Effects of fish oil on ventricular tachyarrhythmia in patients with implantable defibrillators: A pooled analysis

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published in
Circulation
2007

document version
Publisher's PDF, also known as Version of record

Oral Presentations

1

Metabolic Syndrome (MetS) in Young Adulthood and Incident Diabetes in Middle Age: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

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Background: Several studies have shown that MetS is associated with type-2 diabetes in middle and older age. Little is known about MS in young adulthood and early development of diabetes. **Objectives**: To examine the relationship between baseline MetS and incidence of type-2 diabetes during the 20 years of follow-up in the CARDIA Study. **Methods**: CARDIA is a NHLBI sponsored multi-center longitudinal study on evolution of the cardiovascular risk factors in young adults. The sample consists of 4,656 black and white men and women ages 18 to 30 years who were not diabetic at baseline (1985–86). MetS is defined based on the modified NCEP-ATPIII criteria and incident diabetes is defined as a fasting glucose $\geq$126 mg/dl or on diabetes medication at any of the six follow-up examinations (Year 2, 5, 7, 10, 15 and 20). **Results**: Among the 106 participants with MetS at baseline (2.3%), only 6.7% were not overweight (i.e., BMI $<$25 kg/m^2). After 20 years of follow-up, when the average age of the cohort was 44, the incidence rate of type-2 diabetes for participants free of MetS at baseline is 3.2 per 1,000 person-years compared to 25.6 per 1,000 person-years for participants with MetS at baseline. Gender-race specific incidence rates are 26.4, 30.7, 29.8, and 11.5 per 1,000 person-years for black men, white men, black women, and white women, respectively. The age, race, gender-adjusted hazard ratio (HR) for incident type-2 diabetes of baseline MetS is 8.8 ($p < 0.001$); the corresponding age-adjusted HRs are 6.9, 15.4, 6.3 and 7.3 (all $p < 0.001$) for black men, white men, black women and white women, respectively. **Conclusion**: MetS in young adulthood is strongly associated with the development of type-2 diabetes in early middle age. To control the epidemic of diabetes, efforts starting at a young age are needed to prevent the development of MetS.

2

Development of the Metabolic Syndrome Through Menopause: The Study of Women's Health Across the Nation (SWAN)

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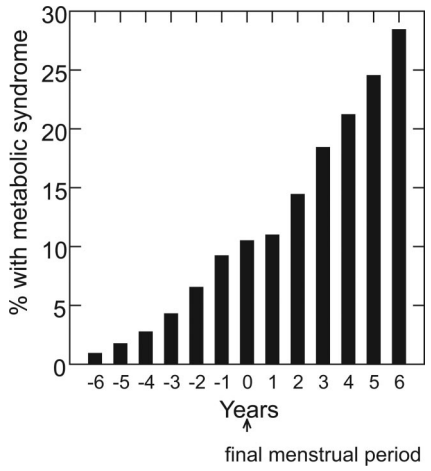
Background. Cross-sectional studies suggest an age-independent association between menopausal status and prevalence of metabolic syndrome (MetS). Using a longitudinal design, we hypothesized that MetS increases with progression through the menopause and that increasing androgenicity accounts for this increase. **Methods**. This is a longitudinal, 7-year study of 839 women in SWAN who reached natural menopause and never took hormone therapy. Data were anchored at time of final menstrual period (FMP). All models included age, ethnicity, study site, smoking, Framingham Risk Score, baseline BMI, BMI change, and the respective hormone (SHBG, free androgen index, estradiol) at baseline and its change from baseline. Generalized estimating equations and repeated measures mixed models were used. **Results**. The figure shows that MetS increases with progression through menopause ($p<.0001$). At FMP, 10% had a new onset of MetS after adjusting for covariates. The final model showed that the odds of MetS increased by 24% for every SD decrease in SHBG over time ($p=0.004$). Unadjusted Spearman correlations between SHBG and components of MetS were all significant ($p<.0001$). In adjusted models, SHBG was predictive only of waist circumference and HDL. **Conclusions**. As SHBG declines over the menopausal transition, the prevalence of MetS increases, independently of age and other important covariates. Since SHBG may be a marker of the androgen/estrogen balance, these data suggest that CVD in women results from menopause-related increasing androgenicity of the hormonal milieu. SWAN has support from grants NR004061; AG012505, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495.



