Original Article

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Relationship of calcium and magnesium intakes with the dietary approaches to stop hypertension score and blood pressure: the International Study of Macro/micronutrients and Blood Pressure

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Objective: Research investigating calcium and magnesium intakes from the Dietary Approaches to Stop Hypertension (DASH) pattern and other sources in association with blood pressure is limited. We aimed to characterize sources/intake levels of calcium and magnesium in relation to overall diet quality (DASH-score) and determine modification effects with DASH score and blood pressure.

Methods: Cross-sectional United States data (average dietary and supplement intake from four 24 h recalls and eight blood pressure measurements) from two separate visits, 2195 men and women (40–59 years) in the International Study of Macro/Micronutrients and Blood Pressure were analysed. Food-based adherence to the DASH diet was estimated. Linear models tested associations between each 1-point DASH score with blood pressure. Participants were stratified by adherence to sex-specific recommended allowance for magnesium and calcium intakes. Effect-modification was tested across DASH-score quintiles and median of urinary sodium.

Results: DASH-score was inversely associated with SBP in fully adjusted models (−0.27; 95%CI: −0.38 to −0.15 mmHg). SBP was inversely associated with dietary calcium intake from DASH food groups: −1.54 (95% CI: −2.65 to −0.43) mmHg; calcium intake from other non-DASH food groups: −1.62 (95% CI: −2.94 to −0.29) mmHg. Dietary magnesium intake from DASH food groups (−1.59; 95% CI: −2.79, −0.40 mmHg) and from other non-DASH foods (−1.92; 95% CI: −3.31, −0.53 mmHg) was inversely associated with SBP.

Conclusion: A higher DASH score showed a consistent association with lower BP suggesting a relationship between intakes of calcium and Mg with BP regardless of whether the source is part of the DASH diet or not, even when adjusted for supplement intakes.
The INTERMAP is registered as NCT00005271 at www.clinicaltrials.gov.

Keywords: 24-h dietary recall, blood pressure, calcium, , Dietary Approaches to Stop Hypertension, hypertension, magnesium

Abbreviations: BP, blood pressure; Ca, calcium; CI, confidence intervals; CVD, cardiovascular diseases; DASH, Dietary Approaches to Stop Hypertension; K, potassium; Mg, magnesium; Na, sodium; Q1, lowest quintile; Q5, highest quintile; RDA, recommended daily allowance; SD, Standard deviation; SSB, sugar sweetened beverages; US, United States

INTRODUCTION

Elevated blood pressure (BP), or hypertension, defined as SBP over 120 mmHg or DBP over 80 mmHg [1,2], is a key independent risk factor for major cardiovascular diseases (CVD) and deaths [3]. CVD afflicts a high and growing proportion of the adult population worldwide [4] and is a leading cause of death in the United States [5]. A potential nonpharmacological strategy for the primary prevention of prehypertension and hypertension is

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a healthier diet [6,7]. For example, reducing exposure to dietary factors that have a detrimental impact on BP, such as positive energy balance, excess alcohol use, high salt intake, and inadequate potassium (K) intake, while increasing exposure to factors that have a beneficial effect, such as dietary patterns with high intakes of vegetables, fruits, whole grains, fish, nuts, and low-fat dairy products, for instance, the Dietary Approaches to Stop Hypertension (DASH) and Mediterranean type diets [6–11].

The DASH diet was developed for a landmark American feeding study and clinical trial testing a holistic dietary intervention to reduce BP [8]. Subsequent studies concurred that DASH dietary pattern adherence is associated with lower BP [8,12]. Moreover, it is recommended as an evidence-based dietary pattern for the management of BP by the American Heart Association [13]. The DASH diet recommendations limit the intakes of sugar-sweetened beverages (SSB), processed red meat, and sodium (Na) [8,12]. Furthermore, the DASH diet incorporates dairy and other foods that are rich sources of dietary calcium (Ca) and magnesium (Mg) – minerals associated with favourable impact on BP [14,15] but are typically under-consumed by the US population [16]. As approximately half of Americans report dietary supplement use [17], total Ca and Mg intakes may be substantially above those reported solely from dietary sources alone and are not always captured in dietary assessment studies [18]. Systematic reviews of randomized controlled trials have shown that supplemental intakes of Ca and Mg may contribute to the primary prevention and management of hypertension [19,20]. However, limited research has combined intakes of Ca and Mg from all sources in relation to DASH adherence, urinary Na and their relationships with BP.

The current study analysed data from the International Study of Macro/Micronutrients and Blood Pressure (INTERMAP), US cohort, to document the relationships between diet and BP, involving interviewer-administered 24-h recalls, data on supplemental intake, 24-h urine samples, and multiple robust BP measurements [21,22]. The US population reported that 52% of the participants were taking dietary supplements [21]. This study aimed to characterize sources of Ca and Mg and its intake levels in relation to overall diet quality (DASH score) and determine modification effects of Ca and Mg intakes with DASH score and BP.

METHODS

Population sample

Between 1996 and 1999, INTERMAP surveyed 2195 men and women 40–59 years of age from eight samples in the United States [22]. Participants were selected randomly from community or workplace population lists and arrayed into four age/sex strata. Each participant attended four clinic visits, two on consecutive days and two further visits on consecutive days about 3 weeks later. Institutional ethics committee approval was obtained for each site; all participants provided written informed consent. INTERMAP was approved by the Institutional Review Board of Northwestern University (STU00204462-CR0002) and the Research Ethics Committee of the Health Research Authority (United Kingdom, #EC3169). INTERMAP was registered as NCT00005271 at www.clinicaltrials.gov (Supplemental Figure 1, http://links.lww.com/HJH/C370).

Dietary data

Dietary intakes were assessed with four 24-h dietary recalls administered by staff trained and certified according to a standardized protocol following the tri-phasic method [23,24]. The recall data were entered electronically via the Nutrition Data System (NDS), Nutrition Coordinating Centre (Version 2.91, University of Minnesota) to generate nutrient intake data [25]. Food intake was disaggregated into constituent parts, and each item was allocated to a predefined food group required for each dietary score (Supplemental Table 1, http://links.lww.com/HJH/C370). Intakes by food groups and nutrients were estimated from the mean of the four 24-h dietary recalls. Alcohol intake during the previous week was estimated from 7-day diaries.

The DASH score was calculated as previously described by Fung *et al.* [26] with a perfect adherence score of 35 [27]. The scores among INTERMAP participants ranged from 8 to 35, with a higher score corresponding with a healthier diet pattern. Supplemental Table 1, http://links.lww.com/HJH/C370 and Supplemental Table 2, http://links.lww.com/HJH/C370 provide an overview of the score calculation. Dietary Ca and Mg intakes from foods were derived from the four 24-h dietary recalls, two per visit. Dietary supplement use was also obtained during the 24-h dietary recalls as previously reported [21]. Briefly, participants were asked if they had taken any vitamin/mineral or other supplements at the initial visit and were requested to bring these to the second visit in order to document the details and/or packaging of all supplements taken. The following details were recorded for each supplement during the interview: name, description, unit and dosage (amount and frequency). The composition of each nutritional supplement was taken from the NDS, if available. If the supplement was not listed on the NDS, the product label information was used to calculate intake. All supplement data were re-entered and rechecked as part of the quality control process [21], the mean score on 12-item review of recall audiotapes was 42.7 (ours of 48) [28].

