Published in final edited form as:
*J Hypertens*. 2009 February ; 27(2): 231–236. doi:10.1097/HJH.0b013e32831a7294.

# Dietary Starch Intake of Individuals and Their Blood Pressure: The INTERMAP Study

**Ian J Brown**[a], **Paul Elliott**[a], **Claire E Robertson**[b], **Queenie Chan**[a], **Martha L Daviglus**[c], **Alan R Dyer**[c], **Chiang-Ching Huang**[c], **Beatriz L Rodriguez**[d], **Kiyomi Sakata**[e], **Hirotsugu Ueshima**[f], **Linda Van Horn**[c], **Liancheng Zhao**[g], **Jeremiah Stamler**[c], and **the INTERMAP Research Group**

[a]Department of Epidemiology and Public Health, Imperial College London, St Mary's Campus, London, UK

[b]Department of Human and Health Sciences, School of Biosciences, University of Westminster, London, UK

[c]Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, USA

[d]Department of Geriatric Medicine, Pacific Health Research Institute, University of Hawaii at Manoa, Honolulu, Hawaii, USA

[e]Department of Hygiene and Preventive Medicine, Iwate Medical University, Morioka, Japan

[f]Department of Health Science, Shiga University of Medical Science, Otsu, Shiga, Japan

[g]Cardiovascular Institute and Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

## Abstract

**Objective—**Data from the Multiple Risk Factor Intervention Trial (MRFIT) show an independent direct association between starch intake and blood pressure (BP) in American men at higher risk of coronary heart disease (CHD). Cross-sectional INTERMAP data were used to assess relations of dietary starch intake to BP in men and women from four countries.

**Methods—**Data include 83 nutrients from four multi-pass 24-h dietary recalls and two timed 24-h urine collections; eight BP readings; and questionnaire data, for 4,680 participants ages 40–59 yr from 17 population samples in Japan, People's Republic of China, United Kingdom, and United States of America.

**Results—**In multiple linear regression analyses – adjusted for urinary sodium, urinary potassium, consumption of alcohol, cholesterol, saturated fatty acids, polyunsaturated fatty acids, calcium, and other variables – starch intake higher by two standard deviations (14.1% kJ) was associated with systolic/diastolic BP differences of −1.0/−0.9 mm Hg ($p = 0.09$, $p < 0.05$). Results were similar with additional control for fibre, magnesium, or phosphorus; reduced to −0.5/−0.7 mm Hg ($p = 0.47$, $p = 0.13$) with separate adjustment for vegetable protein. Findings were similar for all INTERMAP men, for American men, and for American men at higher CHD risk.

**CORRESPONDING AUTHOR:** Professor Paul Elliott, Department of Epidemiology and Public Health, Faculty of Medicine, Imperial College London, St Mary's Campus, London W2 1PG, UK. Tel +44 20 7594 3328, Fax +44 20 7262 1034, p.elliott@imperial.ac.uk..

**CONFLICTS OF INTEREST:** None

**Conclusions—**INTERMAP data indicate that – if any – relations of starch intake to BP are modestly inverse. Current dietary guidelines for hypertension prevention and control remain relevant.

### Keywords

Blood pressure; cross-sectional studies; diet; dietary carbohydrates; dietary starch; epidemiology

## INTRODUCTION

Adverse high blood pressure (BP) levels – prehypertensive and hypertensive – pose a health risk to a significant proportion of the adult population worldwide.[1] Given that elevated BP is a potent risk factor for cardiovascular disease (CVD) with no apparent threshold,[2] public health measures are needed to address the problem throughout the population, with an emphasis on its primary and primordial prevention.[3]

High sodium intake, inadequate potassium intake, high body mass index (BMI), and excessive alcohol intake are established independent risk factors for elevated BP.[4–7] Other dietary factors implicated in BP modification include calcium, magnesium, phosphorus, vegetable protein, cholesterol, saturated fatty acids (SFA), and polyunsaturated fatty acids (PFA).[8–12]

Effects of dietary starch – glycemic polysaccharide carbohydrate composed of glucose molecules; major sources cereals, root vegetables, and legumes[13] – on BP are less studied. [14] Several randomized trials have compared the effects on BP of substituting total glycemic carbohydrate (sugars and starch combined) for other macronutrients,[15, 16] but few have tested starch in isolation.[17, 18] Observational findings of the Multiple Risk Factor Intervention Trial (MRFIT) indicate a direct association between dietary starch intake and BP in American men at higher coronary heart disease (CHD) risk. Based on these data, the INTERMAP Study formed a prior hypothesis that the starch intake of individuals was directly related to their BP. [19] Here we present findings on that hypothesis.

