ABSTRACT

Title of Document: **DIETARY PATTERNS, METABOLIC RISK AND SURVIVAL IN OLDER ADULTS**

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Background: Recent evidence suggests that older adults' diets can appreciably impact their health. Dietary patterns may better capture the multifaceted effects of diet on health than individual nutrients or foods.

Objectives: The purpose of this study was to identify the dietary patterns of a cohort of older adults, and examine relationships with body composition, insulin sensitivity, systemic inflammation, and survival. The influence of a polymorphism in the peroxisome proliferator-activated receptor-γ (PPAR-γ) gene was considered.

Design: The Health, Aging and Body Composition (Health ABC) Study is a prospective cohort study of 3075 older adults. Participants' body composition, genetic variation, glucose metabolism, systemic inflammation, and vital status were evaluated in detail. Food intake was assessed with a modified Block food frequency questionnaire (FFQ), and dietary patterns were derived by cluster analysis.

Results: Six clusters were identified, including a 'Healthy foods' cluster characterized by higher intake of lowfat dairy products, fruit, whole grains, poultry, fish and vegetables. An interaction was found between dietary pattern and PPAR-γ Pro12Ala genotype in relation to body composition. While Pro homozygotes in the

‘Healthy foods’ cluster did not differ significantly in body composition from those in other clusters, men with the Ala allele in the ‘Healthy foods’ cluster had significantly lower adiposity than those in other clusters. The ‘Healthy foods’ cluster had lower fasting insulin and HOMA-IR values than the ‘High-fat dairy products’ and ‘Breakfast cereal’ clusters, while no differences were found in fasting or 2-hour glucose. With respect to inflammation, the ‘Healthy foods’ cluster had lower levels of IL-6 than the ‘High-fat dairy products’ and ‘Sweets and desserts’ clusters, and did not differ in CRP or TNF-α. The ‘Healthy foods’ cluster also had a lower risk of mortality than the ‘High-fat dairy products’ and ‘Sweets and desserts’ clusters, and more years of healthy life and more optimal nutritional status than the other clusters.

Conclusion: A dietary pattern consistent with current guidelines to consume relatively high amounts of vegetables, fruit, whole grains, poultry, fish and lowfat dairy products may reduce the metabolic risk and improve the nutritional status, quality of life and survival of older adults.

DIETARY PATTERNS, METABOLIC RISK AND SURVIVAL IN OLDER ADULTS

By

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Chapter 1: Introduction

Between 2008 and 2030, the number of adults worldwide aged 65 or older is projected to almost double to 1 billion, or 1 in 8 of the earth's inhabitants (1). In the U.S. in 2030, when baby boomers will be aged 65 or older, nearly 1 in 5 persons is expected to be age 65 or older (**Figures 1.1 and 1.2**) (2).

In the last century, the leading causes of death have shifted from infectious diseases to chronic diseases such as cardiovascular disease and cancer, which are influenced by diet (3). This has drawn more attention to the effects of diet on health and survival. Recent research suggests that older adults' diets can significantly impact their risk of developing adverse metabolic conditions (4,5,6). There is an imminent need to identify how diet can improve health, quality of life and survival in the growing older adult population.

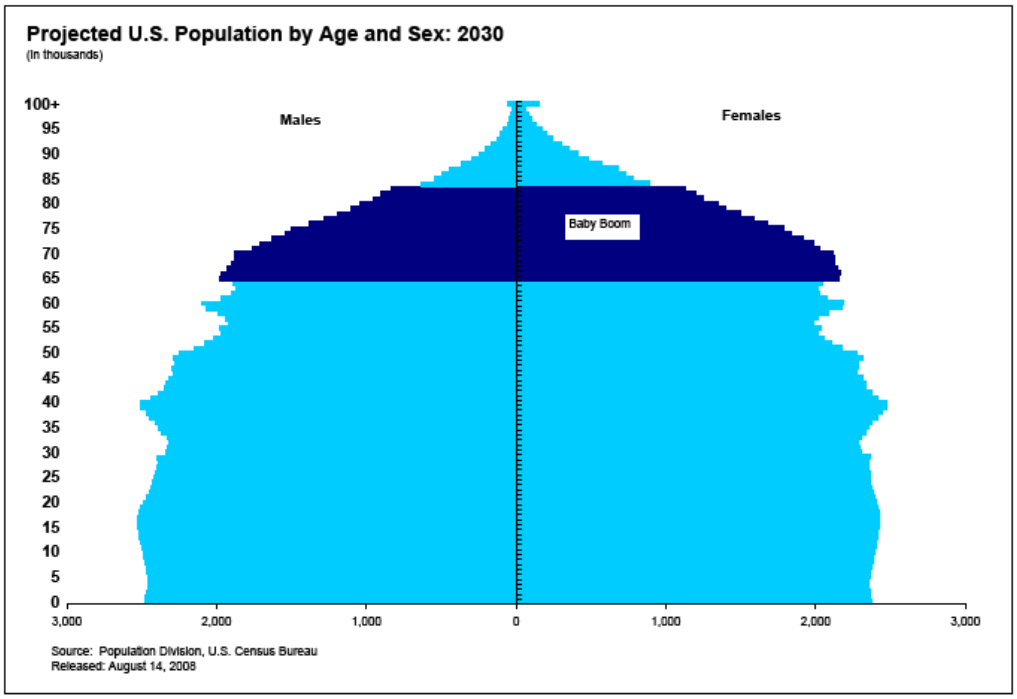

Figure 1.1. Projected U.S. population by age and sex: 2030 (7)

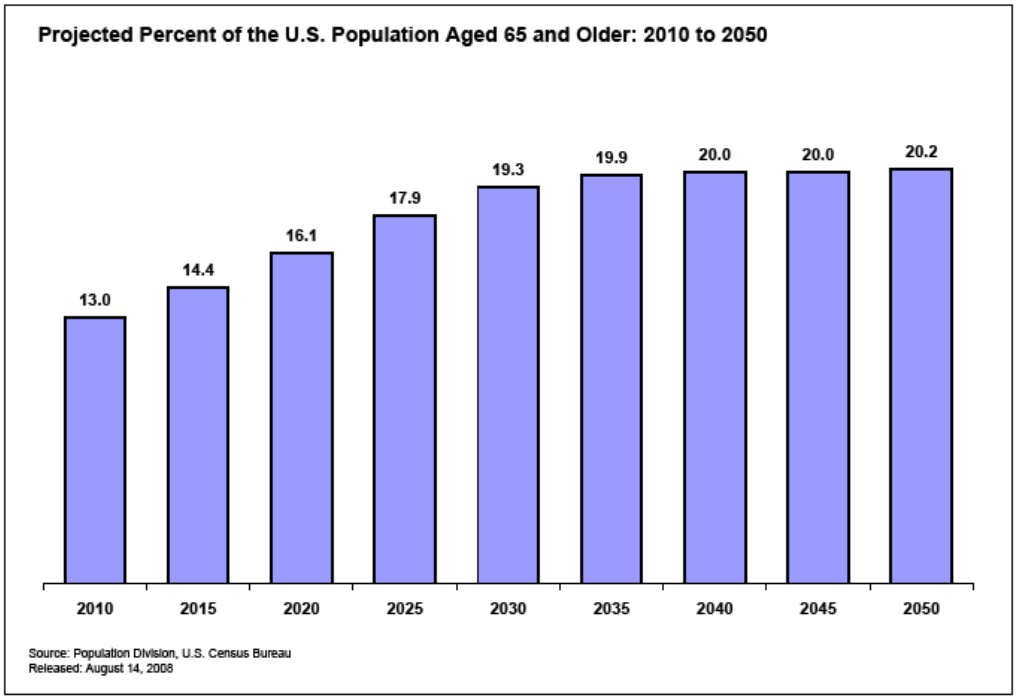

Figure 1.2. Projected percent of the U.S. population aged 65 and older: 2010 to 2050 (7)

Abdominal adiposity, insulin resistance and inflammation have all been implicated in the pathogenesis of multiple chronic diseases, and associated with decreased survival (8,9,10). It is important to determine the influence of diet on these metabolic risk factors in older adults.

Past research in nutritional epidemiology has focused mainly on dietary components in relation to health. Dietary pattern analysis, which examines the diet as a whole, has recently emerged as an alternative approach. People consume complex combinations of foods, nutrients and non-nutrients, which are often interdependent in their bioavailability. Dietary patterns can capture the complexity of the diet, as they account for the high correlation among intakes of foods and nutrients as well as their interactive effects. Dietary patterns are likely more relevant to risk of complex chronic conditions than individual dietary components. Furthermore, the effects of

specific foods or nutrients may be more difficult to detect than that of the diet as a whole. Dietary pattern analysis can enhance our understanding of current dietary practices, and show what combinations of foods are culturally acceptable to a population. Hypothetical "ideal" diets are only useful if they can be incorporated into the culture. In addition, dietary pattern analysis provides a way to evaluate health outcomes of people who generally adhere to dietary guidelines, and produces results that can be directly applied to updating guidelines.

Dietary patterns have been examined in several ways: an 'a priori' approach involves calculating a score of the overall quality of the diet based on the purported health effects of specific dietary constituents, while an empirical 'a posteriori' approach uses the dietary data at hand to identify dietary patterns of the study population independently of their relevance to health.

The purpose of the current study was to determine the overall dietary patterns of a cohort of older adults, and to examine whether dietary pattern groups differed in:

- measures of body composition, including abdominal visceral and subcutaneous fat, thigh intermuscular fat, total lean body mass, total percent body fat, BMI, abdominal circumference and sagittal diameter
- indicators of insulin sensitivity, including fasting serum insulin, fasting plasma glucose, homeostasis model assessment of insulin resistance (HOMA-IR), and glucose tolerance
- markers of systemic inflammation, including C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor- α (TNF-α)

- survival over a 10-year period

Secondary objectives were to:

- investigate the possible influence of variation in the peroxisome proliferator-activated receptor-γ (PPAR-γ) gene on relationships between diet and metabolic risk factors
- evaluate participants' quality of life and nutritional status according to their dietary patterns

Chapter 2: Literature Review

A) Dietary patterns and health

Abdominal adiposity, insulin resistance and inflammation are all believed to increase risk of multiple chronic diseases and mortality (8,9,10). Dietary patterns may better capture the multifaceted effects of diet on these metabolic risk factors and on survival than individual nutrients or foods. A number of studies have recently examined dietary patterns in relation to body composition, insulin sensitivity, inflammation and survival.

Body composition

Several studies have examined dietary patterns of older adults in relation to adiposity. Ledikwe et al. assessed dietary patterns and weight of rural men and women age 66 to 87, and showed that those in a low-nutrient-dense cluster, with high intake of breads, sweet breads and desserts, processed meat, eggs, and fats/oils, were twice as likely to be obese as those in a high-nutrient-dense cluster, with high intake of cereals, vegetables, fruit, milk, poultry, fish, and beans (11). In the Baltimore Longitudinal Study of Aging, Newby et al. inversely associated a dietary pattern high in lowfat dairy products, fruit, and fiber to annual change in BMI in women, and to annual change in waist circumference in both sexes (12).

Insulin sensitivity

The diet of older adults may considerably impact their risk of developing insulin resistance (4,5,6). Several studies have associated dietary patterns with insulin sensitivity (13,14,15,16,17,18). In the Cork and Kerry Diabetes and Heart Disease Study of Irish adults aged 50 to 69 years, a 'prudent' diet, high in pasta and rice, brown breads and unrefined cereals, spreads, poultry, fish, lowfat dairy products, salad dressing, fruit and vegetables, was linked to higher insulin sensitivity (14). Additionally, in a study of Tehrani female teachers aged 40–60 years, a 'healthy' dietary pattern, high in fruit, vegetables, poultry, legumes, tea, fruit juice and whole grains, was inversely associated with insulin resistance, while a 'Western' pattern, high in refined grains, red meat, butter, processed meat, high-fat dairy products, sweets and desserts, pizza, potatoes, eggs, hydrogenated fats and soft drinks, was positively associated with insulin resistance (16). Similarly, in the Health Professionals Follow-up Study of men aged 40-75 years, Fung et al. inversely associated a 'prudent' pattern, high in fruit, vegetables, whole grains and poultry, with fasting insulin, and positively associated a 'Western' pattern, high in red meat, high-fat dairy products and refined grains, with fasting insulin (17).

Inflammation

Dietary patterns have recently been linked to markers of systemic inflammation, such as C-reactive protein (CRP), an acute-phase reactant, and proinflammatory cytokines interleukin-6 (IL-6) and tumor necrosis factor- α (TNF-α) (17,19,20,21,22). In a study of women aged 40-60 years, Esmaillzadeh et al.

inversely associated a ‘healthy’ pattern, high in fruit, vegetables, poultry, legumes, tea, fruit juice and whole grains, to plasma CRP, and positively related a ‘western’ pattern, high in refined grains, red meat, butter, processed meat, high-fat dairy products, sweets and desserts, pizza, potatoes, eggs, hydrogenated fats and soft drinks, to plasma CRP and IL-6 (19). Similarly, in the Multi-Ethnic Study of Atherosclerosis (MESA) of adults aged 45–84 years, Nettleton et al. positively associated a ‘fats and processed meats’ pattern to CRP and IL-6, inversely associated a ‘whole grains and fruit’ pattern to CRP and IL-6, and inversely related a ‘vegetables and fish’ pattern to IL-6 (20). Furthermore, in the Nurses' Health Study of women aged 43-69 years, a ‘prudent’ pattern, high in fruit, vegetables, legumes, fish, poultry and whole grains, was inversely associated with plasma CRP, while a ‘Western’ pattern, high in red and processed meats, sweets, desserts, French fries and refined grains, was positively related to CRP and IL-6 (21). In the Health Professionals Follow-up Study of men aged 40-75 years, Fung et al. also positively associated a “Western” dietary pattern with CRP (17). Additionally, in a study of Japanese adults aged 50-74 years, a “healthy” pattern, high in vegetables, fruit, soy products and fish, was inversely associated with CRP (22).

Survival

Dietary patterns have been associated with mortality in a number of studies (23,24,25,26,27,28,29,30,31,32,33,34). Several studies inversely related a Mediterranean dietary pattern to all-cause and cardiovascular mortality (25,33,35), while others inversely associated a plant-based diet with all-cause and cardiovascular

mortality (23,24,27,28,29,31,32,34,36). Bamia et al., for example, linked increased adherence to a plant-based diet to lower all-cause mortality in adults 60 years and older in the European Prospective Investigation into Cancer and Nutrition (EPIC) Elderly Study (23). Similarly, in a prospective study of adults in Denmark aged 30-70 years at baseline, Osler et al. inversely associated a pattern high in wholemeal bread, vegetables, fruit and fish with both all-cause and cardiovascular mortality (24). Also, in the Seven Countries Study, Menotti et al. positively related a pattern high in butter, dairy products and other animal products to mortality due to coronary heart disease (CHD), and inversely associated a pattern high in cereals, legumes, vegetables, fish, oils and wine with CHD mortality (34).

Diet, the peroxisome proliferator-activated receptor-γ2 (PPAR-γ2) gene and metabolic risk

Both environmental and genetic factors are believed to affect body composition, insulin resistance, and other indicators of metabolic risk (37,38). Recent results from the Finnish Diabetes Prevention Study and other studies suggest that polymorphisms in several genes, including the peroxisome proliferator-activated receptor-γ (PPAR-γ) gene, interact with diet in their effects on body composition and insulin sensitivity (39,40,41,42,43,44,45). PPAR-γ is expressed in adipose tissue and regulates adipocyte differentiation and gene expression in adipocytes. Multiple studies have associated a common polymorphism (Pro12Ala) in the PPAR-γ2 isoform with risk of type 2 diabetes. A meta-analysis linked the common Pro allele to a 25%

increase in risk of type 2 diabetes (46). This polymorphism has also been related to body weight, body composition and insulin sensitivity (43,47,48,49,50,51,52.53).

Effects of the PPAR-γ2 Pro12Ala polymorphism may depend on the composition of the diet (40,41,42,43,44). Memisoglu et al. found the relationship between dietary fat and BMI to differ according to PPAR-γ2 Pro12Ala genotype (40). Robitaille et al. similarly showed that the association between dietary fat and components of the metabolic syndrome varied by PPAR-γ2 Pro12Ala genotype (41). While Luan et al. did not find an interaction between PPAR-γ2 Pro12Ala genotype and total dietary fat in relation to BMI, they did report an inverse association of the dietary polyunsaturated fat to saturated fat ratio with BMI and plasma insulin among Ala allele-carriers but not Pro homozygotes (42). In a diet and exercise intervention study of subjects with impaired glucose tolerance by Lindi et al., Ala homozygotes lost more weight than Pro allele carriers (43). Nicklas et al. also showed metabolic differences in response to diet among persons with different PPAR-γ2 Pro12Ala genotypes (44).

Research at the cellular level has associated the Ala variant with reduced PPAR-γ transcriptional activity compared to the Pro variant (54,55). Surprisingly, both activation of PPAR-γ by thiazolidinediones and reduced transcriptional activity of PPAR-γ due to the Pro12Ala polymorphism have been linked to greater insulin sensitivity (46,48,49,50,51,52,53,56). It is thought that different metabolic pathways mediate the insulin sensitizing effects of both increased and moderately decreased PPAR-γ activity.

Polymorphisms in genes such as the PPAR-γ gene may need to be considered when examining the influence of diet on body composition, insulin sensitivity and other indicators of metabolic risk.

Chapter 3: Methods

A) The Health, Aging and Body Composition (Health ABC) Study

Study design

The Health, Aging and Body Composition (Health ABC) Study is a prospective cohort study to investigate relations among health conditions, body composition, behavioral and social factors, and physical function in older adults. Health ABC was developed by the Laboratory of Epidemiology, Demography, and Biometry of the National Institute on Aging (NIA) of the National Institutes of Health (NIH).

Participants aged 70 to 79 years were recruited for Health ABC from a random sample of white Medicare-eligible residents of selected areas of Pittsburgh, Pennsylvania, and Memphis, Tennessee, and from all age-eligible black residents of these areas. Individuals were eligible for Health ABC if they planned to remain in the area for at least 3 years and reported no life-threatening cancers and no difficulty with basic activities of daily living, walking 1/4 mile or climbing 10 steps. Those who used assistive devices were excluded, as were participants in any research studies which involved medications or modification of eating or exercise habits. Protocols were approved by institutional review boards at the University of Pittsburgh and the University of Tennessee, and participants provided written, informed consent. An interview on behavior, health status, and social, demographic and economic factors, and a clinical examination of body composition, biochemical variables, weight-

related health conditions and physical function were administered between 1997 and 1998, with annual follow-up assessments.

3075 participants were recruited for Health ABC. The study population was approximately balanced for gender, with 52% women. 42% of recruited participants were African American and 58% Caucasian, to ensure adequate numbers to examine whether results varied by race/ethnicity. Participants self reported their race/ethnicity from a fixed set of options (Asian/Pacific Islander, black/African American, white/Caucasian, Latino/Hispanic, do not know, other).

Dietary assessment

Food intake was measured in year 2 of the Health ABC study with a 108-item food frequency questionnaire (FFQ). The FFQ reference period was the preceding year. This FFQ was designed specifically for the Health ABC study by Block Dietary Data Systems (Berkeley, CA), based on reported intakes of non-Hispanic white and black residents of the Northeast and South over age 65 in the third National Health and Nutrition Examination Survey. The FFQ was administered by a trained dietary interviewer, and interviews were periodically monitored to assure quality and consistency. Wood blocks, real food models, and flash cards were used to help participants estimate portion sizes. Nutrient and food group intakes were determined by Block Dietary Data Systems, as were participants' dietary glycemic index (GI) and glycemic load (GL) values, as described previously (57). A Healthy Eating Index (HEI) score, which reflects how well the diet conforms to the recommendations of the

Dietary Guidelines for Americans and the Food Guide Pyramid, was also calculated for each participant.

B) Dietary pattern analysis

In this study, individuals were grouped according to their overall dietary patterns by cluster analysis. The purpose of the cluster analysis was to place individuals into mutually exclusive groups such that persons in a given cluster had similar diets which differed from those of persons in other clusters.

First, the 108 FFQ food items were consolidated into 40 food groups according to similarity in nutrient content. Definitions of food groups are shown in **Appendix A**. Intake from food groups could be entered into a cluster analysis as weight in grams, number of servings, or percentage of total energy intake, for example. In this study, the percentage of energy contributed by each food group for each participant was calculated and used in the cluster analysis. This standardization by energy accounts for differences in total energy needs due to gender, age, body size and level of physical activity. It helps to avoid biased grouping due to variation in energy needs and retains proportionally-based food intake patterns.

The FASTCLUS procedure in SAS (version 9.1; SAS Institute Inc., Cary, NC) was used to generate dietary pattern clusters. This procedure requires the number of clusters to be specified in advance, and creates mutually exclusive clusters by comparing Euclidean distances between each person and each cluster center in an interactive process using a k-means method. The k-means method produces k different clusters of greatest possible distinction. Cluster seeds are first assigned at

approximate cluster locations. The Euclidean distance from each person to each cluster center is calculated, and each person is assigned to the nearest cluster center. The seeds are then replaced within the revised clusters, and the distance calculation and assignment are repeated in an iterative process until there are no further changes. The k-means method moves people between clusters with the goal to 1) minimize variability within clusters and 2) maximize variability between clusters.

K-means clustering is sensitive to outliers, which tend to be selected as the original cluster centers. For this reason, an initial cluster analysis was conducted with a predefined number of 20 clusters, and only seeds of clusters with more than 20 members from this initial analysis were used in subsequent analyses with different numbers of clusters.

Cluster analysis requires advance selection of the number of clusters, which is a subjective decision. To determine an appropriate number of clusters, 2 to 8 cluster solutions were run. Plots of R^2, the proportion of variance accounted for by the clusters, and within-cluster variance versus the number of clusters were examined to assess the ability of the clusters to segregate the study population (**Figures 3.1 and 3.2**). The inflection points in the curves, which are sometimes ambiguous, can indicate an appropriate number of clusters. As seen in **Figure 3.1**, the first clusters explain a large proportion of variance, and then the marginal gain decreases.

Cluster sample sizes were also considered in determining the number of clusters. If clusters have relatively large and similar sample sizes, this can increase the statistical power to detect differences in subsequent regression analyses. In

addition, the differences in food consumption were examined within each set of clusters to find which set of clusters best described distinct eating patterns.

A set of 6 clusters was selected. This solution most clearly identified distinct and nutritionally meaningful dietary patterns, included a pattern generally consistent with dietary guidelines, and maintained a reasonable sample size in each group for ensuing regression analyses. Inflection points in the graphs of R^2 and within-cluster variance versus the number of clusters also suggested a 5 or 6-cluster solution (**Figures 3.1 and 3.2**).