The reliability of dietary intakes of interest (DASH, Ca and Mg) for individuals was estimated using the following formula: $1/[1+(\text{ratio}/2)] \times 100$. The ratio is intraindividual variance divided by interindividual variance. The averages of the first two and second two visits accounted for a higher correlation between dietary intakes on consecutive days. The reliability estimate indicates of the effect of random error (day-to-day variability) [29]. (Supplemental Table 3, http://links.lww.com/HJH/C370)

Clinical measurements

At clinical visits, height and weight were measured twice, and BMI was calculated as weight/height^2 (kg/m^2). BP was measured with a random zero sphygmomanometer by trained staff according to a standardized protocol at each visit following at least 5 min rest [22]. The mean of the eight BP measurements was calculated for use in the analyses. Education, occupation, physical activity, smoking, medical history, family history of high BP, and current medication data were collected using interviewer-guided questionnaires.

Urine collection and analysis

Each participant provided two borate-preserved timed 24-h urine collections approximately 3 weeks apart; aliquots of urine were frozen on-site (−20 °C) and air-freighted frozen to the Central Laboratory (Leuven, Belgium) for biochemical analyses [22]. Urinary Na and K concentrations were measured using emission flame photometry and excretion values were calculated per participant as the product of concentrations in urine and urinary volumes corrected to 24 h. The mean of the two samples was calculated for use in the current study. Because urinary measures offer objective data for Na and K that have greater validity than self-reported dietary data for individuals, these were used here throughout.

Statistical methods

Statistical analyses were applied using SAS software version 9.4 (SAS Institute Inc., Cary, North Carolina, USA). Two-tailed probability values ($P < 0.05$) were considered statistically significant. Associations across categorical variables were analysed using the Chi-squared (χ^2) test. Baseline characteristics of participants are presented across quintile of DASH score. Partial Spearman rank correlation coefficients were calculated between DASH score and dietary Ca and Mg. Multivariable linear regression was used to examine associations between each 1-point DASH score or 2 SD differences in dietary Ca and Mg (total from food and supplements and from DASH score only) with BP. Multiple cross-tabulation analysis, based on quintiles of DASH score and urinary excretion of sodium, was used to further examine the relationship between DASH, Ca, Mg and BP. In the multivariable models we adjusted for the following covariates: model 1 was adjusted for: age (years, continuous), sex, study centre. Model 2 was additionally adjusted for education (years), physical activity (hours/day), alcohol (g/day, continuous), smoking (yes/no), vitamin supplement usage (from food only and food and supplements combined) (yes/no), special diet reported (yes/no), history of CVD (yes/no), anti-hypertensive medication (yes/no), family history of hypertension (yes/no), and mean energy intake (kcal/day, continuous), Model 3 was additionally adjusted for urinary Na. As obesity may lie on the causal pathway between diet and BP, all models were computed with and without adjustment for BMI (continuous variable). As vitamin D intake is important in mediating Ca bioavailability, we adjusted for average vitamin D (mg/d) in model 4b.

Additionally, we conducted stratified analyses to determine if associations between DASH and BP were modified by Mg and Ca intakes [based on sex-specific adherence to recommended daily amount (RDA) from food only and food and supplements combined], and by Ca to Mg intake (sex-specific median value). The RDA used for Ca was greater than 1000 mg/day for men and women aged 50 or less and greater than 1200 mg/day for women aged 51 years or more and for Mg was greater than 320 mg/day for women and greater than 420 mg/day for men [30]. For Na, chronic disease risk reduction (CDRR) level of greater than 2300 mg/day was used for analyses [30,31].

RESULTS

Characteristics

The mean age of the population sample was 49.1 (SD 5.4) years and the sample was comprised of 50% men. Mean SBP/DBP was 118.6 (SD 13.9)/73.4 (SD 9.4) mmHg and the mean DASH score was 21.0 (SD 4.8) (Table 1). Participants in the highest quintile (Q5) of DASH adherence compared with the lowest (Q1) were older, completed more years of education, had lower BMI, were more likely to take vitamin/mineral supplements and were less likely to be a current smoker, they also had higher K excretion. Mean alcohol intake, total energy intake and urinary Na excretion were similar across the DASH quintiles. Overall, 12.5% of participants met CDRR level for Na estimated from their 24-h urine excretion (Table 1). Mean total dietary intake from food and supplements was 938 (SD 498) mg/day for Ca and 359 (SD 162) mg/day for Mg; 30.7% participants reported taking both Ca and Mg supplements (Table 1). Average vitamin D intake was 5.1 (3.6) mg/d. Intake from diet alone showed that 26.7% of men and 23.6% of women met the RDA for Mg, 29.8% of men and 12% of women achieved the RDA for Ca. Combined diet and supplement intakes showed that 35.3% of men and 37.6% of women achieved the RDA for Mg, and 37.3% of men and 27.6% of women achieved the RDA for Ca (Supplemental Table 4, http://links.lww.com/HJH/C370).

Dietary Approaches to Stop Hypertension score, calcium, and magnesium

Participants in Q5 (highest DASH score) compared with Q1 (lowest DASH score) were more likely to meet the RDA for Mg from diet alone at 57.3%, compared with 7.9% ($P < 0.0001$), for Ca the proportions were 35.1% compared with 8.6% ($P < 0.0001$) (Table 1). Participants in Q5 were more likely to report Mg and Ca supplement usage than those in Q1. About 39% of Ca intake was acquired from DASH designated foods (Fig. 1a) primarily from low-fat dairy. Also, 41% of Mg intake was derived from DASH food groups, primarily from vegetables, excluding white potatoes (Fig. 1b). For men, 41% of Ca and Mg intakes were derived from DASH food groups and 50% from other food, and for women, 23% of Ca and 14% of Mg were acquired from supplements and 37% of Ca and 41% of Mg from DASH food groups (Supplemental Table 5, http://links.lww.com/HJH/C370). DASH score showed a stronger partial Spearman correlation with dietary Mg from food ($r = 0.64$, $P < 0.0001$) than dietary Ca from food ($r = 0.42$, $P < 0.0001$) with adjustment for model 2 covariates (Supplemental Table 6, http://links.lww.com/HJH/C370).