## METHODS

### Population Samples, Field Methods (1996–1999)

INTERMAP surveyed 4,680 men and women ages 40–59 years from Japan (4 samples), the People's Republic of China (PRC, 3), the United Kingdom (UK, 2), and the United States of America (USA, 8). Participants were randomly recruited from general and occupational populations, stratified by age and gender.[19] Each participant attended 4 times, visits 1 and 2 on consecutive days, visits 3 and 4 on consecutive days on average 3 weeks later. For BP measurement, each participant – having emptied his/her bladder – was seated for 5 minutes, feet flat on the floor, in a quiet room, with no physical activity, eating, drinking, or smoking in the preceding half hour. Blood pressure was measured twice at each visit with a random-zero sphygmomanometer. Korotkoff sounds I and V were criteria for systolic BP and diastolic BP (SBP, DBP). Measurements of height and weight, and questionnaire data on daily alcohol consumption over the previous 7 days were obtained at 2 visits. Dietary data were collected at each visit by a trained interviewer with use of the in-depth multi-pass 24-hour recall method.[20] All foods and drinks consumed in the previous 24 hours were recorded, including dietary supplements. Questionnaire data were obtained on demographic and other possible confounders. Quality control was extensive, international, national, and local.

Each participant provided two 24-hour urine collections, start and end timed at the research center (visits 1 to 2 and 3 to 4); measurements included urinary volume, sodium, potassium, creatinine, urea; 8% of specimens were split locally and sent to the Central Laboratory for blinded estimation of technical error.[19]

Individuals were excluded if they did not attend all 4 visits; diet data were considered unreliable; energy intake from any 24-hour dietary recall was below 2,092 or greater than 20,920 kJ/24-hour for women, 33,472 kJ/24-hour for men; 2 urine collections were not available; data on other variables were incomplete or indicated protocol violation (total exclusions: 215 people). For each exclusion, a supplementary participant was recruited.

The study received institutional ethics committee approval for each site; all participants gave written consent; all procedures followed were in accordance with institutional guidelines.

## Statistical Methods

Dietary data were converted to nutrient intakes (83 nutrients) with use of enhanced country-specific food tables, standardized across countries by the Nutrition Coordinating Center, University of Minnesota.[20, 21] For nutrients supplying energy, intake was calculated as percent total energy; for others, as intake/1,000 kJ; nutrients were calculated also as amounts/24-hour. Urinary values/24-hour were calculated as products of urinary concentrations and timed volume standardized to 24 hours. Measurements/person were averaged for BP and nutrient variables across the 4 visits; for urinary excretions, across the two 24-hour collections. For descriptive statistics, means and standard deviations (SD), or frequencies and percentages, were calculated by country. To identify food sources of starch, food items were assigned to food groups (automatically by Nutrition Data System software for the USA,[21] manually for the other countries).

Percentage reliability of SBP, DBP, and starch intake from the mean of the four visits was estimated from the formula $1/[1+(\text{ratio}/4)]\times 100$, where the ratio is intra-individual variance divided by inter-individual variance, calculated separately for 8 gender/country strata and pooled by weighting each stratum-specific estimate by sample size minus 1.[22] We are estimating – as a first approximation – the effect of random error (day-to-day variability) on reliability of associations of starch intake with BP, expressed as the size of an observed coefficient as a per cent of the theoretical coefficient in a univariate regression analysis;[22, 23] this does not address the potential effect on starch-BP associations of systematic bias – likely minimized in INTERMAP by observer training, standardization, certification, multi-pass methods, open non-leading questioning, and extensive ongoing quality control throughout the fieldwork.

Associations of dietary variables were explored first by partial Pearson correlation, adjusted for age, gender, and sample, pooled by country. Multiple regression analyses were used to assess relations of the dietary starch intake of individuals (% kJ) to their SBP and DBP (mm Hg). Four sequential regression models were used: Model 1 adjusted for sample, age, gender, weight (kg); height (m);[24] medical history of CVD or diabetes (yes/no), family history of hypertension (yes/no/missing), special diet at time of study (yes/no), reported dietary supplement use at time of study (yes/no), and moderate or heavy physical activity (hours per day); Model 2: addition of 24-hour urinary sodium and potassium excretion (mmol/24-h), and 14-day alcohol intake (g/24-h); Model 3: addition of SFA, PFA (both % kJ), dietary cholesterol, and calcium intake (both mg/1,000 kJ); Models 4a to 4d: all variables in Model 3 plus vegetable protein (% kJ), or dietary fiber (g/1,000 kJ), or magnesium (mg/1,000 kJ), or phosphorus (mg/1,000 kJ) regressed separately to avoid multicollinearity.[25] Country-specific regression coefficients were pooled (weighted by

inverse of their variance). A chi-square test was used to assess cross-country heterogeneity of regression coefficients.[26]

