DASH Dietary Pattern, Mediation by Mineral Intakes, and the Risk of Coronary Artery Disease and Stroke Mortality

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Background—The association of the Dietary Approaches to Stop Hypertension (DASH) dietary pattern with stroke and coronary artery disease (CAD) mortality has not been evaluated in Asian populations, and the role of mineral intakes as potential mediators is not clear.

Methods and Results—We used data from 57 078 participants of the Singapore Chinese Health Study aged 45 to 74 years at baseline (1993–1998). Information on usual diet was collected by a validated 165-item food frequency questionnaire at recruitment, and mortality information was obtained via registry linkage up to December 31, 2014. We constructed DASH scores based on quintiles of intake of 7 predefined food items and sodium. Cox proportional hazard models were used to calculate hazard ratios and corresponding 95% CIs. Greater adherence to the DASH dietary pattern was significantly associated with a lower risk of CAD (hazard ratio between extreme quintiles, 0.76; 95% CI, 0.65–0.90; *P* trend<0.001) and stroke (hazard ratio, 0.62; 95% CI, 0.50–0.78; *P* trend<0.001) mortality. We found an inverse association between potassium intake and CAD mortality and a direct association between sodium intake and stroke mortality. No other significant associations were observed for potassium, sodium, magnesium, and calcium intakes in relation to CAD or stroke mortality. Adjustment for mineral intakes did not materially change the association of the DASH score with CAD or stroke mortality.

Conclusions—Adherence to the DASH dietary pattern was associated with substantially lower risk of CAD and stroke mortality in an Asian population, and this inverse association did not appear to be substantially mediated by intakes of sodium, potassium, magnesium, and calcium. (*J Am Heart Assoc.* 2019;8:e011054. DOI: 10.1161/JAHA.118.011054.)

Key Words: calcium • cardiovascular disease • Chinese • coronary artery disease • Dietary Approaches to Stop Hypertension • magnesium • potassium • prospective cohort study • sodium • stroke

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The Dietary Approaches to Stop Hypertension (DASH) diet is an eating pattern rich in fruits, vegetables, whole grains, and low-fat dairy and low in red meat, saturated fat, sugar-sweetened beverages, and sodium. This diet has been shown to substantially decrease blood pressure.[1] High blood pressure is among the leading risk factors for cardiovascular diseases (CVDs).[2] Hence, the impact of the DASH diet on CVD, coronary artery disease (CAD), and stroke has been evaluated in several prospective cohort studies, but with mixed results composed of nonsignificant[3–6] and inverse significant associations.[7–12] A meta-analysis of 9 cohort studies showed an inverse association between adherence to the DASH diet and CVD mortality.[13] However, all those studies were conducted in Western populations except for 1 small cohort in Taiwan.[9] In the Multiethnic Cohort study, the DASH dietary pattern was significantly associated with lower CVD mortality in whites, African Americans, and Japanese American men. However, no significant association was

Clinical Perspective

What Is New?

- Adherence to the Dietary Approaches to Stop Hypertension (DASH) dietary pattern was associated with lower risk of both coronary artery disease and stroke mortality in a Singapore Chinese population.
- High potassium intake was inversely associated with coronary artery disease mortality, whereas high sodium intake was directly associated with stroke mortality; however, the association between the DASH dietary pattern and cardiovascular disease mortality was largely independent of sodium, potassium, magnesium, and calcium intakes.
- Almost all aspects of the diet considered in the DASH diet appeared to contribute to its inverse association with cardiovascular disease mortality risk.

What Are the Clinical Implications?

- Our findings underscore the importance of overall quality of diet.
- Health benefits of adherence to the DASH dietary pattern against cardiovascular disease risk may go beyond benefits of a low-sodium, high-potassium diet.
- The DASH dietary pattern may thus provide a useful model for cardiovascular disease prevention in Asian populations.

observed in Japanese American women, Native Hawaiians, and Latinos.[14] The inverse association between the DASH diet and CVD mortality has recently been reported in our ethnic Chinese population,[15] but the association with more specific CVD outcomes, namely, CAD and stroke, as well as the role of mineral intakes as potential mediators are yet to be explored.

The DASH diet was primarily designed to promote intake of a collection of nutrients, particularly higher intakes of potassium, calcium, and magnesium, and lower intakes of saturated fat and cholesterol.[16,17] Given the observed associations of potassium, calcium, and magnesium with CVD risk,[18–20] it is plausible to hypothesize that the benefits of the DASH diet may be at least partly mediated through provision of higher intakes of these dietary minerals.

We therefore evaluated adherence to the DASH dietary pattern and mineral intakes in relation to CVD, CAD, and stroke mortality risk in an ethnic Chinese population. We also assessed whether mineral intakes may mediate the DASH diet–CVD relationship and the association between individual DASH components and CVD risk.

Methods

The data that support the findings of this study as well as analytic methods and study materials are available from the corresponding author upon reasonable request and in compliance with National Institutes of Health guidelines.

Study Population

We used data from the Singapore Chinese Health Study, a population-based cohort study conducted among 35 303 Chinese women and 27 954 Chinese men aged 45 to 74 years at baseline between April 1993 and December 1998. The participants were recruited from Hokkiens and Cantonese, the 2 major dialect groups in Singapore, mostly originated from the Fujian and Guangdong provinces in Southern China, respectively.