To graphically check the separation of the clusters, canonical discriminant analysis, a dimension-reduction technique, was used. Canonical discriminant analysis generates linear combinations of the quantitative variables that best summarize the differences among the clusters and provide maximal separation of the clusters. The CANDISC procedure in SAS was used to compute canonical variables. The resulting plot (**Figure 3.3**) illustrates the spatial separation of the clusters.

Mean percent energy contributions from food groups were examined according to the 6 dietary pattern clusters. Clusters were named according to food groups that on average contributed relatively more to total energy intake.

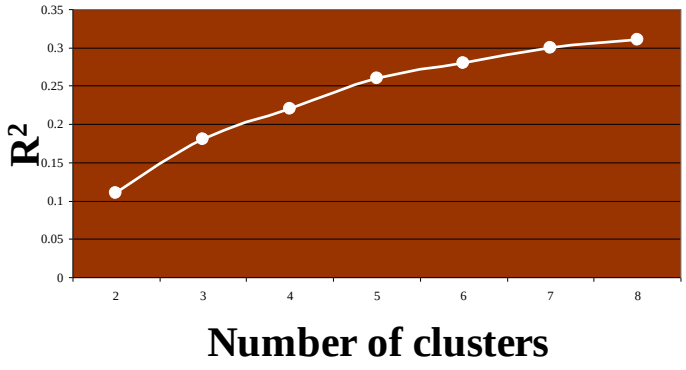

Figure 3.1. The proportion of variance accounted for by the clusters (R^2) versus the number of clusters

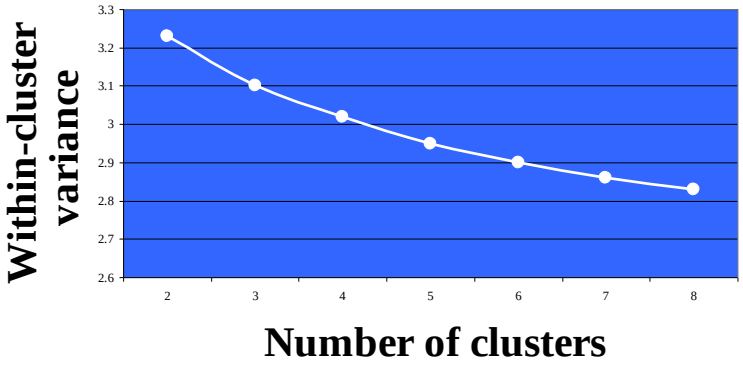

Figure 3.2. Within-cluster variance versus the number of clusters

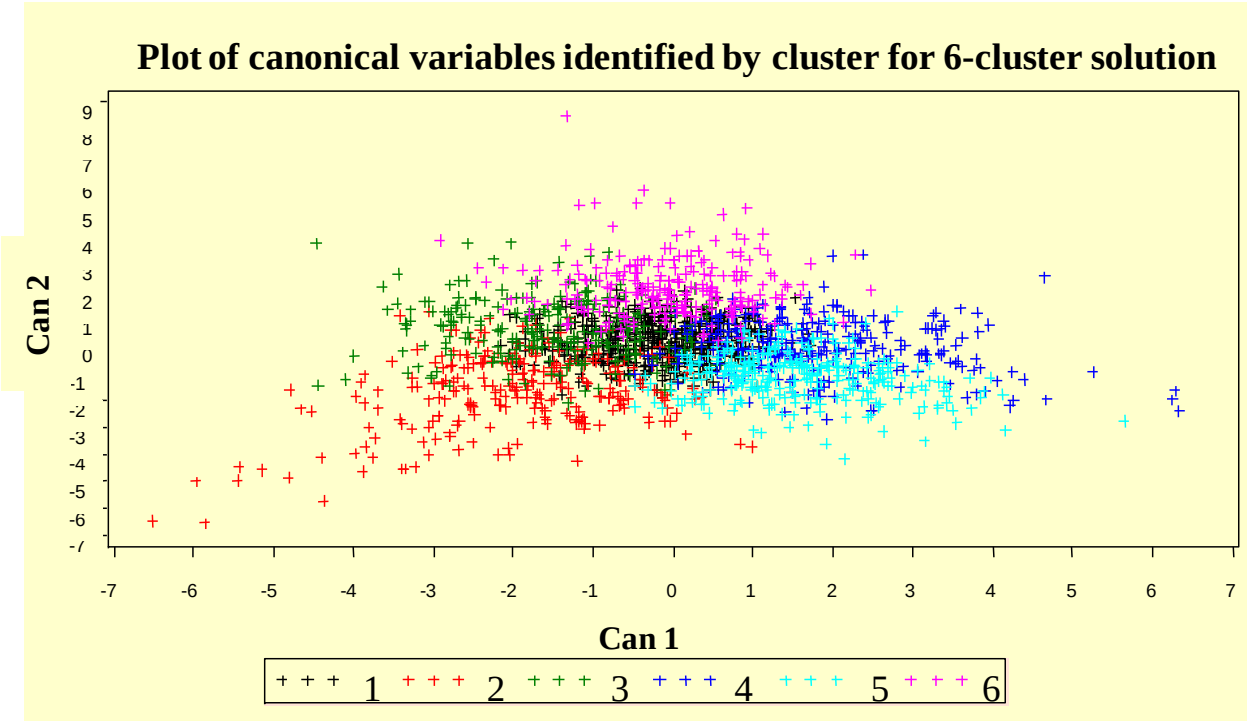

Figure 3.3. Graphical assessment of cluster separation for the 6-cluster solution

Chapter 4: Results

A) Relationships of dietary patterns with body composition in older adults differ by gender and PPAR-γ Pro12Ala genotype

Abstract

Background: Dietary patterns may better capture the multifaceted effects of diet on body composition than individual nutrients or foods.

Objectives: The purpose of this study was to investigate the dietary patterns of a cohort of older adults, and examine relationships of dietary patterns with body composition. The influence of a polymorphism in the peroxisome proliferator-activated receptor-γ (PPAR-γ) gene was considered.

Design: The Health, Aging and Body Composition (Health ABC) Study is a prospective cohort study of 3075 older adults. Participants' body composition and genetic variation were measured in detail. Food intake was assessed with a modified Block food frequency questionnaire (FFQ), and dietary patterns of 1,809 participants with complete data were derived by cluster analysis.

Results: Six clusters were identified, including a 'Healthy foods' cluster characterized by higher intake of lowfat dairy products, fruit, whole grains, poultry, fish and vegetables. An interaction was found between dietary patterns and PPAR-γ Pro12Ala genotype in relation to body composition. While Pro homozygous men and women in the 'Healthy foods' cluster did not differ significantly in body composition from those in other clusters, men with the Ala allele in the 'Healthy foods' cluster had significantly lower levels of adiposity than those in other clusters. Women with the

Ala allele in the 'Healthy foods' cluster differed only in right thigh intermuscular fat from those in one other cluster.

Conclusion: Relationships between diet and body composition in older adults may differ by gender and by genetic factors such as PPAR-γ Pro12Ala genotype.

Introduction

While obesity is considered a major health risk, the regional distribution of body fat may be of greater consequence than overall body fat. Excess fat in the abdominal visceral area in particular has been associated with higher risk for multiple metabolic complications and chronic diseases, as well as increased mortality (58,59,60,61,62,63,64).

Dietary pattern analysis examines the overall diet, and thus takes into account correlation among nutrient intakes as well as nutrient-nutrient interactions. Compared to a focus on individual nutrients or foods, dietary pattern analysis may better capture the complexity of dietary exposure thought to affect body composition.

Both environmental and genetic factors likely influence body composition and body fat distribution (37,38). The peroxisome proliferator-activated receptor-γ (PPAR-γ) is expressed in adipose tissue and regulates adipocyte differentiation and gene expression in adipocytes. A common polymorphism (Pro12Ala) in the PPAR-γ2 isoform of the PPAR-γ gene has been linked to greater adiposity in some studies (47,65,66,67,68), but not in others (48,53,69,70). Polymorphisms in genes such as the PPAR-γ gene may need to be considered when examining the influence of diet on body composition.

The purpose of the current study was to determine the main dietary patterns of a cohort of older adults, and to examine whether dietary pattern groups differed in measures of body composition, including abdominal visceral fat. A secondary goal was to investigate the possible influence of variation in the PPAR-γ gene on the relationship between diet and body composition.

Subjects and methods

Study population

Participants age 70 to 79 were recruited for the Health, Aging and Body Composition (Health ABC) Study, a prospective cohort study, from a random sample of white Medicare-eligible residents of selected areas of Pittsburgh, Pennsylvania, and Memphis, Tennessee, and from all age-eligible black residents of these areas. Individuals were eligible for Health ABC if they planned to remain in the area for at least 3 years and reported no life-threatening cancers and no difficulty with basic activities of daily living, walking 1/4 mile or climbing 10 steps. Those who used assistive devices were excluded, as were participants in any research studies which involved medications or modification of eating or exercise habits. Protocols were approved by institutional review boards at both study sites, and participants provided written, informed consent. An interview on behavior, health status, and social, demographic and economic factors, and a clinical examination of body composition, biochemical variables, weight-related health conditions and physical function were administered between 1997 and 1998, with annual follow-up assessments.

Data from baseline and year 2 of the Health ABC study were used in the current analyses. The sample size for most analyses in this study was 1809, after excluding participants who did not have a dietary assessment (n = 343); those diagnosed with type 2 diabetes before dietary intake was assessed (n = 662); men who reported an energy intake of less than 800 kcal/day or more than 4000 kcal/day and women who reported an energy intake of less than 500 kcal/day or more than 3500 kcal/day (n = 77); and those with incomplete information on other relevant measures (n = 184). Further exclusions were made in some analyses if outcome variables of interest were missing or implausible.

Dietary assessment

Food intake was measured in year 2 of the Health ABC study with a 108-item food frequency questionnaire (FFQ). This FFQ was designed specifically for the Health ABC study by Block Dietary Data Systems (Berkeley, CA), based on reported intakes of non-Hispanic white and black residents of the Northeast and South over age 65 in the third National Health and Nutrition Examination Survey. The FFQ was administered by a trained dietary interviewer, and interviews were periodically monitored to assure quality and consistency. Wood blocks, real food models, and flash cards were used to help participants estimate portion sizes. Nutrient and food group intakes, including daily servings of vegetables and frequency of fruit and fruit juice intake, were determined by Block Dietary Data Systems, as were participants' dietary GI and GL values, as described previously (57). A Healthy Eating Index (HEI) score, which reflects how well the diet conforms to the recommendations of the

Dietary Guidelines for Americans and the Food Guide Pyramid, was also calculated for each participant.

In this study, individuals were grouped according to their overall dietary patterns by cluster analysis, based on methods used in previous studies (71,72). The purpose of the cluster analysis was to place individuals into mutually exclusive groups such that persons in a given cluster had similar diets which differed from those of persons in other clusters. First, the 108 FFQ food items were consolidated into 40 food groups according to similarity in nutrient content. The percentage of energy contributed by each food group for each participant was calculated and used in the cluster analysis. The reason for this standardization was to account for differences in total energy needs due to gender, age, body size and level of physical activity.

The FASTCLUS procedure in SAS (version 9.1; SAS Institute Inc., Cary, NC) was used to generate dietary pattern clusters. This procedure requires the number of clusters to be specified in advance, and generates mutually exclusive clusters by comparing Euclidean distances between each subject and each cluster center in an interactive process using a K-means method. To determine the most appropriate number of clusters, 2 to 8 cluster solutions were run. Plots of R^2 by the number of clusters and of the ratio of between-cluster variance to within-cluster variance by the number of clusters were examined. A set of 6 clusters was selected, as this solution most clearly identified distinct and nutritionally meaningful dietary patterns while maintaining a reasonable sample size in each group for subsequent regression analyses. Mean percent energy contributions from food groups were

examined according to dietary pattern clusters. Clusters were named according to food groups that on average contributed relatively more to total energy intake.

Measures of body composition

At baseline of the Health ABC study, participants underwent axial computed tomography scanning of the abdomen and thigh. Abdominal visceral and subcutaneous fat and thigh intermuscular fat were quantified from scans performed on a General Electric 9800 Advantage in Pittsburgh and a Siemens Somatron and Picker PQ2000S in Memphis. Data from computed tomography scans were analyzed at the University of Colorodo Health Sciences Center according to a standardized protocol (73). Total fat mass and lean mass were assessed at baseline and year 2 by dual energy x-ray absorptiometry (Hologic QDR 4500A, software version 8.21, Hologic, Waltham, MA). Abdominal sagittal diameter was measured at baseline with a Holtain-Kahn abdominal calliper (Holtain Ltd., U.K.), and abdominal circumference was measured at baseline with a tape measure at the level of the largest circumference. Weight in kilograms was measured annually with a standard balance beam scale, and height in meters measured twice at baseline with a Harpenden stadiometer (Holtain Ltd., Crosswell, U.K.). After averaging the two height measurements, BMI (kg/m^2) was calculated as weight divided by the square of height.

Sociodemographic and lifestyle variables

Sociodemographic variables including age, gender, self-identified racial group and education, and lifestyle variables including smoking status, alcohol consumption,

and physical activity were assessed at baseline of the Health ABC study. Lifetime pack-years of cigarette smoking were calculated by multiplying cigarette packs smoked per day by the number of years of smoking. Physical activity was evaluated by a standardized questionnaire specifically designed for the Health ABC study. This questionnaire was derived from the leisure time physical activity questionnaire and included activities commonly performed by older adults (74). The frequency, duration, and intensity of specific activities were determined, and approximate metabolic equivalent unit (MET) values assigned to each activity category to estimate weekly energy expenditure.

Genotyping

The Health ABC cohort was genotyped, using polymerase chain reaction restriction fragment length polymorphism analysis (PCR-RFLP), for the Pro12Ala polymorphism of the PPAR-γ gene by Beamer et al. (75). In the current study population, PPAR-γ Pro12Ala genotype frequencies were found to be in Hardy-Weinberg equilibrium.

Statistical analysis

Characteristics of men and women were compared with Student's *t* test and chi-square test. Characteristics of men and women were also examined by dietary pattern cluster, and each cluster was compared to the 'Healthy foods' cluster with Dunnett's test for continuous variables and chi-square test for categorical variables. Multiple regression models were constructed to compare mean body composition

measures of each cluster to the 'Healthy foods' cluster, controlled for possible confounding factors including age, race, clinical site, education, physical activity, smoking and total calorie intake. The interaction of dietary pattern and gender was tested, as was the interaction of dietary pattern and PPAR-γ Pro12Ala genotype. As these interactions were found to be significant, subsequent analyses were conducted by gender and additionally by PPAR-γ Pro12Ala genotype. Statistical significance was set at $p \leq 0.05$, and analyses were performed using SAS (version 9.1; SAS Institute Inc., Cary, NC).

Results

Table 4.1 shows characteristics of men and women in the study population. Six clusters were identified: 1) 'Meat, snacks, fats and alcohol' (n=480); 2) 'Sweets and desserts' (n=257); 3) 'Refined grains' (n=247); 4) 'Breakfast cereal' (n=273); 5) 'Healthy foods' (n=306); and 6) 'High-fat dairy products' (n=246). **Table 4.2** shows mean percent energy contributions from food groups to dietary pattern clusters. The 'Healthy foods' cluster was characterized by relatively higher intake of lowfat dairy products, fruit, whole grains, poultry, fish and vegetables, and lower consumption of red meat, sweets, added fats and high-calorie drinks.

Tables 4.3 and 4.4 show characteristics of men and women by dietary pattern cluster. The 'Healthy foods' cluster had a significantly higher percent of women than any of the other 5 clusters. Both men and women in the 'Healthy foods' cluster had a higher percent energy intake from protein, lower percent energy from total fat and saturated fat, and higher intake of fiber than those in other clusters. The 'Healthy

foods' cluster also had a higher percent energy from carbohydrate, and a lower dietary glycemic index and glycemic load than most other clusters. In addition, the 'Healthy foods' cluster had a significantly higher Healthy Eating Index score than any other cluster.

Tables 4.5 and 4.6 show selected body composition measures of men and women according to dietary pattern cluster. After adjustment for age, race, clinical site, education, physical activity, smoking and total calorie intake, men in the 'Healthy foods' cluster had a significantly lower total percent body fat than those in the 'Meat, snacks, fats and alcohol' and 'Breakfast cereal' clusters. Men in the 'Healthy foods' cluster also had less abdominal visceral fat than those in the 'Breakfast cereal' cluster. No differences were found between men in the 'Healthy foods' and other clusters in BMI, abdominal circumference, sagittal diameter, abdominal subcutaneous fat, right thigh intermuscular fat or total lean body mass. Women in the 'Healthy foods' cluster showed no significant differences in any measures of body composition from any other clusters.

Tables 4.7 and 4.8 show body composition measures of men and women by PPAR-γ genotype according to dietary pattern cluster. Pro homozygous men and women in the 'Healthy foods' cluster did not differ significantly in any measures of body composition from those in other clusters, after adjustment for age, race, clinical site, education, physical activity, smoking and total calorie intake. Conversely, men with the Ala allele in the 'Healthy foods' cluster differed significantly in almost all measures of body composition from those in other clusters. Men with the Ala allele in the 'Healthy foods' cluster had a significantly lower BMI, total percent body fat,

sagittal diameter, and abdominal visceral and subcutaneous fat areas than those in the 'Meat, snacks, fats and alcohol' and 'Breakfast cereal' clusters. Men with the Ala allele in the 'Healthy foods' cluster also had a lower total percent body fat and sagittal diameter than those in the 'High-fat dairy products' cluster, and a smaller abdominal circumference than those in the 'Refined grains' cluster. Additionally, men with the Ala allele in the 'Healthy foods' cluster had significantly less right thigh intermuscular fat than those in the 'Meat, snacks, fats and alcohol' cluster. On the other hand, women with the Ala allele in the 'Healthy foods' cluster had significantly less right thigh intermuscular fat than those in the 'High-fat dairy products' cluster, but showed no significant differences in any other measures of body composition from any other clusters.

Discussion

In this study of older adults, a variety of distinct dietary patterns were identified. Men in the 'Healthy foods' cluster had a lower total percent body fat than those in the 'Meat, snacks, fats and alcohol' and 'Breakfast cereal' clusters, and less abdominal visceral fat than those in the 'Breakfast cereal' cluster. On the other hand, women in the 'Healthy foods' cluster showed no significant differences in any measures of body composition from any other clusters.

Several other studies have examined dietary patterns of older adults and their associations with adiposity. Ledikwe et al. studied dietary patterns of rural men and women age 66 to 87 in relation to weight, and showed that those in a low-nutrient-dense cluster, with high intake of breads, sweet breads and desserts, processed meats,

eggs, and fats/oils, were twice as likely to be obese as those in a high-nutrient-dense cluster, with high intake of cereals, dark green/yellow vegetables, other vegetables, citrus/melons/berries, fruit juices, other fruits, milks, poultry, fish, and beans (11). In the Baltimore Longitudinal Study of Aging, Newby et al. found a dietary pattern high in reduced-fat dairy products, fruit, and fiber to be inversely associated with annual change in BMI in women, and inversely associated with annual change in waist circumference in both sexes (12).

In the current study, dietary patterns were found to interact with PPAR-γ Pro12Ala genotype in relation to body composition. Specifically, while Pro homozygous men and women in the 'Healthy foods' cluster did not differ significantly in body composition from those in other clusters, men with the Ala allele in the 'Healthy foods' cluster had significantly lower levels of all measures of adiposity than those in other clusters. Women with the Ala allele in the 'Healthy foods' cluster differed only in right thigh intermuscular fat from those in one other cluster.

Previous studies have found interactions between diet and PPAR-γ Pro12Ala genotype in relation to body composition, but results have been inconsistent. Some studies, including the current one, suggest that Ala allele-carriers may be more sensitive to the composition of the diet than Pro homozygotes, while other studies indicate the reverse. In the Nurses' Health Study, Pro homozygous women in the highest quintile of total fat intake had a significantly higher BMI than those in the lowest quintile, while Ala allele-carriers showed no relationship between total fat intake and BMI (40). However, monounsaturated fat intake was not associated with

BMI among Pro homozygotes, but was inversely associated with BMI among Ala allele-carriers. In the Québec Family Study, which included men and women, total fat and saturated fat intake were positively associated with waist circumference in Pro homozygotes but not in Ala allele-carriers (41). Also, in a study by Adamo et al. of obese women on a 900-kcal formula diet, the Ala variant was associated with resistance to diet-induced weight loss (76).

In addition to the current study, several others have implied that diet may affect the body composition of Ala allele-carriers more than that of Pro homozygotes. In the Isle of Ely Study, which included men and women, the dietary polyunsaturated fat to saturated fat ratio was inversely related to BMI among Ala allele-carriers but not Pro homozygotes (42). There was no interaction between total fat intake and PPAR-γ Pro12Ala genotype in relation to BMI, however. Furthermore, in a diet and exercise intervention in men and women with impaired glucose tolerance, Ala homozygotes lost more weight than Pro allele-carriers (43). Similarly, Ala allele-carriers in the weight-loss lifestyle intervention group of the Diabetes Prevention Program lost more weight than Pro homozygotes (77). Also, in a study of men and women with type 2 diabetes, BMI was similar in Ala carriers and Pro homozygotes in the lower quartile of energy intake but significantly higher in Ala carriers in the upper quartile (78). Ala allele-carriers were found to have a significantly lower energy intake per kilogram body weight than Pro homozygotes, and it was suggested that Ala allele-carriers might have a higher food efficiency. In a study of Hispanic American men and women, the Ala allele was associated with increased BMI in those with high intake of polyunsaturated fat, or a high polyunsaturated fat to saturated fat ratio, in an

initial model, but not in a subsequent model (70). Additionally, in a study of overweight women on a hypocaloric diet, weight loss was similar in Ala allele-carriers and Pro homozygotes, but weight regain during follow-up was greater in Ala allele-carriers (44).

Results of studies have thus been inconsistent and indicate that other factors are likely influencing the relationships among diet, PPAR-γ Pro12Ala genotype, and body composition. While gender and weight status may play a role, their impact is not clear from studies to date. The mechanisms behind the effects of the PPAR-γ Pro12Ala genotype are also uncertain. Research at the cellular level has associated the Ala variant with reduced PPAR-γ transcriptional activity compared to the Pro variant (54,55). Surprisingly, both activation of PPAR-γ by thiazolidinediones and reduced transcriptional activity of PPAR-γ due to the Pro12Ala polymorphism have been linked to greater insulin sensitivity (46,48,49,50,51,52,53,56). It is thought that different metabolic pathways mediate the insulin sensitizing effects of both increased and moderately decreased PPAR-γ activity. In the current study, men with the Ala allele may have shown stronger associations between diet and body composition due to potentially higher insulin sensitivity, although this could not be inferred as insulin sensitivity was not examined in this study.