Age-starch and gender-starch interactions were assessed by interaction terms in regression models. Departures from linearity were tested with quadratic terms. Sensitivity analyses involved: use of nutrient densities adjusted for energy; use of g/24-h intake adjusted for energy; urinary sodium/creatinine ratio and potassium/creatinine ratio instead of sodium and potassium; censored normal regression to adjust for antihypertensive treatment effect;[27] restricting analyses to 2,238 “non-intervened” persons (not on a special diet, not consuming dietary supplements, not with diagnosed CVD or diabetes mellitus (DM), not taking medication for high BP, CVD, or DM, i.e., characteristics that could bias observed starch-BP associations); also 3,671 non-hypertensive persons (SBP <140, DBP <90 mm Hg, not taking antihypertensive medication); exclusion of pre-identified people with marked intra-individual variability in nutrient intake and/or SBP, DBP (n=3,473 remain);[19] men only (n=2,359), USA men only (n=1,103),USA men at higher CHD risk (any one or more of: systolic BP ≥140 mm Hg, or diastolic BP ≥90 mm Hg, or body mass index ≥30.0 kg/$m^2$, or current smoker, or history of CVD or DM, or diabetic diet, or taking antidiabetic/antihypertensive/lipid-lowering/cardiovascular-influencing drugs; n=717). Analyses were performed with SAS 9.1 (SAS Institute, Cary, NC, USA) by I.J.B. P-values of <0.05 (uncorrected for multiple-testing) were considered statistically significant. Statistical tests were two-sided except for the chi-square test for cross-country heterogeneity.

## RESULTS

### Descriptive Statistics

Mean SBP ranged from 117.2 in Japan to 121.3 mm Hg in the PRC (Table S1 at http://www.jhypertension.com). Mean DBP was lowest in the PRC (73.2 mm Hg) and highest in the UK (77.3 mm Hg). Energy intake was highest in the USA, lowest in the PRC. Mean starch intake was highest in the PRC (56.5% kJ), intermediate in Japan (35.5% kJ) and lower in the UK and USA (25.5 and 22.8% kJ). The USA was the only country where mean estimated dietary total sugars (26.7% kJ) exceeded starch intake. Rice, noodles, grains, and flour were the predominant sources of starch in Japan (79.2%), the PRC (85.6%), and the USA (38.4%) (data not tabulated). Bread products were the predominant source of starch in the UK (43.1%); second in Japan (7.9%) and the USA (25.7%); negligible in the PRC (0.8%). Vegetables and beans provided 22.4% of starch in the UK; less in the USA (13.3%), the PRC (6.4%), and Japan (5.4%).

The univariate estimate of reliability for starch, based on mean of four 24-hour recalls for each of the 4,680 participants was 73.1% of theoretical coefficient. This is a first approximation of the likely attenuation of starch-BP associations attributable to day-to-day variability in starch intake. Country-specific reliability estimates were higher for Japan and PRC compared to UK and USA (78.4% and 78.8% vs. 69.8% and 69.5%). Blood pressure reliability estimates were 94.3% for SBP and 93.0% for DBP, uniformly high across countries.

### Partial Correlation

Starch intake (% kJ, adjusted for sample, age, gender) exhibited highest correlation (positive) with vegetable protein (r= +0.58). Correlation with fiber was r= +0.28, SFA r= −0.41, 14-day alcohol r= −0.29. Calcium, magnesium, and phosphorus were not highly correlated with starch (r ranging from −0.11 to +0.11).

### Multiple Regression

In Model 1 – adjusted for multiple non-dietary factors – starch intake higher by 2 SD (14.1% kJ) was associated with a SBP difference of −1.5 mm Hg and a DBP difference of −1.0 mm Hg (both $p < 0.001$) (Table 1). Blood pressure differences were reduced with control for urinary and dietary factors (Model 2 onwards). In Model 3 – adjusted for urinary sodium, potassium, dietary alcohol, cholesterol, PFA, SFA, calcium – starch intake higher by 2 SD (14.1% kJ) was associated with SBP/DBP differences of −1.0/−0.9 mm Hg ($p = 0.09$, $p < 0.05$). With additional control for vegetable protein (Model 4a), BP differences were further reduced (SBP/DBP −0.5/−0.7 mm Hg, $p = 0.47$, $p = 0.13$). Separate adjustment for fiber, magnesium, or phosphorus (Models 4b to 4d) yielded similar results to Model 3.