Association of Dietary Approaches to Stop Hypertension score and its components with blood pressure

DASH score was inversely associated with SBP across all models including adjustment for BMI (mean difference −0.27; 95% CI: −0.38 to −0.15 mmHg per 1-point change

TABLE 1. Characteristics across quintiles of Dietary Approaches to Stop Hypertension score for INTERMAP United States participants (*N* = 2195)

DASH quintiles	Q1 (*n* = 417)	Q2 (*n* = 440)	Q3 (*n* = 487)	Q4 (*n* = 427)	Q5 (*n* = 424)	ALL (*n* = 2195)
DASH score, median (range)	14 (8–16)	18 (17–19)	21 (20–22)	24 (23–25)	28 (26–35)	21 (8–35)
Male [*n* (%)]	195 (46.8)	237 (53.9)	260 (53.4)	206 (48.2)	205 (48.4)	1103 (50.2)
Female [*n* (%)]	222 (53.2)	203 (46.1)	227 (46.6)	221 (51.8)	219 (51.6)	1092 (49.8)
Age at screening (years)	47.9 (5.2)	48.8 (5.5)	49.2 (5.3)	49.8 (5.5)	50.0 (5.1)	49.1 (5.4)
Education completed (years)	13.7 (3.1)	14.3 (2.7)	15.2 (3.0)	15.3 (2.9)	16.2 (2.9)	15.0 (3.0)
BMI (kg/m^2)	30.5 (6.3)	29.6 (5.7)	28.9 (6.0)	28.5 (6.0)	27.0 (5.0)	28.9 (5.9)
SBP (mmHg)	120.8 (13.7)	120.9 (14.1)	118.2 (13.4)	118.2 (14.1)	114.8 (13.3)	118.6 (13.9)
DBP (mmHg)	73.7 (9.8)	74.7 (9.9)	73.6 (9.7)	73.5 (9.5)	71.5 (9.2)	73.4 (9.7)
Current smoker [*n* (%)]	132 (31.7)	103 (23.4)	66 (13.6)	45 (10.5)	23 (5.4)	369 (16.8)
Taking vitamin/mineral supplement [*n* (%)]	145 (34.8)	192 (43.6)	255 (52.4)	257 (60.2)	287 (67.7)	1136 (51.8)
Following a special diet [*n* (%)]	54 (12.9)	67 (15.2)	74 (15.2)	96 (22.5)	110 (25.9)	401 (18.3)
Diagnosed with cardiovascular disease [*n* (%)]	176 (42.2)	190 (43.2)	200 (41.1)	165 (38.6)	144 (34.0)	875 (39.9)
Take medication for blood pressure management [*n* (%)]	89 (21.3)	118 (26.8)	111 (22.8)	92 (21.5)	73 (17.2)	483 (22.0)
Family history of hypertension [*n* (%)]	278 (66.7)	304 (69.1)	327 (67.1)	304 (71.2)	278 (65.6)	1491 (67.9)
Hours physical activity	4.0 (3.6)	3.4 (3.1)	3.4 (3.1)	3.4 (3.1)	3.4 (3.1)	3.2 (3.1)
Wholegrain (mg/day)	10 (17)	18 (25)	28 (32)	43 (48)	62 (50)	32 (41)
Vegetable excluding potato (mg/day)	111 (77)	148 (110)	181 (105)	204 (115)	256 (129)	180 (119)
Fruit (mg/day)	86 (116)	153 (153)	230 (224)	274 (209)	371 (228)	223 (215)
Nuts and legume (mg/day)	33 (43)	39 (45)	43 (45)	46 (41)	67 (56)	46 (48)
Low fat dairy (mg/day)	40 (89)	101 (173)	154 (198)	203 (213)	286 (240)	157 (207)
Red meat including processed (mg/day)	123 (66)	101 (72)	88 (67)	63 (49)	47 (43)	85 (66)
Sugar sweetened beverages (mg/day)	622 (466)	454 (397)	333 (385)	238 (295)	137 (265)	356 (404)
Energy intake (kcal/day)	2237 (718)	2243 (743)	2286 (742)	2230 (676)	2222 (597)	2245 (699)
Alcohol intake (g/day)	7 (16)	9 (17)	7 (14)	6 (10)	6 (9)	7 (14)
Urinary sodium (mmol/24-h)	158.4 (62.4)	166.6 (61.8)	163.6 (58.4)	162.8 (58.3)	161.1 (55.9)	162.6 (59.4)
< CDRR level sodium[a] [*n* (%)]	63 (15.1)	52 (11.8)	64 (13.1)	42 (9.8)	53 (12.5)	274 (12.5)
Calcium from food (mg/day)	621 (315)	700 (327)	803 (366)	856 (362)	975 (384)	791 (372)
> RDA calcium from food [*n* (%)]	36 (8.6)	63 (14.3)	107 (22.0)	105 (24.6)	149 (35.1)	460 (21.0)
Take calcium supplement [*n* (%)]	100 (24.0)	126 (28.6)	173 (35.5)	207 (48.5)	222 (52.4)	828 (37.7)
Calcium from supplement (mg/day) (consumer only)	259 (304)	356 (477)	334 (354)	381 (381)	513 (530)	388 (436)
Total calcium (mg/day)	683 (358)	802 (435)	921 (445)	1041 (480)	1244 (563)	938 (498)
> RDA calcium from food + supplements [*n* (%)]	54 (12.9)	94 (21.4)	149 (30.6)	179 (41.9)	236 (55.7)	712 (32.4)
Magnesium from food (mg/24 h)	252 (93)	281 (94)	317 (100)	345 (105)	399 (109)	319 (112)
> RDA magnesium from food [*n* (%)]	33 (7.9)	49 (11.1)	98 (20.1)	129 (30.2)	243 (57.3)	552 (25.1)
Take magnesium supplement [*n* (%)]	82 (19.7)	100 (22.7)	138 (28.3)	169 (39.6)	200 (47.2)	689 (31.4)
Magnesium from supplement (mg/24 h) (consumer only)	99 (89)	114 (164)	124 (178)	120 (121)	158 (186)	129 (158)
Total magnesium (mg/24 h)	272 (108)	307 (131)	352 (156)	392 (145)	473 (184)	359 (162)
> RDA magnesium from food + supplements [*n* (%)]	56 (13.4)	89 (20.2)	152 (31.2)	192 (45.0)	311 (73.3)	800 (36.4)
Take calcium and/or magnesium supplement [*n* (%)]	101 (24.2)	127 (28.9)	176 (36.1)	210 (49.2)	229 (54.0)	843 (38.4)
Take calcium and magnesium supplement [*n* (%)]	81 (19.4)	99 (22.5)	135 (27.7)	166 (38.9)	193 (45.5)	674 (30.7)
Average vitamin D intake (mg/day)	4.2 (3.9)	4.6 (3.3)	5.1 (3.4)	5.5 (3.2)	6.1 (3.7)	5.1 (3.7)

Chronic disease risk reduction (CDRR) level for sodium: 2,300 mg/day. Recommended daily amount (RDA) for calcium: women aged 50 years or less and men 1000 mg/day, women aged 51 years or more 1200 mg/day; for magnesium: women 320 mg/day and men 420 mg/day; for vitamin D: 600 IU/day.
[a]Urinary excretion.

in DASH score for model 2). The association between DASH score and DBP was attenuated following adjustment by BMI (Table 2). SBP was consistently lower for those in the highest quantile (DASH score 26–35 points), versus the lowest quartile of DASH score (8–16 points) for those having urinary Na excretion above sex-specific median and those below median (Supplemental Figure 2, http://links.lww.com/HJH/C370).