Structured questionnaires were used to collect information through in-person interviews on demographic characteristics, lifestyle factors (physical activity, tobacco use, and alcohol intake), usual diet, and medical history at the time of recruitment. The study was approved by the Institutional Review Board at the National University of Singapore, and informed consent was obtained from each study participant. Further details of study design can be found in a previous publication.[21]

Assessment of Diet and Covariates

During the baseline interview, a semiquantitative food frequency questionnaire (FFQ) was administered, which included 165 food items commonly consumed in Singapore. The respondents were required to choose the portion size (small, medium, or large) from provided photographs and select from 8 frequency categories (ranging from "never or hardly ever" to "2 or more times a day"). We derived nutrient intakes including calcium, potassium, magnesium, and sodium (in milligrams) from FFQ data using the Singapore Food Composition Database that was specifically developed for this cohort study.[21]

The FFQ was validated among a subset of 810 participants from this cohort survey by two 24-hour recalls collected for 1 weekday and 1 weekend day and by a repeat administration of the FFQ. The intake values from the FFQ and 24-hour recall methods showed similar distributions, with most mean pairs for energy and nutrients within 10% of each other's values. Moreover, the correlation coefficient for energy and nutrients between these 2 methods ranged from 0.24 to 0.79, which is comparable with previous validation studies in diverse populations.[22] Specifically for calcium intake, correlation coefficients between FFQ and 24-hour recall methods ranged from 0.51 to 0.62 among the 4 groups by sex and dialect group for energy-adjusted values.[21]

We calculated a DASH dietary pattern score for each participant based on the method developed by Fung et al[7] that considers 7 food groups and 1 mineral: high intake of

fruits, vegetables, nuts, dairy products, and whole grain, and low intake of sodium, sugar–sweetened beverages, and red meats (fresh and processed). The quintiles for intake of favorable items were used directly as scores, while they were used in the reverse direction for unfavorable items (sodium, sweetened beverages, and red meats). For example, a participant in the highest quintiles of fruits and red meat intakes received a component score of 5 for the former but 1 for the latter. The overall DASH score for each participant was a sum of the individual component scores that hypothetically could range from 8 to 40.

Self-reported information about age, body weight, height, educational level, smoking status, and physical activity was also collected through the baseline questionnaire. Body mass index (in kg/m^2) was calculated by body weight in kilograms divided by square of height in meters. To obtain past medical conditions of the participants including type 2 diabetes mellitus, hypertension, cancer, CAD, and stroke, participants were asked if they had been told by a doctor that they have these conditions.

Assessment of Mortality

Data on death occurrence and its causes were obtained through linkage with the nationwide registry of birth and death in Singapore. Vital status for the cohort participants was updated through December 31, 2014. In this cohort, as of December 31, 2014, only 52 subjects (0.08%) were known to be lost to follow-up for reasons such as emigration from Singapore, rendering vital statistics during follow-up virtually complete. The *International Classification of Diseases, Ninth Revision* (*ICD-9*) was employed to specify underlying cause of death, using 390 to 459 codes for CVD deaths, 410 to 414 for CAD deaths, 430 to 438 for stroke deaths, 430 to 432 for hemorrhagic stroke, and 433 to 438 for ischemic/ill-defined stroke.

Statistical Analysis

Among 63 257 participants who were interviewed at baseline, we excluded participants with self-reported CAD or stroke at recruitment (n=3220) and those with either a self-reported cancer history or cancer identified via linkage with the nationwide Singapore Cancer Registry at baseline (n=1936). Participants with extreme energy intakes (<600 or >3000 kcal/day for women and <700 or >3700 kcal/day for men, n=1023) were also excluded, and a total of 57 078 subjects remained for the current analysis.

Energy-adjusted values were used for all foods and nutrients using the residual method.[23] Person-years of follow-up for each participant were calculated from the date of recruitment until the reported time of death, lost to follow-

up, or December 31, 2014, whichever came first. We employed Cox proportional hazards models to examine associations of quintiles of independent variables with CVD mortality risk using the lowest quintiles of intake or score as the reference category. Accordingly, we first examined the associations of adherence to the DASH diet with CVD mortality and its subtypes of CAD and stroke. Next, we determined the associations of intake of minerals (sodium, calcium, magnesium, and potassium) with these outcomes and then assessed the extent to which associations of the DASH diet with CVD mortality and its subtypes are mediated by these minerals. Finally, we examined the associations of components of the DASH diet.

In the multivariable model, we adjusted for age (continuous), sex, interview year (1993–1995, 1996–1998), dialect group (Hokkien, Cantonese), level of education (none, primary school, secondary school or more), physical activity of moderate intensity (<0.5, 0.5–3.9, ≥4 h/week), body mass index (continuous), cigarette smoking (never smoker, ex-smoker, current smoker), alcohol consumption (never or monthly, weekly, daily), self-reported history of hypertension and diabetes mellitus, and total energy intake (continuous). For models with dietary minerals as the exposure of interest, we further adjusted for quartiles of the intake ratio of polyunsaturated to saturated fatty acids, as well as quartiles of dietary cholesterol, long-chain omega-3 polyunsaturated fatty acid, other omega-3 fatty acids, fiber, and use of dietary supplements (weekly and more; yes/no).

The proportionality assumption was tested using Schoenfeld residuals, and no violation was detected. We tested for linear trends across categories of exposures by assigning the median intake to each of the quintiles of intake and modeling these as continuous variables in multivariable regression models. We calculated Pearson's correlation coefficients among intakes of minerals and between minerals and the DASH score. The strongest correlation between any of the examined minerals and other dietary factors was 0.73 for potassium and fiber. To assess multicollinearity in models with several dietary factors included, we calculated the variance inflation factor in the fully adjusted model and found that all were <2.5 except for potassium, which had a slightly higher value (2.69). Hence, multicollinearity was not a significant issue in these models. We tested interactions through cross-product terms between median values of DASH score quintiles and sex, age (categorized based on cohort median at 55 years), body mass index (<23 and ≥23 kg/m^2), current smoking (yes/no), and alcohol use (at least weekly/no or occasionally). All statistical analyses were conducted using Stata Statistical Software, Release 14.2 (Stata Corporation, College Station, TX), with 2-sided *P*<0.05 as the threshold for statistical significance.