Significant cross-country heterogeneity was not detected in any regression models. Gender-starch and age-starch interactions were nonsignificant, and there was no evidence of non-linearity in starch-BP associations.

### Sensitivity Analyses

Results of sensitivity and main analyses were generally compatible (summarized for regression Model 3 in Table 2). Absolute magnitudes of inverse associations between starch and BP were increased consistently in analyses restricted to 2,238 “non-intervened” participants. In Model 3, absolute magnitude of the SBP/DBP difference increased from −1.0/−0.9 to −1.5/−1.2 mm Hg. In analyses restricted to 717 USA men with higher CHD risk, associations were nonsignificantly inverse.

## DISCUSSION

Among the men and women of the INTERMAP Study we found starch intake to inversely associated with BP – statistically significant in 5 of 7 nutrient-controlled diastolic BP models – though associations were generally of low-order, and reduced further with control for vegetable protein.

Thus, INTERMAP findings do not lend support to its prior hypothesis – based on MRFIT data – of a direct relationship between starch intake and BP. Rather they are similar to findings among 615 Japanese-Hawaiian men of the Honolulu Heart Program where starch intake (g/24-h assessed by single 24-hour dietary recall) was inversely associated with SBP and DBP with adjustment for age, body mass, and alcohol (no adjustment for energy).[29] In MRFIT, among 11,342 American men ages 35 to 57 years at baseline, with elevated CHD risk, 6 year mean starch intake (% kJ) was found to be directly associated with 6 year mean SBP and DBP with multiple adjustments (including energy, alcohol, micro- and macronutrients).[12, 28]

INTERMAP and MRFIT used similar dietary data collection methods, nutrient calculations, BP measurements and analyses; nonetheless, study differences may account for disparity in results: MRFIT volunteers were selected on the basis of higher CHD risk; survey timescales differed (MRFIT 6 years, INTERMAP 3 weeks); INTERMAP participants were more diverse (men and women from population or occupational samples in four countries compared to male volunteers from 18 USA cities). In INTERMAP analyses on 717 American men with higher CHD risk, BP differences were nonsignificantly inverse (not direct).

The OmniHeart feeding trial found high protein (half from plant sources) or high monounsaturated fat (MFA) diets reduced BP more effectively than an isocaloric high carbohydrate diet (based on the DASH [Dietary Approaches to Stop Hypertension] diet, rich in fruit, vegetables, grains, legumes, nuts/seeds, and low-fat/fat-free dairy products, with

reduced total and saturated fats, and cholesterol) consumed for 6 weeks by 164 untreated prehypertensive and hypertensive men and women.[15] Compared to the high carbohydrate arm, mean BP reductions were: for high protein, −1.4/−1.2 mm Hg; for high-MFA, −1.3/−0.8 mm Hg. In a recent meta-analysis of 10 trials (including OmniHeart, total n=400, duration 3 to 14 weeks) that substituted carbohydrate with MFA, high-MFA diet was associated with significantly lower average systolic/diastolic BP of −2.6/−1.8; this difference was reduced and non-significant when analyses were restricted to randomized crossover trials (6 trials remained, total n=281, duration 3 to 14 weeks).[16] Most of these trials however substituted both sugars and starch, and – given the varying physiological effects of different carbohydrates[30] – the effect on BP of starch cannot be deduced. The only large, isocaloric, micronutrient-controlled trial to investigate starch compared a 40g wheat starch cookie consumed daily for 12 weeks with an isocaloric soybean cookie in 302 prehypertensive and hypertensive Chinese men and women.[18] Participants were counseled to reduce their usual intake to compensate for the additional energy from the cookie. Compared to baseline (habitual diet), both interventions resulted in significant BP reductions, however a larger reduction was observed in the soy protein group (e.g., a mean SBP change of −13.0 mm Hg, compared to −8.7 mm Hg in the starch group). This result is consistent with INTERMAP data on independent, inverse associations between vegetable protein intake and BP;[11] also with the present finding, that modest inverse associations of starch intake and BP are attenuated by control for vegetable protein. Given the positive correlation and the coincident sources (e.g., vegetables, grains, nuts, seeds), it is possible that the observed associations of starch and BP are a proxy for the relations of vegetable protein to BP (or vice versa). Dietary fiber may also relate inversely to BP[14] and like vegetable protein, may be found in concert with starch.[31] However, control for dietary fiber (or magnesium, correlated with both fiber and vegetable protein) did not reduce starch-BP associations to the same extent as vegetable protein. The relationship of animal protein intake to BP has historically been more contentious than vegetable protein.[14] In a recent trial, partial substitution of carbohydrate with protein from lean red meat – equivalent to 5.3% total energy – in 60 hypertensive persons for 8 weeks reduced mean clinic SBP by 5.2 mm Hg (p=0.04).[32] In contrast, INTERMAP data indicate a possible direct associations of animal protein to BP,[11] and direct associations of red meat to BP: 2 SD higher red meat intake (102.6 g/24-h) associated with SBP higher by 1.3 mm Hg ($p < 0.01$, adjusted for multiple confounders including total energy intake and SFA).[33]