Strengths of this study include its unique age group and thorough measures of body composition. While several studies had examined associations between dietary patterns and anthropometric measures of adiposity, this study was unique in assessing dietary patterns of older adults in relation to more detailed measures of adiposity, by CT scan and DEXA, in addition to anthropometric assessments. A possible limitation

of this study was that the sample size did not allow subdivision of the study population beyond gender and PPAR-γ Pro12Ala genotype in the analyses.

In conclusion, the current and previous studies suggest that at least in certain populations, the relationship between diet and body composition differs according to PPAR-γ Pro12Ala genotype. Additional genetic and lifestyle factors which influence the relationships of diet, PPAR-γ Pro12Ala genotype, and body composition still need to be identified, as do the underlying mechanisms and the specific populations affected. If these questions can be elucidated, eventually diets could be tailored to persons with specific genotypes to minimize their risks of adverse health conditions and promote optimal health.

Tables

Table 4.1. Characteristics of the study population[1]

	Men	Women
n (%)	831 (45.9%)	978 (54.1%[2])
Sociodemographic factors		
Age (years)[3]	75.3 ± 0.1	75.0 ± 0.1[2]
Race (% White)	71.6	63.6[2]
Education (% completed high school)[4]	79.2	81.5
Behavioral factors[4]		
Smoking (lifetime pack-years)	25.1 ± 1.1	12.0 ± 0.7[2]
Alcohol (% any consumption)	62.6	47.7[2]
Physical activity (kcal/week)	1469 ± 74	788 ± 43[2]
Biochemical variables		
Fasting glucose (mg/dL)[3]	94.4 ± 0.3	91.4 ± 0.3[2]
Fasting insulin (μU/mL)[4]	7.7 ± 0.2	7.9 ± 0.2
Body composition		
BMI (kg/m^2)[3]	26.6 ± 0.1	27.0 ± 0.2[2]
Total body fat (%)[3]	29.2 ± 0.2	40.4 ± 0.2[2]
Visceral abdominal fat (cm^2)[4]	149.3 ± 2.3	124.9 ± 1.8[2]
Right thigh intermuscular fat (cm^2)[4]	9.3 ± 0.2	10.2 ± 0.2[2]
Dietary factors[3]		
Total calorie intake (kcal)	2014 ± 23	1677 ± 18[2]
% kcal from carbohydrate	53.1 ± 0.3	53.8 ± 0.3[2]
% kcal from protein	14.2 ± 0.1	14.5 ± 0.1
% kcal from fat	33.0 ± 0.3	33.2 ± 0.2
% kcal from saturated fat	9.6 ± 0.1	9.4 ± 0.1
Total dietary fiber (g)	18.3 ± 0.3	16.6 ± 0.2[2]
Genotype[5]		
PPAR-γ Pro12Ala genotype (n (%))		
Pro/Pro	665 (81.9)	820 (85.6[2])
Ala/Pro and Ala/Ala	147 (18.1)	138 (14.4[2])

[1] Means ± SEM, unless otherwise specified.
[2] Significantly different from men, $P \leq 0.05$ (Student's *t* test for continuous variables and chi-square test for categorical variables).
[3] Values from year 2 of the Health ABC study.
[4] Values from baseline of the Health ABC study.
[5] Genotype information not available for 39 participants.

Table 4.2. Percent energy contribution from selected food groups for the 6 dietary pattern clusters[1]

Food group	Percent energy contribution[2]					
	Healthy foods (n=306)	**Meat, snacks, fats and alcohol** (n= 480)	**Sweets and desserts** (n=257)	**Refined grains** (n=247)	**Breakfast cereal** (n=273)	**High-fat dairy products** (n=246)
Processed meat	**1.7 ± 2.0**	**4.0 ± 3.3**	2.6 ± 2.5	3.6 ± 3.2	2.4 ± 2.3	3.0 ± 3.0
Meat	**2.8 ± 2.7**	**4.0 ± 3.1**	3.4 ± 2.7	3.5 ± 2.9	3.5 ± 3.1	3.7 ± 3.4
Fish and other seafood	**2.7 ± 2.7**	1.7 ± 2.1	1.3 ± 1.6	1.4 ± 2.1	2.0 ± 2.5	**1.3 ± 1.5**
Poultry (not fried)	**3.4 ± 4.3**	2.2 ± 2.7	2.0 ± 2.3	2.0 ± 2.5	2.0 ± 2.0	**1.9 ± 2.4**
Fried poultry	**0.4 ± 1.0**	**1.5 ± 2.8**	0.6 ± 1.1	1.1 ± 1.9	0.6 ± 1.1	0.9 ± 1.8
Lowfat dairy products	**9.4 ± 6.7**	1.0 ± 2.0	1.8 ± 3.0	1.6 ± 3.2	2.7 ± 3.9	**0.5 ± 1.4**
Higher-fat dairy products	**3.5 ± 2.8**	5.1 ± 2.9	6.2 ± 4.5	5.5 ± 3.9	6.3 ± 3.8	**16.7 ± 5.6**
Beer	**0.3 ± 1.4**	**1.4 ± 4.5**	0.3 ± 1.3	0.4 ± 2.3	0.5 ± 1.9	0.4 ± 1.9
Liquor	0.6 ± 2.4	**1.1 ± 3.6**	0.6 ± 2.1	**0.4 ± 1.6**	0.7 ± 2.0	0.6 ± 1.9
Fruit	**8.2 ± 5.0**	4.0 ± 3.1	**3.6 ± 3.0**	3.9 ± 3.3	4.7 ± 3.8	4.3 ± 3.7
Dark green vegetables	**0.4 ± 0.5**	0.2 ± 0.3	**0.2 ± 0.2**	0.3 ± 0.3	0.2 ± 0.3	0.3 ± 0.3
Dark yellow vegetables	**1.1 ± 1.4**	0.7 ± 1.0	0.7 ± 1.1	0.9 ± 1.4	**0.7 ± 0.7**	0.8 ± 1.0
Other vegetables	**1.4 ± 1.4**	1.1 ± 1.3	**1.1 ± 1.2**	1.3 ± 1.2	1.2 ± 1.1	1.3 ± 1.4
Whole grains	**5.8 ± 5.4**	3.2 ± 3.5	2.4 ± 2.8	**2.1 ± 3.5**	2.7 ± 3.0	3.1 ± 3.8
Cold breakfast cereal – fiber/bran	2.9 ± 3.5	1.5 ± 2.4	1.5 ± 2.6	**1.0 ± 1.9**	**3.7 ± 4.9**	2.0 ± 2.9
Other cold breakfast cereal	6.7 ± 4.3	4.5 ± 3.4	5.3 ± 4.2	**4.1 ± 4.3**	**18.4 ± 6.3**	5.9 ± 4.2
Refined grains	9.5 ± 5.0	10.7 ± 4.3	10.1 ± 5.4	**25.3 ± 6.8**	**8.7 ± 4.7**	11.0 ± 4.9

Food group	Percent energy contribution[2]					
	Healthy foods (n=306)	**Meat, snacks, fats and alcohol** (n= 480)	**Sweets and desserts** (n=257)	**Refined grains** (n=247)	**Breakfast cereal** (n=273)	**High-fat dairy products** (n=246)
Rice, pasta and mixed dishes	**4.2 ± 4.2**	4.0 ± 3.8	3.0 ± 2.7	2.9 ± 2.7	3.0 ± 2.5	**2.9 ± 2.6**
Snacks	**1.4 ± 2.9**	**2.8 ± 5.1**	2.1 ± 3.9	1.5 ± 2.6	1.4 ± 2.5	1.7 ± 3.1
Nuts	3.3 ± 4.0	**4.7 ± 6.7**	3.0 ± 3.6	3.2 ± 3.9	**2.6 ± 3.9**	3.2 ± 4.0
High-calorie drinks	**0.8 ± 1.8**	**4.0 ± 5.2**	1.7 ± 3.0	2.7 ± 4.2	2.1 ± 3.5	2.9 ± 4.9
Mayonnaise and salad dressing	3.0 ± 2.8	**4.9 ± 4.2**	3.0 ± 2.7	**2.9 ± 2.7**	3.6 ± 3.2	3.9 ± 3.2
Sweets and desserts	**6.3 ± 4.7**	7.8 ± 4.7	**26.2 ± 8.8**	8.0 ± 5.5	7.2 ± 5.0	6.7 ± 4.7
Miscellaneous fats	**3.6 ± 3.5**	**5.9 ± 4.5**	4.0 ± 3.5	5.3 ± 4.1	3.8 ± 3.2	4.6 ± 3.7

[1] Means ± SD, unless otherwise specified.
[2] Clusters with the highest and lowest percent energy contributions from each food group are in bold.

Table 4.3. Characteristics of men by dietary pattern cluster[1]

	Healthy Foods (reference) (n=306)	**Meat, snacks, fats and alcohol** (n= 480)	**Sweets and desserts** (n=257)	**Refined grains** (n=247)	**Breakfast cereal** (n=273)	**High-fat dairy products** (n=246)
n (% men in cluster)	102 (33.3)	234 (48.8[2])	123 (47.9[2])	122 (49.4[2])	145 (53.1[2])	105 (42.7[2])
Characteristics						
Age (years)[3]	75.3 ± 0.3	75.0 ± 0.2	75.7 ± 0.3	75.1 ± 0.3	75.3 ± 0.2	75.5 ± 0.3
Race (% White)	88.2	60.7[2]	75.6[2]	57.4[2]	85.5	72.4[2]
Education (% completed high school)[4]	87.3	76.1[2]	80.5	60.7[2]	89.7	83.8
Smoking (lifetime pack-years)[4]	16.5 ± 2.3	25.1 ± 2.1	28.5 ± 3.2[2]	23.9 ± 2.6	27.7 ± 2.6[2]	27.0 ± 2.9
Alcohol (% any consumption)[4]	68.6	69.7	49.6[2]	46.7[2]	68.3	66.7
Physical activity (kcal/week)[4]	2129 ± 240	1420 ± 171[2]	1337 ± 175[2]	1321 ± 191[2]	1473 ± 116	1255 ± 156[2]
PPAR-γ Pro12Ala genotype (n (%))[5]						
Pro/Pro	79 (79.0)	203 (87.5[2])	95 (81.9)	106 (88.3)	110 (76.9)	72 (71.3)
Ala/Pro and Ala/Ala	21 (21.0)	29 (12.5[2])	21 (18.1)	14 (11.7)	33 (23.1)	29 (28.7)
Dietary factors[3]						
Total calorie intake (kcal)	1848 ± 53	2007 ± 42	2232 ± 67[2]	1996 ± 58	1885 ± 48	2130 ± 68[2]
% kcal from carbohydrate	57.2 ± 0.7	48.9 ± 0.5[2]	53.4 ± 0.6[2]	53.2 ± 0.6[2]	58.2 ± 0.6	50.8 ± 0.7[2]
% kcal from protein	16.5 ± 0.3	14.0 ± 0.2[2]	12.5 ± 0.2[2]	14.1 ± 0.2[2]	14.1 ± 0.2[2]	14.5 ± 0.2[2]
% kcal from fat	27.0 ± 0.6	36.0 ± 0.4[2]	35.4 ± 0.6[2]	33.5 ± 0.6[2]	28.1 ± 0.5	35.3 ± 0.6[2]
% kcal from saturated fat	7.4 ± 0.2	10.1 ± 0.1[2]	10.4 ± 0.2[2]	9.4 ± 0.2[2]	8.2 ± 0.2[2]	11.8 ± 0.2[2]

	Healthy Foods (reference) (n=306)	**Meat, snacks, fats and alcohol** (n= 480)	**Sweets and desserts** (n=257)	**Refined grains** (n=247)	**Breakfast cereal** (n=273)	**High-fat dairy products** (n=246)
Total dietary fiber (g)	22.2 ± 0.8	17.3 ± 0.5[2]	19.1 ± 0.7[2]	17.3 ± 0.7[2]	18.2 ± 0.6[2]	17.3 ± 0.8[2]
Dietary glycemic index (glucose scale)	54.5 ± 0.4	55.2 ± 0.3	56.3 ± 0.3[2]	59.8 ± 0.3[2]	59.2 ± 0.2[2]	55.5 ± 0.4
Dietary glycemic load (glucose scale)	132.2 ± 4.5	125.7 ± 3.0	155.2 ± 4.7[2]	149.0 ± 4.8[2]	151.7 ± 4.4[2]	139.4 ± 4.6
Healthy Eating Index score	80.9 ± 0.8	66.3 ± 0.8[2]	64.3 ± 1.1[2]	67.1 ± 1.1[2]	73.3 ± 0.8[2]	66.1 ± 1.2[2]

[1] Means ± SEM, unless otherwise specified.
[2] Significantly different from the 'Healthy foods' cluster, $P \leq 0.05$ (Dunnett's test for continuous variables and chi-square test for categorical variables).
[3] Values from year 2 of the Health ABC study.
[4] Values from baseline of the Health ABC study.
[5] Genotype information not available for 19 men.

Table 4.4. Characteristics of women by dietary pattern cluster[1]

	Healthy Foods (reference) (n=306)	**Meat, snacks, fats and alcohol** (n= 480)	**Sweets and desserts** (n=257)	**Refined grains** (n=247)	**Breakfast cereal** (n=273)	**High-fat dairy products** (n=246)
n (% women in cluster)	204 (66.7)	246 (51.3[2])	134 (52.1[2])	125 (50.6[2])	128 (46.9[2])	141 (57.3[2])
Characteristics						
Age (years)[3]	75.0 ± 0.2	74.7 ± 0.2	75.0 ± 0.3	74.9 ± 0.2	75.4 ± 0.2	75.4 ± 0.2
Race (% White)	77.9	44.3[2]	83.6	52.0[2]	68.8	63.1[2]
Education (% completed high school)[4]	91.7	74.8[2]	90.3	66.4[2]	81.3[2]	83.7[2]
Smoking (lifetime pack-years)[4]	9.5 ± 1.3	16.5 ± 1.8[2]	13.4 ± 1.9	11.4 ± 1.9	9.1 ± 1.6	9.8 ± 1.7
Alcohol (% any consumption)[4]	55.9	44.3[2]	60.5	36.8[2]	42.2[2]	44.0[2]
Physical activity (kcal/week)[4]	989 ± 107	659 ± 63[2]	765 ± 85	638 ± 97	811 ± 141	859 ± 149
PPAR-γ Pro12Ala genotype (n (%))[5]						
Pro/Pro	166 (83.0)	219 (91.3[2])	106 (80.3)	109 (89.3)	107 (84.9)	113 (81.9)
Ala/Pro and Ala/Ala	34 (17.0)	21 (8.8[2])	26 (19.7)	13 (10.7)	19 (15.1)	25 (18.1)
Dietary factors[3]						
Total calorie intake (kcal)	1566 ± 33	1707 ± 39[2]	1873 ± 46[2]	1695 ± 61	1542 ± 47	1703 ± 45
% kcal from carbohydrate	57.6 ± 0.5	49.8 ± 0.5[2]	52.2 ± 0.5[2]	53.2 ± 0.6[2]	60.4 ± 0.6[2]	51.5 ± 0.6[2]
% kcal from protein	16.7 ± 0.3	13.9 ± 0.2[2]	12.9 ± 0.2[2]	13.5 ± 0.2[2]	14.0 ± 0.2[2]	14.8 ± 0.2[2]
% kcal from fat	27.4 ± 0.4	37.3 ± 0.5[2]	36.3 ± 0.5[2]	34.5 ± 0.6[2]	27.9 ± 0.6	35.2 ± 0.5[2]
% kcal from saturated fat	7.5 ± 0.1	10.0 ± 0.1[2]	10.7 ± 0.2[2]	9.4 ± 0.2[2]	7.9 ± 0.2	11.4 ± 0.2[2]

	Healthy Foods (reference) (n=306)	**Meat, snacks, fats and alcohol** (n= 480)	**Sweets and desserts** (n=257)	**Refined grains** (n=247)	**Breakfast cereal** (n=273)	**High-fat dairy products** (n=246)
Total dietary fiber (g)	19.3 ± 0.5	15.8 ± 0.4[2]	15.9 ± 0.5[2]	15.5 ± 0.6[2]	16.7 ± 0.6[2]	15.7 ± 0.6[2]
Dietary glycemic index (glucose scale)	53.8 ± 0.2	54.9 ± 0.3[2]	55.2 ± 0.3[2]	57.9 ± 0.3[2]	59.4 ± 0.3[2]	55.4 ± 0.3[2]
Dietary glycemic load (glucose scale)	111.1 ± 2.7	108.4 ± 2.9	126.3 ± 3.4[2]	121.7 ± 4.8	127.9 ± 4.1[2]	112.7 ± 3.3
Healthy Eating Index score	80.8 ± 0.5	65.9 ± 0.7[2]	64.8 ± 1.0[2]	67.3 ± 1.0[2]	73.3 ± 0.8[2]	69.9 ± 1.0[2]

[1] Means ± SEM, unless otherwise specified.
[2] Significantly different from the 'Healthy foods' cluster, $P \leq 0.05$ (Dunnett's test for continuous variables and chi-square test for categorical variables).
[3] Values from year 2 of the Health ABC study.
[4] Values from baseline of the Health ABC study.
[5] Genotype information not available for 20 women.

Table 4.5. Multivariate-adjusted means of body composition measures in men by dietary pattern cluster[1]

	Healthy Foods (reference)	Meat, snacks, fats and alcohol	Sweets and desserts	Refined grains	Breakfast cereal	High-fat dairy products
n	102	234	123	122	145	105
BMI (kg/m2)						
Model 1[2]	26.0 ± 0.4	26.7 ± 0.2	26.4 ± 0.3	26.4 ± 0.3	27.1 ± 0.3	26.5 ± 0.4
Model 2[3]	26.1 ± 0.4	26.7 ± 0.2	26.4 ± 0.3	26.4 ± 0.4	27.1 ± 0.3	26.6 ± 0.4
Total body fat (%)						
Model 1[2]	27.6 ± 0.5	29.5 ± 0.3[4]	29.2 ± 0.5	29.0 ± 0.5	30.0 ± 0.4[4]	29.1 ± 0.5
Model 2[3]	27.9 ± 0.5	29.4 ± 0.3[4]	29.2 ± 0.5	28.8 ± 0.5	30.1 ± 0.4[4]	29.1 ± 0.5
Abdominal circumference (cm)						
Model 1[2]	97.3 ± 1.1	100.4 ± 0.7	99.9 ± 1.0	100.7 ± 1.0	100.6 ± 0.9	99.8 ± 1.1
Model 2[3]	97.8 ± 1.1	100.4 ± 0.7	99.9 ± 1.0	100.2 ± 1.0	100.8 ± 0.9	99.8 ± 1.1
Sagittal diameter (cm)						
Model 1[2]	21.5 ± 0.3	22.4 ± 0.2[4]	22.1 ± 0.3	22.0 ± 0.3	22.5 ± 0.2[4]	22.5 ± 0.3
Model 2[3]	21.6 ± 0.3	22.4 ± 0.2	22.0 ± 0.3	22.0 ± 0.3	22.5 ± 0.2	22.5 ± 0.3
Abdominal visceral fat (cm^2)						
Model 1[2]	131.4 ± 6.4	155.1 ± 4.2[4]	147.7 ± 5.8	147.9 ± 5.9	155.1 ± 5.4[4]	149.5 ± 6.3
Model 2[3]	135.4 ± 6.5	154.3 ± 4.2	148.1 ± 5.8	144.1 ± 5.9	157.0 ± 5.4[4]	148.7 ± 6.2
Right thigh intermuscular fat (cm^2)						
Model 1[2]	8.2 ± 0.6	9.4 ± 0.4	9.0 ± 0.5	9.8 ± 0.5	9.4 ± 0.5	9.5 ± 0.6

	Healthy Foods (reference)	Meat, snacks, fats and alcohol	Sweets and desserts	Refined grains	Breakfast cereal	High-fat dairy products
Model 2[3]	8.7 ± 0.6	9.4 ± 0.4	8.9 ± 0.5	9.2 ± 0.5	9.8 ± 0.5	9.5 ± 0.5

[1] Least squares means ± SEM.
[2] Adjusted for age and race.
[3] Adjusted for age, race, clinical site, education, physical activity, smoking status and total calorie intake.
[4] Significantly different from the 'Healthy foods' cluster, $P \leq 0.05$ (Dunnett's test).

Table 4.6. Multivariate-adjusted means of body composition measures in women by dietary pattern cluster[1]

	Healthy Foods (reference)	Meat, snacks, fats and alcohol	Sweets and desserts	Refined grains	Breakfast cereal	High-fat dairy products
n	204	246	134	125	128	141
BMI (kg/m2)						
Model 1[2]	27.1 ± 0.3	27.7 ± 0.3	26.7 ± 0.4	26.7 ± 0.4	26.6 ± 0.4	26.6 ± 0.4
Model 2[3]	27.1 ± 0.3	27.7 ± 0.3	26.6 ± 0.4	26.7 ± 0.4	26.6 ± 0.4	26.7 ± 0.4
Total body fat (%)						
Model 1[2]	40.1 ± 0.4	41.1 ± 0.4	40.1 ± 0.5	40.1 ± 0.5	40.6 ± 0.5	39.8 ± 0.5
Model 2[3]	40.1 ± 0.4	41.1 ± 0.4	40.2 ± 0.5	40.0 ± 0.5	40.5 ± 0.5	39.9 ± 0.5
Abdominal circumference (cm)						
Model 1[2]	96.1 ± 0.9	98.4 ± 0.8	95.1 ± 1.1	97.8 ± 1.2	95.7 ± 1.1	97.4 ± 1.1
Model 2[3]	96.8 ± 0.9	98.2 ± 0.8	95.7 ± 1.1	96.4 ± 1.2	95.6 ± 1.1	97.4 ± 1.1
Sagittal diameter (cm)						
Model 1[2]	21.1 ± 0.3	21.9 ± 0.3	22.0 ± 0.3	21.6 ± 0.3	21.1 ± 0.3	21.2 ± 0.3
Model 2[3]	21.3 ± 0.3	21.8 ± 0.3	21.9 ± 0.3	21.6 ± 0.3	21.1 ± 0.3	21.3 ± 0.3
Abdominal visceral fat (cm^2)						
Model 1[2]	118.2 ± 4.0	130.0 ± 3.7	125.3 ± 4.9	132.9 ± 5.1	116.1 ± 5.0	126.3 ± 4.8
Model 2[3]	120.7 ± 4.0	128.7 ± 3.7	127.0 ± 5.0	129.0 ± 5.1	116.2 ± 5.0	126.7 ± 4.7
Right thigh intermuscular fat (cm^2)						
Model 1[2]	9.8 ± 0.4	10.8 ± 0.4	9.7 ± 0.5	10.4 ± 0.5	9.9 ± 0.5	9.9 ± 0.5

	Healthy Foods (reference)	Meat, snacks, fats and alcohol	Sweets and desserts	Refined grains	Breakfast cereal	High-fat dairy products
Model 2[3]	10.0 ± 0.4	10.8 ± 0.4	9.8 ± 0.5	10.2 ± 0.5	9.9 ± 0.5	9.9 ± 0.5

[1] Least squares means ± SEM.
[2] Adjusted for age and race.
[3] Adjusted for age, race, clinical site, education, physical activity, smoking status and total calorie intake.
[4] Significantly different from the 'Healthy foods' cluster, $P \leq 0.05$ (Dunnett's test).