Table 1. Participant Characteristics According to Quintiles of DASH Score in the Singapore Chinese Health Study

Characteristics	Quintiles of DASH Score				
	Q1 (Low)	Q2	Q3	Q4	Q5 (High)
n (%)	8431 (14.0)	13 454 (22.3)	11 015 (18.3)	14 271 (23.7)	13 127 (21.8)
Age, y	55.1±7.7	56.3±8.0	56.5±8.0	56.7±8.1	56.8±7.9
Female sex, n (%)	3304 (39.2)	6783 (50.4)	6136 (55.7)	8521 (59.7)	8720 (66.4)
Dialect group, n (%)					
Hokkien	3396 (40.3)	5820 (43.3)	5043 (45.8)	6828 (47.8)	6836 (52.1)
Cantonese	5035 (59.7)	7634 (56.7)	5972 (54.2)	7443 (52.2)	6291 (47.9)
Education, n (%)					
No formal education	2245 (26.6)	3933 (29.2)	3189 (29.0)	3775 (26.5)	3135 (23.9)
Primary school	4080 (48.4)	6122 (45.5)	4840 (43.9)	6326 (44.3)	5473 (41.7)
Secondary school	2106 (25.0)	3399 (25.3)	2986 (27.1)	4170 (29.2)	4519 (34.4)
Smoking, n (%)					
None	4500 (53.4)	8556 (63.6)	7609 (69.1)	10 606 (74.3)	10 639 (81.0)
Ex-smoker	1036 (12.3)	1533 (11.4)	1196 (10.9)	1542 (10.8)	1270 (9.7)
Current smoker	2895 (34.3)	3365 (25.0)	2210 (20.1)	2123 (14.9)	1218 (9.3)
Alcohol drinker, at least weekly, n (%)	1671 (19.8)	1821 (13.5)	1269 (11.5)	1354 (9.5)	894 (6.8)
Moderate physical activity, n (%)					
<0.5 h/wk	7282 (86.4)	11 084 (82.4)	8729 (79.2)	10 834 (75.9)	9032 (68.8)
0.5 to 3 h/wk	765 (9.1)	1581 (11.8)	1462 (13.3)	2139 (15.0)	2453 (18.7)
≥4 h/wk	384 (4.6)	789 (5.9)	824 (7.5)	1298 (9.1)	1642 (12.5)
Hypertension, n (%)	1732 (20.5)	3096 (23.0)	2598 (23.6)	3518 (24.7)	3344 (25.5)
Diabetes mellitus, n (%)	547 (6.5)	1118 (8.3)	933 (8.5)	1353 (9.5)	1402 (10.7)
Body mass index, kg/m^2	23.2±3.4	23.2±3.2	23.2±3.3	23.2±3.2	23.0±3.2
Dietary intake					
Total energy, kcal/d	1594±522	1513±540	1530±539	1552±524	1565±472
PUFA/SFA ratio	0.55±1.4	0.56±0.4	0.63±2.0	0.65±1.7	0.77±1.5
Cholesterol, mg/d	202±83.4	187±76.9	176±69.1	165±66.3	146±66.7
Long-chain omega-3 PUFA, g/d	0.31±0.2	0.32±0.2	0.33±0.2	0.33±0.2	0.31±0.2
Other omega-3 PUFA, g/d	0.47±0.2	0.53±0.2	0.56±0.2	0.59±0.2	0.65±0.3
Fiber, g/d	9.04±2.7	10.8±2.8	12.1±3.0	13.6±3.3	16.4±4.1
Calcium, mg/d	292±126.9	351±137	396±154	445±170	541±203
Potassium, mg/d	1477±338	1640±339	1751±360	1868±3833	2085±432
Sodium, mg/d	1226±373	1159±345	1118±323	1078±321	1007±308
Magnesium, mg/d	216±27.3	231±26.3	241±27.9	252±29.9	275±35.5
Supplemental calcium use, n (%)	264 (3.1)	537 (4.0)	591 (5.4)	1030 (7.2)	1369 (10.4)

The data are expressed as n (%) or mean±standard deviation. DASH indicates Dietary Approaches to Stop Hypertension; PUFA, polyunsaturated fatty acids; SFA, saturated fatty acids.

Results

Among the 57 078 participants in our study, the DASH score ranged from 8 to 39 with a mean (±SD) of 24.1±4.3. Those in the highest quintile of the DASH score (best adherence) were more likely to be women and highly educated (Table 1). They also generally had more healthful lifestyle profiles than those in the lowest quintile with lower smoking and regular alcohol drinking and higher physical activity level. A higher adherence to the DASH pattern was also associated with a higher polyunsaturated to saturated fatty acid ratio; higher intakes of fiber, vitamin D, folate, calcium, potassium, and magnesium;

Table 2. Hazard Ratio (95% CI) of Cardiovascular Mortality According to DASH Score