Limitations of the INTERMAP findings include: their cross-sectional nature; underestimation of effect size, attributable to limited reliability in the measurement of nutrients (i.e., regression dilution bias, despite repeated measures) and systematic bias (likely minimized by observer training, standardization, certification, multi-pass methods, open non-leading questioning, and extensive ongoing quality control throughout the fieldwork); and possible residual confounding. There was little evidence from multiple sensitivity analyses to indicate substantial uncontrolled bias; analyses limited to “non-intervened” participants tended to show stronger associations.

Physiological mechanisms for inverse associations between starch and BP are not forthcoming. Glycemic index (GI) studies show that metabolic effects of different carbohydrate-containing foods vary.[34] Kopp hypothesized that consumption of high-GI foods could lead to elevated BP compared to low-GI foods.[35] High glycemic load (GL, the product of GI and carbohydrate content) foods elicit an elevated insulin response,[36] possible chronic over-stimulation of pancreatic β-cells, hyperinsulinaemia and insulin resistance.[37] Hyperinsulinaemia may – hypothetically – raise BP through (for example) inactivation of nitric oxide (a potent vasodilator), or increased tissue aldehydes leading to elevated cytosolic free calcium and peripheral vascular resistance.[38] The GI of starch-containing foods varies widely depending on such factors as variety, ripeness, maturation,

processing, and preparation,[34] e.g., the GI of pasta ranges from 27 to 78, potatoes 25–111 (white bread=100).[39] Research is needed on relations of dietary GI and GL to BP.

## CONCLUSION

The inverse associations of starch intake and BP observed here are potentially at odds with the literature from feeding trials where BP reductions were observed when starch (or total carbohydrate) was replaced with soy protein, protein (in particular vegetable), or MFA.[15, 18] Given limited (few studies) and inconsistent observational and trial data, possible confounding, high correlations, and inability to separate out the specific effects on BP of starch in the majority of carbohydrate feeding trials, we have no ability at present to draw etiological conclusions on starch and BP, beyond rejecting the MRFIT inference (direct relation). These data underscore the value of the DASH diet guidelines for BP maintenance and control − 55% kJ from carbohydrate and a diet rich in fruit, vegetables, and low-fat/fat-free dairy products, with reduced total and saturated fats, and cholesterol.[40]

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

The INTERMAP Study was accomplished through the fine work of staff at local, national, and international centers – a partial listing of colleagues is published in *J Hum Hypertens* (2003;17:603–606).

**FUNDING:** I.J.B.'s Ph.D. was supported by a UK Medical Research Council studentship. The INTERMAP Study has been funded by grant R01HL50490 from the National Heart, Lung, and Blood Institute, Bethesda, Maryland; by the Chicago Health Research Foundation; by grant 090357003 from the Ministry of Education, Science, Sports, and Culture, Tokyo, Japan; and by national agencies in the People's Republic of China and in the United Kingdom.

## REFERENCES

1. Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJL. Selected major risk factors and global and regional burden of disease. Lancet. 2002; 360:1347–1360. [PubMed: 12423980]
2. Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002; 360:1903–1913. [PubMed: 12493255]
3. Lenfant C. Task force on research in epidemiology and prevention of cardiovascular diseases. Circulation. 1994; 90:2609–2617. [PubMed: 7994799]
4. Cutler JA, Allender PS. Randomized trials of sodium reduction: An overview. Am J Clin Nutr. 1997; 65(suppl):643S–651S. [PubMed: 9022560]
5. Whelton PK, He J, Cutler JA, Brancati FL, Appel LJ, Follmann D, Klag MJ. Effects of oral potassium on blood pressure: Meta-analysis of randomized controlled clinical trials. J Am Med Assoc. 1997; 277:1624–1632.
6. Trials of Hypertension Prevention Collaborative Research Group. Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure. The Trials of Hypertension Prevention, Phase II. Arch Intern Med. 1997; 157:657–667. [PubMed: 9080920]
7. Xin X, He J, Frontini MG, Ogden LG, Motsamai OI, Whelton PK. Effects of alcohol reduction on blood pressure. A meta-analysis of randomized controlled trials. Hypertension. 2001; 38:1112–1117. [PubMed: 11711507]
8. Allender PS, Cutler JA, Cappuccio FP, Pryer J, Elliott P. Dietary calcium and blood pressure: a meta-analysis of randomized clinical trials. Ann Intern Med. 1996; 124:825–831. [PubMed: 8610952]