In multivariate analyses adjusted for model 3 covariates including urinary Na, 2 SD higher DASH foods aligned with the diet pattern was associated with significantly lower SBP/DBP; for example, 2 SD higher intake of wholegrain (82 g/day) was associated with SBP lower by 1.74 (95% CI: −2.83 to −0.66) mmHg (Table 3). For red meat (2 SD 132 g/day) and SSB (2 SD 808 g/day) with reverse scoring of DASH diet pattern, 2 SD higher intakes were associated with SBP higher by 2.85 (95% CI: 1.61–4.10) mmHg for red meat and 2.12 (95% CI: 2.12–0.96) mmHg for SSB.

Association of calcium with blood pressure

In multiple cross-tabulation analysis, SBP was consistently lower for those with urinary Na excretion below median values across Q1 (lowest DASH score) to Q5 (highest DASH score), and those with total Ca above RDA had the lowest SBP and DBP across Q1–Q5 (Fig. 2). SBP and DBP were inversely associated with Ca intake from DASH food groups (2 SD 582 mg/day) across all models with and without BMI, except for DBP with BMI for models 2 and 3, for example, linear regression model 3, −1.89/−0.93 mmHg ($P < 0.05$) controlled for multiple confounders; with additional adjustment for BMI −1.54/−0.74 mmHg (Table 4). For 2 SD (440 mg/day) higher in Ca intake from other foods (e.g. non-low-fat dairy, bread, eggs), SBP and DBP were −1.62/−0.99 mmHg with BMI in model 3 ($P < 0.05$). After adjusting for dietary vitamin D (model 4b), the relation between Ca intake from DASH and SBP attenuated, but remained significant for SBP, but

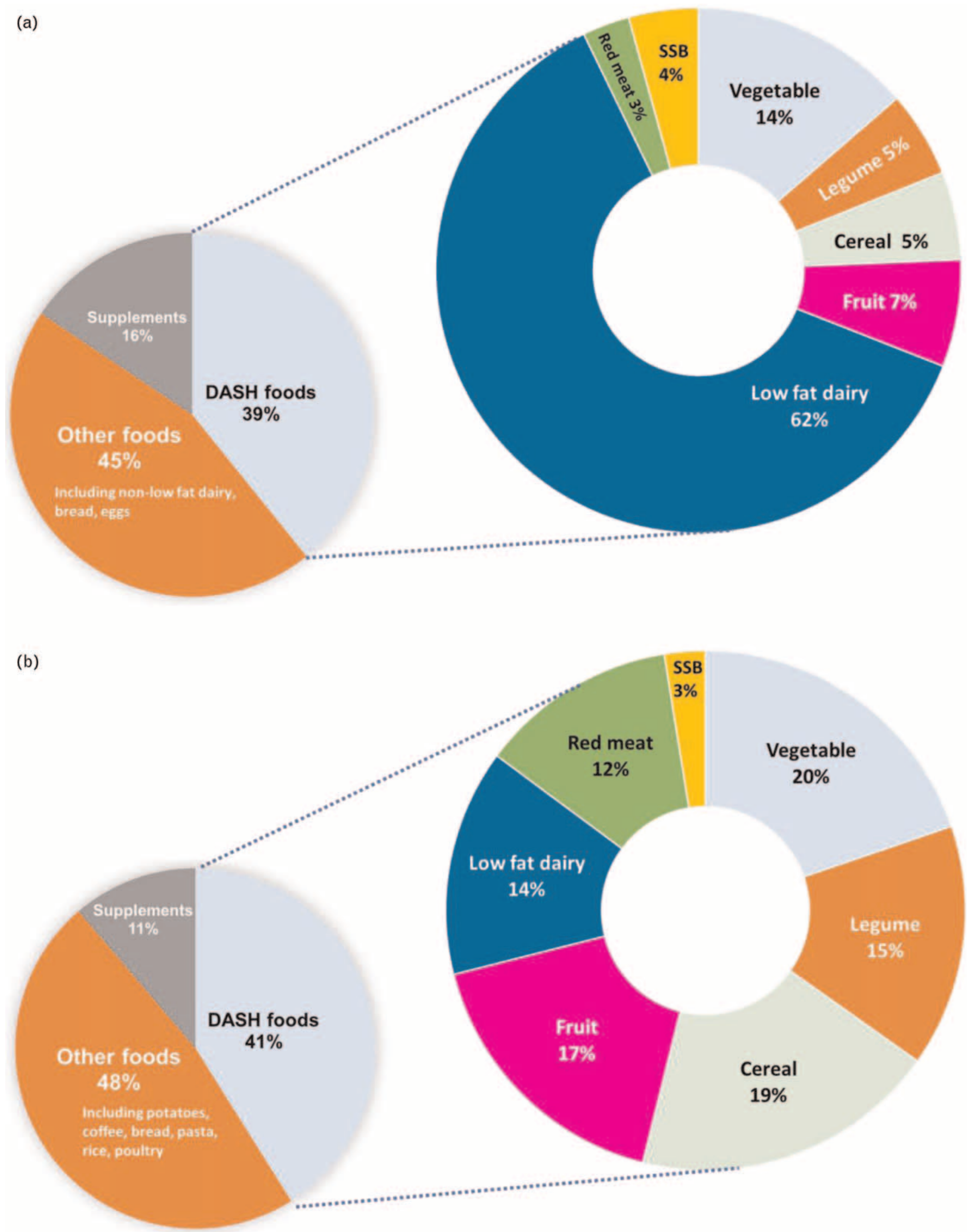

FIGURE 1 Food sources from Dietary Approaches to Stop Hypertension score components, other food and supplements (a) for calcium intake (b) for magnesium intake.

TABLE 2. Estimated mean difference in blood pressure per 1-point change in Dietary Approaches to Stop Hypertension score for INTERMAP US participants ($N = 2195$)[a,b]

	SBP (mmHg)		DBP (mmHg)	
		With BMI		With BMI
	Difference (95% CI)	Difference (95% CI)	Difference (95% CI)	Difference (95% CI)
Model 1	−0.49 (−0.61, −0.37)***	−0.32 (−0.44, −0.21)***	−0.24 (−0.32, −0.16)***	−0.15 (−0.23, −0.07)**
Model 2	−0.39 (−0.51, −0.27)***	−0.27 (−0.38, −0.15)***	−0.19 (−0.27, −0.11)***	−0.12 (−0.21, −0.04)**
Model 3	−0.39 (−0.51, −0.27)***	−0.27 (−0.39, −0.15)***	−0.19 (−0.27, −0.11)***	−0.12 (−0.20, −0.03)**
Model 4	−0.37 (−0.50, −0.24)***	−0.19 (−0.32, −0.06)**	−0.17 (−0.26, −0.08)**	−0.07 (−0.16, 0.02)
Model 5	−0.34 (−0.47, −0.21)***	−0.19 (−0.32, −0.06)**	−0.16 (−0.25, −0.07)**	−0.07 (−0.16, 0.02)

[a]Values are presented as mean (95% CI); *$P < 0.05$; **$P < 0.01$; ***$P < 0.0001$.
[b]Model 1 adjusted for age (continuous), sex, study centre. Model 2 additional adjustment for years in education, physical activity, mean daily alcohol intake (g/day continuous), smoker, vitamin/mineral supplement usage, special diet reported, cardiovascular disease diagnosed, antihypertensive medication, family history hypertension, mean daily energy intake (kcal/day, continuous). Model 3 = model 2 + urinary sodium excretion. Model 4 = model 3 + total dietary magnesium. Model 5 = model 3 + total dietary calcium.

not DBP, with similar findings observed for Ca intake from other foods.