	Quintiles of DASH score					
	Q1	Q2	Q3	Q4	Q5	P for Trend*
Median (IQR)	18 (17–19)	21 (20–22)	23 (23–24)	26 (25–27)	30 (28–31)	
CVD mortality						
Cases/person-years	763/136 023	1221/217 734	913/179 137	1101/233 318	873/215 770	
Multivariable model[†]	1.00	0.89 (0.81–0.98)	0.82 (0.74–0.90)	0.78 (0.71–0.86)	0.70 (0.64–0.78)	<0.001
+ Na	1.00	0.90 (0.82–0.98)	0.82 (0.75–0.91)	0.79 (0.71–0.87)	0.71 (0.64–0.79)	<0.001
+ Ca, Mg, Na, K	1.00	0.90 (0.82–0.99)	0.83 (0.75–0.92)	0.79 (0.71–0.88)	0.72 (0.63–0.82)	<0.001
CAD mortality						
Cases/person-years	418/136 023	666/217 734	486/179 137	587/233 318	453/215 770	
Multivariable model[†]	1.00	0.90 (0.80–1.02)	0.81 (0.71–0.92)	0.77 (0.68–0.88)	0.69 (0.60–0.79)	<0.001
+ Na	1.00	0.90 (0.80–1.02)	0.81 (0.71–0.93)	0.78 (0.68–0.89)	0.69 (0.60–0.80)	<0.001
+ Ca, Mg, Na, K	1.00	0.92 (0.81–1.05)	0.83 (0.72–0.96)	0.80 (0.69–0.93)	0.72 (0.60–0.85)	<0.001
Stroke mortality						
Cases/person-years	222/136 023	357/217 734	267/179 137	319/233 318	248/215 770	
Multivariable model[†]	1.00	0.86 (0.73–1.02)	0.79 (0.66–0.94)	0.74 (0.62–0.88)	0.64 (0.53–0.78)	<0.001
+ Na	1.00	0.87 (0.74–1.03)	0.80 (0.66–0.96)	0.75 (0.63–0.90)	0.66 (0.54–0.80)	<0.001
+ Ca, Mg, Na, K	1.00	0.86 (0.73–1.03)	0.79 (0.65–0.96)	0.73 (0.60–0.89)	0.62 (0.49–0.78)	<0.001

CAD indicates coronary artery disease; CVD, cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension; IQR, interquartile range.

*Linear trend was tested by treating the median values of quintiles as a continuous variable.

[†]Multivariable model 1: adjusted for age, sex, dialect, year of interview, educational level, body mass index, physical activity, smoking status, alcohol use, history of diabetes mellitus, history of hypertension, total energy intake, and dietary supplement use.

and a lower intake of cholesterol. Those with higher DASH scores were more likely to have a history of diabetes mellitus and hypertension. The highest correlation among the 3 minerals of interest was between potassium and magnesium (r=0.75) followed by potassium and calcium (r=0.62) and calcium and magnesium (0.56). The correlation coefficient between the DASH score and intakes of calcium, potassium, sodium, and magnesium were 0.47, 0.49, −0.22, and 0.57, respectively.

During 981 983 person-years of follow-up (mean 17.2 years), we documented 4871 cases of CVD mortality, including 2610 cases of CAD mortality and 1413 cases of stroke mortality. Higher adherence to the DASH dietary pattern was associated with a lower risk of CVD, CAD, and stroke mortality, with dose-response relationships in multivariable models. These associations were not substantially weakened by further adjustment for intakes of sodium, calcium, magnesium, and potassium (Table 2).

Higher calcium (hazard ratio [HR] for extreme quintiles, 0.91; 95% CI, 0.83–1.00; *P* for trend=0.02) and magnesium (HR, 0.87; 95% CI, 0.79–0.95; *P* for trend=0.003) intake were associated with a lower risk of CVD mortality in multivariable adjusted models (Tables S1 and S2). However, after further adjustment for intakes of other dietary factors, the association

for both minerals was weakened and lost statistical significance (Table 3). Fiber intake was mostly responsible for this attenuation (HR, 0.97, 95% CI, 0.88–1.07 for calcium; and HR, 0.99, 95% CI, 0.89–1.10 for magnesium) while fiber itself remained inversely associated with lower risk. Higher potassium intake was inversely associated with CVD risk, whereas a higher sodium intake was directly associated with CVD risk regardless of the adjustment for other risk factors including dietary factors. Considering CAD and stroke mortality separately, the same patterns of association were generally observed, but potassium was only inversely associated with CAD. We observed no statistically significant interaction between intake of these minerals and age and sex regarding risk of CVD, CAD, and stroke mortality (*P*>0.10).

We tested if our findings were sensitive to the inclusion of *ICD-9* code 438 labeled as "Late effects of cerebrovascular diseases," but exclusion of those deaths yielded almost identical associations (data not shown). We further tested subtypes of stroke mortality, hemorrhagic and ischemic/ill-defined, and observed the same patterns of inverse associations without a mediation role for these minerals (data not shown). We also examined interactions between DASH scores and other risk factors and observed a stronger association with stroke mortality in participants with at least weekly

Table 3. Hazard Ratio (95% CI) of Cardiovascular Mortality According to Calcium, Potassium, and Magnesium Intakes in Fully Adjusted Model

Quintiles	Minerals			
	Ca	Mg	K	Na
CVD mortality				
Q1	1.00	1.00	1.00	1.00
Q2	1.02 (0.93–1.11)	0.98 (0.89–1.07)	0.98 (0.89–1.07)	1.04 (0.95–1.15)
Q3	0.94 (0.85–1.04)	1.02 (0.93–1.13)	0.87 (0.79–0.97)	1.04 (0.94–1.15)
Q4	0.92 (0.82–1.02)	1.03 (0.93–1.15)	0.91 (0.82–1.02)	1.10 (0.99–1.22)
Q5	1.01 (0.90–1.12)	1.06 (0.94–1.19)	0.89 (0.78–1.01)	1.16 (1.05–1.29)
P for trend	0.98	0.22	0.04	0.003
CAD mortality				
Q1	1.00	1.00	1.00	1.00
Q2	0.99 (0.87–1.12)	0.95 (0.84–1.08)	0.92 (0.81–1.04)	1.06 (0.93–1.20)
Q3	0.89 (0.78–1.03)	0.98 (0.86–1.12)	0.85 (0.74–0.98)	1.02 (0.89–1.17)
Q4	0.90 (0.78–1.04)	1.04 (0.90–1.20)	0.85 (0.73–0.99)	1.09 (0.94–1.25)
Q5	1.00 (0.87–1.16)	1.03 (0.87–1.21)	0.82 (0.69–0.97)	1.12 (0.97–1.30)
P for trend	0.83	0.48	0.02	0.11
Stroke mortality				
Q1	1.00	1.00	1.00	1.00
Q2	1.05 (0.89–1.25)	0.96 (0.81–1.14)	1.08 (0.91–1.27)	1.07 (0.90–1.28)
Q3	0.97 (0.80–1.17)	0.97 (0.81–1.16)	1.00 (0.83–1.21)	1.10 (0.91–1.32)
Q4	0.88 (0.72–1.08)	0.99 (0.81–1.20)	0.97 (0.79–1.19)	1.13 (0.93–1.37)
Q5	0.97 (0.79–1.19)	1.04 (0.84–1.30)	0.97 (0.77–1.23)	1.28 (1.05–1.56)
P for trend	0.53	0.61	0.60	0.01