9. Jee SH, Miller ER III, Guallar E, Singh VK, Appel LJ, Klag MJ. The effect of magnesium supplementation on blood pressure: A meta-analysis of randomized clinical trials. Am J Hypertens. 2002; 15:691–696. [PubMed: 12160191]
10. Elliott P, Kesteloot H, Appel LJ, Dyer AR, Ueshima H, Chan Q, et al. Dietary phosphorus and blood pressure: INTERMAP Study. Hypertension. 2008; 51:669–675. [PubMed: 18250363]
11. Elliott P, Stamler J, Dyer AR, Appel L, Dennis B, Kesteloot H, et al. Association between protein intake and blood pressure: The INTERMAP Study. Arch Intern Med. 2006; 166:79–87. [PubMed: 16401814]
12. Stamler J, Caggiula A, Grandits GA, Kjelsberg M, Cutler JA. Relationship to blood pressure of combinations of dietary macronutrients. Findings of the Multiple Risk Factor Intervention Trial (MRFIT). Circulation. 1996; 94:2417–2423. [PubMed: 8921782]
13. Brand-Miller, JC. Carbohydrates. In: Mann, J.; Truswell, AS., editors. Essentials of Human Nutrition. Oxford University Press; Oxford: 2002. p. 11-29.
14. Appel, LJ.; Elliott, P. The effects of macronutrients, fiber, cholesterol, and dietary patterns on blood pressure. In: Whelton, PK.; He, J.; Louis, GT., editors. Lifestyle Modification for the Prevention and Treatment of Hypertension. Marcel Dekker, Inc; New York, NY: 2003. p. 243-273.
15. Appel LJ, Sacks FM, Carey VJ, Obarzanek E, Swain JF, Miller ER III, et al. Effects of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids. Results of the OmniHeart randomized trial. J Am Med Assoc. 2005; 294:2455–2464.
16. Shah M, Adams-Huet B, Garg A. Effect of high-carbohydrate or high-cis-monounsaturated fat diets on blood pressure: a meta-analysis of intervention trials. Am J Clin Nutr. 2007; 85:1251–1256. [PubMed: 17490960]
17. Sacks FM, Rouse IL, Stampfer MJ, Bishop LM, Lenherr CF, Walther RJ. Effect of dietary fats and carbohydrate on blood pressure of mildly hypertensive patients. Hypertension. 1987; 1:452–460. [PubMed: 3308702]
18. He J, Gu D, Wu X, Chen J, Duan X, Chen J, Whelton PK. Effect of soybean protein on blood pressure: A randomized, controlled trial. Ann Intern Med. 2005; 143:1–9. [PubMed: 15998749]
19. Stamler J, Elliott P, Dennis B, Dyer AR, Kesteloot H, Liu K, et al. INTERMAP: Background, aims, design, methods, and descriptive statistics (non-dietary). J Hum Hypertens. 2003; 17:591–608. [PubMed: 13679950]
20. Dennis B, Stamler J, Buzzard M, Conway R, Elliott P, Moag-Stahlberg A, et al. INTERMAP: The dietary data - process and quality control. J Hum Hypertens. 2003; 17:609–622. [PubMed: 13679951]
21. Schakel SF, Dennis BH, Wold AC, Conway R, Zhao L, Okuda N, et al. Enhancing data on nutrient composition of foods eaten by the participants in the INTERMAP Study in China, Japan, the United Kingdom, and the United States. J Food Comp Anal. 2003; 16:395–408.
22. Grandits GA, Bartsch GE, Stamler J. Chapter 4. Method issues in dietary data analysed in the Multiple Risk Factor Intervention Trial. Am J Clin Nutr. 1997; 65(suppl):211S–227S. [PubMed: 8988939]
23. Dyer AR, Shipley M, Elliott P. Urinary electrolyte excretion in 24 hours and blood pressure in the INTERSALT Study. I. Estimates of reliability. The INTERSALT Cooperative Research Grou. Am J Epidemiol. 1994; 139:927–939. [PubMed: 8166143]
24. Dyer AR, Elliott P, Shipley M. Body mass index versus height and weight in relation to blood pressure. Findings for the 10,079 persons in the INTERSALT Study. Am J Epidemiol. 1990; 131:589–597. [PubMed: 2180281]
25. Reed D, McGee D, Yano K, Hankin J. Diet, blood pressure, and multicollinearity. Hypertension. 1985; 7:405–410. [PubMed: 3838968]
26. Hedges, LV.; Olkin, I. Statistical methods for meta-analysis. Academic Press; Orlando, NY: 1985.
27. Tobin MD, Sheehan NA, Scurrah KJ, Burton PR. Adjusting for treatment effects in studies of quantitative traits: antihypertensive therapy and systolic blood pressure. Stat Med. 2005; 24:2911–2935. [PubMed: 16152135]