Association of magnesium with blood pressure

In multiple cross-tabulation analysis, SBP was consistently lower for those with urinary Na excretion below median values across Q1 (lowest DASH score) to Q5 (highest DASH score), and those with total Mg above RDA had the lowest SBP across Q1–Q5 (Fig. 3). SBP and DBP were inversely associated with Mg intake from DASH food groups (2 SD (146 mg/day) across all models with and without BMI, except for DBP with BMI for models 2 and 3, for example, lower by 2.5/1.3 mmHg ($P < 0.001$) controlled for model 3 covariates and lower by 1.3/0.8 mmHg including BMI as an additional confounder (Table 5). For dietary Mg intake from other foods (e.g. potatoes, coffee, bread, pasta, rice, poultry), the difference in SBP/DBP with increasing Mg was −1.92/−0.97 mmHg per 2 SD (145 mg/day) in Model 3 with BMI ($P < 0.05$).

DISCUSSION

Limited research has previously investigated the intake of Ca and Mg from food sources relative to DASH adherence as associated with BP. We studied the associations between levels of DASH diet adherence and measures of BP to identify food groups and supplements that contributed most to Ca and Mg intakes and tested for potential effect modification by Ca and Mg intakes with DASH score and BP. This study presents evidence suggesting a relationship between intakes of Ca and Mg with BP regardless of whether the source comes from foods that are part of the DASH score or not, even when adjusted for supplement intakes.

Results identified that DASH foods contributed to 39 and 41% of Ca and Mg intake, respectively. The primary dietary sources of Ca and Mg in the United States are milk, yogurt, cheese [32] and green leafy vegetables, nuts, seeds, and whole grains, respectively [33]. Thus, unsurprisingly, in the present study, low-fat dairy was a major contributor to Ca intakes, and vegetables, fruits, and cereals were top contributors to Mg intakes. We found that other food sources not specified in the DASH score contributed more to Ca and Mg intakes than the DASH score foods themselves. These other food sources of Ca and Mg (e.g. non-low-fat dairy, bread, eggs, pasta, potatoes, coffee, rice, poultry) contributed similarly to BP as DASH score foods.

Supplemental intakes of Ca and/or Mg were reported by 39% of the sample population and contributed 15.6 and 11.2%, respectively, to total intakes. Participants who had the highest adherence to the DASH diet were also more likely to report Mg and Ca supplement intake, which aligns with other findings demonstrating a positive relationship between healthy lifestyles and the use of dietary supplements [34–37]. Overall, dietary supplement use among US adults is similar to those presented here and has remained

TABLE 3. Estimated mean differences in blood pressure associated with 2SD higher Dietary Approaches to Stop Hypertension component intake for INTERMAP US participants ($n = 2195$)[a,b]

	SBP (mmHg)		DBP (mmHg)	
		With BMI		With BMI
DASH-designated foods (2SD)	Difference (95% CI)	Difference (95% CI)	Difference (95% CI)	Difference (95% CI)
Wholegrain (82 g/day)	−1.74 (−2.83, −0.66)**	−1.10 (−2.16, −0.04)*	−1.32 (−2.07, −0.56)**	−0.97 (−1.71, −0.22)*
Vegetables (237 g/day)	−1.57 (−2.67, −0.46)**	−1.18 (−2.26, −0.10)*	−0.62 (−1.39, 0.15)	−0.35 (−1.12, 0.41)
Fruit (430 g/day)	−1.51 (−2.61, −0.42)**	−1.04 (−2.11, 0.03)	−0.15 (−0.92, 0.62)	0.09 (−0.67, 0.84)
Nuts and legumes (95 g/day)	−0.25 (−1.36, 0.85)	0.14 (−0.94, 1.21)	−0.18 (−0.95, 0.59)	0.05 (−0.71, 0.81)
Low fat dairy (415 g/day)	−1.77 (−2.87, −0.66)**	−1.59 (−2.67, −0.52)**	−1.09 (−1.86, −0.32)**	−0.99 (−1.75, −0.23)*
Red meat (132 g/day)	2.85 (1.61, 4.10)***	1.74 (0.51, 2.97)**	1.24 (0.37, 2.11)**	0.67 (−0.20, 1.54)
Sugar sweetened beverages (808 g/day)	2.12 (0.96, 3.27)**	1.61 (0.48, 2.74)*	0.77 (−0.04, 1.58)	0.43 (−0.37, 1.23)

[a]Values are presented as mean (95% CI); *$P < 0.05$; **$P < 0.01$; ***$P < 0.0001$.
[b]Model 3: adjustment for age (continuous), sex, study centre, years in education, physical activity, mean daily alcohol intake (g/day continuous), smoker, vitamin/mineral supplement usage, special diet reported, cardiovascular disease diagnosed, antihypertensive medication, family history hypertension, mean daily energy intake (kcal/day, continuous), urinary sodium excretion.