Multivariable model: adjusted for age, sex, dialect, year of interview, educational level, body mass index, physical activity, smoking status, alcohol use, history of diabetes mellitus, history of hypertension, total energy intake, ratio of polyunsaturated to saturated fatty acids intake, dietary intake of cholesterol, long-chain omega-3 fatty acid, other omega-3 fatty acids, fiber, and dietary supplements use. CAD indicates coronary artery disease; CVD, cardiovascular disease.

alcohol consumption (HR, 0.46 for extreme quintiles; 95% CI, 0.23–0.91) compared with those with less-than-weekly intake (0.66; 0.51–0.85; *P*-interaction=0.04). Furthermore, adherence to the DASH was associated with lower CVD mortality in nonsmokers (0.68; 0.58–0.78) but not in current smokers (1.02; 0.81–1.28); however, this interaction had only borderline statistical significance (*P*-interaction=0.08). A similar interaction was observed for stroke mortality (0.53, 0.41–0.69 in nonsmokers versus 0.92, 0.58–1.46 in smokers; *P*-interaction=0.08) but not CAD mortality (0.75, 0.61–0.92 versus 0.93, 0.69–1.25; *P*-interaction=0.70). Interactions were not statistically significant with age, sex, body mass index for CVD, CAD, and stroke mortality (*P*-interaction>0.19).

We assessed individual components of the DASH score (Table 4) and found that 6 of 8 components were inversely associated with CVD risk (vegetables, fruits, whole grains, nuts and legumes, red meat, and sodium) following dose-response relationships (all *P*s-trend≤0.04) while the remaining

2 components (dairy and sugar-sweetened beverages) tended to be inversely associated but with borderline statistical significance (*P*-trend=0.07 for both). The associations of these components with CAD and stroke mortality were generally the same as for CVD mortality except that the intake of sugar-sweetened beverages was significantly associated with stroke mortality but not with CAD mortality.

Discussion

In this longitudinal study in ethnic Chinese adults, we observed that adherence to the DASH diet was associated with lower risk of CVD, CAD, and stroke mortality independent of intakes of sodium, calcium, potassium, and magnesium. Moreover, the majority of DASH diet components were associated with lower CVD, CAD, and stroke mortality risk with few exceptions.

A meta-analysis of 9 studies found 20% lower risk comparing the highest DASH diet adherence to the lowest

Table 4. Hazard Ratio (95% CI) of Cardiovascular Mortality According to Individual DASH Scores (Higher Scores Reflect More Favorable Intakes)

