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Prospective investigation of major dietary patterns and risk of cardiovascular mortality in Bangladesh

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Abstract

Background—Dietary pattern analysis is emerging as a practical, effective tool for relating comprehensive dietary intake to risk of cardiovascular disease mortality. However, no studies have applied this technique to a population outside of the developed world.

Methods—We conducted prospective cohort analyses in 11,116 participants enrolled in the Health Effects of Arsenic Study in Araihazar, Bangladesh, measuring deaths attributable to disease of circulatory system, heart disease, and cerebrovascular disease. Participants were enrolled in 2000 and followed up for an average of 6.6 years. Dietary information was obtained through a previously validated food-frequency questionnaire at baseline.

Results—Principal component analysis based on our comprehensive, 39 item FFQ yielded 3 dietary patterns: (i) a “balanced” pattern, comprised of steamed rice, red meat, fish, fruit and vegetables; (ii) an “animal protein” diet, which was more heavily weighted towards eggs, milk, red meat, poultry, bread, and vegetables; and (iii) a “gourd and root vegetable” diet that heavily relied on a variety of gourds, radishes, pumpkin, sweet potato, and spinach. We observed a

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Ethical approval: The study procedures were approved by the Ethical Committee of the Bangladesh Medical Research Council and the Institutional Review Boards of Columbia University and the University of Chicago. Verbal consent was obtained from study participants.

positive association between increasing adherence to the animal protein diet and risk of death from both disease of the circulatory system and heart disease; the hazard ratio was 1.13 (95% CI, 1.00-1.28, p = 0.05) and 1.17 (95% CI, 0.99-1.38, p = 0.07), respectively, in relation to one standard deviation increase in the factor scores for the animal protein diet pattern, after controlling for age, sex, body mass index, smoking status, and energy intake. The positive association was more significant among ever smokers; the hazard ratios (95% CI) for deaths from disease of the circulatory system and heart disease was 1.17 (1.02-1.34) and 1.20 (1.00-1.45), respectively, in relation to one standard deviation increase in the factor scores for the animal protein diet pattern.

Conclusions—An animal protein-rich diet in rural Bangladesh may increase risk of heart disease mortality, especially among smokers. This emphasizes the need to further explore and address the impact of dietary patterns on cardiovascular disease in populations undergoing epidemiologic transition into a future of higher chronic disease burden.

Keywords

Dietary patterns; cardiovascular disease; Bangladesh; coronary heart disease; epidemiologic transition

INTRODUCTION

Cardiovascular disease (CVD) is a vitally important, yet often overlooked, health burden in developing countries. Compared to the developed world, it contributes less, proportionally, to total mortality (~23% compared to ~49%). However, with the vast majority of the global population within its borders, over 60% of worldwide CVD mortality is attributable to the developing world (1). As these regions undergo further industrialization, a decrease in infectious disease mortality and concurrent increase in chronic disease mortality will only enhance the burden of CVD (2-4). Thus, it has become advantageous to better understand modifiable risk factors that contribute to development of this disease. One such factor is diet, which can influence development of obesity, hypertension, dyslipidemia, diabetes, and, ultimately, CVD.

Rather than analyzing intake of specific foods or nutrients, it has been suggested that evaluation of whole diet patterns may yield a more comprehensive understanding of how this complex factor affects the etiology of disease (5). Compared to the “single nutrient” approach, this analysis more fully accounts for biochemical interactions between nutrients, as well as interrelationships between dietary components that cause difficulty in distinguishing individual food or nutrient effects (6). Multiple studies have examined CVD risk and mortality based on food intake patterns (7-13). However, very few have studied the association in non-Western populations, and none have included populations in low-income or developing countries.

We have identified three major dietary patterns among participants of the Health Effects of Arsenic Longitudinal Study (HEALS) in rural Bangladesh (14). In the present study, we evaluate the association between diet patterns and the risk of deaths due to disease of the circulatory system, heart disease, and cerebrovascular disease.

SUBJECTS AND METHODS

Study participants

The HEALS is a prospective cohort study based in Araihazar, Bangladesh, designed to investigate adverse health outcomes associated with chronic exposure to arsenic in groundwater. An abbreviated explanation of study design is presented here, as full details are available elsewhere (Ahsan, 2006). Using population-based sampling, 11,746 men and women were recruited between 2000 and 2002, under the criteria that all were married (to reduce loss to follow-up), between 18-75 years old, and had resided in the study area for at least 5 years. Study participants underwent baseline clinical assessment, and detailed interviews were conducted with each to characterize lifestyle, demographics, and environmental exposures.