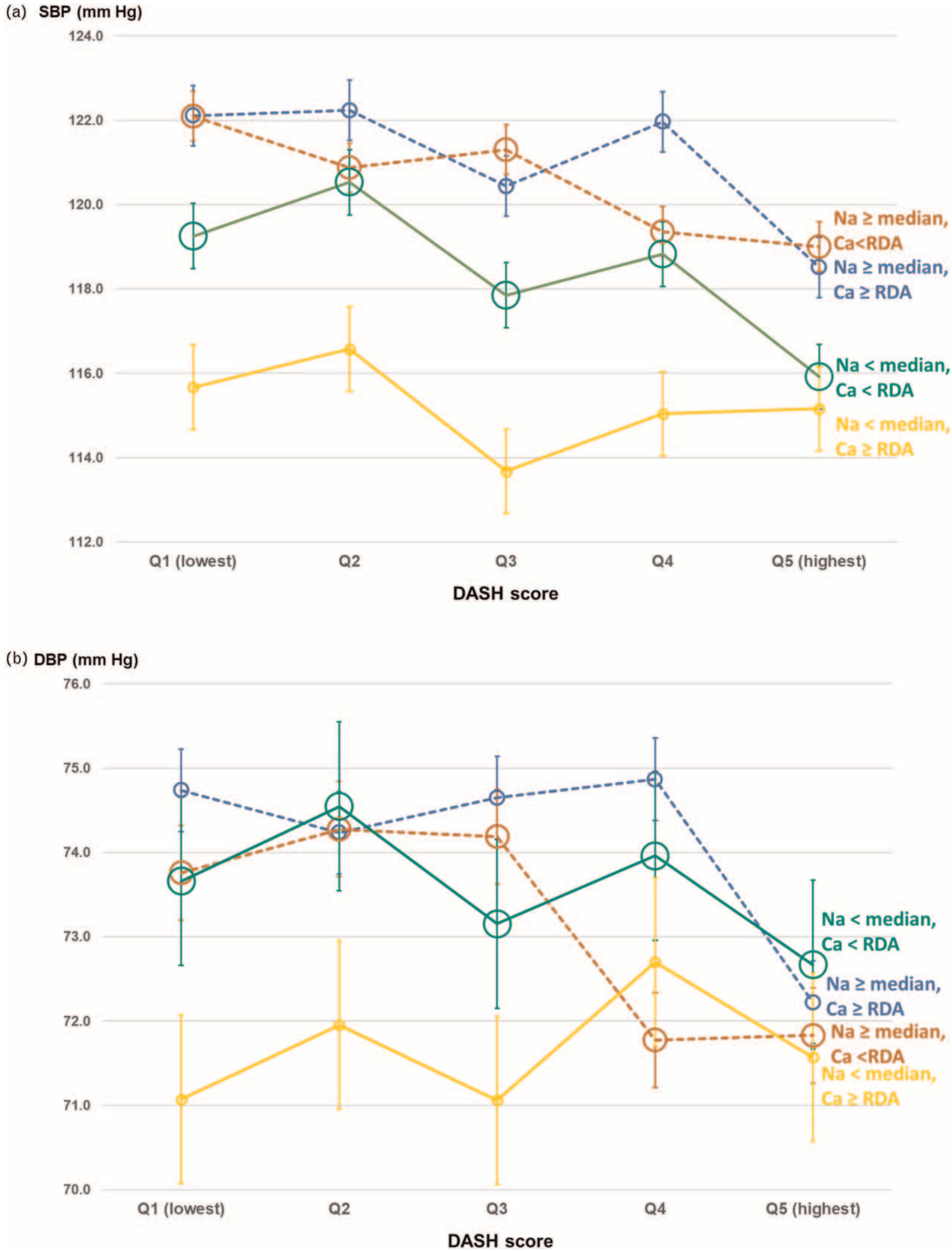

FIGURE 2 Mean blood pressure by quintile of DASH score ($N = 2195$) adjusted for age, sex, study center, education, physical activity, alcohol, smoking, vitamin supplement usage, special diet reported, history of cardiovascular disease, anti-hypertensive medication, family history of hypertension, mean energy intake and BMI: (a) SBP (b) DBP. Median for urinary Na excretion (mmol/24 h) were 173.9 for male individuals and 137.4 for female individuals. RDA of calcium intake for women aged 50 or less and men was 1000 mg/day, and for women aged 51 years or more was 1200 mg/day. Quintiles for DASH score was 8–16, 17–19, 20–22, 23–25 and 26–35. The circle size represents sample size for each quintile of DASH score and error bars indicate standard error of mean BP. DASH, Dietary Approaches to Stop Hypertension; Na, Sodium; Q, Quintile; RDA, recommended daily amount.

TABLE 4. Estimated mean differences in blood pressure associated with 2SD higher dietary calcium from Dietary Approaches to Stop Hypertension food groups and other foods for INTERMAP US participants ($n = 2195$)[a,b]

	SBP (mmHg)		DBP (mmHg)	
		With BMI		With BMI
	Difference (95% CI)	Difference (95% CI)	Difference (95% CI)	Difference (95% CI)
Calcium intake from DASH food groups (2SD = 582 mg/day)				
Model 1	−1.96 (−3.13, −0.79)**	−1.75 (−2.86, −0.65)**	−1.05 (−1.84, −0.26)**	−0.94 (−1.70, −0.18)*
Model 2	−1.85 (−2.99, −0.71)**	−1.54 (−2.65, −0.43)**	−0.92 (−1.72, −0.12)*	−0.75 (−1.54, 0.03)
Model 3	−1.89 (−3.03, −0.74)**	−1.54 (−2.65, −0.43)**	−0.93 (−1.73, −0.13)*	−0.74 (−1.52, 0.05)
Model 4a	−2.07 (−3.22, −0.91)**	−1.78 (−2.90, −0.66)**	−1.05 (−1.86, −0.24)*	−0.89 (−1.68, −0.09)*
Model 4b	−1.87 (−3.20, −0.57)**	−1.33 (−2.60, −0.07)*	−0.73 (−1.64, 0.18)	−0.42 (−1.31, 0.47)
Calcium intake from other food groups[c] (2SD = 440 mg/day)				
Model 1	0.24 (−0.97, 1.46)	−0.87 (−2.02, 0.28)	−0.15 (−0.98, 0.67)	−0.76 (−1.56, 0.04)
Model 2	−1.03 (−2.39, 0.33)	−1.61 (−2.93, −0.29)*	−0.71 (−1.66, 0.24)	−1.03 (−1.96, −0.10)*
Model 3	−1.24 (−2.60, 0.13)	−1.62 (−2.94, −0.29)*	−0.78 (−1.73, 0.18)	−0.99 (−1.93, −0.05)*
Model 4b	−1.14 (−2.50, 0.24)	−1.51 (−2.90, −0.18)*	−0.68 (−1.60, 0.28)	−0.89 (−1.80, 0.05)
Model 4c	−1.61 (−2.98, −0.23)*	−1.93 (−3.27, −0.59)**	−0.97 (−1.94, −0.002)*	−1.15 (−2.10, −0.20)*

[a]Values are presented as mean (95% CI); *P value <0.05; **P value <0.01; ***P value <0.0001.
[b]Model 1 adjusted for age (continuous), sex, study centre. Model 2 additional adjustment for years in education, physical activity, mean daily alcohol intake (g/day continuous), smoker, vitamin/mineral supplement usage, special diet reported, cardiovascular disease diagnosed, antihypertensive medication, family history hypertension, mean daily energy intake (kcal/day, continuous). Model 3 = model 2 + urinary sodium excretion. Model 4a = model 3 + calcium intake from supplement + calcium intake from other food groups other than DASH or supplement. Model 4b = model 3 + vitamin D intake (mg/day). Model 4c = model 3 + calcium intake from supplement + calcium intake from DASH score.
[c]Other than calcium intake from DASH or supplement.

stable in the 10–15 years. Supplementation use along with food intakes of Ca and Mg in this study demonstrated inverse relations with BP. This is in contrast with other studies that show intakes of Ca and Mg from supplementation may pose a risk in terms of CVD outcomes [38] or have shown inconsistent benefits [39], which may be due to methodological limitations in study designs. For example, the use of self-reported food frequency questionnaires to estimate intake may have introduced bias, making comparisons with our findings difficult.

Despite higher intakes of Ca and Mg among participants in the highest quintile of DASH adherence, levels of both fell below the RDA for almost 70% of the sample even when considering intakes from supplements. Intakes of these nutrients remain lower than recommended [16] and were identified as nutrients of concern in the 2020–2025 Dietary Guidelines for Americans for which low intakes are associated with health issues [30].