	DASH Components Scores					P for Trend*
	1	2	3	4	5	
CVD mortality						
Vegetables score	1.00	0.95 (0.87–1.02)	0.90 (0.83–0.98)	0.81 (0.74–0.89)	0.80 (0.72–0.89)	<0.001
Fruits score	1.00	0.90 (0.83–0.97)	0.77 (0.71–0.85)	0.78 (0.71–0.85)	0.75 (0.68–0.83)	<0.001
Whole grains score	1.00	0.97 (0.88–1.07)	1.00 (0.90–1.12)	0.97 (0.88–1.06)	0.90 (0.83–0.99)	0.04
Nuts and legumes score	1.00	0.90 (0.83–0.98)	0.94 (0.86–1.02)	0.90 (0.82–0.99)	0.86 (0.78–0.95)	0.008
Dairy score	1.00	0.99 (0.91–1.08)	0.94 (0.86–1.03)	0.94 (0.86–1.03)	0.93 (0.85–1.02)	0.07
Low sugar-sweetened beverage score	1.00	0.95 (0.82–1.10)	0.95 (0.83–1.08)	0.83 (0.73–0.95)	0.90 (0.81–1.01)	0.07
Low red meat score	1.00	0.90 (0.82–0.99)	0.86 (0.77–0.94)	0.83 (0.75–0.92)	0.84 (0.76–0.94)	0.002
Low sodium score	1.00	0.94 (0.85–1.03)	0.89 (0.81–0.93)	0.90 (0.82–0.99)	0.90 (0.82–0.98)	0.02
CAD mortality						
Vegetables score	1.00	0.91 (0.81–1.02)	0.90 (0.80–1.02)	0.81 (0.71–0.92)	0.76 (0.66–0.88)	<0.001
Fruits score	1.00	0.85 (0.76–0.95)	0.73 (0.65–0.82)	0.74 (0.66–0.84)	0.69 (0.60–0.79)	<0.001
Whole grains score	1.00	0.99 (0.86–1.13)	0.98 (0.84–1.14)	1.05 (0.92–1.18)	0.87 (0.77–0.98)	0.13
Nuts and legumes score	1.00	0.87 (0.77–0.98)	0.91 (0.81–1.03)	0.89 (0.79–1.01)	0.87 (0.76–0.99)	0.08
Dairy score	1.00	0.92 (0.82–1.03)	0.89 (0.79–1.00)	0.95 (0.85–1.08)	0.89 (0.79–1.01)	0.15
Low sugar-sweetened beverage score	1.00	1.16 (0.95–1.42)	1.07 (0.88–1.28)	0.96 (0.80–1.16)	1.00 (0.85–1.17)	0.24
Low red meat score	1.00	0.88 (0.77–1.00)	0.85 (0.74–0.97)	0.81 (0.71–0.93)	0.81 (0.70–0.94)	0.007
Low sodium score	1.00	0.96 (0.84–1.08)	0.89 (0.79–1.01)	0.93 (0.82–1.05)	0.89 (0.79–1.01)	0.08
Stroke mortality						
Vegetables score	1.00	0.97 (0.83–1.12)	0.94 (0.80–1.10)	0.82 (0.68–0.97)	0.81 (0.67–0.99)	0.01
Fruits score	1.00	0.90 (0.77–1.04)	0.75 (0.64–0.88)	0.79 (0.67–0.94)	0.76 (0.63–0.91)	0.001
Whole grains score	1.00	0.95 (0.80–1.14)	0.99 (0.81–1.21)	0.80 (0.66–0.96)	0.91 (0.78–1.07)	0.06
Nuts and legumes score	1.00	0.88 (0.76–1.03)	0.87 (0.74–1.02)	0.86 (0.72–1.02)	0.82 (0.69–0.99)	0.04
Dairy score	1.00	1.01 (0.87–1.18)	0.97 (0.82–1.13)	0.86 (0.72–1.02)	0.92 (0.78–1.09)	0.11
Low sugar-sweetened beverage score	1.00	0.75 (0.57–1.00)	0.79 (0.62–1.01)	0.71 (0.56–0.91)	0.79 (0.64–0.97)	0.17
Low red meat score	1.00	0.79 (0.66–0.95)	0.78 (0.65–0.94)	0.79 (0.65–0.96)	0.81 (0.67–0.99)	0.16
Low sodium score	1.00	0.87 (0.74–1.04)	0.85 (0.72–1.01)	0.85 (0.72–1.01)	0.85 (0.71–1.01)	0.07

CAD indicates coronary artery disease; CVD, cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension.
*Linear trend was tested by treating the median values of quintiles as a continuous variable.
Multivariable model: adjusted for age, sex, dialect, year of interview, educational level, body mass index, physical activity, smoking status, alcohol use, history of diabetes mellitus, history of hypertension, total energy intake, and dietary supplement use.

for CVD mortality.[13] The association between adherence to the DASH diet and more specific CVD outcomes, CAD and stroke, was assessed in few previous cohort studies. A meta-analysis of 3 studies found an inverse association with CAD risk (relative risk [RR], 0.79; 95% CI, 0.71–0.88) and stroke risk (RR, 0.81; 95% CI, 0.72–0.92).[24] All these studies were done in Western countries except for a small study in 2061 Taiwanese (123 cases) in which the DASH score was not associated with stroke risk.[9] However, a "DASH nutrient score," a combination of 5 DASH targeted nutrients (saturated fat, dietary fiber, calcium, potassium, and magnesium), was

significantly associated with lower risk of stroke in that study, although among all these items, only magnesium reached statistical significance.[9] Hence, the benefits of the DASH diet was mainly attributed to its mineral content in this Asian population.[9] This hypothesis was also supported by the inverse associations of higher calcium[25] or potassium[26] intake with CVD risk in the Japan Collaborative Cohort Study.

Our findings for dietary calcium intake corroborate a meta-analysis of 17 prospective cohort studies that also found no significant association with CVD mortality risk (HR, 0.97; 95% CI, 0.88–1.06). However, an inverse association was observed

in a subgroup analysis of 8 studies with <10 years' follow-up (HR, 0.88; 95% CI, 0.78–0.99) in this meta-analysis.[27] A dose-response meta-regression of 11 prospective studies also showed no significant association between dietary calcium intake and CVD/CAD or stroke mortality.[28] In contrast, in a recent study in a Korean population with low calcium intake comparable to the intake level in our population, higher calcium intake was associated with lower risk of incident CVD in women, while a nonsignificant higher risk was observed in men.[29] No significant association with stroke was observed in that study in either sex.[29] Our findings did not support sex-specific associations between mineral intakes and mortality of CAD, stroke, or CVD.

The contrast between the highest and lowest quintile of magnesium intake in our study was relatively small (205 mg/day versus 290 mg/day), which may have contributed to a weaker association for magnesium as compared with potassium intake, for which the contrast was larger (1301 mg/day versus 2306 mg/day). Our findings for magnesium intake were in line with a dose-response meta-analysis that found no significant association with CVD mortality (RR, 0.93 per 100 mg/day; 95% CI, 0.82–1.05; 8 studies) and stroke mortality (RR, 1.07 per 100 mg/day; 95% CI, 0.90–1.28; 4 studies).[19] However, in the same meta-analysis, magnesium intake was significantly associated with a lower risk of CAD mortality (RR, 0.81 per 100 mg/day; 95% CI, 0.69–0.95; 5 studies).[19] The majority of the studies included in this meta-analysis did not control for any other nutrients (comparable with our findings before full adjustment) and thus could not rule out confounding by other dietary factors.