Measurement of food intakes

Trained interviewers administered a 39-item food-frequency questionnaire (FFQ) during baseline assessment of all participants in the HEALS. Details of this questionnaire and its subsequent validation are available elsewhere (15). Briefly, prior to baseline, local nutrition experts were consulted to identify all locally available food, and a sequence of focus groups further refined food items for inclusion. A FFQ pilot study among 120 local individuals not included in the cohort study was used to create the final form questionnaire, ensuring that only common foods were included and deeming any items consumed less than once per month in the previous year as insignificant. US Department of Agriculture Nutrient Database for Standard Reference (abbreviated version) (16) and an Indian food nutrient database (17) were used to convert food intakes to nutrient intake values.

To assess the validity of the FFQ, 200 HEALS participants were randomly selected to maintain 7 day food diaries during 2 different seasons. Analysis of the 189 respondents with complete diaries showed sufficient correlation (0.30 to 0.76) with data previously obtained in the FFQ, including common food items, macronutrients, and many major micronutrients (namely total fat, monounsaturated fat, polyunsaturated fat, saturated fat, protein, carbohydrate, dietary fiber, sodium, potassium, vitamin B-6, vitamin B-12, riboflavin, manganese, thiamine, and iron). The present study included 11,116 participants from the 11,746 cohort members who filled out a FFQ at baseline.

Assessment of cardiovascular mortality

The study endpoint of interest was cardiovascular disease deaths, defined as deaths due to disease of circulatory system (ICD-10 I00-I99), among cohort participants during the period from baseline to March 18, 2009 (end of third follow-up). Details of the methods for the assessment of causes of deaths are described elsewhere (18). Briefly, we adapted a validated verbal autopsy procedure, developed by International Centre for Diarrhea Disease Research, Bangladesh, in collaboration with the WHO, to ascertain the causes of deaths. During the follow-up, upon receipt of a death reported by family or neighbors, a study physician and a trained social worker administered the verbal autopsy form to the next of kin. Medical records from physicians who had treated the deceased were collected. For deaths that occurred in the hospital, information on death certificates and biopsies was ascertained. These data were reviewed monthly by an outcome assessment committee, consisting of physicians and consulting medical specialists blinded to the exposure status. Causes of deaths were coded according to the WHO classification (19) and the International Classification of Diseases, 10th Revision (ICD-10) (20). International Centre for Diarrhea Disease Research, Bangladesh has used this method to ascertain causes of deaths since 1971 (21-22) and documented an overall 95% specificity, with a 85% sensitivity for cancer deaths and up to 85% sensitivity for cardiovascular deaths (23).

Food pattern derivation

Details of the methods were presented elsewhere (14). Briefly, we performed principal component analysis using the PROC FACTOR procedure in SAS to identify dietary patterns. An orthogonal rotation (the varimax option in SAS) was used to derive factors (dietary patterns) uncorrelated to one another for better interpretability. To determine the number of meaningful factors, conventional criteria for principle component analysis including eigenvalue, the scree test, proportion of variance accounted for, and the interpretation criterion were considered (24). For each factor, each food item received a factor loading, which represents the correlation coefficient between the food item and the factor. Three major dietary patterns, namely the “balanced” diet, “animal protein”, and “root vegetable” diet, were identified and named accordingly to the foods that loaded most heavily on the pattern (Appendix 1). The first of these was a “balanced” pattern, comprised of steamed rice, red meat, fish, fruit and vegetables. An “animal protein” diet was more heavily weighted towards eggs, milk, red meat, poultry, bread, and vegetables. The “gourd and root vegetable” diet was heavily reliant on a variety of gourds, radishes, pumpkin, sweet potato and spinach. To indicate a subject’s relative standing for each dietary pattern in the population, a factor score, which is a linear composite of the optimally-weighted food items by factor loadings, was constructed for each dietary pattern. We have previously evaluated association of these diet patterns in relation to blood pressure at baseline (14) and the risk of skin lesions (25).