In addition to not meeting the RDA, the bioavailability of Ca may be compromised by adherence to the fibre-rich DASH diet [40]. Ca bioavailability and absorption are increased in the presence of vitamin D, with the richest source being fortified cow's milk but not always found in non-dairy milk sources. Without vitamin D, only 10–15% of dietary Ca is absorbed, as compared with absorption of 30–40% with vitamin D [41]. Among participants of our study, dietary vitamin D intake was low (≈5 mg/day), and associations between Ca intake and BP attenuated after adjustment for vitamin D, suggesting it may mediate Ca bioavailability. Thus, low Ca intakes among these participants may be further compromised as a secondary analysis of the DASH trial revealed that participants adhering to the DASH diet had lower blood levels of active vitamin D [42].

Of note is that even participants who had the highest adherence to the DASH diet in the present study reported Ca and Mg intakes below those reported in the DASH trial [8]. Design differences in the prospective interventional DASH study versus the observational, cross-sectional diet assessment performed in INTERMAP to calculate ad libitum DASH adherence likely contribute to these differences in intakes. As a cross-sectional study, these results cannot be viewed as casual, but rather, in associations with urinary measures of Ca/Mg the potential for identifying possible mechanisms is enhanced, and offers rationale for future testing of these hypotheses.

Suggested mechanisms underlying the benefits of the DASH diet include the beneficial role of Ca and Mg [43]. In this study, higher Ca and Mg intakes from DASH and all other sources were associated with lower SBP and DBP. These findings corroborate prior research demonstrating the prevention or reduction of high BP with increased intakes of Ca [20,44,45] and Mg [46,47]. It has been proposed that Mg acts as a Ca channel blocker, thereby improving endothelial function [48]. Ca intake plays a crucial role in regulating BP through various mechanisms. It can modify intracellular Ca in vascular smooth muscle cells, thereby affecting vascular volume and the renin–angiotensin–aldosterone system [49]. When Ca intake is low, it leads to an increase in parathyroid gland activity, resulting in the production of parathyroid hormone. This hormone increases intracellular calcium in vascular smooth muscles, causing vasoconstriction. Furthermore, low Ca intake can increase the synthesis of calcitriol, either directly or mediated by parathyroid hormone. Calcitriol increases intracellular Ca in vascular smooth muscle cells. Both low Ca intake and parathyroid hormone can stimulate renin release, leading to the synthesis of angiotensin II and aldosterone, which increases BP levels [49].

Other studies also support the association between Ca and Mg intakes and lower CVD risk. The Singapore Chinese Health Study reported that Ca and Mg intakes were associated with a lower risk of coronary artery disease and stroke mortality (hazard ratio for extreme quintiles 0.91 and 0.87, for Ca and Mg, respectively). However, after adjusting for intakes of other dietary factors (e.g. cholesterol, omega-3 fatty acids, fibre, polyunsaturated to saturated fats ratio), the

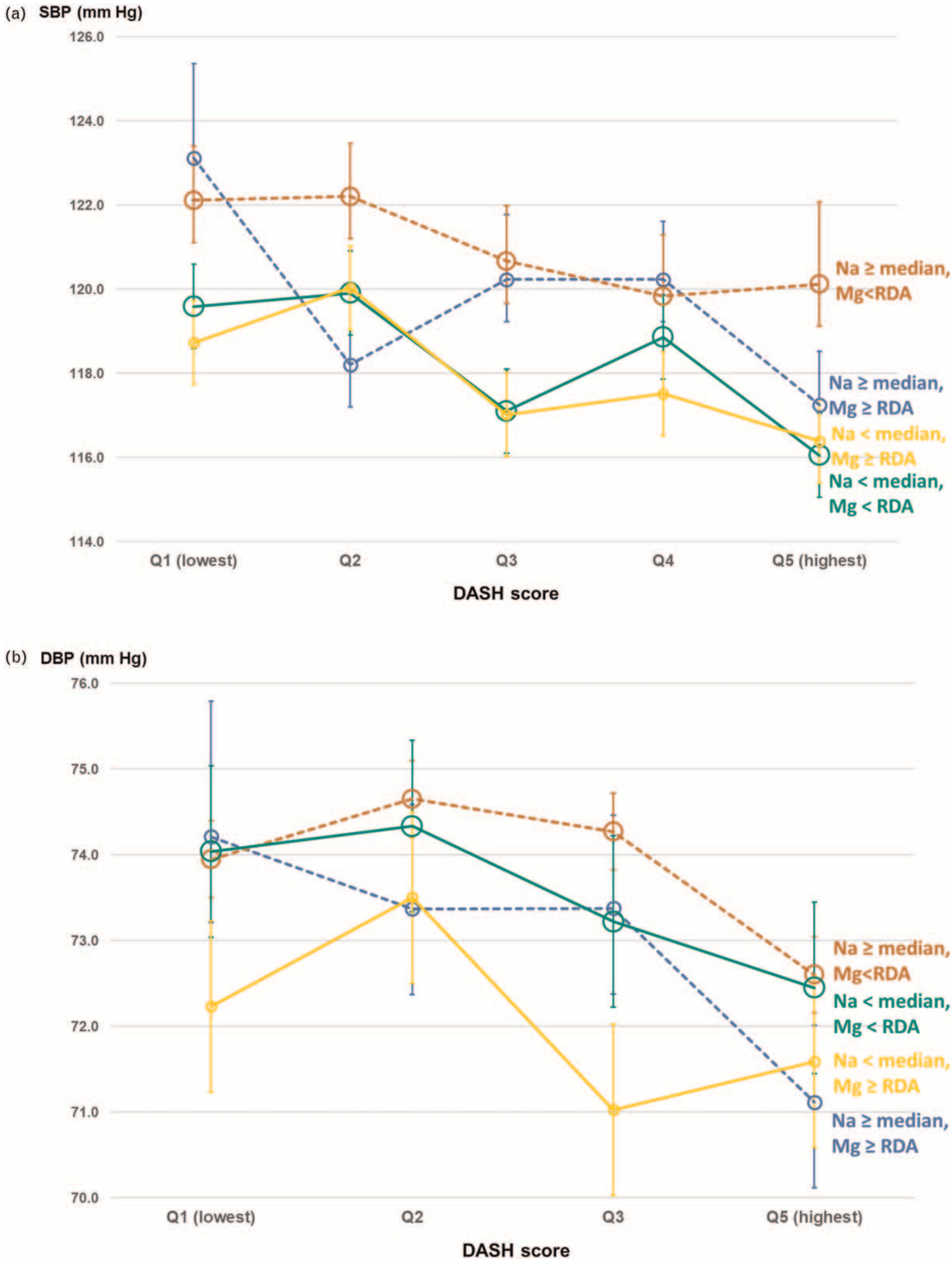

FIGURE 3 Mean blood pressure by quintile of Dietary Approaches to Stop Hypertension score ($N = 2195$) adjusted for age, sex, study centre, education, physical activity, alcohol, smoking, vitamin supplement usage, special diet reported, history of cardiovascular disease, anti-hypertensive medication, family history of hypertension, mean energy intake and BMI: (a) SBP (b) DBP. Median for urinary Na excretion (mmol/24 h) were 173.9 for male individuals and 137.4 for female individuals. RDA of magnesium intake (mg/day) was 320 for women and 420 for men. Quintiles for DASH score was 8–16, 17–19, 20–22, 23–25 and 26–35. The circle size represents sample size for each quintile of DASH score and error bars indicate standard error of mean BP. DASH, Dietary Approaches to Stop Hypertension; Na, Sodium; Q, Quintile; RDA, recommended daily amount.