Table 4.7. Multivariate-adjusted means of body composition measures in men by dietary pattern cluster and PPAR-γ Pro12Ala genotype[1]

	Healthy Foods (reference)	Meat, snacks, fats and alcohol	Sweets and desserts	Refined grains	Breakfast cereal	High-fat dairy products
Pro/Pro (n)	79	203	95	106	110	72
BMI (kg/m2)						
Model 1[2]	26.2 ± 0.4	26.4 ± 0.3	26.4 ± 0.4	26.2 ± 0.4	26.7 ± 0.4	26.3 ± 0.4
Model 2[3]	26.2 ± 0.4	26.4 ± 0.3	26.4 ± 0.4	26.2 ± 0.4	26.7 ± 0.4	26.4 ± 0.4
Total body fat (%)						
Model 1[2]	28.2 ± 0.6	29.1 ± 0.4	29.1 ± 0.5	28.7 ± 0.5	29.4 ± 0.5	29.0 ± 0.6
Model 2[3]	28.3 ± 0.6	29.1 ± 0.4	29.1 ± 0.5	28.4 ± 0.5	29.5 ± 0.5	29.0 ± 0.6
Abdominal circumference (cm)						
Model 1[2]	98.0 ± 1.2	99.6 ± 0.7	100.1 ± 1.1	99.0 ± 1.0	99.8 ± 1.0	98.9 ± 1.2
Model 2[3]	98.3 ± 1.3	99.6 ± 0.8	99.9 ± 1.1	98.7 ± 1.1	99.1 ± 1.1	99.0 ± 1.3
Sagittal diameter (cm)						
Model 1[2]	21.8 ± 0.3	22.2 ± 0.2	22.0 ± 0.3	21.9 ± 0.3	22.2 ± 0.3	22.3 ± 0.3
Model 2[3]	21.9 ± 0.3	22.2 ± 0.2	22.0 ± 0.3	21.9 ± 0.3	22.2 ± 0.3	22.4 ± 0.3
Abdominal visceral fat (cm^2)						
Model 1[2]	136.1 ± 7.4	148.4 ± 4.6	149.1 ± 6.7	145.4 ± 6.4	148.4 ± 6.3	143.8 ± 7.7
Model 2[3]	138.7 ± 7.4	148.3 ± 4.6	148.8 ± 6.7	142.4 ± 6.5	150.1 ± 6.3	143.3 ± 7.6
Right thigh intermuscular fat (cm^2)						
Model 1[2]	8.8 ± 0.6	9.0 ± 0.4	8.8 ± 0.6	9.8 ± 0.5	8.9 ± 0.5	9.4 ± 0.7

	Healthy Foods (reference)	Meat, snacks, fats and alcohol	Sweets and desserts	Refined grains	Breakfast cereal	High-fat dairy products
Model 2[3]	9.2 ± 0.6	9.1 ± 0.4	8.6 ± 0.6	9.3 ± 0.5	9.2 ± 0.5	9.4 ± 0.6
Ala/Pro and Ala/Ala (n)	21	29	21	14	33	29
BMI (kg/m2)						
Model 1[2]	24.9 ± 0.8	28.2 ± 0.7[4]	26.3 ± 0.8	27.5 ± 1.0	28.3 ± 0.6[4]	27.2 ± 0.7
Model 2[3]	24.9 ± 0.8	28.3 ± 0.7[4]	26.3 ± 0.8	27.6 ± 1.0	28.2 ± 0.6[4]	27.2 ± 0.7
Total body fat (%)						
Model 1[2]	25.1 ± 1.1	31.7 ± 0.9[4]	29.3 ± 1.1[4]	30.0 ± 1.3[4]	32.0 ± 0.8[4]	30.2 ± 0.9[4]
Model 2[3]	25.8 ± 1.2	31.6 ± 0.9[4]	29.2 ± 1.1	29.9 ± 1.3	31.9 ± 0.9[4]	30.1 ± 1.0[4]
Abdominal circumference (cm)						
Model 1[2]	95.2 ± 2.8	104.6 ± 2.4[4]	99.6 ± 2.8	110.7 ± 3.4[4]	103.7 ± 2.2	102.8 ± 2.5
Model 2[3]	95.2 ± 3.0	104.0 ± 2.5	100.6 ± 2.9	109.9 ± 3.5[4]	103.6 ± 2.3	103.2 ± 2.5
Sagittal diameter (cm)						
Model 1[2]	20.2 ± 0.6	23.8 ± 0.5[4]	22.1 ± 0.6	22.4 ± 0.7	23.5 ± 0.5[4]	23.1 ± 0.5[4]
Model 2[3]	20.4 ± 0.6	23.9 ± 0.5[4]	22.1 ± 0.6	22.5 ± 0.7	23.4 ± 0.5[4]	23.0 ± 0.5[4]
Abdominal visceral fat (cm^2)						
Model 1[2]	114.7 ± 13.3	196.5 ± 11.3[4]	150.9 ± 13.3	159.9 ± 16.4	183.7 ± 10.7[4]	168.0 ± 11.7[4]
Model 2[3]	123.2 ± 14.1	192.8 ± 11.7[4]	152.8 ± 13.6	154.2 ± 16.8	185.9 ± 10.9[4]	164.4 ± 11.9

	Healthy Foods (reference)	Meat, snacks, fats and alcohol	Sweets and desserts	Refined grains	Breakfast cereal	High-fat dairy products
Right thigh intermuscular fat (cm^2)						
Model 1[2]	6.3 ± 1.4	12.1 ± 1.2[4]	9.7 ± 1.4	9.5 ± 1.7	11.2 ± 1.1[4]	9.7 ± 1.2
Model 2[3]	7.4 ± 1.4	11.2 ± 1.2[4]	10.4 ± 1.3	8.3 ± 1.7	11.7 ± 1.1	9.4 ± 1.2

[1] Least squares means ± SEM.
[2] Adjusted for age and race.
[3] Adjusted for age, race, clinical site, education, physical activity, smoking status and total calorie intake.
[4] Significantly different from the 'Healthy foods' cluster, $P \leq 0.05$ (Dunnett's test).

Table 4.8. Multivariate-adjusted means of body composition measures in women by dietary pattern cluster and PPAR-γ Pro12Ala genotype[1]

	Healthy Foods (reference)	Meat, snacks, fats and alcohol	Sweets and desserts	Refined grains	Breakfast cereal	High-fat dairy products
Pro/Pro (n)	166	219	106	109	107	113
BMI (kg/m2)						
Model 1[2]	27.4 ± 0.4	27.8 ± 0.3	26.6 ± 0.5	26.9 ± 0.5	26.8 ± 0.5	26.7 ± 0.5
Model 2[3]	27.5 ± 0.4	27.7 ± 0.3	26.5 ± 0.5	26.9 ± 0.5	26.8 ± 0.5	26.8 ± 0.5
Total body fat (%)						
Model 1[2]	40.1 ± 0.5	41.2 ± 0.4	40.0 ± 0.6	40.0 ± 0.6	40.7 ± 0.6	39.7 ± 0.5
Model 2[3]	40.1 ± 0.5	41.2 ± 0.4	40.1 ± 0.6	40.0 ± 0.6	40.5 ± 0.6	39.8 ± 0.5
Abdominal circumference (cm)						
Model 1[2]	96.5 ± 1.0	98.4 ± 0.9	95.1 ± 1.3	98.1 ± 1.3	96.1 ± 1.3	97.7 ± 1.2
Model 2[3]	97.4 ± 1.0	98.1 ± 0.9	95.8 ± 1.3	96.7 ± 1.2	96.0 ± 1.2	97.9 ± 1.2
Sagittal diameter (cm)						
Model 1[2]	21.4 ± 0.2	22.0 ± 0.2	21.7 ± 0.3	21.7 ± 0.3	21.2 ± 0.3	21.3 ± 0.3
Model 2[3]	21.5 ± 0.2	21.9 ± 0.2	21.7 ± 0.3	21.7 ± 0.3	21.2 ± 0.3	21.4 ± 0.3
Abdominal visceral fat (cm^2)						
Model 1[2]	121.6 ± 4.5	129.9 ± 4.0	125.2 ± 5.6	133.1 ± 5.5	115.3 ± 5.6	128.7 ± 5.4
Model 2[3]	124.2 ± 4.5	128.1 ± 4.0	127.3 ± 5.7	129.6 ± 5.5	115.4 ± 5.5	129.8 ± 5.4
Right thigh intermuscular fat (cm^2)						
Model 1[2]	10.1 ± 0.5	11.1 ± 0.4	9.9 ± 0.6	10.8 ± 0.6	10.4 ± 0.6	9.6 ± 0.5

	Healthy Foods (reference)	Meat, snacks, fats and alcohol	Sweets and desserts	Refined grains	Breakfast cereal	High-fat dairy products
Model 2[3]	10.3 ± 0.5	10.9 ± 0.4	10.0 ± 0.6	10.6 ± 0.6	10.4 ± 0.6	9.6 ± 0.5
Ala/Pro and Ala/Ala (n)	34	21	26	13	19	25
BMI (kg/m2)						
Model 1[2]	25.6 ± 0.8	27.6 ± 1.0	27.3 ± 0.9	25.7 ± 1.2	25.4 ± 1.0	25.9 ± 0.9
Model 2[3]	25.6 ± 0.8	27.8 ± 1.0	27.1 ± 0.9	25.4 ± 1.3	25.1 ± 1.0	26.3 ± 0.9
Total body fat (%)						
Model 1[2]	39.7 ± 1.0	40.9 ± 1.3	40.7 ± 1.2	41.5 ± 1.6	40.3 ± 1.4	39.7 ± 1.2
Model 2[3]	39.9 ± 1.0	41.3 ± 1.3	40.7 ± 1.2	40.5 ± 1.7	39.9 ± 1.4	39.9 ± 1.2
Abdominal circumference (cm)						
Model 1[2]	93.4 ± 2.1	97.9 ± 2.7	95.4 ± 2.4	95.3 ± 3.6	94.4 ± 2.9	96.1 ± 2.5
Model 2[3]	93.5 ± 2.2	98.6 ± 2.7	96.0 ± 2.6	94.3 ± 3.8	94.0 ± 2.9	95.6 ± 2.5
Sagittal diameter (cm)						
Model 1[2]	20.0 ± 1.2	21.9 ± 1.5	23.6 ± 1.3	20.8 ± 1.9	20.1 ± 1.6	20.4 ± 1.4
Model 2[3]	20.1 ± 1.2	22.1 ± 1.5	23.3 ± 1.5	20.8 ± 2.0	20.0 ± 1.6	20.6 ± 1.4
Abdominal visceral fat (cm^2)						
Model 1[2]	103.1 ± 9.0	136.6 ± 11.6	128.7 ± 10.4	128.5 ± 14.7	121.9 ± 12.2	115.4 ± 10.5
Model 2[3]	105.5 ± 9.1	139.9 ± 11.5	132.0 ± 11.1	114.7 ± 15.6	120.5 ± 12.2	114.2 ± 10.7

	Healthy Foods (reference)	Meat, snacks, fats and alcohol	Sweets and desserts	Refined grains	Breakfast cereal	High-fat dairy products
Right thigh intermuscular fat (cm^2)						
Model 1[2]	8.0 ± 0.8	9.6 ± 1.0	8.8 ± 0.9	8.1 ± 1.3	7.6 ± 1.1	11.1 ± 0.9[4]
Model 2[3]	8.0 ± 0.8	9.8 ± 1.0	8.6 ± 1.0	8.0 ± 1.4	7.4 ± 1.1	11.3 ± 1.0[4]

[1] Least squares means ± SEM.
[2] Adjusted for age and race.
[3] Adjusted for age, race, clinical site, education, physical activity, smoking status and total calorie intake.
[4] Significantly different from the 'Healthy foods' cluster, $P \leq 0.05$ (Dunnett's test).

B) Dietary patterns, insulin sensitivity and inflammation in older adults

Abstract

Background: Several studies have linked overall dietary patterns to insulin sensitivity and systemic inflammation, which affect risk of multiple chronic diseases.

Objectives: The purpose of this study was to investigate the dietary patterns of a cohort of older adults, and examine relationships of dietary patterns with markers of insulin sensitivity and systemic inflammation.

Design: The Health, Aging and Body Composition (Health ABC) Study is a prospective cohort study of 3075 older adults. In Health ABC, multiple indicators of glucose metabolism and markers of systemic inflammation were assessed. Food intake was estimated with a modified Block food frequency questionnaire (FFQ). In this study, dietary patterns of 1,751 participants with complete data were derived by cluster analysis.

Results: Six clusters were identified, including a 'Healthy foods' cluster, characterized by higher intake of lowfat dairy products, fruit, whole grains, poultry, fish and vegetables. The 'Healthy foods' cluster had significantly lower fasting insulin and HOMA-IR values than the 'Breakfast cereal' and 'High-fat dairy products' clusters, while no differences were found in fasting or 2-hour glucose. With respect to inflammation, the 'Healthy foods' cluster had

significantly lower levels of IL-6 than the 'Sweets and desserts' and 'High-fat dairy products' clusters, and no differences were seen in CRP or TNF-α.
Conclusion: Results of this study indicate that a dietary pattern high in lowfat dairy products, fruit, whole grains, poultry, fish and vegetables may be associated with greater insulin sensitivity and lower systemic inflammation in older adults.

Introduction

Recent research suggests that older adults' diets can significantly influence their risk of developing adverse metabolic conditions, including insulin resistance and type 2 diabetes (4,5,6). A number of studies have also linked dietary composition to markers of systemic inflammation, such as C-reactive protein (CRP), an acute-phase reactant, and proinflammatory cytokines interleukin-6 (IL-6) and tumor necrosis factor- α (TNF-α) (19,20,21,22). Inflammation has been implicated in the pathogenesis of multiple chronic conditions, including cardiovascular disease and type 2 diabetes, though underlying mechanisms have not been fully elucidated (79,80,81).

One method of assessing the overall dietary influence on metabolic risk is through dietary pattern analysis. Unlike studies that focus on specific nutrients or foods, dietary pattern analysis accounts for the combined effects of individual nutrients and foods.

Though insulin resistance has been linked to inflammation, and both of these metabolic risk factors have been implicated in a number of adverse chronic conditions, few studies have simultaneously examined the associations of overall dietary patterns with markers of insulin resistance and systemic inflammation, particularly in the older adult population. The objective of this study was to determine whether older adults who follow different dietary patterns differ in indicators of insulin sensitivity and systemic inflammation.

Subjects and methods

Study population

Participants age 70 to 79 were recruited for the Health, Aging and Body Composition (Health ABC) Study, a prospective cohort study, from a random sample of white Medicare-eligible residents of selected areas of Pittsburgh, Pennsylvania, and Memphis, Tennessee, and from all age-eligible black residents of these areas. Individuals were eligible for Health ABC if they planned to remain in the area for at least 3 years and reported no life-threatening cancers and no difficulty with basic activities of daily living, walking 1/4 mile or climbing 10 steps. Those who used assistive devices were excluded, as were participants in any research studies which involved medications or modification of eating or exercise habits. Protocols were approved by institutional review boards at both

study sites, and participants provided written, informed consent. An interview on behavior, health status, and social, demographic and economic factors, and a clinical examination of body composition, biochemical variables, weight-related health conditions and physical function were administered between 1997 and 1998, with annual follow-up assessments.

Data from baseline and year 2 of the Health ABC study were used in the current analyses. The sample size for this study was 1751, after excluding participants who did not have a dietary assessment (n = 343); those diagnosed with type 2 diabetes before dietary intake was assessed (n = 548); men who reported an energy intake of less than 800 kcal/day or more than 4000 kcal/day and women who reported an energy intake of less than 500 kcal/day or more than 3500 kcal/day (n = 81); and those with incomplete information on outcome variables or control variables of interest (n = 352).

Dietary assessment

Food intake was measured in year 2 of the Health ABC study with a 108-item food frequency questionnaire (FFQ). This FFQ was designed specifically for the Health ABC study by Block Dietary Data Systems (Berkeley, CA), based on reported intakes of non-Hispanic white and black residents of the Northeast and South over age 65 in the third National Health and Nutrition Examination Survey. The FFQ was administered by a trained dietary interviewer, and interviews were

periodically monitored to assure quality and consistency. Wood blocks, real food models, and flash cards were used to help participants estimate portion sizes. Nutrient and food group intakes, including daily servings of vegetables and frequency of fruit and fruit juice intake, were determined by Block Dietary Data Systems, as were participants' dietary GI and GL values, as described previously (57). A Healthy Eating Index (HEI) score, which reflects how well the diet conforms to the recommendations of the Dietary Guidelines for Americans and the Food Guide Pyramid, was also calculated for each participant.

In this study, individuals were grouped according to their overall dietary patterns by cluster analysis, based on methods used in previous studies (71,72).

The purpose of the cluster analysis was to place individuals into mutually exclusive groups such that persons in a given cluster had similar diets which differed from those of persons in other clusters. First, the 108 FFQ food items were consolidated into 40 food groups according to similarity in nutrient content. The percentage of energy contributed by each food group for each participant was calculated and used in the cluster analysis. The reason for this standardization was to account for differences in total energy needs due to gender, age, body size and level of physical activity.

The FASTCLUS procedure in SAS (version 9.1; SAS Institute Inc., Cary, NC) was used to generate dietary pattern clusters. This procedure requires the number of clusters to be specified in advance, and generates mutually exclusive

clusters by comparing Euclidean distances between each subject and each cluster center in an interactive process using a K-means method. To determine the most appropriate number of clusters, 2 to 8 cluster solutions were run. Plots of R^2 by the number of clusters and of the ratio of between-cluster variance to within-cluster variance by the number of clusters were examined. A set of 6 clusters was selected, as this solution most clearly identified distinct and nutritionally meaningful dietary patterns while maintaining a reasonable sample size in each group for subsequent regression analyses. Mean percent energy contributions from food groups were examined according to dietary pattern clusters. Clusters were named according to food groups that on average contributed relatively more to total energy intake.

Measures of glucose metabolism

Fasting glucose and fasting insulin were assessed at baseline of the Health ABC study, from blood drawn through venipuncture after an overnight fast and stored at -70°C. Plasma glucose was measured by an automated glucose oxidase reaction (YSI 2300 Glucose Analyzer; Yellow Springs Instruments, Yellow Springs, OH), and serum insulin with a commercially available radioimmunoassay kit (Pharmacia, Uppsala, Sweden). Homeostasis model assessment of insulin resistance (HOMA-IR), an estimate of insulin resistance derived from fasting glucose and insulin levels, was calculated according to the

formula: [fasting insulin (μU/mL) x fasting glucose (mmol/L)/22.5]. To evaluate glucose tolerance, an oral glucose tolerance test (OGTT) was administered at baseline to participants without diagnosed type 2 diabetes. After blood was drawn for glucose and insulin measurements, participants ingested 75 g of glucose in solution (glucola), and another blood sample was drawn after 2 hours. Biological specimens were processed according to standardized protocols by the Laboratory of Clinical Biochemistry at the University of Vermont (82).

Markers of inflammation

CRP, IL-6 and TNF-α were measured in fasting blood samples at baseline of Health ABC. IL-6 and TNF-α levels were measured in duplicate with enzyme-linked immunosorbent assay (ELISA) kits from R&D Systems (Minneapolis, MN). The detectable limit was 0.10 pg/mL for IL-6 (using HS600 Quantikine kit) and 0.18 pg/mL for TNF-α (using HSTA50 kit). Serum CRP levels were also measured in duplicate using ELISA based on purified protein and polyclonal anti-CRP antibodies (Calbiochem, San Diego, CA). The CRP assay was standardized according to the World Health Organization First International Reference Standard, with a sensitivity of 0.08 μg/mL.

Measures of body composition

Total fat mass was assessed in the Health ABC study by dual energy x-ray absorptiometry (Hologic QDR 4500A, software version 8.21, Hologic, Waltham, MA). Weight in kilograms was measured with a standard balance beam scale, and height in meters measured twice at baseline with a Harpenden stadiometer (Holtain Ltd., Crosswell, U.K.). After averaging the two height measurements, BMI (kg/m^2) was calculated as weight divided by the square of height.

Sociodemographic and lifestyle variables

Sociodemographic variables including age, gender, self-identified racial group and education, and lifestyle variables including smoking status, alcohol consumption, and physical activity were assessed at baseline of the Health ABC study. Lifetime pack-years of cigarette smoking were calculated by multiplying cigarette packs smoked per day by the number of years of smoking. Physical activity was evaluated by a standardized questionnaire specifically designed for the Health ABC study. This questionnaire was derived from the leisure time physical activity questionnaire and included activities commonly performed by older adults (74). The frequency, duration, and intensity of specific activities were determined, and approximate metabolic equivalent unit (MET) values assigned to each activity category to estimate weekly energy expenditure.

Genotyping

The Health ABC cohort was genotyped, using polymerase chain reaction restriction fragment length polymorphism analysis (PCR-RFLP), for the Pro12Ala polymorphism of the PPAR-γ gene by Beamer et al. (75). In the current study population, PPAR-γ Pro12Ala genotype frequencies were found to be in Hardy-Weinberg equilibrium.

Statistical analysis

Characteristics of men and women were compared with Student's *t* test and chi-square test. Characteristics of men and women were also examined by dietary pattern cluster, and each cluster was compared to the 'Healthy foods' cluster with Dunnett's test for continuous variables and chi-square test for categorical variables. Multiple regression models were constructed to compare mean measures of glucose metabolism and inflammation of each cluster to the 'Healthy foods' cluster, controlled for possible confounding factors including gender, age, race, clinical site, education, physical activity, smoking, total calorie intake and PPAR-γ genotype. The interaction of dietary pattern and gender was tested, as was the interaction of dietary pattern and race. As these interactions were not found to be significant, analyses were conducted in the study population as a whole. Statistical significance was set at $p \leq 0.05$, and analyses were performed using SAS (version 9.1; SAS Institute Inc., Cary, NC).