3

Association Between Fitness and Incident Diabetes Over 20 Years in Young- to Middle-Aged Adults: CARDIA Fitness Study

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Background: Cardiorespiratory fitness (CRF) is inversely associated with the development of type 2 diabetes (DM) in longitudinal studies. The few prior studies with repeated measures of CRF demonstrate that improvements in CRF are associated with a lower incidence of DM as compared with declining CRF. In a longitudinal study of adults initially aged 18 to 30, we tested the hypothesis that baseline CRF is inversely associated with the 20-year incidence of DM, and that marked declines CRF are associated with a higher incidence of DM. **Methods**: In 1985–86 (baseline) and 2005–06 (year 20), 2048 men and women (59%) from the Coronary Artery Risk Development in Young Adults (CARDIA) study achieved $>=$85% of their age-predicted heart rate (HR) maximum during symptom-limited graded exercise treadmill (GXT) testing. GXT duration was used to estimate CRF; change in CRF was defined as the difference in CRF between baseline and year 20. Incident DM is defined as fasting glucose $>=$126 mg/dL or the use of DM control medications among those free from DM at baseline. **Results**: Over 20 years, 120 (5.9%) persons developed DM. Mean GXT duration (minutes) at baseline was 9.0 (SD $=$2.2) in women and 12.3 (SD $=$ 2.0) in men. For each 2.7 (SD) minutes shorter GXT duration at baseline, the Cox proportional hazard ratio of developing incident DM is 1.48 (95% CI: 1.19, 1.85) higher, adjusted for age, sex, race, baseline body mass index (BMI) and 20-year BMI change. GXT duration declined 3.1 minutes (SD $=$ 1.9) in over 20 years, or 29% (SD $=$ 19%). The incidence of DM was highest in participants with the greatest declines in CRF (Table). **Conclusions**: A single measure of CRF demonstrates a strong inverse association with incident DM. On average, CRF declines over 20-years in healthy adults, but a significantly elevated risk of developing DM is restricted to those with the greatest declines in CRF. This effect is partially confounded by changes in BMI.

Table: Odds Ratios (95% Confidence Intervals) of Incident Diabetes by Quartiles* of Percent Change in Cardiorespiratory Fitness (CRF) Over 20 Years

% Change in CRF	Quartile 1 (212% to -19%)	Quartile 2 (<-19% to -30%)	Quartile 3 (<-30% to -41%)	Quartile 4 (<-41% to -81%)
N events (%)	21 (4.1%)	15 (2.9%)	30 (6%)	54 (10.6%)
Model 1	1 (Ref)	0.68 (0.34, 1.33)	1.33 (0.75, 2.37)	2.33 (1.38, 3.96)
Model 2	1 (Ref)	0.76 (0.38, 1.51)	1.38 (0.76, 2.51)	1.96 (1.13, 3.39)
Model 3	1 (Ref)	0.71 (0.35, 1.42)	1.20 (0.65, 2.23)	1.51 (0.81, 2.82)

*512 participants per quartile; Model 1: Adjusted for age, race (black vs. white), sex; Model 2: Adjusted for Model 1 + baseline BMI; Model 3: Adjusted for Model 2 + BMI change

4

Initial Body Mass Index in Young Adults Predicts 20-Year Risk of Incident Diabetes: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

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Objectives: Increases in prevalence of overweight/obesity have led to projections of a disturbing rise in Type-2 diabetes. We used data from the CARDIA Study to examine the roles of initial body mass index (BMI) and 20-year change in BMI in risk of incident diabetes among normal ($18.5\leq$BMI<25), overweight ($25\leq$BMI<30), and moderately obese ($30\leq$BMI<35) African-American and white adults, initially aged 18–30 in 1985–86. **Methods**: Incident diabetes is defined as fasting glucose$>$126 mg/dL or on diabetes medication at any follow-up exam (Year 2, 5, 7, 10, 15 and 20). Change in BMI is defined as (1) increased ($>$2 kg/m^2 increase by Year 20), (2) stable/decreased ($>$2 kg/m^2 decrease by Year 20 or baseline BMI $\pm$2 kg/m^2 at every exam), (3) fluctuating ($\pm$2 kg/m^2 of baseline BMI at Year 20 but $\geq$1 interim BMI$>$2 kg/m^2 from baseline). After exclusions (diabetes at baseline and participants who at any exam were pregnant or missing data), 142 of 2156 adults had incident diabetes. **Results**: At baseline, 68%, 26%, and 5% were normal, overweight, or obese, respectively. BMI increased over 20 years in most adults in all baseline BMI groups (74%, 78%, and 100% respectively) while only 16%, 9% and 0%, respectively, had stable/decreased BMI. Among normal weight young adults at baseline, risk of incident diabetes did not differ for those whose BMI increased or fluctuated vs. remained stable/decreased (Table). However for those already overweight or obese at baseline, increased or fluctuating BMI substantially increased risk of incident diabetes (7–23 fold higher). Very few overweight adults maintained stable BMI, which may explain why diabetes risk, although elevated, was not statistically significant. **Conclusions**: Our