Statistical Analyses

Descriptive analyses were first conducted to assess relationships of diet patterns with baseline lifestyle and CVD risk factors. We computed person-time from the baseline to the date of death from any cause or the date of third active in-person follow-up visit, whichever came first. Because deaths from other forms of heart disease were often a consequence of previous ischemic heart disease in our study population, we *a priori* estimated the hazard ratios for the combined category heart disease that included deaths from ischemic heart disease and other types of heart disease (26). Cox proportional hazards regression was used to compute the hazard ratios for deaths from disease of circulatory system, heart disease, and cerebrovascular disease, first in relation to baseline lifestyle and cardiovascular disease risk factors. For main analyses, we estimated hazard ratios in relation to quartiles of factor scores as well as one standard deviation (SD) increase of the factor scores for each diet pattern. The assumption of proportional hazards was examined by testing the cross-product terms between covariate variables and log function of survival time, and p-values for all the terms were > 0.10. We first adjusted for age at baseline, sex and energy intake. A second model was constructed to additionally adjust for *a priori* defined potential confounders including baseline body mass index (m/kg^2) and smoking status (never, past, and current). In addition, we conducted stratified analyses by smoking status, one of the most important risk factors for cardiovascular disease mortality, to assess whether the association between diet patterns and cardiovascular disease mortality was similar within ever and never smokers. All analysis was conducted using SAS 9.2 (SAS Institute, Inc., Cary, North Carolina).

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RESULTS

A total of 185 deaths of disease of circulatory system were observed. Among the 185 deaths, 82 were due to cerebrovascular disease (I60-I69); 96 were due to ischemic heart disease (I20-I25, n = 64) or other forms of heart disease (I30-I52, n = 32), which included mostly deaths due to heart failure (I50.0-I50.9, n = 31) and ventricular tachycardia (I47, n = 1); and 7 deaths were due to pulmonary heart disease, hypertensive heart disease, or multiple valve diseases (I08, I11, and I27). Each diet pattern was divided into quartiles by factor score and analyzed for differences in various sociodemographic, lifestyle, and CVD risk factors (Table 1). Adherence to the animal protein diet was associated with a higher proportion of males, television and land ownership, older age, longer education, and higher BMI. Conversely, those following the root vegetable diet were more likely to be women, not television or land owners, and less educated.

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Higher levels of body mass index and diabetes status were associated with an increased risk of death due to heart disease (Table 2). There was no association of educational level with mortality from either disease of the circulatory system overall or any of the subtypes of cardiovascular disease. Diastolic and systolic hypertension were related to increased risk of death from disease of the circulatory system overall and all subtypes of cardiovascular disease, and the associations were stronger for cerebrovascular disease. Participants who were current smokers were 1.7 times more likely to die from disease of circulatory system and 2.3 times more likely to die from heart disease.

Adjusted hazard ratios for disease of circulatory system, heart disease, and cerebrovascular disease in relation to each dietary pattern are shown in Table 3. An inverse association was observed between the balanced diet pattern and disease of the circulatory system; when diet pattern was used as a continuous variable, HR for disease of circulatory system was 0.86 (95% CI = 0.73-1.01, p = 0.07, model 2) for each SD increase in the balanced diet pattern. Individuals in the highest quartile of the balanced diet pattern had reduced risk for death from disease of the circulatory system (HR = 0.86, 95% CI = 0.57-1.30, model 2) and heart disease (HR = 0.79, 95% CI = 0.44-1.40, model 2). However, the point estimates were not statistically significance. Adherence to the animal protein diet was positively related to death from disease of the circulatory system, especially heart disease mortality. When the diet pattern was a continuous variable, the HRs for deaths from disease of the circulatory system and heart disease was 1.13 (95% CI = 1.00-1.28, p = 0.05, model 2) and 1.17 (95% CI = 0.99-1.38, p = 0.07, model 2), respectively, in relation to one standard deviation increase in factor scores of the animal protein diet pattern. There was a dose-response relationship between animal protein diet pattern and risk of heart disease mortality, with the highest quartile of the animal protein diet possessing a risk increase of more than 100% (HR (95% CI): 1.0 (reference), 1.43 (0.68-3.01), 1.65 (0.81-3.38), 2.11 (0.81-4.17); (p for trend = 0.02, model 1)). The significance of the association was slightly attenuated after controlling for body mass index, and smoking status, in addition to age, gender, and energy intake (p for trend=0.05, model 2). A non-significant inverse association between increasing adherence to the animal protein diet and stroke mortality was also observed (p for trend =0.22). Adherence to gourd and root vegetable diet pattern was not related to risk of overall circulatory system disease, heart disease, or cerebrovascular disease.