We observed an inverse association between potassium intake and CVD and CAD mortality even after controlling for other dietary factors. In a meta-analysis by Aburto et al,[18] potassium intake was not significantly associated with incident CVD (RR, 0.88; 95% CI, 0.70–1.10) or CAD (RR, 0.96; 95% CI, 0.78–1.19), but these were pooled analysis of only 4 and 3 studies, respectively. In contrast, their meta-analysis of potassium intake and incident stroke risk based on 9 studies showed an inverse association (RR, 0.76; 95% CI, 0.39–0.90).[18] Of note, the majority of these studies also did not control for other dietary factors. Several underlying mechanisms have been proposed for the potential protective role of potassium on cardiovascular risk including modulation of blood pressure, reduction of free radical formation, improvement of endothelial function, increase in arterial compliance, and reduction of left ventricular mass.[30]

Higher adherence to the DASH dietary pattern in our study was associated with higher intakes of calcium, potassium, and magnesium. However, the inverse association of DASH adherence was not substantially mediated by intake of these 3 minerals. Other aspects of the diet as reflected in the DASH diet could improve cardiovascular health,[1] through different mechanisms such as providing sufficient dietary fiber,[31] folate,[32] and flavonoids.[33] In our study, the inverse associations of the DASH diet with CVD and stroke mortality were observed only in nonsmokers, with a stronger association for stroke mortality in alcohol drinkers. These findings indicate a potential offsetting impact of smoking against the beneficial effects of the DASH diet, while a synergistic effect for moderate alcohol and the DASH diet may exist.

As for components of the DASH diet, most individual items were inversely associated with a lower risk of CVD, CAD, and stroke mortality. These findings emphasize the importance of diet quality as a whole rather than a specific food group or nutrient. In contrast to our findings, no significant association with stroke was observed for food components of DASH in a small Taiwanese population.[9] The only other study, to our knowledge, that considered the association of DASH components with CVD risk was the Women's Health Study, in which only fruit intake had a significant inverse association.[5] Despite our borderline findings for the dairy component, we have previously reported an inverse association between dairy intake and stroke mortality risk at a slightly shorter period of follow-up and different classification of dairy consumption.[34] The DASH diet uses a data-driven approach in scoring of components (quintiles), whereas a priori criteria with regional calibration may improve its efficacy through a better utilization of components such as dairy. As for the sodium component, our findings were in line with current dietary guidelines highlighting the adverse effects of high sodium intake despite debates about optimal dose.[35] However, inconclusive findings were observed in a meta-analysis for CVD (incident and mortality) and incident CAD whereas a significant 24% to 32% higher risk was observed for CAD mortality and stroke (incident and mortality).[20] The adverse effect of a higher sodium intake is mediated through blood pressure and non–blood pressure mechanisms.[36] In the PURE (Prospective Urban Rural Epidemiology) study, sodium intake was associated with cardiovascular disease and strokes but only in communities with a mean intake over 5 g/day like Chinese.[37] The mean daily sodium intake of Chinese Singaporean adults was 3.7 g concurrent to our study baseline[38] and 3.3 g based on 24-hour urine measurements in 2010[39]; however, we still have observed the direct associations in our study.

The strengths of our study include the prospective design and the large sample size with long follow-up and a large number of CVD mortality cases. Other strengths include negligible loss to follow-up and use of a locally validated dietary assessment tool. However, some misclassification in the assessment of the DASH score or nutrient intakes due to measurement error in the reporting of food consumption and changes in diet over time is unavoidable. Because of the prospective design, this misclassification should have been nondifferential but still could have obscured existing

relationships by biasing HRs toward the null. In particular, the absence of any direct question about added salt in the FFQ may have led to misclassification. An underestimation of sodium intake often occurs with dietary assessment tools due to underreporting and inherent difficulties in capturing information about recipes and discretionary salt use.[40] This may have led to dilution of DASH-CVD and sodium-CVD associations in our study. Another limitation is that adherence to the DASH diet may be a marker of health consciousness that in turn may affect other health-related behaviors including access to health care. It is not clear if we have sufficiently captured these confounding factors despite our adjustment for a wide range of covariates. Hence, like any other epidemiological study, a potential role of residual confounding could not be ruled out. Members of this cohort were of Chinese ethnicity, and our results may not be generalizable to other ethnic groups.

In conclusion, adherence to the DASH dietary pattern was associated with lower risk of CVD, CAD, and stroke mortality in an ethnic Chinese population. High potassium intake and low sodium intake were also associated with lower CAD and CVD mortality. However, the association between the DASH dietary pattern and CVD mortality was largely independent of mineral intakes. Almost all aspects of the diet considered in the DASH diet appeared to contribute to its inverse association, underscoring the importance of overall dietary quality. Our results support the hypothesis that the DASH dietary pattern can be used as a potential model for CVD prevention in Asian populations.

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Author Contributions

Dr Talaei analyzed data and wrote the first draft; Dr Koh designed and conducted the whole study; Drs Koh, Yuan, and van Dam assisted in interpreting the data and critically edited the manuscript. This paper was the idea of Dr van Dam, who has primary responsibility for final content. All authors read and approved the final manuscript.

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Disclosures

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Supplemental Material

Table S1. Cardiovascular mortality cases (and person years) according to quintiles of calcium, potassium, sodium, and magnesium intakes.