TABLE 5. Estimated mean differences in blood pressure associated with 2 SD higher dietary magnesium from Dietary Approaches to Stop Hypertension food groups and other food for INTERMAP US participants ($n = 2195$)[a,b]

	SBP (mmHg)		DBP (mmHg)	
		With BMI		With BMI
	Difference (95% CI)	Difference (95% CI)	Difference (95% CI)	Difference (95% CI)
Magnesium intake from DASH score (2SD = 146 mg/day)				
Model 1	−2.21 (−3.38, −1.03)**	−1.54 (−2.65, −0.43)**	−1.28 (−2.07,−0.48)**	−0.91 (−1.69, −0.14)*
Model 2	−2.50 (−3.72, −1.28)**	−1.59 (−2.79, −0.40)**	−1.30 (−2.16, −0.45)**	−0.81 (−1.66, 0.03)
Model 3	−2.49 (−3.71, −1.27)**	−1.59 (−2.79, −0.40)**	−1.30 (−2.15, −0.45)**	−0.80 (−1.64, 0.05)
Model 4a	−2.67 (−3.90, −1.44)***	−1.78 (−2.99, −0.57)**	−1.39 (−2.25, −0.53)**	−0.89 (−1.74, −0.03)*
Magnesium intake from other food groups[c] (2SD = 145 mg/day)				
Model 1	−0.47 (−1.72, 0.78)	−0.62 (−1.80, 0.56)	−0.48 (−1.33, 0.36)	−0.56 (−1.38, 0.25)
Model 2	−2.09 (−3.53, −0.66)**	−1.92 (−3.30, −0.53)*	−1.11 (−2.11, −0.11)*	−1.01 (−2.00, −0.03)*
Model 3	−2.28 (−3.71, −0.85)**	−1.92 (−3.31, −0.53)**	−1.17 (−2.17, −0.16)*	−0.97 (−1.95, 0.02)*
Model 4b	−2.64 (−4.07, −1.20)**	−2.17 (−3.58, −0.77)**	−1.35 (−2.36, −0.34)**	−1.09 (−2.09, −0.10)*

[a]Values are presented as mean (95% CI); *P value <0.05; **P value <0.01; ***P value <0.0001.
[b]Model 1 adjusted for age (continuous), sex, study centre. Model 2 additional adjustment for years in education, physical activity, mean daily alcohol intake (g/day continuous), smoker, vitamin/mineral supplement usage, special diet reported, cardiovascular disease diagnosed, antihypertensive medication, family history hypertension, mean daily energy intake (kcal/day, continuous). Model 3 = model 2 + U Na. Model 4a = model 3 + Mg intake from supplement + Mg intake from other food groups other than Mg intake from DASH score or supplement. Model 4b = model 3 + Mg intake from supplement + Mg intake from DASH score.
[c]Other than magnesium intake from DASH or supplement.

association was weakened, primarily because of fibre intakes derived from plant based sources [50]. Although these other dietary factors were not included in the present analysis, it is possible that the relationship between Ca and Mg with BP would be attenuated, however, it is noteworthy that intakes of Ca from food in the present study were about twice those in the Singapore Chinese Health Study and Mg intakes were also slightly higher, although much more comparable. The same study also found that adjustments for mineral intakes (K, Na, Mg, Ca) did not change the significant relationship between DASH scores and stroke or coronary artery disease mortality [50]. These results are similar to the findings in this study with BP significantly and inversely relating to DASH scores even with adjustments for Ca and Mg, except for with DBP, which was not significant after adjustments for Ca and Mg when including BMI in the model.

INTERMAP has several strengths related to the standardized protocol across all population samples for multiple BP and clinical measurements at two-time points. Likewise, repeated 24-h dietary recalls were collected according to a detailed methodology used by trained and certified interviewers providing variability not fully captured with food frequency questionnaires. Detailed assessment of dietary supplement use was used to determine comprehensive Mg and Ca intakes. As dietary Na and increased BMI are established risk factors for elevated BP, objective measures of clinical rather than self-reported weight and height and 24-h urinary sodium were used. Limitations of this study are also acknowledged. Despite the collection of several multi-pass 24-h recalls with rigorous quality check procedures, potential reporting error is an established limitation of self-reported dietary intakes, and the same issue could apply to the self-reported intakes of supplements [28]. A detailed protocol was followed to calculate Mg and Ca intake from supplements; however, additional intake of these minerals from medications (e.g. antacids) was not captured. Furthermore, we could not differentiate the types of mineral supplements used (e.g. Mg citrate/oxide/chloride and Ca citrate/carbonate/phosphate), but these may have different physiological effects on vascular function [51]. The population sample used was ethnically diverse; however, the generalizability of results to the current US population may be limited because of changes in the food supply since the 1990s. Nonetheless, DASH score only increased modestly between 1990 and 2018, reaching 23 in high-income countries in 2018 [52], whereas our study reported a mean score of 21. Lastly, cross-sectional analyses test associations and not causality. Regardless, the findings presented here warrant further exploration in clinical trials with replication in other cohorts.

In conclusion, this study showed a higher intake of Ca and Mg is associated with BP regardless of whether the source is part of the DASH diet or not, and even when adjusted for supplement intakes. Previous reports on the INTERMAP study have presented the findings of urinary Ca and Mg in relation to BP [53], while the current analysis adds to the existing literature by focusing on dietary Ca and Mg in relation to DASH adherence and its association with BP. We also show that the benefit of following a DASH diet pattern may be enhanced by meeting the RDA for Ca and Mg through diet and supplements. These findings can be helpful to inform future research, dietary recommendations, and clinical practice.

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Statement of authors' contributions to manuscript: L.M. S., L.J.A., B.L.R., P.E., L.V.H., J.S.: designed the INTERMAP Study, conducted the fieldwork and collected data; R.G., G.

A., Q.C.: performed the analysis; R.G., G.A., L.V.H., Q.C.: interpreted the data, and prepared the manuscript; L.M.O. G., L.M.S., B.L.R. contributed to the dietary data analysis and revised the work critically for important intellectual content; T.H.V., L.J.A., M.L.D., P.E., J.S. revised the work critically for important intellectual content; L.V.H. and Q.C. were responsible for final content, and all authors read and approved the final manuscript. Q.C. is an employee and shareholder of Amgen Inc. The work presented here was conducted while Q.C. was an employee of Imperial College London. Amgen Inc was not involved in this study.

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Conflicts of interest

There are no conflicts of interest.

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