Results

Table 4.9 shows characteristics of men and women in the study population. Six clusters were identified: 1) 'Breakfast cereal' (n=258); 2) 'Meat and alcohol' (n=31); 3) 'Healthy foods' (n=319); 4) 'Sweets and desserts' (n=289); 5) 'Refined grains' (n=284); and 6) 'High-fat dairy products' (n=570). **Table 4.10** shows mean percent energy contributions from food groups to dietary pattern clusters. The 'Healthy foods' cluster was characterized by relatively higher intake of lowfat dairy products, fruit, whole grains, poultry, fish and vegetables, and lower consumption of red meat, added fats and high-calorie drinks.

Table 4.11 shows characteristics of participants by dietary pattern cluster. The 'Healthy foods' cluster had a significantly higher percent of women than all other clusters, as well as a higher percent of white participants, a higher level of education, and fewer pack-years of smoking. The 'Healthy foods' cluster had a significantly higher percent energy intake from protein, lower percent energy from saturated fat, and higher intake of fiber than all other clusters. The 'Healthy foods' cluster also had a significantly lower percent energy from total fat, higher percent energy from carbohydrate, and lower dietary glycemic index and glycemic load than most other clusters. In addition, the 'Healthy foods' cluster had a significantly higher Healthy Eating Index score than any other cluster.

Table 4.12 shows mean measures of glucose metabolism and inflammation according to dietary pattern cluster. The 'Healthy foods' cluster had significantly lower fasting insulin and HOMA-IR values than both the 'Breakfast cereal' cluster and the 'High-fat dairy products' cluster, after adjusting for gender, age, race, clinical site, education, physical activity, smoking, total calorie intake and PPAR-γ genotype. No significant differences were found between the 'Healthy foods' and other clusters in fasting glucose or 2-hour glucose after adjusting for all covariates. With respect to inflammatory markers, the 'Healthy foods' cluster had significantly lower levels of IL-6 than both the 'Sweets and desserts' cluster and the 'High-fat dairy products' cluster. No significant differences were seen between the 'Healthy foods' and other clusters in CRP or TNF-α after adjusting for all covariates.

Discussion

In this study of older adults, dietary patterns were associated with specific indicators of insulin sensitivity and inflammation. The 'Healthy foods' cluster had significantly lower fasting insulin and HOMA-IR values than the 'Breakfast cereal' and 'High-fat dairy products' clusters, while no differences were found in fasting or 2-hour glucose. With respect to inflammation, the 'Healthy foods'

cluster had significantly lower levels of IL-6 than the 'Sweets and desserts' and 'High-fat dairy products' clusters, and no differences were seen in CRP or TNF-α.

Several previous studies also found associations between dietary patterns and insulin sensitivity (13,14,15,16,17,18). In the Cork and Kerry Diabetes and Heart Disease Study of Irish adults aged 50 to 69 years, a 'prudent' diet was linked to higher insulin sensitivity (14). Additionally, in a study of Tehrani female teachers aged 40–60 years, a 'healthy' dietary pattern was inversely associated with insulin resistance, while a 'Western' dietary pattern was positively associated with insulin resistance (16). Furthermore, in the Health Professionals Follow-up Study of men aged 40-75 years, Fung et al. inversely associated a 'prudent' pattern with fasting insulin and positively associated a 'Western' dietary pattern with fasting insulin (17).

Previous research has also linked dietary patterns to markers of systemic inflammation (17,19,20,21,22). In a study of women aged 40-60 years, Esmaillzadeh et al. inversely associated a 'healthy' dietary pattern to plasma CRP, and positively related a 'western' pattern to plasma CRP and IL-6 (19). Similarly, in the Multi-Ethnic Study of Atherosclerosis (MESA) of adults aged 45–84 years, Nettleton et al. positively associated a 'fats and processed meats' pattern to CRP and IL-6, inversely associated a 'whole grains and fruit' pattern to CRP and IL-6, and inversely related a 'vegetables and fish' pattern to IL-6 (20). Furthermore, in the Nurses' Health Study of women aged 43-69 years, a 'prudent' pattern was

inversely associated with plasma CRP, while a 'Western' pattern was positively related to CRP and IL-6 (21). In the Health Professionals Follow-up Study of men aged 40-75 years, Fung et al. also positively associated a "Western" dietary pattern with CRP (17). Additionally, in a study of Japanese adults aged 50-74 years, a "healthy" dietary pattern was inversely associated with CRP (22).

It is difficult to compare results of different dietary pattern studies, as derived patterns are unique to each study population. However, in the current and previous studies, dietary patterns associated with insulin resistance and inflammation have consistently included certain food groups. Results of the current and previous studies suggest that a dietary pattern high in food groups such as whole grains, vegetables, fruit, poultry, fish and lowfat dairy products, and low in food groups such as refined grains, red meat, sugar-sweetened beverages, added fats, sweets and desserts, and high-fat dairy products, is associated with higher insulin sensitivity compared to other dietary patterns. With respect to inflammation, this and previous studies suggest that a dietary pattern high in food groups such as vegetables, fruit, whole grains, fish, poultry and legumes, and low in food groups such as refined grains, red meat and processed meat, sweets and desserts, sugar-sweetened beverages, and fried potatoes, is linked to lower measures of systemic inflammation compared to other dietary patterns. It is possible that these dietary patterns contribute to lower metabolic risk because they are high in specific protective nutrients, some perhaps not yet

identified, but the current study was not intended to investigate the effects of individual nutrients.

While this study showed significant differences among dietary pattern clusters in IL-6, but not in CRP or TNF-α, the inflammatory markers did follow similar trends. This would be expected, as inflammation involves a cascade in which tissue injury stimulates cells to produce pro-inflammatory cytokines, which in turn stimulate hepatocytes to produce acute-phase proteins. TNF-α and IL-6 thereby promote increased production of CRP by the liver. Additionally, while this study showed significant differences among dietary pattern clusters in fasting insulin and HOMA-IR, but not in fasting or 2-hour glucose, measures of glucose metabolism also displayed similar trends. One unexpected finding was that the 'Meat and alcohol' dietary pattern cluster did not exhibit significantly higher metabolic risk than the 'Healthy foods' cluster, and in some cases even tended to have lower risk. Because the 'Meat and alcohol' cluster had a substantially smaller sample size than the other clusters, however, these findings may not be highly meaningful.

The mechanisms to explain associations of diet with inflammation and insulin resistance have not been fully elucidated, though several theories have been suggested. Excess body fat has been linked to both insulin resistance and a state of chronic low-grade systemic inflammation, and it is thought that inflammation may contribute to insulin resistance. Adipose tissue expresses

cytokines such as TNF-α and IL-6, which may induce insulin resistance by impairing insulin signaling (83). Body fat measures were not included as covariates in this study, as they were considered potential intermediaries in the pathway between diet and metabolic risk factors.

Strengths of this study include its focus on adults aged 70 and older, a little-studied population, and simultaneous examination of multiple measures of insulin sensitivity and systemic inflammation. A limitation of this study is that the cross-sectional design does not allow inference of a causal relationship between diet and metabolic risk factors. Furthermore, this study population consisted of relatively well-functioning older adults at presumably lower metabolic risk, and it is possible that associations between diet and insulin sensitivity and inflammation would be stronger in a study population of less healthy older adults.

In conclusion, the current and previous studies suggest that a 'healthy' dietary pattern, high in food groups such as whole grains, vegetables, fruit, poultry, and fish, and low in food groups such as refined grains, red and processed meat, high-fat dairy products, sweets and desserts, and sugar-sweetened beverages, is associated with both greater insulin sensitivity and a lower level of systemic inflammation when compared to other dietary patterns. Because indicators of insulin sensitivity and systemic inflammation have been linked to risk of multiple chronic diseases, diets that promote high insulin sensitivity and

low systemic inflammation should be encouraged in older adults. Dietary interventions to lower metabolic risk in older adults could be targeted to groups according to their current dietary patterns.

Tables

Table 4.9. Characteristics of the study population[1]

	Men	Women
n (%)	825 (47.1%)	926 (52.9%)
Sociodemographic factors		
Age (years)[2]	75.3 ± 0.1	74.9 ± 0.1[3]
Race (% White)	70.3	63.5[3]
Education (% completed high school)[4]	76.6	81.8[3]
Behavioral factors[4]		
Smoking (lifetime pack-years)	25.0 ± 1.1	11.7 ± 0.7[3]
Alcohol (% any consumption)	63.4	47.4[3]
Physical activity (kcal/week)	1461 ± 74	780 ± 44[3]
Biochemical variables		
Fasting glucose (mg/dL)[4]	94.7 ± 0.3	91.5 ± 0.3[3]
Fasting insulin (μU/mL)[4]	7.7 ± 0.2	7.9 ± 0.2
2-hour glucose (mg/dL)[4]	122.7 ± 1.4	129.3 ± 1.4[3]
HOMA-IR[4]	1.8 ± 0.0	1.8 ± 0.0
C-reactive protein (μg/mL)	2.3 ± 0.1	2.9 ± 0.1[3]
Interleukin-6 (pg/mL)	2.3 ± 0.1	2.2 ± 0.1
Tumor necrosis factor- α (pg/mL)	3.4 ± 0.1	3.3 ± 0.1[3]
Body composition		
BMI (kg/m^2)[4]	26.6 ± 0.1	27.1 ± 0.2[3]
Total body fat (%)[4]	29.0 ± 0.2	40.5 ± 0.2[3]
Dietary factors[2]		
Total calorie intake (kcal)	2010 ± 23	1686 ± 19[3]
% kcal from carbohydrate	53.2 ± 0.3	54.0 ± 0.3[3]
% kcal from protein	14.2 ± 0.1	14.4 ± 0.1
% kcal from fat	32.8 ± 0.3	33.3 ± 0.2
% kcal from saturated fat	9.5 ± 0.1	9.4 ± 0.1
Total dietary fiber (g)	18.2 ± 0.3	16.9 ± 0.2[3]

Genotype[5]		
PPAR-γ Pro12Ala genotype (n (%))		
Pro/Pro	663 (82.1)	774 (85.3)
Ala/Pro and Ala/Ala	145 (18.0)	133 (14.7)

[1] Means ± SEM, unless otherwise specified.
[2] Values from year 2 of the Health ABC study.
[3] Significantly different from men, $P \leq 0.05$ (Student's *t* test for continuous variables and chi-square test for categorical variables).
[4] Values from baseline of the Health ABC study.
[5] Genotype information not available for 36 participants.

Table 4.10. Percent energy contribution from selected food groups for the 6 dietary pattern clusters[1]

Food group	Percent energy contribution[2]					
	Healthy foods (n=319)	**Breakfast cereal** (n= 258)	**Meat and alcohol** (n=31)	**Sweets and desserts** (n=289)	**Refined grains** (n=284)	**High-fat dairy products** (n=570)
Processed meat	**1.7 ± 1.8**	2.6 ± 2.7	**4.2 ± 3.0**	2.7 ± 2.6	3.7 ± 3.0	3.6 ± 3.1
Meat	**2.8 ± 2.6**	3.3 ± 2.9	**4.6 ± 3.5**	3.7 ± 2.9	3.7 ± 3.1	3.7 ± 2.9
Fish and other seafood	**2.6 ± 2.4**	1.8 ± 2.4	**1.2 ± 1.9**	1.3 ± 1.5	1.5 ± 2.1	1.6 ± 2.9
Poultry (not fried)	**3.0 ± 3.7**	2.0 ± 2.0	**1.6 ± 1.8**	2.0 ± 2.3	1.9 ± 2.4	2.1 ± 2.6
Fried poultry	**0.4 ± 1.0**	0.7 ± 1.4	**2.1 ± 3.5**	0.8 ± 1.4	1.2 ± 2.0	1.2 ± 2.3
Lowfat dairy products	**9.1 ± 6.0**	2.2 ± 3.6	1.1 ± 2.4	1.7 ± 3.0	1.2 ± 2.4	**0.7 ± 1.6**
Higher-fat dairy products	**3.1 ± 2.4**	7.0 ± 4.6	6.6 ± 4.6	6.4 ± 4.7	5.4 ± 4.0	**9.8 ± 6.9**
Beer	**0.2 ± 0.9**	0.3 ± 1.4	**17.1 ± 8.3**	0.4 ± 1.5	0.3 ± 1.4	0.4 ± 1.1
Liquor	0.7 ± 2.5	0.6 ± 1.9	**3.3 ± 9.4**	**0.5 ± 1.9**	0.6 ± 1.8	0.9 ± 2.6
Fruit	**7.6 ± 5.0**	4.6 ± 3.7	**2.8 ± 2.0**	3.6 ± 2.9	3.9 ± 3.5	4.4 ± 3.5
Dark green vegetables	**0.4 ± 0.5**	0.2 ± 0.3	0.3 ± 0.3	**0.2 ± 0.2**	0.2 ± 0.4	0.3 ± 0.3
Dark yellow vegetables	**1.1 ± 1.3**	0.7 ± 0.7	**0.4 ± 0.5**	0.7 ± 0.9	0.8 ± 1.1	0.8 ± 1.0
Other vegetables	**1.3 ± 1.2**	1.2 ± 1.5	**0.9 ± 0.8**	1.0 ± 1.0	1.3 ± 1.2	1.2 ± 1.2
Whole grains	**5.5 ± 5.1**	2.8 ± 3.1	**1.7 ± 2.0**	2.2 ± 2.6	1.8 ± 3.1	3.6 ± 4.0
Cold breakfast cereal – fiber/bran	3.0 ± 3.6	**3.7 ± 5.0**	**0.6 ± 1.3**	1.6 ± 2.6	1.0 ± 1.9	1.7 ± 2.5
Other cold breakfast cereal	7.2 ± 4.4	**18.7 ± 6.3**	**3.7 ± 4.3**	5.5 ± 4.3	4.3 ± 4.3	4.8 ± 3.6
Refined grains	9.9 ± 5.0	**8.8 ± 5.0**	10.0 ± 5.1	9.9 ± 5.3	**24.5 ± 6.9**	10.5 ± 4.2

Food group	Percent energy contribution[2]					
	Healthy foods (n=319)	**Breakfast cereal** (n= 258)	**Meat and alcohol** (n=31)	**Sweets and desserts** (n=289)	**Refined grains** (n=284)	**High-fat dairy products** (n=570)
Rice, pasta and mixed dishes	**3.9 ± 3.7**	**2.9 ± 2.4**	3.5 ± 2.9	3.2 ± 2.7	3.1 ± 2.9	3.6 ± 3.5
Snacks	1.5 ± 3.3	**1.4 ± 2.6**	1.5 ± 2.7	2.3 ± 4.1	1.6 ± 2.7	**2.6 ± 4.8**
Nuts	3.8 ± 4.3	2.4 ± 3.8	**2.3 ± 3.5**	3.2 ± 3.7	3.1 ± 3.8	**4.3 ± 5.9**
High-calorie drinks	**0.9 ± 2.1**	2.0 ± 3.4	1.4 ± 2.1	2.4 ± 3.8	3.1 ± 4.5	**3.5 ± 5.0**
Mayonnaise and salad dressing	3.3 ± 3.0	3.5 ± 3.1	3.7 ± 3.1	3.1 ± 2.9	**3.1 ± 2.8**	**4.5 ± 2.9**
Sweets and desserts	6.6 ± 4.8	7.0 ± 5.0	**5.2 ± 3.7**	**24.4 ± 8.3**	7.7 ± 5.4	6.7 ± 4.2
Miscellaneous fats	**3.6 ± 3.4**	3.9 ± 3.3	5.3 ± 3.7	4.1 ± 3.5	5.2 ± 4.0	**5.5 ± 4.4**

[1] Means ± SD, unless otherwise specified.
[2] Clusters with the highest and lowest percent energy contributions from each food group are in bold.

Table 4.11. Characteristics of the study population by dietary pattern cluster[1]

	Healthy foods (n=319)	**Breakfast cereal** (n= 258)	**Meat and alcohol** (n=31)	**Sweets and desserts** (n=289)	**Refined grains** (n=284)	**High-fat dairy products** (n=570)
Characteristics						
Gender (% men)	36.7	53.9[2]	83.9[2]	47.4[2]	51.1[2]	45.8[2]
Age (years)[3]	75.0 ± 0.2	75.4 ± 0.2	74.1 ± 0.5	75.1 ± 0.2	75.1 ± 0.2	75.0 ± 0.1
Race (% White)	83.4	75.6[2]	64.5[2]	75.8[2]	53.9[2]	55.3[2]
Education (% completed high school)[4]	90.6	83.3[2]	71.0[2]	84.8[2]	61.6[2]	77.7[2]
Smoking (lifetime pack-years)[4]	12.5 ± 1.2	18.4 ± 1.7[2]	42.5 ± 7.7[2]	20.3 ± 1.8[2]	18.8 ± 1.5[2]	17.9 ± 1.1[2]
Alcohol (% any consumption)[4]	61.8	55.4	100.0[2]	56.1	46.1[2]	52.3[2]
Physical activity (kcal/week)[4]	1431 ± 111	1155 ± 103	1640 ± 674	1012 ± 90[2]	953 ± 102[2]	981 ± 70[2]
PPAR-γ Pro12Ala genotype (n (%))[5]						
Pro/Pro	260 (82.5)	203 (80.2)	27 (87.1)	233 (82.6)	247 (88.9)[2]	467 (84.0)
Ala/Pro and Ala/Ala	55 (17.5)	50 (19.8)	4 (12.9)	49 (17.4)	31 (11.2)[2]	89 (16.0)
Body composition						
BMI (kg/m^2)[4]	26.3 ± 0.3	27.1 ± 0.3	27.1 ± 0.9	26.2 ± 0.2	26.8 ± 0.3	27.4 ± 0.2[2]
Total body fat (%)[4]	35.7 ± 0.4	35.1 ± 0.5	30.7 ± 1.1[2]	34.9 ± 0.4	34.3 ± 0.5	35.5 ± 0.3
Dietary factors[3]						
Total calorie intake (kcal)	1688 ± 29	1722 ± 35	2013 ± 116[2]	2051 ± 40[2]	1853 ± 40[2]	1853 ± 27[2]
% kcal from carbohydrate	57.4 ± 0.4	59.3 ± 0.5[2]	43.3 ± 1.3[2]	52.5 ± 0.4[2]	53.3 ± 0.4[2]	50.4 ± 0.3[2]
% kcal from protein	16.2 ± 0.2	14.0 ± 0.2[2]	13.0 ± 0.5[2]	12.9 ± 0.1[2]	13.8 ± 0.1[2]	14.4 ± 0.1[2]

	Healthy foods (n=319)	**Breakfast cereal** (n= 258)	**Meat and alcohol** (n=31)	**Sweets and desserts** (n=289)	**Refined grains** (n=284)	**High-fat dairy products** (n=570)
% kcal from fat	27.7 ± 0.3	28.1 ± 0.4	31.9 ± 1.1[2]	36.0 ± 0.3[2]	34.0 ± 0.4[2]	36.3 ± 0.3[2]
% kcal from saturated fat	7.5 ± 0.1	8.2 ± 0.1[2]	9.4 ± 0.4[2]	10.6 ± 0.1[2]	9.4 ± 0.1[2]	10.7 ± 0.1[2]
Total dietary fiber (g)	20.3 ± 0.4	17.3 ± 0.4[2]	15.1 ± 1.2[2]	17.1 ± 0.4[2]	16.4 ± 0.4[2]	17.0 ± 0.3[2]
Dietary glycemic index (glucose scale)	54.4 ± 0.2	59.6 ± 0.2[2]	50.2 ± 1.0[2]	55.8 ± 0.2[2]	58.8 ± 0.2[2]	55.2 ± 0.2[2]
Dietary glycemic load (glucose scale)	120.6 ± 2.3	141.8 ± 3.2[2]	103.2 ± 7.3	140.1 ± 2.8[2]	135.5 ± 3.3[2]	119.0 ± 1.9
Healthy Eating Index score	80.5 ± 0.4	72.7 ± 0.6[2]	66.5 ± 2.0[2]	64.2 ± 0.7[2]	67.6 ± 0.7[2]	67.6 ± 0.5[2]

[1] Means ± SEM, unless otherwise specified.
[2] Significantly different from the 'Healthy foods' cluster, $P \leq 0.05$ (Dunnett's test for continuous variables and chi-square test for categorical variables).
[3] Values from year 2 of the Health ABC study.
[4] Values from baseline of the Health ABC study.
[5] Genotype information not available for 36 participants.

Table 4.12. Multivariate-adjusted means of biochemical variables by dietary pattern cluster[1]

	Healthy foods (n=319)	Breakfast cereal (n=258)	Meat and alcohol (n=31)	Sweets and desserts (n=289)	Refined grains (n=284)	High-fat dairy products (n=570)
Fasting glucose (mg/dL)						
Model 1[2]	91.7 ± 0.5	93.0 ± 0.6	95.4 ± 1.7	91.6 ± 0.5	91.7 ± 0.6	93.5 ± 0.4[3]
Model 2[4]	91.7 ± 0.5	92.9 ± 0.6	94.9 ± 1.7	91.3 ± 0.6	92.1 ± 0.6	93.4 ± 0.4
Fasting insulin (µU/mL)						
Model 1[2]	6.1 ± 0.2	7.0 ± 0.2[3]	5.6 ± 0.6	6.5 ± 0.2	6.8 ± 0.2	7.0 ± 0.2[3]
Model 2[4]	6.1 ± 0.2	7.0 ± 0.2[3]	5.5 ± 0.5	6.6 ± 0.2	6.7 ± 0.2	7.0 ± 0.2[3]
2-hour glucose (mg/dL)						
Model 1[2]	118.3 ± 2.1	122.5 ± 2.4	123.1 ± 7.1	119.5 ± 2.2	117.4 ± 2.2	121.2 ± 1.6
Model 2[4]	118.9 ± 2.2	122.1 ± 2.5	121.9 ± 7.1	119.1 ± 2.3	117.7 ± 2.3	121.2 ± 1.7
HOMA-IR						
Model 1[2]	1.4 ± 0.0	1.6 ± 0.1[3]	1.3 ± 0.1	1.5 ± 0.1	1.5 ± 0.1	1.6 ± 0.0[3]
Model 2[4]	1.4 ± 0.0	1.6 ± 0.1[3]	1.3 ± 0.1	1.5 ± 0.1	1.5 ± 0.1	1.6 ± 0.0[3]
C-reactive protein (µg/mL)						
Model 1[2]	1.6 ± 0.1	1.8 ± 0.1	1.6 ± 0.2	1.8 ± 0.1	1.8 ± 0.1	1.8 ± 0.1
Model 2[4]	1.7 ± 0.1	1.8 ± 0.1	1.4 ± 0.2	1.9 ± 0.1	1.7 ± 0.1	1.8 ± 0.1
Interleukin-6 (pg/mL)						
Model 1[2]	1.6 ± 0.1	1.7 ± 0.1	2.2 ± 0.3[3]	1.9 ± 0.1[3]	1.8 ± 0.1[3]	1.9 ± 0.1[3]

	Healthy foods (n=319)	**Breakfast cereal** (n=258)	**Meat and alcohol** (n=31)	**Sweets and desserts** (n=289)	**Refined grains** (n=284)	**High-fat dairy products** (n=570)
Model 2[4]	1.7 ± 0.1	1.7 ± 0.1	2.0 ± 0.2	1.9 ± 0.1[3]	1.8 ± 0.1	1.9 ± 0.1[3]
Tumor necrosis factor- α (pg/mL)						
Model 1[2]	2.9 ± 0.1	2.9 ± 0.1	2.9 ± 0.2	3.1 ± 0.1	3.2 ± 0.1[3]	3.2 ± 0.1[3]
Model 2[4]	2.9 ± 0.1	2.9 ± 0.1	2.7 ± 0.2	3.1 ± 0.1	3.2 ± 0.1	3.2 ± 0.1

[1] Geometric means ± SEM.
[2] Adjusted for gender, age and race.
[3] Significantly different from the 'Healthy foods' cluster, $P \leq 0.05$ (Dunnett's test).
[4]Adjusted for gender, age, race, clinical site, education, physical activity, smoking status, total calorie intake and PPAR-γ genotype.