Stratified analyses by smoking status are shown in Table 4. The association between the balanced diet pattern and risk of disease of circulatory system remained among never smokers, with an HR of 0.67 (95% CI, 0.45-1.01; p=0.05) for each SD increase in the score for the balanced diet pattern. Smokers adhering to the animal protein diet were shown to have significantly increased risk of disease of the circulatory system (HR=1.17, 95% CI, 1.02-1.34; p=0.03) and heart disease (HR=1.20, 95% CI, 1.00-1.45; p=0.05), although the test for interaction by smoking status was not significant.

DISCUSSION

We evaluated the impact of dietary patterns on cardiovascular mortality in a cohort of 11,116 participants in rural Bangladesh. The most noteworthy finding was increased risk of mortality due to overall cardiovascular disease (disease of the circulatory system) and heart disease in those adhering to the animal protein diet, especially among smokers.

Our study population presented a novel context within which to explore these topics, as FFQ-based pattern analyses of diet and cardiovascular mortality have thus far been presented mainly for westernized societies (7-11, 27) and, to a much lesser extent, some populations in East Asia (12-13). Bangladesh provides an especially interesting backdrop for such a study, with the country in the midst of an “epidemiologic transition” from the major causes of mortality being based in nutritional deficiencies and infectious diseases to primarily degenerative diseases, such as cancer, cardiovascular disease, and diabetes (2-4). Though Bangladesh is still in the early stages of this transition, they are rapidly improving nutritional status while adopting a diet that is higher in fat, iron, and calcium (28, 29). In the 15 years preceding 1996, this contributed to the prevalence of chronic energy deficiency falling from 78% to 64% (28).

Several studies have explored the relationship between dietary patterns and CHD, yielding somewhat inconsistent results. A prospective cohort study of US male health professionals showed significant CHD risk associated with a “Western diet,” characterized by more frequent intake of red meat, refined starch, sweets, and high-fat dairy (7). A Western diet was similarly associated with increased CHD risk among women in the Nurses’ Health Study (9). Two recent studies of Asian populations compared more “Westernized,” meat-heavy diets with traditional Chinese or Japanese dietary patterns, finding higher risk of CHD in the former (P(trend)=0.05 [12]; P(trend)=0.176 [13]). Additionally, two studies found a positive association between Western diet and plasma biomarkers of cardiovascular risk (c-peptide, insulin, glycated hemoglobin [30], leptin and homocysteine [31]), while negatively correlating with concentration of plasma folate, a cardioprotective agent (30, 31). It should be noted that two published reports have not supported the correlation between a Western or animal protein diet and CHD (10, 11).

A recent literature review summarized factors that are “protective” against CHD to include vegetables, nuts, and monounsaturated fats, as well as Mediterranean, prudent, and high-quality diets. “Harmful” factors included *trans*-fatty acids, foods with a high glycemic index, and a Western dietary pattern (32). It has been suggested that failure to detect increased CHD risk among Western diet adherents in some countries could be due to a given culture’s propensity to include healthy or cardioprotective food items (such as plants [11], light breads, or juices [10]) in their diet, even if they are consumed in lesser proportion because of displacement by more unhealthy, Western food items. This may explain the marginal significance observed for the meat-based diet of our study as well, considering that the animal protein diet still displayed high factor loadings for multiple fruits. This tendency for cardioprotective foods to appear across dietary patterns in Bangladesh could also explain our marginal significance for decreased risk of cardiovascular disease associated with consumption of a balanced diet.

Our finding that a diet higher in saturated fat may be protective against stroke, though not statistically significant, has been suggested in previous studies (33-36). Among a cohort of Japanese and Japanese-American men, Reed and colleagues observed that low-fat and low-protein diets correlated with higher cerebral infarction mortality (33). Similarly, an analysis of ischemic stroke in the Framingham Heart Study yielded a decline in risk associated with increased intake of total fat, saturated fat, and monounsaturated fat (35). The paradoxical findings in the associations of animal protein diet with heart disease and cerebrovascular disease may be explained through a pathological difference in occlusive processes of small and large arteries, in particular a potential protective effect of cholesterol on small vessel endothelium (35, 37, 38). Risk of large vessel stroke correlates with risk of CHD (also a large vessel process), and is the predominant cause of stroke in Western countries. Small vessel strokes are the predominant cause of stroke in non-Western countries, with this subtype having been shown to account for 76% of cerebral infarctions in a Japanese autopsy study (39) (compared to 20% in Western countries [38]). Future studies are needed to further investigate diet patterns and subtypes of stroke.