	Quintiles of minerals				
	Q1	Q2	Q3	Q4	Q5
Calcium					
Median, mg/d (IQR)	242 (194-269)	319 (305-333)	373 (359-389)	449 (425-482)	646 (586-746)
Cases/person-years					
CVD mortality	1107/195779	1112/195526	944/197782	827/197576	873/193528
CAD mortality	615/195779	588/195526	486/197782	448/197576	472/193528
Stroke mortality	306/195779	337/195526	282/197782	232/197576	250/193528
Magnesium					
Median, mg/d (IQR)	205 (193-212)	226 (222-230)	242 (238-246)	259 (254-265)	290 (280-308)
Cases/person-years					
CVD mortality	1036/195766	1012/197116	1007/198002	949/196436	867/194661
CAD mortality	574/195766	542/197116	521/198002	516/196436	457/194661
Stroke mortality	296/195766	294/197116	287/198002	275/196436	261/194661
Sodium					
Median, mg/d (IQR)	702 (539-800)	955 (913-994)	1102 (1067-1137)	1252 (1211-1298)	1507 (1417-1662)
Cases/person-years					
CVD mortality	979/197009	1021/197371	978/196275	967/196114	926/195213
CAD mortality	521/197009	548/197371	514/196275	523/196114	504/195213
Stroke mortality	276/197009	302/197371	291/196275	275/196114	269/195213
Potassium					
Median, mg/d (IQR)	1301 (1132-1400)	1579 (1528-1625)	1755 (1712-1801)	1955 (1901-2017)	2306 (2182-2513)
Cases/person-years					
CVD mortality	1186/190639	1150/194429	937/197871	879/198913	719/200131
CAD mortality	663/190639	599/194429	511/197871	460/198913	377/200131
Stroke mortality	321/190639	346/194429	288/197871	249/198913	209/200131

IQR: interquartile range, Ca: calcium, Mg: magnesium, Na: sodium, K: potassium, CVD: cardiovascular disease, CAD: coronary artery disease.

Table S2. Hazard ratio (95% Confidence Interval) of cardiovascular mortality according to calcium, sodium, potassium, and magnesium intakes in simpler multivariable models.

	Ca		Mg		Na		K	
Quintiles	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
CVD mortality								
Q1	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Q2	1.01 (0.93-1.10)	0.97 (0.89-1.06)	0.98 (0.90-1.07)	0.93 (0.85-1.01)	1.08 (0.99-1.18)	1.00 (0.92-1.10)	1.00 (0.92-1.08)	0.95 (0.88-1.04)
Q3	0.92 (0.84-1.00)	0.88 (0.80-0.96)	0.98 (0.90-1.07)	0.93 (0.85-1.02)	1.08 (0.99-1.18)	0.99 (0.91-1.09)	0.88 (0.81-0.96)	0.83 (0.76-0.91)
Q4	0.86 (0.79-0.94)	0.83 (0.76-0.91)	0.95 (0.87-1.04)	0.90 (0.82-0.99)	1.18 (1.07-1.29)	1.04 (0.95-1.14)	0.89 (0.81-0.97)	0.85 (0.78-0.93)
Q5	0.91 (0.83-0.99)	0.91 (0.83-1.00)	0.89 (0.81-0.98)	0.87 (0.79-0.95)	1.26 (1.15-1.38)	1.11 (1.02-1.22)	0.81 (0.74-0.89)	0.80 (0.73-0.88)
P-trend	0.01	0.02	0.01	0.003	<0.001	0.01	<0.001	<0.001
CAD mortality								
Q1	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Q2	1.00 (0.89-1.12)	0.95 (0.84-1.07)	0.97 (0.86-1.09)	0.91 (0.80-1.02)	1.11 (0.99-1.26)	1.04 (0.92-1.17)	0.95 (0.85-1.06)	0.91 (0.81-1.02)
Q3	0.88 (0.78-1.00)	0.84 (0.74-0.95)	0.94 (0.83-1.06)	0.89 (0.78-1.00)	1.10 (0.97-1.24)	1.00 (0.88-1.13)	0.88 (0.79-0.99)	0.83 (0.73-0.93)
Q4	0.87 (0.77-0.98)	0.83 (0.73-0.94)	0.96 (0.85-1.09)	0.90 (0.80-1.02)	1.23 (1.08-1.39)	1.07 (0.94-1.21)	0.85 (0.75-0.96)	0.81 (0.71-0.91)
Q5	0.93 (0.82-1.05)	0.91 (0.80-1.03)	0.88 (0.77-0.99)	0.83 (0.73-0.94)	1.30 (1.15-1.47)	1.12 (0.99-1.27)	0.78 (0.68-0.88)	0.76 (0.66-0.86)
P-trend	0.12	0.11	0.05	0.01	0.00	0.07	<0.001	<0.001
Stroke mortality								
Q1	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Q2	1.05 (0.90-1.23)	1.00 (0.85-1.18)	0.96 (0.82-1.13)	0.91 (0.77-1.07)	1.08 (0.92-1.28)	1.01 (0.85-1.19)	1.06 (0.91-1.24)	1.02 (0.87-1.20)
Q3	0.94 (0.79-1.10)	0.90 (0.76-1.06)	0.93 (0.79-1.09)	0.89 (0.75-1.05)	1.09 (0.92-1.29)	1.01 (0.85-1.20)	0.97 (0.83-1.14)	0.93 (0.79-1.09)
Q4	0.83 (0.70-0.99)	0.82 (0.69-0.97)	0.92 (0.78-1.08)	0.88 (0.74-1.04)	1.14 (0.96-1.35)	1.03 (0.87-1.23)	0.91 (0.77-1.08)	0.88 (0.74-1.05)
Q5	0.88 (0.74-1.05)	0.90 (0.76-1.08)	0.90 (0.76-1.06)	0.89 (0.75-1.06)	1.28 (1.08-1.52)	1.18 (0.99-1.40)	0.87 (0.73-1.04)	0.88 (0.73-1.05)
P-trend	0.03	0.10	0.17	0.21	0.00	0.06	0.04	0.05

Ca: calcium, Mg: magnesium, Na: sodium, K: potassium, CVD: cardiovascular disease, CAD: coronary artery disease.

Multivariable model 1: adjusted for age, sex, dialect, year of interview, educational level;

Multivariable model 2: further adjusted for body mass index, physical activity, smoking status, alcohol use, history of diabetes, history of hypertension, total energy intake, and dietary supplements use.