C) Dietary patterns and survival of older adults

Abstract

Background: Recent research has linked overall dietary patterns to survival in older adults.

Objectives: The objective of this study was to determine the dietary patterns of a cohort of older adults, and to explore associations of these dietary patterns with survival over a 10-year period. A secondary goal was to evaluate participants' quality of life and nutritional status according to their dietary patterns.

Design: The Health, Aging and Body Composition (Health ABC) Study is a prospective cohort study of 3075 older adults. In Health ABC, all-cause mortality was assessed from baseline through year 10. Food intake was estimated with a modified Block food frequency questionnaire (FFQ), and dietary patterns of 2582 participants with complete data were derived by cluster analysis.

Results: Six clusters were identified, including a 'Healthy foods' cluster, characterized by higher intake of lowfat dairy products, fruit, whole grains, poultry, fish and vegetables. The 'Healthy foods' cluster had a significantly lower risk of mortality than both the 'High-fat dairy products' and 'Sweets and desserts' clusters after adjusting for potential confounders. The 'Healthy foods' cluster also had significantly more years of healthy life and more favorable levels of selected nutritional biomarkers than the other clusters.

Conclusion: A dietary pattern consistent with current guidelines to consume relatively high amounts of vegetables, fruit, whole grains, poultry, fish and lowfat

dairy products may improve the nutritional status and quality of life and reduce the risk of mortality in older adults.

Introduction

Between 2000 and 2030, the number of adults worldwide aged 65 years and older is projected to more than double from approximately 420 million to 973 million (84). In the last century, the leading causes of death have shifted from infectious diseases to chronic diseases such as cardiovascular disease and cancer, which are influenced by diet (3). This has drawn more attention to the effect of diet on mortality. As the older adult population increases, so does the need to identify how diet may improve quality of life and survival.

Past studies have primarily considered specific dietary components in relation to health. Dietary pattern analysis, which examines the overall diet, has recently emerged as an alternative approach. Dietary pattern analysis can capture the complexity of the diet, as it accounts for the high correlation among intakes of specific foods and nutrients, as well as interactive effects of foods or nutrients, which are often interdependent in their bioavailability. Furthermore, the effects of individual foods or nutrients may be more difficult to detect than that of the diet as a whole. In addition, dietary pattern analysis can enhance our understanding of current dietary practices, provide a way to evaluate health outcomes of those who adhere to dietary guidelines, and produce results that may be directly applicable to updating dietary guidelines.

Dietary patterns have been examined in several ways: an 'a priori' approach involves calculating a score of the overall quality of the diet based on the purported health effects of specific dietary constituents, while an empirical 'a posteriori' approach uses the dietary data at hand to identify dietary patterns of the study population independently of their relevance to health. Several studies, predominantly in Europe, have explored associations of diet scores with mortality, and many have employed a Mediterranean diet score (23,24,25,26,27,35,36,85,86,87). Fewer studies have investigated the associations of empirical dietary patterns with mortality, especially in the U.S. The objective of this study was to determine the dietary patterns of a U.S. cohort of older adults and to explore associations of these dietary patterns with survival over a 10-year period.

Subjects and methods

Study population

Participants age 70 to 79 were recruited for the Health, Aging and Body Composition (Health ABC) Study, a prospective cohort study, from a random sample of white Medicare-eligible residents of selected areas of Pittsburgh, Pennsylvania, and Memphis, Tennessee, and from all age-eligible black residents of these areas. Individuals were eligible for Health ABC if they planned to remain in the area for at least 3 years and reported no life-threatening cancers and no difficulty with basic activities of daily living, walking 1/4 mile or climbing 10 steps. Those who used assistive devices were excluded, as were participants in any research studies which involved medications or modification of eating or exercise habits. Protocols were

approved by institutional review boards at both study sites, and participants provided written, informed consent. An interview on behavior, health status, and social, demographic and economic factors, and a clinical examination of body composition, biochemical variables, weight-related health conditions and physical function were administered between 1997 and 1998, with annual follow-up assessments.

Data from baseline through year 10 of the Health ABC study were used in the current analyses. The sample size for this study was 2582, after excluding participants who did not have a dietary assessment (n = 343); men who reported an energy intake of less than 800 kcal/day or more than 4000 kcal/day and women who reported an energy intake of less than 500 kcal/day or more than 3500 kcal/day (n = 103); and those with incomplete information on control variables of interest (n = 47).

Dietary assessment

Food intake was measured in year 2 of the Health ABC study with a 108-item food frequency questionnaire (FFQ). This FFQ was designed specifically for the Health ABC study by Block Dietary Data Systems (Berkeley, CA), based on reported intakes of non-Hispanic white and black residents of the Northeast and South over age 65 in the third National Health and Nutrition Examination Survey. The FFQ was administered by a trained dietary interviewer, and interviews were periodically monitored to assure quality and consistency. Wood blocks, real food models, and flash cards were used to help participants estimate portion sizes. Nutrient and food group intakes were determined by Block Dietary Data Systems, as were participants' dietary glycemic index (GI) and glycemic load (GL) values, as described previously

(57). A Healthy Eating Index (HEI) score, which reflects how well the diet conforms to the recommendations of the Dietary Guidelines for Americans and the Food Guide Pyramid, was also calculated for each participant.

In this study, individuals were grouped according to their overall dietary patterns by cluster analysis, based on methods used in previous studies (71,72). The purpose of the cluster analysis was to place individuals into mutually exclusive groups such that persons in a given cluster had similar diets which differed from those of persons in other clusters. First, the 108 FFQ food items were consolidated into 40 food groups according to similarity in nutrient content. The percentage of energy contributed by each food group for each participant was calculated and used in the cluster analysis. The reason for this standardization was to account for differences in total energy needs due to gender, age, body size and level of physical activity.

The FASTCLUS procedure in SAS (version 9.1; SAS Institute Inc., Cary, NC) was used to generate dietary pattern clusters. This procedure requires the number of clusters to be specified in advance, and generates mutually exclusive clusters by comparing Euclidean distances between each subject and each cluster center in an interactive process using a K-means method. To determine the most appropriate number of clusters, 2 to 8 cluster solutions were run. Plots of R^2 by the number of clusters and of the ratio of between-cluster variance to within-cluster variance by the number of clusters were examined. A set of 6 clusters was selected, as this solution most clearly identified distinct and nutritionally meaningful dietary patterns while maintaining a reasonable sample size in each group for subsequent regression analyses. Mean percent energy contributions from food groups were

examined according to dietary pattern clusters. Clusters were named according to food groups that on average contributed relatively more to total energy intake.

Biochemical measures

Fasting glucose and fasting insulin were assessed at baseline of the Health ABC study, from blood drawn through venipuncture after an overnight fast and stored at -70°C. Plasma glucose was measured by an automated glucose oxidase reaction (YSI 2300 Glucose Analyzer; Yellow Springs Instruments, Yellow Springs, OH), and serum insulin with a commercially available radioimmunoassay kit (Pharmacia, Uppsala, Sweden). Specimens were processed according to standardized protocols by the Laboratory of Clinical Biochemistry at the University of Vermont (Health, Aging and Body Composition Study Operations Manual). Serum concentrations of folate, homocysteine, vitamin B_{12} and holotranscobalamin, the biologically active fraction of vitamin B_{12}, and possibly a more pertinent marker of vitamin B_{12} status, were quantified in a subset of participants in year 3 of Health ABC. Homocysteine was measured by a fluorescence polarization immunoassay, vitamin B_{12} and folate by microbiological methods, and holotranscobalamin by a solid phase radioimmunoassay (88). In year 2 of Health ABC, the antioxidants vitamin C, beta-carotene and alpha-tocopherol, the predominant and most active form of vitamin E, were also determined in a subset of participants. Vitamin C was measured by a spectrophotometric assay performed on a robotic chemical analyzer, and beta-carotene and alpha-tocopherol by high pressure liquid chromatography (HPLC).

Body composition

Total fat mass was assessed in the Health ABC study by dual energy x-ray absorptiometry (Hologic QDR 4500A, software version 8.21, Hologic, Waltham, MA). Weight in kilograms was measured with a standard balance beam scale, and height in meters measured twice at baseline with a Harpenden stadiometer (Holtain Ltd., Crosswell, U.K.). After averaging the two height measurements, BMI (kg/m^2) was calculated as weight divided by the square of height.

Survival assessment

All-cause mortality was evaluated from baseline of Health ABC through November 26, 2007. Deaths were identified through attempts to contact participants, notification by proxy, hospital records, local newspaper obituaries, and Social Security Death Index data, and were confirmed by death certificates. Immediate and underlying causes of death were adjudicated by a committee. Survival time was defined as the time between the baseline clinical examination and the date of death and/or date of last contact.

Participants were asked to report their general health every 6 months during in-person examinations or telephone interviews. The number of years of healthy life for each participant was defined as the number of years from baseline through year 9 of Health ABC in which the participant reported either excellent, very good, or good general health, as opposed to fair or poor health, or if the person was no longer alive.

Sociodemographic and lifestyle variables

Sociodemographic variables including age, gender, self-identified racial group and education, and lifestyle variables including smoking status, alcohol consumption, and physical activity were assessed at baseline of the Health ABC study. Lifetime pack-years of cigarette smoking were calculated by multiplying cigarette packs smoked per day by the number of years of smoking. Physical activity was evaluated by a standardized questionnaire specifically designed for the Health ABC study. This questionnaire was derived from the leisure time physical activity questionnaire and included activities commonly performed by older adults (74). The frequency, duration, and intensity of specific activities were determined, and approximate metabolic equivalent unit (MET) values assigned to each activity category to estimate weekly energy expenditure.

Statistical analysis

Characteristics of men and women were compared with Student's *t* test and chi-square test. Characteristics of men and women were also examined by dietary pattern cluster, and each cluster was compared to the 'Healthy foods' cluster with Dunnett's test for continuous variables and chi-square test for categorical variables. For the all-cause mortality analyses, the censor date was the reported date of death and/or the documented date of last contact with the participant. The sample size was not sufficient to examine cause-specific mortality by dietary pattern cluster. Cox proportional hazards regression was used to compare the risk of all-cause mortality of each cluster to the 'Healthy foods' cluster, controlled for possible confounding factors

including gender, age, race, clinical site, education, physical activity, smoking and total calorie intake. None of the covariates deviated from the proportional hazards assumption required by the Cox regression model. The interaction of dietary pattern and gender was tested, as was the interaction of dietary pattern and race. As these interactions were not found to be significant, analyses were conducted in the study population as a whole. Statistical significance was set at $p \leq 0.05$, and analyses were performed using SAS (version 9.1; SAS Institute Inc., Cary, NC).

Results

Characteristics of men and women in the study population are shown in **Table 4.13**. Six clusters were identified: 1) 'Healthy foods' (n=374); 2) 'High-fat dairy products' (n=332); 3) 'Meat, fried foods, and alcohol' (n=693); 4) 'Breakfast cereal' (n=386); 5) 'Refined grains' (n=458); and 6) 'Sweets and desserts' (n=339). **Table 4.14** presents mean percent energy contributions from food groups to dietary pattern clusters. The 'Healthy foods' cluster was characterized by relatively higher intake of lowfat dairy products, fruit, whole grains, poultry, fish and vegetables, and lower consumption of meat, fried foods, sweets, high-calorie drinks and added fats.

As shown in **Table 4.15**, the 'Healthy foods' cluster had a significantly higher percent of women than all other clusters, as well as a higher percent of white participants, a higher level of education, and fewer pack-years of smoking. The 'Healthy foods' cluster also had a significantly higher percent energy intake from protein, higher intake of fiber, lower percent energy from saturated fat, and lower dietary glycemic index than all other clusters. In addition, the 'Healthy foods' cluster

had a significantly higher level of physical activity, higher percent energy from carbohydrate, lower total calorie intake, lower percent energy from total fat, and lower dietary glycemic load than most other clusters. The 'Healthy foods' cluster also had a significantly higher Healthy Eating Index score and more years of healthy life than any other cluster.

Nutrition-related biomarkers of two subsets of the study population by dietary pattern cluster are presented in **Table 4.16**. In these subsets, participants were relatively evenly distributed throughout the six clusters. The 'Healthy foods' cluster had a significantly higher level of folate, vitamin B_{12}, holotranscobalamin and beta-carotene and a significantly lower level of homocysteine than most other clusters. The 'Healthy foods' cluster also had significantly higher levels of vitamin C and alpha-tocopherol than the 'Refined grains' cluster.

In the all-cause mortality analysis, the mean follow-up time from baseline was 8.4 years, with a range of 1.1 to 10.4 years. During the follow-up period, 739 participants (29.5%) died. **Table 4.17** displays the relative risk of mortality according to dietary pattern cluster. The 'Healthy foods' cluster had a significantly lower risk of mortality than the 'High-fat dairy products' cluster, the 'Meat, fried foods, and alcohol' cluster, and the 'Sweets and desserts' cluster, after controlling for gender, age and race. After further adjustment for clinical site, education, physical activity, smoking and total calorie intake, the 'Healthy foods' cluster still showed significantly lower risk of mortality than the 'High-fat dairy products' and 'Sweets and desserts' clusters. No significant differences in risk of mortality were seen

between the ‘Healthy foods’ cluster and the ‘Breakfast cereal’ or ‘Refined grains’ clusters.

Discussion

Dietary patterns were significantly associated with mortality in this study of older adults. The ‘Healthy foods’ cluster, with relatively higher intake of lowfat dairy products, fruit, whole grains, poultry, fish and vegetables, and lower intake of meat, fried foods, sweets, high-calorie drinks and added fats, showed lower risk of mortality than both the ‘High-fat dairy products’ and ‘Sweets and desserts’ clusters after adjusting for relevant confounders. The ‘High-fat dairy products’ cluster had higher intake of foods such as ice cream, cheese, and 2% and whole milk and yogurt, and lower intake of poultry, lowfat dairy products, rice and pasta, while the ‘Sweets and desserts’ cluster had relatively higher consumption of foods such as doughnuts, cake, cookies, pudding, chocolate and candy, and lower intake of fruit, fish, other seafood, and dark green vegetables.

Previous studies have also found associations between dietary patterns and mortality (23,24,25,26,27,28,29,30,31,32,33,34). Several studies inversely related a Mediterranean dietary pattern to all-cause and cardiovascular mortality (24,25,33), while multiple others inversely associated a plant-based diet with all-cause and cardiovascular mortality (23,24,27,28,29,31,32,34,36). Bamia et al., for example, linked increased adherence to a plant-based diet to lower all-cause mortality in adults 60 years and older in the European Prospective Investigation into Cancer and Nutrition (EPIC) Elderly Study (23). Similarly, in a prospective study of adults in

Denmark aged 30-70 years at baseline, Osler et al. inversely associated a pattern high in wholemeal bread, vegetables, fruit and fish with both all-cause and cardiovascular mortality (24). Also, in the Seven Countries Study, Menotti et al. positively related food patterns high in butter, dairy products and other animal products to mortality due to coronary heart disease (CHD), and inversely associated food patterns high in cereals, legumes, vegetables, fish, oils and wine with CHD mortality (34).

While culture influences dietary patterns, which are specific to each study population, patterns associated with mortality in this and previous studies have features in common. Virtually all studies linked a dietary pattern high in food groups such as vegetables, fruit, whole grains, poultry, fish and lowfat dairy products to lower mortality compared to other dietary patterns. Multiple studies also related a dietary pattern high in plant foods to reduced risk of mortality. Unexpectedly, in this and several other studies, a pattern higher in red meat was not significantly associated with increased risk of mortality when controlled for relevant confounding factors. One suggested explanation is that plant-based diets may lower health risk because plant foods are protective, while diets high in animal foods may be more likely to increase risk if the animal foods displace protective plant foods in the diet (24,33). In the current study, the 'Meat, fried foods, and alcohol' cluster did have a slightly higher percentage of total calories from vegetables, fruit and whole grains than both the 'High-fat dairy products' and 'Sweets and desserts' clusters which showed higher risk of mortality.

In the current study, the 'Healthy foods' cluster had more optimal levels of nutritional biomarkers than the other clusters, particularly the 'Refined grains' cluster.

Older adults are at risk of inadequate vitamin B_{12} and folate status, which has been linked to increased levels of homocysteine (89). Elevated homocysteine has itself been related to poor cognitive function, dementia, Alzheimer's disease, coronary heart disease, stroke and mortality (90,91,92,93,94). Inadequate antioxidant status is also of concern to older adults, as it has been linked to risk of multiple chronic diseases (95,96,97). The more favorable nutritional status of those in the 'Healthy foods' cluster, who generally adhered to dietary guidelines, provides additional support for current guidelines.

Healthy People 2010 is a set of health objectives for the U.S. to achieve in the first decade of the 21st century. A primary goal of Healthy People 2010 is to increase quality and years of healthy life (98). In the current study, those in the 'Healthy foods' cluster had significantly more years of healthy life than any other cluster. Similarly, in the U.S. Cardiovascular Health Study of adults aged 65 years and older, a dietary pattern higher in fiber and total carbohydrate and lower in total fat was associated with more years of healthy life (29).

Strengths of this study include its thorough assessment of participants' health status, relatively long 10-year follow-up period, and measurement of many potential confounding factors, unlike several previous studies which evaluated few confounders. A limitation of this study is that the study population consisted of relatively well-functioning older adults, which may limit the applicability of findings to the well-functioning older adult population. Also, participants may have changed their dietary patterns over the 10-year follow-up period, though changes in diet would most likely attenuate differences in health risk between the 'Healthy foods' and other

clusters. Furthermore, as dietary patterns have been found to be part of specific lifestyles, it may be difficult by statistical methods to fully separate effects of diet from effects of physical activity and other lifestyle characteristics.

In conclusion, results of this study suggest that older adults who follow a dietary pattern consistent with current guidelines to consume relatively high amounts of vegetables, fruit, whole grains, lowfat dairy products, poultry and fish, may lower their risk of mortality. Because a substantial percentage of older adults in this study followed the 'Healthy foods' dietary pattern, adherence to such a diet appears a feasible and realistic recommendation for improved survival and quality of life in the growing older adult population.

Tables

Table 4.13. Characteristics of the study population[1]

	Men	Women
n (%)	1243 (48.1)	1339 (51.9)
Sociodemographic factors[2]		
Age (years)	74.3 ± 0.1	73.9 ± 0.1[3]
Race (% White)	66.9	57.5[3]
Education (% completed high school)	75.7	79.1[3]
Behavioral factors[2]		
Smoking (lifetime pack-years)	26.0 ± 0.9	12.0 ± 0.6[3]
Alcohol (% any consumption)	58.3	43.5[3]
Physical activity (kcal/week)	1494 ± 69	734 ± 36[3]
Biochemical variables[2]		
Fasting glucose (mg/dL)	107.1 ± 1.0	100.8 ± 0.9[3]
Fasting insulin (μU/mL)	8.4 ± 0.2	8.3 ± 0.2
Body composition[2]		
BMI (kg/m^2)	27.0 ± 0.1	27.6 ± 0.1[3]
Total body fat (%)	29.3 ± 0.2	40.5 ± 0.2[3]
Dietary factors[4]		
Total calorie intake (kcal)	2013 ± 19	1689 ± 16[3]
% kcal from carbohydrate	52.9 ± 0.2	53.7 ± 0.2[3]
% kcal from protein	14.3 ± 0.1	14.6 ± 0.1[3]
% kcal from fat	33.2 ± 0.2	33.4 ± 0.2
% kcal from saturated fat	9.6 ± 0.1	9.4 ± 0.1[3]
Total dietary fiber (g)	18.3 ± 0.2	16.9 ± 0.2[3]
Dietary glycemic index (glucose scale)	57.0 ± 0.1	55.9 ± 0.1[3]
Dietary glycemic load (glucose scale)	140.7 ± 1.5	116.9 ± 1.2[3]
Healthy Eating Index score	68.6 ± 0.3	70.9 ± 0.3[3]
Survival		
All-cause mortality (n (%))	429 (35.5)	310 (23.9)[3]
Years of healthy life	6.0 ± 0.1	6.2 ± 0.1

[1] Means ± SEM, unless otherwise specified.
[2] Values from baseline of the Health ABC study.
[3] Significantly different from men, $P \leq 0.05$ (Student's *t* test for continuous variables and chi-square test for categorical variables).
[4] Values from year 2 of the Health ABC study.