Cigarette smoking has been shown in multiple studies to have a cumulative effect on development of cardiovascular disease, a finding that was supported in our population (among smokers, HR in relation to one SD diet pattern score for animal protein pattern: p = 0.03, disease of the circulatory system; p = 0.05, heart disease) (40-42). It is most strongly associated with increased risk of aortic aneurysm and peripheral vascular disease, with cardiovascular dysfunction mediated by oxidative stress that yields inflammation, thrombosis, and oxidation of low-density lipoprotein cholesterol (43, 44). Future studies within our population would be needed to analyze the degree of increase in inflammatory markers or carotid artery intima-medial thickness relative to smoking status and dietary intake.

Strengths of our study include a large, population-based sample size and a comprehensive, validated FFQ (15). Additionally, religious motivations lead to restricted alcohol consumption in Bangladesh, thus removing a potential cofounder. Furthermore, because health screening is not as robust as in more developed countries, there is a smaller chance of participants changing their diet because of risk factors for chronic disease. For example, similar studies of CHD in the United States have had to consider whether dietary groupings were skewed by individuals following a defined “healthy” or “fruits and vegetables” diet only because screening tests or medical intervention caused them to change their diet after decades of more unhealthy food consumption. Limitations include the delineation of food patterns itself. Though pattern analysis can be argued to be a more effective, realistic method of assessing food consumption and risk of cardiovascular disease, there is still a measure of subjectivity in selection of food groups for factor analysis, post-analysis identification of patterns, and choosing the method of vector rotation (5, 45). Furthermore, identification of diet patterns in Bangladesh is more nuanced than in countries where dramatically different patterns may exist; even among higher economic classes in Bangladesh, there is still a prioritized consumption of staple foods (46). This dietary homogeneity also limits the generalizability of our results to populations of more varied culture or socioeconomic background.

Our results underscore the importance of better understanding epidemiologic transition in developing countries such as Bangladesh, and responding with appropriate public health measures – not only in consideration of communicable diseases, environmental contamination, and nutrition deficiency, but also recognizing the potential for additional, widespread health issues on the horizon. As economic development continues in this country, changes in dietary patterns will usher in a future of more overweight individuals and higher chronic disease mortality. Recent studies have shown that from 1996 to 2004 alone, the proportion of overweight females has increased drastically in both urban (from 10 to 20%) and rural areas (from 2 to 6%) (47). This could be explained through the consumption of higher fat foods correlating closely with socioeconomic advances. A recent study in Bangladesh identified meat and dairy consumption as increasing to a greater degree than any other food items when comparing the richest economic class to the poorest (46). Though this trend will produce a double burden of overnutrition and undernutrion in Bangladesh, certain geographical, economic, or social characteristics will likely dictate which epidemic is present in a given subset of the population. Herein lies the need for focused interventions that will not only address those currently afflicted by malnourishment and communicable illness, but also stave off the burden of chronic disease that will otherwise coincide with increased prosperity and development in Bangladesh as well as other developing countries.

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [48].

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Appendix 1

Factor Loading Matrix[1] for Dietary Patterns Derived from Principle component Analysis

	"Balanced" diet	"Animal protein"	"Root vegetable"
Tea	-	0.48	-
Big fish (fresh water)	-	0.44	-
Eggs (hen eggs)	-	0.49	-
Milk	-	0.49	-
Poultry (fowl)	-	0.47	-
Puffed rice	-	0.22	-
Lentil	-	0.37	-
Wheat bread (brown)	−0.16	0.49	-
Beef or mutton	0.21	0.45	-
Bitter gourd (a kind of squash)	0.43	0.18	0.28
Banana	0.16	0.47	-
Jack Fruit	0.30	0.22	-
Watermelon	0.20	0.29	-
Mango	0.39	0.22	-
Steamed rice	0.24	−0.29	-
Guava	0.27	-	-
Beans (scarlet runner)	0.62	-	-
Potato	0.22	-	-
Bottle gourd (a kind of squash)	0.46	-	-
Small fish (fresh water)	0.39	-	-
Eggplant	0.33	-	0.17
Cauliflower	0.64	-	0.16
Parwar/patol (a kind of squash)	0.22	0.17	0.37
Green papaya	0.22	-	0.35
Cabbage	0.51	-	0.24
Okra	0.29	-	0.37
Yam	0.31	-	0.26
Spinach	0.24	-	0.25
Dried fish	-	-	0.22
Ridge gourd/jhinga (a kind of squash)	-	-	0.53
Snake gourd/chachinga (a kind of squash)	-	-	0.57
Ghosala/dhundal (a kind of squash)	-	-	0.51
Radish	-	-	0.48