data suggest that to avoid a diabetes epidemic among middle-age adults, prevention of overweight/obesity before or early in adulthood may be pivotal. Preventing additional weight gain in young adults already overweight may further reduce diabetes risk.

Table: Hazard Ratios (95% Confidence Interval) for Incident Diabetes by Baseline BMI and 20-Year Change in BMI

Baseline BMI	BMI Change	n	Hazard Ratio*	95% CI
Normal	Stable	230	1.0	
Normal	Increased	1091	2.6	0.8–8.5
Normal	Fluctuating	149	1.5	0.3–7.6
Overweight	Stable	53	2.7	0.4–16.1
Overweight	Increased	448	7.4	2.3–23.9
Overweight	Fluctuating	71	11.2	3.1–40.4
Obese	Increased	114	23.5	7.2–77.3

* Age-, race-, gender-adjusted

5

Absolute Risk of CHD and Diabetes Varies Considerably as a Function of the Presence of Specific Components of the Metabolic Syndrome

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Although the link between metabolic syndrome (MetS) and both coronary heart disease (CHD) and diabetes mellitus (DM) is well-established, few studies have investigated the variability in absolute risk as a function of the component composition among adults with MetS. Such information can be used to identify relatively higher-risk subgroups for CHD and DM prevention among the overall MetS population. **Methods**: Current NIH-AHA criteria for MetS ($\geq$3 of large waist, low HDL, high triglycerides, high blood pressure, and impaired fasting glucose) were applied to 12,213 black and white middle-aged individuals free of baseline CHD and DM in the Atherosclerosis Risk in Communities Study. Baseline exams were conducted from 1987–89 and CHD ascertainment was complete through 2002. DM status was ascertained at triennial follow-up exams over 9 years with data analyzed using interval-censored event times. Incidence rates (IR) per 1,000 person-yrs for CHD and DM were estimated using Poisson regression, adjusted for age, sex, race and ARIC field center. **Results**: During follow-up, (mean 13 yrs), 1,196 CHD events occurred. The CHD IR was significantly higher among subjects with MetS (10.0 vs 6.2, $p<0.0001$). IRs of CHD as a function of MetS component composition (all combinations of 3, 4, or 5 factors) ranged from a low of 5.4 (95% CI: 2.6, 11.3) to a high of 13.8 (9.9, 19.4) and tended to increase with increasing number of components. Independent of the number of components present, among subjects with MetS, the IR of CHD was 28% higher among those with low HDL than without, and 23% higher among those with elevated BP than without. The incidence rate of diabetes was also higher among subjects with versus without MetS (35.0 vs 7.3, $p<0.0001$). IRs for diabetes as a function of MetS component composition ranged from a low of 5.4 (95% CI: 2.2, 12.9) to a high of 70.0 (95% CI: 57.7, 80.1). Independent of the number of components present, among subjects with MetS, the IR of DM was nearly 4-fold higher among those with impaired fasting glucose than without (45.1 vs. 12.5) and 70% higher among those with large waist than without. **Conclusion**: Clinicians screening patients for MetS should be aware that CHD and DM risk varies considerably as a function of both the number, and composition, of MetS components.