Table 4.14. Percent energy contribution from selected food groups for the 6 dietary pattern clusters[1]

Food group	Percent energy contribution[2]					
	Healthy foods (n=374)	**High-fat dairy products** (n=332)	**Meat, fried foods, and alcohol** (n=693)	**Breakfast cereal** (n=386)	**Refined grains** (n=458)	**Sweets and desserts** (n=339)
Processed meat	**1.7 ± 1.9**	3.0 ± 2.8	3.9 ± 3.3	2.7 ± 2.8	**4.1 ± 3.6**	2.9 ± 2.6
Meat	**2.8 ± 2.7**	3.7 ± 3.1	**4.0 ± 3.1**	3.5 ± 3.1	3.7 ± 3.0	3.4 ± 2.7
Fish and other seafood	**2.8 ± 2.8**	1.4 ± 1.8	1.7 ± 2.0	1.8 ± 2.3	1.4 ± 1.9	**1.3 ± 1.5**
Poultry (not fried)	**3.4 ± 4.2**	**1.9 ± 2.5**	2.5 ± 3.1	2.1 ± 2.3	1.9 ± 2.4	1.9 ± 2.3
Fried poultry	**0.4 ± 1.1**	1.0 ± 1.8	**1.5 ± 2.6**	0.7 ± 1.4	1.2 ± 2.2	0.8 ± 1.5
Lowfat dairy products	**10.4 ± 6.3**	**0.5 ± 1.4**	1.0 ± 1.9	2.3 ± 3.7	1.3 ± 2.5	1.6 ± 2.9
Higher-fat dairy products	**3.4 ± 2.7**	**17.1 ± 6.0**	5.1 ± 3.0	6.4 ± 3.9	5.7 ± 4.0	6.2 ± 4.3
Beer	**0.3 ± 1.5**	0.4 ± 2.0	**1.2 ± 4.1**	0.5 ± 2.0	0.3 ± 1.8	0.4 ± 1.5
Liquor	0.5 ± 1.8	0.5 ± 1.6	**1.1 ± 3.5**	0.6 ± 1.8	**0.4 ± 1.5**	0.5 ± 2.0
Fruit	**8.3 ± 5.4**	4.2 ± 3.6	4.5 ± 3.7	4.8 ± 3.9	4.2 ± 4.0	**3.5 ± 2.9**
Dark green vegetables	**0.4 ± 0.5**	0.2 ± 0.3	0.3 ± 0.3	0.2 ± 0.3	0.3 ± 0.3	**0.2 ± 0.2**
Dark yellow vegetables	**1.0 ± 1.2**	0.7 ± 0.9	0.8 ± 1.0	**0.7 ± 0.8**	0.9 ± 1.4	0.7 ± 1.0
Other vegetables	**1.4 ± 1.4**	1.2 ± 1.3	1.2 ± 1.3	1.1 ± 1.1	1.3 ± 1.2	**1.0 ± 1.1**
Whole grains	**5.1 ± 4.6**	3.0 ± 3.8	3.8 ± 4.1	2.9 ± 3.7	**2.0 ± 3.1**	2.3 ± 2.9
Cold breakfast cereal – fiber/bran	3.1 ± 3.7	2.0 ± 3.1	1.6 ± 2.5	**3.3 ± 4.9**	**1.0 ± 2.0**	1.6 ± 2.7
Other cold breakfast cereal	6.9 ± 4.3	6.3 ± 4.5	4.4 ± 3.4	**19.3 ± 6.7**	**4.3 ± 4.3**	5.3 ± 4.2
Refined grains	10.1 ± 5.3	10.9 ± 4.8	10.2 ± 4.2	**9.0 ± 4.9**	**24.6 ± 6.7**	10.0 ± 5.3

Food group	Percent energy contribution[2]					
	Healthy foods (n=374)	**High-fat dairy products** (n=332)	**Meat, fried foods, and alcohol** (n=693)	**Breakfast cereal** (n=386)	**Refined grains** (n=458)	**Sweets and desserts** (n=339)
Rice, pasta and mixed dishes	3.9 ± 3.8	**2.9 ± 2.8**	**4.1 ± 3.9**	3.0 ± 2.8	3.1 ± 2.8	2.9 ± 2.5
Snacks	**1.4 ± 2.9**	1.8 ± 3.1	**2.8 ± 5.2**	1.6 ± 3.0	1.6 ± 2.7	2.3 ± 4.0
Nuts	3.6 ± 4.4	3.1 ± 4.0	**4.6 ± 6.4**	**2.9 ± 4.0**	3.2 ± 3.8	3.1 ± 3.7
High-calorie drinks	**0.7 ± 1.8**	2.7 ± 4.7	**3.8 ± 5.4**	1.8 ± 3.2	2.7 ± 4.3	2.1 ± 3.4
Mayonnaise and salad dressing	3.2 ± 3.3	3.9 ± 3.4	**4.3 ± 3.8**	3.5 ± 3.1	3.2 ± 3.1	**3.0 ± 2.6**
Sweets and desserts	**6.0 ± 4.9**	6.8 ± 4.8	7.1 ± 4.6	6.6 ± 5.0	6.9 ± 5.3	**25.8 ± 8.9**
Miscellaneous fats	**3.4 ± 3.3**	4.7 ± 3.8	**5.8 ± 4.5**	3.8 ± 3.3	5.2 ± 4.0	3.9 ± 3.4

[1] Means ± SD, unless otherwise specified.
[2] Clusters with the highest and lowest percent energy contributions from each food group are in bold.

Table 4.15. Characteristics of the study population by dietary pattern cluster[1]

	Healthy foods (n=374)	**High-fat dairy products** (n=332)	**Meat, fried foods, and alcohol** (n=693)	**Breakfast cereal** (n=386)	**Refined grains** (n=458)	**Sweets and desserts** (n=339)
Characteristics						
Gender (% men)	35.8	44.9[2]	48.8[2]	57.0[2]	51.3[2]	49.3[2]
Age (years)[3]	74.1 ± 0.1	74.5 ± 0.2	73.7 ± 0.1	74.2 ± 0.1	74.1 ± 0.1	74.3 ± 0.2
Race (% White)	83.4	64.8[2]	48.1[2]	71.0[2]	47.8[2]	73.2[2]
Education (% completed high school)[3]	91.4	80.1[2]	74.9[2]	83.2[2]	59.4[2]	82.6[2]
Smoking (lifetime pack-years)[3]	13.2 ± 1.2	20.4 ± 1.6[2]	19.6 ± 1.1[2]	18.8 ± 1.4[2]	19.1 ± 1.3[2]	20.7 ± 1.6[2]
Alcohol (% any consumption)[3]	58.8	47.0[2]	53.1	51.0[2]	38.7[2]	55.5
Physical activity (kcal/week)[3]	1538 ± 127	924 ± 85[2]	1071 ± 78[2]	1222 ± 94	875 ± 77[2]	1011 ± 105[2]
Body composition[3]						
BMI (kg/m^2)	26.7 ± 0.2	27.1 ± 0.3	28.1 ± 0.2[2]	27.5 ± 0.2	27.4 ± 0.2	26.5 ± 0.2
Total body fat (%)	35.9 ± 0.4	35.1 ± 0.4	35.5 ± 0.3	34.7 ± 0.4	34.4 ± 0.4[2]	34.8 ± 0.4
Dietary factors[4]						
Total calorie intake (kcal)	1703 ± 28	1903 ± 35[2]	1840 ± 25[2]	1735 ± 28	1848 ± 31[2]	2076 ± 36[2]
% kcal from carbohydrate	56.9 ± 0.4	50.9 ± 0.4[2]	50.2 ± 0.3[2]	59.2 ± 0.4[2]	52.5 ± 0.3[2]	52.6 ± 0.3[2]
% kcal from protein	17.0 ± 0.2	14.8 ± 0.1[2]	14.3 ± 0.1[2]	14.1 ± 0.1[2]	14.0 ± 0.1[2]	12.7 ± 0.1[2]
% kcal from fat	27.5 ± 0.3	35.6 ± 0.4[2]	35.8 ± 0.3[2]	28.4 ± 0.3	34.6 ± 0.3[2]	36.1 ± 0.3[2]
% kcal from saturated fat	7.5 ± 0.1	11.7 ± 0.1[2]	9.9 ± 0.1[2]	8.1 ± 0.1[2]	9.5 ± 0.1[2]	10.6 ± 0.1[2]
Total dietary fiber (g)	20.7 ± 0.4	16.4 ± 0.4[2]	17.2 ± 0.3[2]	17.5 ± 0.3[2]	16.7 ± 0.3[2]	17.5 ± 0.4[2]

	Healthy foods (n=374)	**High-fat dairy products** (n=332)	**Meat, fried foods, and alcohol** (n=693)	**Breakfast cereal** (n=386)	**Refined grains** (n=458)	**Sweets and desserts** (n=339)
Dietary glycemic index (glucose scale)	54.0 ± 0.2	55.6 ± 0.2[2]	54.9 ± 0.2[2]	60.0 ± 0.2[2]	58.8 ± 0.2[2]	55.8 ± 0.2[2]
Dietary glycemic load (glucose scale)	119.5 ± 2.2	124.8 ± 2.5	116.8 ± 1.8	143.2 ± 2.6[2]	133.0 ± 2.5[2]	142.1 ± 2.6[2]
Healthy Eating Index score	80.8 ± 0.4	68.1 ± 0.7[2]	67.2 ± 0.4[2]	72.8 ± 0.5[2]	67.9 ± 0.5[2]	63.8 ± 0.7[2]
Survival						
Years of healthy life	6.8 ± 0.1	6.0 ± 0.2[2]	6.0 ± 0.1[2]	6.3 ± 0.1[2]	5.7 ± 0.1[2]	6.1 ± 0.1[2]

[1] Means ± SEM, unless otherwise specified.
[2] Significantly different from the 'Healthy foods' cluster, $P \leq 0.05$ (Dunnett's test for continuous variables and chi-square test for categorical variables).
[3] Values from baseline of the Health ABC study.
[4] Values from year 2 of the Health ABC study.

Table 4.16. Nutritional biomarkers of two subsets of the study population by dietary pattern cluster[1]

	n	Healthy foods	High-fat dairy products	Meat, fried foods, and alcohol	Breakfast cereal	Refined grains	Sweets and desserts
Folate (nmol/L)[2]	809	83.9 ± 4.0	69.1 ± 4.8[3]	71.4 ± 2.6[3]	76.0 ± 3.5	61.9 ± 3.1[3]	70.7 ± 4.3
Vitamin B_{12} (pmol/L)[2]	803	577.6 ± 31.2	466.3 ± 24.9[3]	455.7 ± 15.9[3]	487.2 ± 38.1	439.0 ± 22.9[3]	405.2 ± 24.3[3]
Holotranscobalamin (pmol/L)[2]	785	174.1 ± 12.7	140.4 ± 13.6	133.0 ± 5.9[3]	131.1 ± 9.9[3]	114.3 ± 6.5[3]	112.5 ± 9.0[3]
Homocysteine (μmol/L)[2]	813	8.6 ± 0.3	9.5 ± 0.3	9.4 ± 0.2	9.8 ± 0.3[3]	9.9 ± 0.3[3]	10.4 ± 0.5[3]
Vitamin C (ascorbic acid + dehydroascorbic acid, mg/dL)[4]	208	35.1 ± 2.2	30.2 ± 2.7	28.6 ± 1.5	29.0 ± 2.1	24.6 ± 2.0[3]	32.1 ± 2.0
Beta-carotene (all-trans, μmol/L)[4]	208	1.1 ± 0.1	0.6 ± 0.2[3]	0.7 ± 0.1[3]	0.6 ± 0.1[3]	0.8 ± 0.1	0.7 ± 0.1
Vitamin E (alpha-tocopherol, μmol/L)[4]	207	50.7 ± 4.3	39.8 ± 4.3	40.0 ± 2.2	43.3 ± 3.6	37.1 ± 2.7[3]	40.3 ± 2.8

[1] Means ± SEM, unless otherwise specified.
[2] Values from year 3 of the Health ABC study.
[3] Significantly different from the 'Healthy foods' cluster, $P \leq 0.05$ (Dunnett's test for continuous variables and chi-square test for categorical variables).
[4] Values from year 2 of the Health ABC study.

Table 4.17. Relative risk of all-cause mortality by dietary pattern cluster

	Healthy foods (n=374)	**High-fat dairy products** (n=332)	**Meat, fried foods, and alcohol** (n=693)	**Breakfast cereal** (n=386)	**Refined grains** (n=458)	**Sweets and desserts** (n=339)
All-cause mortality						
n (%)	77 (21.0)	109 (34.0)	209 (30.9)	105 (28.2)	135 (30.2)	104 (32.0)
Relative risk (95% CI)						
Model 1[1]	1.00	1.59 (1.19, 2.14)[2]	1.39 (1.06, 1.82)[2]	1.25 (0.93, 1.69)	1.32 (0.99, 1.76)	1.52 (1.13, 2.04)[2]
Model 2[3]	1.00	1.40 (1.04, 1.88)[2]	1.21 (0.92, 1.60)	1.16 (0.86, 1.56)	1.08 (0.80, 1.45)	1.37 (1.02, 1.86)[2]

[1] Adjusted for gender, age and race.
[2] Significantly different from the 'Healthy foods' cluster, $P \leq 0.05$ (Cox proportional hazards regression).
[3] Adjusted for gender, age, race, clinical site, education, physical activity, smoking status and total calorie intake.

Chapter 5: Summary and Implications

A) Summary

This study investigated the overall dietary patterns of a cohort of older adults, and examined relationships of dietary patterns with body composition, insulin sensitivity, systemic inflammation, and survival. The influence of a polymorphism in the peroxisome proliferator-activated receptor-γ (PPAR-γ) gene was explored.

A variety of distinct dietary patterns were identified, including a 'Healthy foods' pattern, high in fruit, vegetables, whole grains, poultry, fish and lowfat dairy products, and generally consistent with current dietary recommendations.

An interaction was found between dietary pattern and PPAR-γ Pro12Ala genotype in relation to body composition. Pro homozygous men and women in the 'Healthy foods' cluster did not differ significantly in any measures of body composition from those in other clusters, after adjustment for age, race, clinical site, education, physical activity, smoking and total calorie intake. Conversely, men with the Ala allele in the 'Healthy foods' cluster had significantly lower adiposity than those in other clusters. Men with the Ala allele in the 'Healthy foods' cluster had a significantly lower BMI, total percent body fat, sagittal diameter, and abdominal visceral and subcutaneous fat areas than those in the 'Meat, snacks, fats and alcohol' and 'Breakfast cereal' clusters. Men with the Ala allele in the 'Healthy foods' cluster also had a lower total percent body fat and sagittal diameter than those in the 'High-fat dairy products' cluster, and a smaller abdominal circumference than those in the 'Refined grains' cluster. Additionally, men with the Ala allele in the 'Healthy foods'

cluster had significantly less right thigh intermuscular fat than those in the 'Meat, snacks, fats and alcohol' cluster. On the other hand, women with the Ala allele in the 'Healthy foods' cluster had significantly less right thigh intermuscular fat than those in the 'High-fat dairy products' cluster, but showed no significant differences in any other measures of body composition from any other clusters.

The 'Healthy foods' cluster also had significantly lower fasting insulin and HOMA-IR values than both the 'Breakfast cereal' and 'High-fat dairy products' clusters, after adjusting for gender, age, race, clinical site, education, physical activity, smoking, total calorie intake and PPAR-γ genotype. No significant differences were found between the 'Healthy foods' and other clusters in fasting glucose or 2-hour glucose after adjusting for all covariates. With respect to inflammation, the 'Healthy foods' cluster had significantly lower levels of IL-6 than both the 'Sweets and desserts' and 'High-fat dairy products' clusters. No significant differences were seen between the 'Healthy foods' and other clusters in CRP or TNF-α after adjusting for all covariates.

The 'Healthy foods' cluster also had a significantly lower risk of mortality than the 'High-fat dairy products' and 'Sweets and desserts' clusters, after controlling for gender, age, race, clinical site, education, physical activity, smoking and total calorie intake. No significant differences in risk of mortality were seen between the 'Healthy foods' cluster and the 'Breakfast cereal' or 'Refined grains' clusters. Furthermore, the 'Healthy foods' cluster had more years of healthy life and more optimal levels of nutrition-related biomarkers than the other clusters.

While it is difficult to compare results of different dietary pattern studies, as derived patterns are unique to each study population, the current and previous studies have shown remarkable consistency in their findings. A dietary pattern consistent with current guidelines to consume relatively high amounts of vegetables, fruit, whole grains, poultry, fish and lowfat dairy products is associated with lower adiposity, lower systemic inflammation, higher insulin sensitivity, higher quality of life, more favorable nutritional status, and improved survival in older adults.

Strengths of this study include its focus on adults aged 70 and older, a little-studied population, and thorough assessment of participants' body composition, biochemical measures, genetic information, and health status. In addition, this study had a relatively long 10-year follow-up period, and evaluated many potential confounding variables, including genetic factors, which were not considered in previous studies. A possible limitation of this study is that the study population consisted of relatively well-functioning older adults, which may limit the applicability of findings to the well-functioning older adult population. Furthermore, as dietary patterns have been associated with specific lifestyles, it may be difficult to fully separate effects of diet from effects of physical activity and other lifestyle characteristics by statistical methods.

B) <u>Implications</u>

Studies that focus on single nutrients or foods in relation to complex health conditions may not provide the full context of the dietary impact. An observed association could be due to intake of the specific food or nutrient. However, the food

or nutrient could also be highly correlated with, or could be displacing, other, more relevant foods or nutrients in the diet, and thus lead to a false association. An assessment of the overall diet can provide a more complete picture of the dietary influence on health.

Future research to stem from this project could include investigation of additional genetic factors which may play a role in associations of diet with body composition and metabolic risk. Genome-wide association studies are increasing our knowledge of the genetic variants which may predispose individuals to common chronic diseases. New methods allow identification of up to 500,000 single nucleotide polymorphisms (SNPs) in an individual, and thus facilitate the identification of key SNPs that are likely to influence health. Further studies are needed to determine how dietary patterns affect the expression of relevant genes, and to examine which dietary patterns may be most protective of the genome. One challenge is finding the most appropriate way to analyze the complex relationships of multiple genes, diet, other relevant lifestyle factors, and health outcomes. Once the interactions between genetic variation and dietary patterns become more fully understood, dietary recommendations can be individualized according to specific genotypes (99).

Results of this study can encourage dietary interventions in older adults. Overall dietary patterns can be altered to reduce metabolic risk and improve quality of life and survival. Large-scale dietary interventions can also decrease the rising medical costs of diet-related chronic disease (100,101,102).

Dietary interventions can be targeted to groups according to their current dietary patterns. A substantial percentage of older adults in this study followed a dietary pattern high in vegetables, fruit, whole grains, poultry, fish and lowfat dairy products. Adherence to such a diet is a culturally acceptable and realistic recommendation for improved health and survival in the expanding older adult population.

Appendix A: Food grouping in the dietary pattern analysis

Food groups	Items
Processed meat	Bacon; breakfast sausage, including sausage biscuit; hot dogs; bologna, sliced ham, chicken salad, other lunch meats
Meat	Hamburgers, cheeseburgers, meat loaf; beef, including steak, roast, pot roast, or in a sandwich; pork, including chops, roast, pigs' feet, or dinner ham; mixed dishes with meat, such as corned beef hash, stuffed cabbage, pork chow mein, or frozen meals with meat
Liver and organ meat	Liver, including chicken liver or liverwurst
Fish and other seafood	Shellfish such as shrimp, scallops, crabs; tuna, tuna salad, tuna casserole; other fish, broiled or baked
Fish - fried	Fried fish or fried fish sandwich
Poultry	Chicken or turkey, roasted or broiled, including in sandwiches; chicken stew, chicken casserole, other mixed dishes such as chicken and dumplings, frozen meals with chicken, or chicken pot pies
Poultry – fried	Fried chicken
Eggs	Eggs, including biscuit sandwiches and Egg McMuffins
Lowfat dairy products	Lowfat yogurt or frozen yogurt; skim or 1% milk, chocolate milk or cocoa
Higher-fat dairy products	Cottage cheese; other cheese or cheese spreads, including in sandwiches; ice cream, ice milk, ice cream bars; 2% or whole milk, chocolate milk or cocoa; non-lowfat yogurt or frozen yogurt
Wine	Glasses of wine or wine coolers
Beer	Bottles or cans of beer
Liquor	Glasses or shots of liquor or mixed drinks
Tea	Cups of tea or iced tea (not herbal tea)
Coffee	Cups of coffee, regular or decaf
Fruit	Bananas; fresh apples or pears; oranges or tangerines (not juice); grapefruit (not juice); cantaloupe; raw peaches, apricots,

Food groups	Items
	nectarines; applesauce, fruit cocktail, canned pears; canned, frozen, or stewed peaches or apricots; any other fruit (grapes, honeydew, pineapple, strawberries)
Fruit juice	Orange juice or grapefruit juice; other fruit juices such as apple juice, prune juice, lemonade
Dark green vegetables	Broccoli; spinach; collards, mustard greens, turnip greens
Dark yellow vegetables	Sweet potatoes, yams; carrots, mixed vegetables containing carrots, or stews with carrots
Tomatoes and tomato products	Raw tomatoes; ketchup or salsa; tomato juice or V-8 juice
Salad greens	Green salad
Legumes	Baked beans, chili with beans, blackeyed peas, any other dried beans; soy milk
Other vegetables	Coleslaw, cabbage; corn; green beans or green peas; any other vegetable, such as okra, cooked green peppers, cooked onions
Potatoes	White potatoes (not fried) including boiled, baked, and mashed, potato salad
French fries	French fries and fried potatoes
Whole grains	Whole wheat, rye, or other dark breads
Cold breakfast cereal – fiber/bran	Fiber or bran cereals
Other cold breakfast cereal	Product 19, Just Right or Total cereal; cold cereals such as Corn Flakes, Cheerios, Special K
Refined grains	Pancakes, waffles, or French toast; biscuits, muffins; rolls, hamburger buns, English muffins, bagels; white bread, including French, Italian, or in sandwiches; corn bread, corn muffins, hush puppies; crackers; cooked cereals such as oatmeal, cream of wheat or grits
Rice, pasta, and mixed dishes	Rice or dishes made with rice; spaghetti or other pasta with tomato sauce, such as lasagna; cheese dishes without tomato sauce, such as macaroni and cheese, or cheese grits; stuffing or dressing
Pizza	Pizza

Food groups	Items
Snacks	Snacks, such as potato chips, corn chips, and popcorn (not pretzels)
Nuts	Peanut butter; peanuts, pecans, other nuts or seeds
High-calorie drinks	Hi-C, Kool-Aid, or other drinks with added vitamin C; regular soft drinks, or bottled sweetened teas (not diet)
Meal replacement food products	Instant breakfast milkshakes such as Carnation, diet shakes such as SlimFast, or liquid supplements such as Ensure
Mayonnaise and salad dressing	Salad dressing; mayonnaise, sandwich spreads
Soup	Vegetable, vegetable beef, chicken vegetable, or tomato soup; other soups, such as chicken noodle, chowder
Sweets and desserts	Doughnuts, danish pastry; cake, sweet rolls, coffee cake; cookies; pumpkin pie, sweet potato pie; any other pies or cobbler; pudding; chocolate candy, candy bars
Miscellaneous sugar	Sugar or honey in coffee, tea, or on cereal
Miscellaneous fat	Butter or margarine on bread, potatoes, vegetables, etc.; gravy; cream; olive oil or canola oil; corn oil, vegetable oil; lard, fatback, bacon fat; Crisco

References

1. U.S. Census Bureau. IDB Data - IDB Aggregation - Table 094. http://www.census.gov/ipc/www/idb/tables.html#region (accessed September 16, 2008).