28. Stamler J, Caggiula AW, Grandits GA. Relation of body mass and alcohol, nutrient, fiber, and caffeine intakes to blood pressure in the special intervention and usual care groups in the Multiple Risk Factor Intervention Trial. Am J Clin Nutr. 1997; 65:338S–365S. [PubMed: 8988947]
29. Joffres MR, Reed DM, Yano K. Relationship of magnesium intake and other dietary factors to blood pressure: The Honolulu heart study. Am J Clin Nutr. 1987; 45:469–475. [PubMed: 3812346]
30. Anderson JW, Randles KM, Kendal CWC, Jenkins DJA. Carbohydrate and fiber recommendations for individuals with diabetes: A quantitative assessment and meta-analysis of the evidence. J Am Coll Nutr. 2004; 23:5–17. [PubMed: 14963049]
31. FAO/WHO. FAO food and nutrition paper 66. World Health Organization; Geneva: 1997. Carbohydrates in human nutrition. Report of a joint FAO/WHO expert consultation.
32. Hodgson JM, Burke V, Beilin LJ, Puddey IB. Partial substitution of carbohydrate intake with protein intake from lean red meat lowers blood pressure in hypertensive persons. Am J Clin Nutr. 2006; 83:780–787. [PubMed: 16600928]
33. Tzoulaki I, Brown IJ, Chan Q, Van Horn L, Ueshima H, Zhao L, et al. Relation of iron and red meat intake to blood pressure: cross sectional epidemiological study. Brit Med J. 2008; 337:a258. [PubMed: 18632704]
34. Wolever, TMS. The glycemic index. In: Bourne, GH., editor. Aspects of some vitamins, minerals and enzymes in health and disease. Karger; Basel: 1990. p. 120-185.
35. Kopp W. Pathogenesis and etiology of essential hypertension: role of dietary carbohydrate. Med Hypotheses. 2005; 64:782–787. [PubMed: 15694697]
36. Brand-Miller JC, Thomas M, Swan V, Ahmad ZI, Petocz P, Colagiuri S. Physiological validation of the concept of glycemic load in lean young adults. J Nutr. 2003; 133:2728–2732. [PubMed: 12949357]
37. DeFronzo RA, Bonadonna RC, Ferrannini E. Pathogenesis of NIDDM. A balanced overview. Diabetes Care. 1992; 15:318–368. [PubMed: 1532777]
38. Vasdev S, Longerich L, Gill V. Prevention of fructose-induced hypertension by dietary vitamins. Clin Biochem. 2004; 37:1–9. [PubMed: 14675555]
39. Wolever TMS. Physiological mechanisms and observed health impacts related to the glycaemic index: Some observations. Int J Obes. 2006; 30:S72–S78.
40. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N Engl J Med. 1997; 336:1117–1124. [PubMed: 9099655]

*J Hypertens*. Author manuscript; available in PMC 2011 June 10.

**Table 1**

Estimated Mean Difference in Blood Pressure (mm Hg), Starch Intake (% kJ) Higher by Two Standard Deviations*, Sequential Regression Models, All Men and Women (n=4,680)

| Model | Covariates, added sequentially† | Systolic Blood Pressure | | Diastolic Blood Pressure | |
|---|---|---|---|---|---|
| | | Difference mm Hg | (Z-Score) | Difference mm Hg | (Z-Score) |
| 1 | Sample, age, gender, weight, height, special diet, supplement intake, CVD-DM diagnosis, physical activity, family history of high BP | −1.50 | (−3.53) | −0.96 | (−3.41) |
| 2 | + Urinary Na, urinary K, 14-day alcohol | −0.57 | (−1.23) | −0.51 | (−1.61) |
| 3 | + Dietary cholesterol, PFA, SFA, Calcium | −0.96 | (−1.69) | −0.92 | (−2.36) |
| 4a | + Vegetable protein, or | −0.49 | (−0.73) | −0.70 | (−1.52) |
| 4b | + Fibre, or | −0.88 | (−1.51) | −0.93 | (−2.33) |
| 4c | + Magnesium, or | −0.98 | (−1.69) | −0.99 | (−2.49) |
| 4d | + Phosphorus | −0.90 | (−1.55) | −0.82 | (−2.07) |

Units are hours/24-h moderate or heavy activity (physical activity), mmol/24-h (urinary Na, urinary K), g/24-h (alcohol), mg/1,000 kJ (cholesterol, calcium, magnesium, phosphorus), % kJ (PFA, SFA, vegetable protein), g/1,000 kJ (fibre)

Special diet: Weight loss, weight gain, vegetarian, salt reduced, diabetic, fat modified, or any other diet.