	"Balanced" diet	"Animal protein"	"Root vegetable"
Spinach stalks	-	-	0.48
Sweet potato	-	-	0.29
Water Rice	-	-	0.17
Pumpkin	-	-	0.39
Tomato	-	-	-
Salted fish	-	-	-

[1] Factor loadings represent the correlation between factor scores and intakes of food items. Positive Factor loadings ≤ 0.15 and negative factor loadings ≥ −0.15 were omitted in the table for simplicity

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Table 1

Sociodemographic characteristics by quartile (Q) of dietary factor score

	Quartile of factor scores for the Balanced diet pattern			Quartile of factor scores for the Animal protein diet pattern			Quartile of factor scores for the Gourd and root vegetable diet pattern		
	Q1 Mean	Q4 Mean	p for trend[1] or correlations [2, 3]	Q1 Mean	Q4 Mean	p for trend[1] or correlations [2, 3]	Q1 Mean	Q4 Mean	p for trend[1] or correlations [2, 3]
Male (%)	47.7	42.6	<0.01	31.8	63.7	<0.01	50.4	37.5	<0.01
Nonsmokers (%)	60.8	63.7	0.87	71.9	49.3	0.61	60.7	68.3	0.88
Own a television (%)	35.8	37.8	0.09	20.5	53.8	<0.01	37.9	32.1	<0.01
Own land >1 acre (%)	14.3	18.8	<0.01	8.5	26.3	<0.01	15.9	17.0	0.07
Age (y)	37.3	37.6	0.01	35.7	39.4	0.14 **	37.1	36.7	−0.01
Education (y)	3.6	3.6	0.02	2.2	5.2	0.30 **	3.7	3.4	−0.01
Systolic blood pressure	115.4	114.9	−0.01	113.1	116.9	0.08 **	114.4	115.3	0.02 *
Diastolic blood pressure	75.0	73.7	−0.03 **	72.7	75.5	0.09 **	73.8	74.2	0.01
BMI (kg/m2)	20.0	19.8	0.00	19.3	20.7	0.19 **	19.9	19.7	−0.01

[1]Trend tests were performed by using linear regression that included energy-adjusted factor scores as the dependent variable and age and sex as the independent variables.

[2]Pearson correlations between the factor scores and natural logs of energy-adjusted nutrient values.

[3].01< p <.05,

*.01< p <.05,

**p <.01

Table 2

Relationships between Baseline Risk Factors and Mortality from Disease of the Circulatory System

		Disease of the circulatory system		Heart disease		Cerebrovascular disease	
Risk Factors	**Follow-up Person-years**	**N of Deaths**	**Age and Sex Adjusted HR**	**N of Deaths**	**Age and Sex Adjusted HR**	**N of Deaths**	**Age and Sex Adjusted HR**
Body Mass Index							
<18.5	28768.09	83	1.02 (0.73-1.43)	36	0.91 (0.56-1.47)	44	0.72 (0.39-1.31)
18.5-22	28926.07	58	1.00	30	1.00	25	1.00
>22	15379.07	44	1.34 (0.90-1.98)	30	1.79 (1.08-2.97)	13	0.90 (0.46-1.75)
Education (years)[1]							
0 years	32214.23	84	1.00	43	1.00	38	1.00
1-5 years	21758.49	44	0.85 (0.59-1.22)	23	0.85 (0.51-1.41)	19	0.83 (0.48-1.44)
5+ years	19067.65	57	1.20 (0.87-1.70)	30	1.23 (0.76-1.98)	25	1.23 (0.73-2.05)
Systolic Blood Pressure[2]							
<140 mmHg	67510.56	123	1.00	75	1.00	41	1.00
>140 mmHg	5251.32	61	3.21 (2.33-4.42)	21	2.04 (1.24-3.38)	40	5.55 (3.01-8.77)
Diastolic Blood Pressure[3]							
<90 mmHg	66910.57	144	1.00	85	1.00	53	1.00
>90 mmHg	5819.27	41	2.56 (1.81-3.63)	11	1.23 (0.65-2.30)	29	4,64 (2.95-7.31)
Smoking							
Never	47389.05	48	1.00	26	1.00	20	1.00
Past	4643.23	28	1.14 (0.65-1.98)	11	1.24 (0.54-2.84)	13	0.93 (0.41-2.12)
Current	21040.97	109	1.73 (1.10-2.71)	59	2.30 (1.22-4.35)	49	1.59 (0.81-3.11)