2. U.S. Census Bureau. An Older and More Diverse Nation by Midcentury. http://www.census.gov/Press-Release/www/releases/archives/population/012496.html (accessed September 16, 2008).

3. Gorina Y, Hoyert D, Lentzner H, Goulding M. Trends in causes of death among older persons in the United States. Aging Trends, No 6. Hyattsville, Maryland: National Center for Health Statistics. 2006.

4. Knowler WC, Barrett-Connor E, Fowler SE et al.; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002 Feb 7;346(6):393-403.

5. Ilanne-Parikka P, Eriksson JG, Lindström J et al.; Finnish Diabetes Prevention Study Group. Effect of lifestyle intervention on the occurrence of metabolic syndrome and its components in the Finnish Diabetes Prevention Study. Diabetes Care. 2008 Apr;31(4):805-7.

6. Corpeleijn E, Feskens EJ, Jansen EH et al. Improvements in glucose tolerance and insulin sensitivity after lifestyle intervention are related to changes in serum fatty acid profile and desaturase activities: the SLIM study. Diabetologia. 2006 Oct;49(10):2392-401.

7. U.S. Census Bureau. 2008 National Population Projections Tables and Charts. http://www.census.gov/population/www/projections/tablesandcharts.html (accessed September 16, 2008).

8. Blüher M. The inflammatory process of adipose tissue. Pediatr Endocrinol Rev. 2008 Sep;6(1):24-31.

9. de Ferranti S, Mozaffarian D. The perfect storm: obesity, adipocyte dysfunction, and metabolic consequences. Clin Chem. 2008 Jun;54(6):945-55.

10. Rana JS, Nieuwdorp M, Jukema JW, Kastelein JJ. Cardiovascular metabolic syndrome - an interplay of obesity, inflammation, diabetes and coronary heart disease. Diabetes Obes Metab. 2007 May;9(3):218-32.

11. Ledikwe JH, Smiciklas-Wright H, Mitchell DC, Miller CK, Jensen GL. Dietary patterns of rural older adults are associated with weight and nutritional status. J Am Geriatr Soc. 2004 Apr;52(4):589-95.

12. Newby PK, Muller D, Hallfrisch J, Andres R, Tucker KL. Food patterns measured by factor analysis and anthropometric changes in adults. Am J Clin Nutr. 2004 Aug;80(2):504-13.

13. Liese AD, Schulz M, Moore CG, Mayer-Davis EJ. Dietary patterns, insulin sensitivity and adiposity in the multi-ethnic Insulin Resistance Atherosclerosis Study population. Br J Nutr. 2004 Dec;92(6):973-84.

14. Villegas R, Salim A, Flynn A, Perry IJ. Prudent diet and the risk of insulin resistance. Nutr Metab Cardiovasc Dis. 2004 Dec;14(6):334-43.

15. McNaughton SA, Mishra GD, Brunner EJ. Dietary patterns, insulin resistance and incidence of type 2 diabetes in the Whitehall II study. Diabetes Care. 2008 Apr 4.

16. Esmaillzadeh A, Kimiagar M, Mehrabi Y, Azadbakht L, Hu FB, Willett WC. Dietary patterns, insulin resistance, and prevalence of the metabolic syndrome in women. Am J Clin Nutr. 2007 Mar;85(3):910-8.

17. Fung TT, Rimm EB, Spiegelman D et al. Association between dietary patterns and plasma biomarkers of obesity and cardiovascular disease risk. Am J Clin Nutr. 2001 Jan;73(1):61-7.

18. Wirfält E, Hedblad B, Gullberg B et al. Food patterns and components of the metabolic syndrome in men and women: a cross-sectional study within the Malmö Diet and Cancer cohort. Am J Epidemiol. 2001 Dec 15;154(12):1150-9.

19. Esmaillzadeh A, Kimiagar M, Mehrabi Y, Azadbakht L, Hu FB, Willett WC. Dietary patterns and markers of systemic inflammation among Iranian women. J Nutr. 2007 Apr;137(4):992-8.

20. Nettleton JA, Steffen LM, Mayer-Davis EJ et al. Dietary patterns are associated with biochemical markers of inflammation and endothelial activation in the Multi-Ethnic Study of Atherosclerosis (MESA). Am J Clin Nutr. 2006 Jun;83(6):1369-79.

21. Lopez-Garcia E, Schulze MB, Fung TT et al. Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction. Am J Clin Nutr. 2004 Oct;80(4):1029-35.

22. Nanri A, Yoshida D, Yamaji T, Mizoue T, Takayanagi R, Kono S. Dietary patterns and C-reactive protein in Japanese men and women. Am J Clin Nutr. 2008 May;87(5):1488-96.

23. Bamia C, Trichopoulos D, Ferrari P et al. Dietary patterns and survival of older Europeans: the EPIC-Elderly Study (European Prospective Investigation into Cancer and Nutrition). Public Health Nutr. 2007 Jun;10(6):590-8.

24. Osler M, Heitmann BL, Gerdes LU, Jorgensen LM, Schroll M. Dietary patterns and mortality in Danish men and women: a prospective observational study. Br J Nutr. 2001 Feb;85(2):219-25.

25. Knoops KT, de Groot LC, Kromhout D et al. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project. JAMA. 2004 Sep 22;292(12):1433-9.

26. Huijbregts P, Feskens E, Rasanen L et al. Dietary pattern and 20 year mortality in elderly men in Finland, Italy, and The Netherlands: longitudinal cohort study.BMJ. 1997 Jul 5;315(7099):13-7.

27. Kant AK, Schatzkin A, Graubard BI, Schairer C. A prospective study of diet quality and mortality in women. JAMA. 2000 Apr 26;283(16):2109-15.

28. Hoffmann K, Boeing H, Boffetta P et al. Comparison of two statistical approaches to predict all-cause mortality by dietary patterns in German elderly subjects. Br J Nutr. 2005 May;93(5):709-16.

29. Diehr P, Beresford SA. The relation of dietary patterns to future survival, health, and cardiovascular events in older adults. J Clin Epidemiol. 2003 Dec;56(12):1224-35.

30. Trichopoulou A, Kouris-Blazos A, Wahlqvist ML et al. Diet and overall survival in elderly people. BMJ. 1995 Dec 2;311(7018):1457-60.

31. Masala G, Ceroti M, Pala V et al. A dietary pattern rich in olive oil and raw vegetables is associated with lower mortality in Italian elderly subjects. Br J Nutr. 2007 Aug;98(2):406-15.

32. Waijers PM, Ocke MC, van Rossum CT et al. Dietary patterns and survival in older Dutch women. Am J Clin Nutr. 2006 May;83(5):1170-6.

33. Harriss LR, English DR, Powles J et al. Dietary patterns and cardiovascular mortality in the Melbourne Collaborative Cohort Study. Am J Clin Nutr. 2007 Jul;86(1):221-9.

34. Menotti A, Kromhout D, Blackburn H, Fidanza F, Buzina R, Nissinen A. Food intake patterns and 25-year mortality from coronary heart disease: cross-cultural correlations in the Seven Countries Study. The Seven Countries Study Research Group. Eur J Epidemiol. 1999 Jul;15(6):507-15.

35. Knoops KT, Groot de LC, Fidanza F, Alberti-Fidanza A, Kromhout D, van Staveren WA. Comparison of three different dietary scores in relation to 10-year

mortality in elderly European subjects: the HALE project. Eur J Clin Nutr. 2006 Jun;60(6):746-55.

36. Kant AK, Graubard BI, Schatzkin A. Dietary patterns predict mortality in a national cohort: the National Health Interview Surveys, 1987 and 1992. J Nutr. 2004 Jul;134(7):1793-9.

37. Tuomilehto J, Lindstrom J, Eriksson JG et al.; Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001 May 3;344(18):1343-50.

38. O'Rahilly S, Barroso I, Wareham NJ. Genetic factors in type 2 diabetes: the end of the beginning? Science. 2005 Jan 21;307(5708):370-3.

39. Uusitupa M. Gene-diet interaction in relation to the prevention of obesity and type 2 diabetes: evidence from the Finnish Diabetes Prevention Study. Nutr Metab Cardiovasc Dis. 2005 Jun;15(3):225-33.

40. Memisoglu A, Hu FB, Hankinson SE et al. Interaction between a peroxisome proliferator-activated receptor gamma gene polymorphism and dietary fat intake in relation to body mass. Hum Mol Genet. 2003 Nov 15;12(22):2923-9.

41. Robitaille J, Despres JP, Perusse L, Vohl MC. The PPAR-gamma P12A polymorphism modulates the relationship between dietary fat intake and components of the metabolic syndrome: results from the Quebec Family Study. Clin Genet. 2003 Feb;63(2):109-16.

42. Luan J, Browne PO, Harding AH et al. Evidence for gene-nutrient interaction at the PPARgamma locus. Diabetes. 2001 Mar;50(3):686-9.

43. Lindi VI, Uusitupa MI, Lindstrom J et al.; Finnish Diabetes Prevention Study. Association of the Pro12Ala polymorphism in the PPAR-gamma2 gene with 3-year incidence of type 2 diabetes and body weight change in the Finnish Diabetes Prevention Study. Diabetes. 2002 Aug;51(8):2581-6.

44. Nicklas BJ, van Rossum EF, Berman DM, Ryan AS, Dennis KE, Shuldiner AR. Genetic variation in the peroxisome proliferator-activated receptor-gamma2 gene (Pro12Ala) affects metabolic responses to weight loss and subsequent weight regain. Diabetes. 2001 Sep;50(9):2172-6.

45. Marin C, Perez-Jimenez F, Gomez P et al. The Ala54Thr polymorphism of the fatty acid-binding protein 2 gene is associated with a change in insulin sensitivity after a change in the type of dietary fat. Am J Clin Nutr. 2005 Jul;82(1):196-200.

46. Altshuler D, Hirschhorn JN, Klannemark M et al. The common PPARgamma Pro12Ala polymorphism is associated with decreased risk of type 2 diabetes. Nat Genet. 2000 Sep;26(1):76-80.

47. Pihlajamaki J, Vanhala M, Vanhala P, Laakso M. The Pro12Ala polymorphism of the PPAR gamma 2 gene regulates weight from birth to adulthood. Obes Res. 2004 Feb;12(2):187-90.

48. Gonzalez Sanchez JL, Serrano Rios M, Fernandez Perez C, Laakso M, Martinez Larrad MT. Effect of the Pro12Ala polymorphism of the peroxisome proliferator-activated receptor gamma-2 gene on adiposity, insulin sensitivity and lipid profile in the Spanish population. Eur J Endocrinol. 2002 Oct;147(4):495-501.

49. Buzzetti R, Petrone A, Ribaudo MC et al. The common PPAR-gamma2 Pro12Ala variant is associated with greater insulin sensitivity. Eur J Hum Genet. 2004 Dec;12(12):1050-4.

50. Sramkova D, Kunesova M, Hainer V, Hill M, Vcelak J, Bendlova B. Is a Pro12Ala polymorphism of the PPARgamma2 gene related to obesity and type 2 diabetes mellitus in the Czech population? Ann N Y Acad Sci. 2002 Jun;967:265-73.

51. Kao WH, Coresh J, Shuldiner AR, Boerwinkle E, Bray MS, Brancati FL; Atherosclerosis Risk in Communities Study. Pro12Ala of the peroxisome proliferator-activated receptor-gamma2 gene is associated with lower serum insulin levels in nonobese African Americans: the Atherosclerosis Risk in Communities Study. Diabetes. 2003 Jun;52(6):1568-72.

52. Memisoglu A, Hu FB, Hankinson SE et al. Prospective study of the association between the proline to alanine codon 12 polymorphism in the PPARgamma gene and type 2 diabetes. Diabetes Care. 2003 Oct;26(10):2915-7.

53. Ghoussaini M, Meyre D, Lobbens S et al. Implication of the Pro12Ala polymorphism of the PPAR-gamma 2 gene in type 2 diabetes and obesity in the French population. BMC Med Genet. 2005 Mar 22;6:11.

54. Deeb SS, Fajas L, Nemoto M et al. A Pro12Ala substitution in PPARgamma2 associated with decreased receptor activity, lower body mass index and improved insulin sensitivity. Nat Genet. 1998 Nov;20(3):284-7.

55. Masugi J, Tamori Y, Mori H, Koike T, Kasuga M. Inhibitory effect of a proline-to-alanine substitution at codon 12 of peroxisome proliferator-activated receptor-gamma 2 on thiazolidinedione-induced adipogenesis. Biochem Biophys Res Commun. 2000 Feb 5;268(1):178-82.

56. Yamauchi T, Kamon J, Waki H et al. The mechanisms by which both heterozygous peroxisome proliferator-activated receptor gamma (PPARgamma) deficiency and PPARgamma agonist improve insulin resistance. J Biol Chem. 2001 Nov 2;276(44):41245-54.

57. Sahyoun NR, Anderson AL, Kanaya AM et al. Dietary glycemic index and load, measures of glucose metabolism, and body fat distribution in older adults.Am J Clin Nutr. 2005 Sep;82(3):547-52.

58. Adams KF, Schatzkin A, Harris TB et al. Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. N Engl J Med. 2006 Aug 24;355(8):763-78.

59. Moore SC, Mayne ST, Graubard BI et al. Past body mass index and risk of mortality among women. Int J Obes (Lond). Epub 2008 Jan 22.

60. Wannamethee SG, Shaper AG, Lennon L, Whincup PH. Decreased muscle mass and increased central adiposity are independently related to mortality in older men. Am J Clin Nutr. 2007 Nov;86(5):1339-46.

61. Zhang X, Shu XO, Yang G et al. Abdominal adiposity and mortality in Chinese women. Arch Intern Med. 2007 May 14;167(9):886-92.

62. Lindqvist P, Andersson K, Sundh V, Lissner L, Björkelund C, Bengtsson C. Concurrent and separate effects of body mass index and waist-to-hip ratio on 24-year mortality in the Population Study of Women in Gothenburg: evidence of age-dependency. Eur J Epidemiol. 2006;21(11):789-94.

63. Turcato E, Bosello O, Di Francesco V et al. Waist circumference and abdominal sagittal diameter as surrogates of body fat distribution in the elderly: their relation with cardiovascular risk factors. Int J Obes Relat Metab Disord. 2000 Aug;24(8):1005-10.

64. Menke A, Muntner P, Wildman RP, Reynolds K, He J. Measures of adiposity and cardiovascular disease risk factors. Obesity (Silver Spring). 2007 Mar;15(3):785-95.

65. Canizales-Quinteros S, Aguilar-Salinas CA, Ortiz-López MG et al. Association of PPARG2 Pro12Ala variant with larger body mass index in Mestizo and Amerindian populations of Mexico. Hum Biol. 2007 Feb;79(1):111-9.

66. Kim K, Lee S, Valentine RJ. Association of pro12Ala polymorphism in the peroxisome proliferative-activated receptor gamma2 gene with obesity and hypertension in Korean women. J Nutr Sci Vitaminol (Tokyo). 2007 Jun;53(3):239-46.

67. Danawati CW, Nagata M, Moriyama H et al. A possible association of Pro12Ala polymorphism in peroxisome proliferator-activated receptor gamma2 gene with obesity in native Javanese in Indonesia. Diabetes Metab Res Rev. 2005 Sep-Oct;21(5):465-9.

68. Kim KS, Choi SM, Shin SU, Yang HS, Yoon Y. Effects of peroxisome proliferator-activated receptor-gamma 2 Pro12Ala polymorphism on body fat distribution in female Korean subjects. Metabolism. 2004 Dec;53(12):1538-43.

69. Kawasaki I, Tahara H, Emoto M et al. Impact of Prol2Ala variant in the peroxisome proliferator-activated receptor (PPAR) gamma2 on obesity and insulin resistance in Japanese Type 2 diabetic and healthy subjects. Osaka City Med J. 2002 Jun;48(1):23-8.

70. Nelson TL, Fingerlin TE, Moss L, Barmada MM, Ferrell RE, Norris JM. The PPARgamma Pro12Ala polymorphism is not associated with body mass index or waist circumference among Hispanics from Colorado. Ann Nutr Metab. 2007;51(3):252-7.

71. Newby PK, Muller D, Hallfrisch J, Qiao N, Andres R, Tucker KL. Dietary patterns and changes in body mass index and waist circumference in adults. Am J Clin Nutr. 2003 Jun;77(6):1417-25.

72. Tucker KL, Chen H, Hannan MT et al. Bone mineral density and dietary patterns in older adults: the Framingham Osteoporosis Study. Am J Clin Nutr. 2002 Jul;76(1):245-52.

73. Hill JO, Sidney S, Lewis CE, Tolan K, Scherzinger AL, Stamm ER. Racial differences in amounts of visceral adipose tissue in young adults: the CARDIA (Coronary Artery Risk Development in Young Adults) study. Am J Clin Nutr. 1999 Mar;69(3):381-7.

74. Taylor HL, Jacobs DR Jr, Schucker B, Knudsen J, Leon AS, Debacker G. A questionnaire for the assessment of leisure time physical activities. J Chronic Dis. 1978;31(12):741-55.

75. Health, Aging and Body Composition Study. https://psg-mac43.ucsf.edu/ucsf_cc/version3.1/habc/genetrackinglog.asp (accessed December 11, 2007).

76. Adamo KB, Dent R, Langefeld CD et al. Peroxisome proliferator-activated receptor gamma 2 and acyl-CoA synthetase 5 polymorphisms influence diet response. Obesity (Silver Spring). 2007 May;15(5):1068-75.

77. Franks PW, Jablonski KA, Delahanty L et al; Diabetes Prevention Program Research Group. The Pro12Ala variant at the peroxisome proliferator-activated receptor gamma gene and change in obesity-related traits in the Diabetes Prevention Program. Diabetologia. 2007 Dec;50(12):2451-60.

78. Vaccaro O, Lapice E, Monticelli A et al. Pro12Ala polymorphism of the PPARgamma2 locus modulates the relationship between energy intake and body weight in type 2 diabetic patients. Diabetes Care. 2007 May;30(5):1156-61.

79. Pai JK, Pischon T, Ma J et al. Inflammatory markers and the risk of coronary heart disease in men and women. N Engl J Med. 2004 Dec 16;351(25):2599-610.

80. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. JAMA. 2001 Jul 18;286(3):327-34.

81. Guest CB, Park MJ, Johnson DR, Freund GG. The implication of proinflammatory cytokines in type 2 diabetes. Front Biosci. 2008 May 1;13:5187-94.

82. Health, Aging and Body Composition Study Operations Manual. Internet: https://psg-mac43.ucsf.edu (accessed June 17, 2008).

83. Qatanani M, Lazar MA. Mechanisms of obesity-associated insulin resistance: many choices on the menu. Genes Dev. 2007 Jun 15;21(12):1443-55.

84. Centers for Disease Control and Prevention. Public health and aging: trends in aging--United States and worldwide. JAMA. 2003 Mar 19;289(11):1371-3.

85. Osler M, Schroll M. Diet and mortality in a cohort of elderly people in a north European community. Int J Epidemiol. 1997 Feb;26(1):155-9.

86. Lagiou P, Trichopoulos D, Sandin S et al. Mediterranean dietary pattern and mortality among young women: a cohort study in Sweden. Br J Nutr. 2006 Aug;96(2):384-92.

87. Seymour JD, Calle EE, Flagg EW, Coates RJ, Ford ES, Thun MJ; American Cancer Society. Diet Quality Index as a predictor of short-term mortality in the American Cancer Society Cancer Prevention Study II Nutrition Cohort. Am J Epidemiol. 2003 Jun 1;157(11):980-8.

88. Refsum H, Smith AD. Low vitamin B-12 status in confirmed Alzheimer's disease as revealed by serum holotranscobalamin. J Neurol Neurosurg Psychiatry. 2003 Jul;74(7):959-61.

89. Clarke R, Refsum H, Birks J et al. Screening for vitamin B12 and folate deficiency in older people. Am J Clin Nutr 2003;77:1241–7.

90. Prins ND, den Heijer T, Hofman A et al. Homocysteine and cognitive function in the elderly. The Rotterdam Study. Neurology 2002;59:1375–80.

91. Seshadri S, Beiser A, Selhub J et al. Plasma homocysteine as a risk factor for dementia and Alzheimer's disease.NEngl J Med 2002;346:476–83.

92. The Homocysteine Studies Collaboration. Homocysteine and risk of ischemic heart disease and stroke: a meta-analysis. JAMA. 2002;288:2015–22.

93. Clarke R, Birks J, Nexo E et al. Low vitamin B-12 status and risk of cognitive decline in older adults. Am J Clin Nutr. 2007 Nov;86(5):1384-91.

94. Dangour AD, Breeze E, Clarke R, Shetty PS, Uauy R, Fletcher AE. Plasma homocysteine, but not folate or vitamin B-12, predicts mortality in older people in the United Kingdom. J Nutr. 2008 Jun;138(6):1121-8.

95. van't Veer P, Jansen MC, Klerk M, Kok FJ. Fruits and vegetables in the prevention of cancer and cardiovascular disease. Public Health Nutr. 2000 Mar;3(1):103-7.

96. Lonn E, Bosch J, Yusuf S et al.; HOPE and HOPE-TOO Trial Investigators. Effects of long-term vitamin E supplementation on cardiovascular events and cancer: a randomized controlled trial. JAMA. 2005 Mar 16;293(11):1338-47.

97. Gao X, Martin A, Lin H, Bermudez OI, Tucker KL. Alpha-Tocopherol intake and plasma concentration of Hispanic and non-Hispanic white elders is associated with dietary intake pattern. J Nutr. 2006 Oct;136(10):2574-9.

98. U.S. Department of Health and Human Services. Healthy people 2010. Internet: http://www.healthypeople.gov/About/goals.htm (accessed September 11, 2008).

99. Mead MN. Nutrigenomics: the genome-food interface. Environ Health Perspect. 2007 Dec;115(12):A582-9.

100. American Diabetes Association. Direct and Indirect Costs of Diabetes in the United States. http://www.diabetes.org/diabetes-statistics/cost-of-diabetes-in-us.jsp (accessed September 25, 2008).

101. World Health Organization (WHO). Preventing chronic disease: a vital investment. Geneva: WHO; 2005.

102. Centers for Disease Control and Prevention. Overweight and obesity. Economic consequences.

http://www.cdc.gov/nccdphp/dnpa/obesity/economic_consequences.htm (accessed September 25, 2008).