CVD-DM: History of heart attack, other heart disease, stroke, or diabetes.

Supplement intake: Taking any dietary supplement at time of the study.

Na indicates sodium; K, potassium; PFA, polyunsaturated fatty acids; SFA, saturated fatty acids; MFA, monounsaturated fatty acids.

All nutrients are from food only, exclusive of amounts from dietary supplements.

Z-score ≥1.96: uncorrected $P \leq 0.05$; ≥2.58: uncorrected $P \leq 0.01$; ≥3.29: uncorrected $P \leq 0.001$.

No significant cross-country heterogeneity detected at $p<0.05$.

*Two standard deviation difference is 14.11% kJ for starch.

†Variables are added to each prior model, so that for example, Model 4a contains all the variables listed in Models 1–3 and vegetable protein.

## Table 2

Sensitivity Analyses: Estimated Mean Difference in Blood Pressure (mm Hg) for Starch Intake (% kJ*) Higher by Two Standard Deviations†, Regression Model 3

| Analysis (Number of people) | Systolic Blood Pressure | | Diastolic Blood Pressure | |
|---|---|---|---|---|
| | Difference mm Hg | (Z-score) | Difference mm Hg | (Z-score) |
| (a) % kJ with inclusion of energy intake (kJ/24 hours) (n=4,680) | −0.93 | (−1.63) | −0.94 | (−2.41) |
| (b) g/24 hours adjusted for energy intake (kJ/24 hours) (n=4,680) | −1.10 | (−1.29) | −1.06 | (−1.81) |
| (c) % kJ, adjusted for Na/Cr and K/Cr (n=4,680) | −1.02 | (−1.79) | −0.91 | (−2.33) |
| (d) % kJ censored normal regression, adjusting for antihypertensive treatment (n=4,680) | −1.05 | (−1.65) | −1.05 | (−2.46) |
| (e) % kJ, non-intervened participants (n=2,238)‡ | −1.52 | (−1.89) | −1.23 | (−2.23) |
| (f) % kJ, nonhypertensive participants (n=3,671) | −0.77 | (−1.60) | −0.84 | (−2.33) |
| (g) % kJ with exclusion of people with high day-to-day variability of SBP, DBP, and/or nutrient intakes (n=3,473) | −0.86 | (−1.26) | −0.65 | (−1.40) |
| (h) % kJ, men only (n=2,359)§ | −1.10 | (−1.47) | −0.68 | (−1.26) |
| (i) % kJ, USA men only (n=1,103)§ | −1.99 | (−1.94) | −0.82 | (−1.07) |
| (j) % kJ, USA men with higher CHD risk(n=717)§ | −0.96 | (−0.68) | −0.41 | (−0.40) |

Z-score ≥1.96: uncorrected $P \leq 0.05$; ≥2.58: uncorrected $P \leq 0.01$.

Model 3: Sample, age, gender, weight, height, special diet, supplement use, physical activity, CVD-DM, family history of high BP, urinary Na, urinary K, dietary alcohol, cholesterol, PFA, SFA, calcium.

Na/Cr, sodium-creatinine ratio; K/Cr, potassium-creatinine ratio

Non-intervened: individuals not on a special diet, not consuming nutritional supplements, not with diagnosed CVD/DM, not taking medication for high BP/CVD/DM.

Nonhypertensive: SBP <140 and DBP <90 mm Hg and not taking antihypertensive medication.

Higher CHD risk, any one or more of: systolic BP ≥140 mm Hg, or diastolic BP ≥90 mm Hg, or body mass index 90 mm Hg, or body mass index 30.0 kg/m$^2$, or current smoker, or history of CVD or DM, or diabetic diet, or taking antidiabetic/antihypertensive/lipid-lowering/cardiovascular-influencing drugs.

No significant cross-country heterogeneity detected at $p<0.05$.

*Unless otherwise stated.

†Two standard deviation differences for starch are 14.11% kJ (analyses a, c-h) and 116.13 g/24-h (analysis b).

‡Regressions not adjusted for special diet, supplement use, or CVD-DM.

§Regressions not adjusted for gender.