[1] n=5 missing education

[2] n=46 missing systolic blood pressure

[3] n=51 missing diastolic blood pressure

Table 3

Hazard Ratios for Disease of the Circulatory System in relation to Diet Patterns

	HR (95% CI) by quartile of diet pattern					HR (95% CI) in relation to one SD diet pattern score	
	Q1	Q2	Q3	Q4	p for trend[2]	HR (95% CI)	p-value
Balanced diet pattern							
Disease of the circulatory system							
Deaths, n/person-years	45/18335	55/18472	45/18779	46/19331		185/73073	
Model 1[*]	1.0	1.30 (0.88-1.94)	0.96 (0.64-1.46)	0.87 (0.56-1.32)	0.26	0.85 (0.72-1.00)	0.05
Model 2[1]	1.0	1.28 (0.86-1.91)	0.96 (0.63-1.46)	0.86 (0.57-1.30)	0.24	0.86 (0.73-1.01)	0.07
Heart disease							
Deaths, n/person-years	25/18335	25/18472	28/18779	23/19331		96/73073	
Model 1[*]	1.0	1.02 (0.58-1.79)	1.07 (0.62-1.85)	0.80 (0.45-1.42)	0.51	0.85 (0.67-1.06)	0.15
Model 2[1]	1.0	1.01 (0.57-1.80)	1.06 (0.61-1.85)	0.79 (0.44-1.40)	0.47	0.86 (0.69-1.08)	0.19
Cerebrovascular disease							
Deaths, n/person-years	17/18335	29/18472	15/18779	22/19331		82/73073	
Model 1[*]	1.0	1.95 (1.07-3.56)	0.87 (0.44-1.75)	1.08 (0.57-2.04)	0.51	0.89 (0.71-1.13)	0.34
Model 2[1]	1.0	1.88 (1.03-3.46)	0.87 (0.43-1.75)	1.05 (0.56-1.99)	0.49	0.89 (0.70-1.13)	0.32
Animal protein pattern							
Disease of the circulatory system							
Deaths, n/person-years	28/18700	40/18625	48/18727	75/18865		185/73073	
Model 1[*]	1.0	1.08 (0.66-1.77)	1.10 (0.68-1.77)	1.25 (0.80-1.97)	0.29	1.16 (1.03-1.31)	0.0146
Model 2[1]	1.0	1.07 (0.65-1.76)	1.11 (0.69-1.81)	1.20 (0.75-1.91)	0.41	1.13 (1.00-1.28)	0.05
Heart disease							
Deaths, n/person-years	11/18700	20/18625	26/18727	44/18865		96/73073	
Model 1[*]	1.0	1.43 (0.68-3.01)	1.65 (0.81-3.38)	2.11(0.81-4.17)	0.02	1.24 (1.06-1.46)	0.0068
Model 2[1]	1.0	1.38 (0.63-3.04)	1.76 (0.84-3.71)	1.94 (0.95-4.00)	0.05	1.17 (0.99-1.38)	0.07
Cerebrovascular disease							
Deaths, n/person-years	17/18700	18/18625	20/18727	28/18865		82/73073	
Model 1[*]	1.0	0.77 (0.40-1.51)	0.70 (0.36-1.36)	0.71 (0.38-1.33)	0.32	1.06 (0.88-1.28)	0.55
Model 2[1]	1.0	0.80 (0.41-1.56)	0.69 (0.36-1.36)	0.74 (0.39-1.41)	0.38	1.08 (0.89-1.31)	0.46
Gourd and Root Vegetable Diet Pattern							
Disease of the circulatory system							
Deaths, n/person-years	46/18732	52/18513	49/18765	44/18906		185/73073	
Model 1[*]	1.0	1.06 (0.71-1.58)	1.04 (0.70-1.56)	1.02 (0.68-1.55)	0.94	1.02 (0.89-1.18)	0.77
Model 2[1]	1.0	1.05 (0.70-1.58)	1.06 (0.70-1.59)	1.04 (0.69-1.59)	0.84	1.03 (0.89-1.18)	0.70

	HR (95% CI) by quartile of diet pattern					HR (95% CI) in relation to one SD diet pattern score	
	Q1	Q2	Q3	Q4	p for trend[2]	HR (95% CI)	p-value
Heart disease							
Deaths, n/person-years	22/18732	33/18513	23/18765	23/18906		96/73073	
Model 1[*]	1.0	1.42 (0.82-2.45)	1.04 (0.58-1.86)	1.13 (0.63-2.02)	0.99	1.09 (0.91-0.32)	0.35
Model 2[1]	1.0	1.40 (0.80-2.44)	1.09 (0.50-1.98)	1.17 (0.64-1.98)	0.86	1.10 (0.92-1.33)	0.30
Cerebrovascular disease							
Deaths, n/person-years	22/18732	17/18513	24/18765	20/18906		82/73073	
Model 1[*]	1.0	0.74 (0.39-1.39)	1.06 (0.59-1.90)	0.97 (0.53-1.79)	0.78	0.94 (0.75-1.18)	0.62
Model 2[1]	1.0	0.75 (0.39-1.41)	1.03 (0.57-1.86)	0.99 (0.54-1.86)	0.79	0.95 (0.76-1.19)	0.65

[*] HRs were adjusted for age, gender, energy intake.

[1] HRs were adjusted for age, gender, energy intake, body mass index, and smoking status.

[2] P-value for trend was estimated using quartile value of dietary pattern as a continuous variable in the model.

Table 4

Hazard Ratios for Disease of the Circulatory System in relation to Diet Patterns by smoking status

	HR (95% CI) in relation to one SD diet pattern score				
	Non-smokers		**Smokers**		
	HR (95% CI)	**p-value**	**HR (95% CI)**	**p-value**	**P for interaction**
Balanced diet pattern					
Disease of the circulatory system					
Deaths, n/person-years	48/47,389		137/25,684		
Model 1*	0.67 (0.45-1.01)	0.05	0.90 (0.74-1.10)	0.29	0.16
Heart disease					
Deaths, n/person-years	26/47,389		70/25,684		
Model 1*	0.83 (0.51-1.35)	0.45	0.85 (0.64-1.13)	0.25	0.76
Cerebrovascular disease					
Deaths, n/person-years	20/47,389		62/25,684		
Model 1*	0.52 (0.25-1.04)	0.06	0.99 (0.76-1.30)	0.96	0.10
Animal protein pattern					
Disease of the circulatory system					
Deaths, n/person-years	48/47389		137/25,684		
Model 1*	1.02 (0.74-1.39)	0.92	1.17 (1.02-1.34)	0.03	0.44
Heart disease					
Deaths, n/person-years	26/47,389		70/25,684		
Model 1*	1.21 (0.84-1.73)	0.30	1.20 (1.00-1.45)	0.05	0.87
Cerebrovascular disease					
Deaths, n/person-years	20/47,389		62/25,684		
Model 1*	0.78 (0.42-1.46)	0.43	1.11 (0.90-1.36)	0.34	0.19
Gourd and Root Vegetable Diet Pattern					
Disease of the circulatory system					
Deaths, n/person-years	48/47,389		137/25,684		
Model 1*	1.16 (0.90-1.49)	0.25	0.98 (0.83-1.16)	0.79	0.36
Heart disease					
Deaths, n/person-years	26/47,389		70/25,684		
Model 1*	1.22 (0.90-1.66)	0.20	1.04 (0.83-1.31)	0.72	0.88
Cerebrovascular disease					
Deaths, n/person-years	20/47,389		62/25,684		
Model 1*	1.01 (0.64-1.59)	0.96	0.94 (0.72-1.21)	0.62	0.86

[1] HRs were adjusted for age, gender, energy intake, body mass index.