6

Hemoblobin A1c as a Risk Factor for Heart Failure Among Persons with Diabetes: The Atherosclerosis Risk in Communities (ARIC) Study

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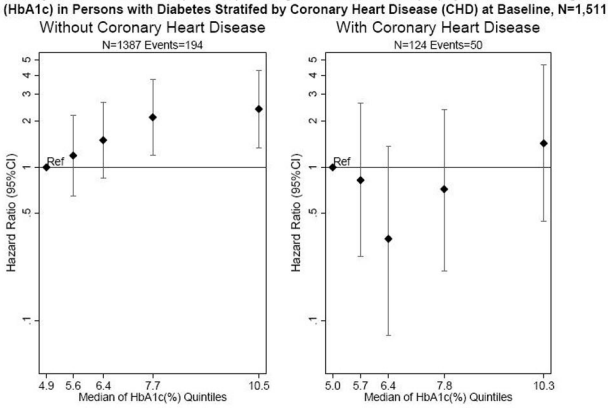
Background: Hemoglobin A1c (A1c) reflects long-term glycemic control. Two cohorts (Kaiser and UKPDS) suggest A1c is a risk factor for HF. We tested this hypothesis in population based cohort of persons with diabetes and stratified by history of coronary heart disease (CHD) at baseline. **Methods**: We studied incidence of HF hospitalization or death among 1822 ARIC cohort participants with diabetes (diagnosis or fasting glucose >126 mg/dl) and no evidence of prevalent HF (58.0$\pm$5.7 years; 48% male; 39% African-American; median follow-up 10.8 years). A1c was measured on stored whole blood samples using HPLC (Tosoh Corp, Tokyo, Japan). Cox proportional hazard ratios (HRs) were adjusted for age, sex, race, education, health insurance status, drinking, body mass index, and waist hip ratio, and major CHD risk factors (blood pressure level and medications, LDL and HDL cholesterol levels, smoking). **Results**: Crude incidence rates per 1,000 persons-years were substantially lower in the absence of CHD (IR 14.7 for CHD- vs. 52.6 for CHD+, $p<0.001$). The HRs increased with each quintile of A1c in persons with diabetes without CHD but no clear association was observed in persons with diabetes and prevalent CHD (see Figure). The HR of HF for each one percentage point increase of A1c was 1.14 (95% CI 1.06–1.22) for the non-CHD group and 1.11 (95% CI 0.91–1.34) for the CHD group. The association was unaltered if cases were limited to HF among individuals free of CHD at the time of onset (HR 1.14, 95% CI 1.05–1.24) **Conclusions**: These data suggest that A1c is an independent risk factor for incident HF in persons with diabetes without prevalent CHD. The number individuals and cases with CHD at baseline was limited.

Figure. Adjusted Hazard Ratios* (95% CIs) of Congestive Heart Failure (HF) by Quintile of Hemoglobin A1c (HbA1c) in Persons with Diabetes Stratifed by Coronary Heart Disease (CHD) at Baseline, N=1,511



* Cox proportional hazard ratios (HRs) were adjusted for age, sex, race, education, health insurance status, drinking, body mass index, and waist hip ratio, and major CHD risk factors (blood pressure level and medications, LDL and HDL cholesterol levels, smoking).

7

Common Genetic and Environmental Contributions to Depression and Inflammatory Markers in Middle-Aged Men: The Twins Heart Study

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Introduction: Both depression and inflammation are risk factors for coronary heart disease (CHD), and it has been suggested that inflammation is a pathway linking depression to CHD. However, this association could be confounded by common genetic and/or environmental factors. We sought to examine the relationship between inflammatory markers and depression and further determine to what extend this association can be explained by common genes. **Methods**: Two inflammatory markers, interleukin-6 (IL-6) and C-reactive protein (CRP), were measured in 298 male twins who were free of symptomatic CHD, including 55 twin pairs discordant for lifetime history of major depression (MD) and 94 normal twin pairs with both members free of MD. MD was diagnosed with the Structured Clinical Interview for Psychiatric Disorders. Current depressive symptoms were assessed using the Beck Depression Inventory. Traditional CHD risk factors were also measured. Generalized estimating equations were used to take into account the relationship within twin pairs. The genetic models were constructed by using the structural equation modeling. **Results**: The mean age of the twins was 54 years (age range: 47–59 years). Neither IL-6 nor CRP showed significantly different levels comparing MD cases to their non-MD co-twins. However, in the normal twin pairs, a strong dose-response relationship was observed between inflammation and severity of depressive symptoms ($P<0.001$ for both IL-6 and CRP). After adjustment for traditional CHD risk factors (physical activity, LDL-cholesterol, smoking and marital status), IL-6 remained independently associated with depressive symptoms ($P=0.03$), but not CRP ($P=0.84$). Genetic modeling found a significant genetic correlation between IL-6 and depressive symptoms ($r_g=0.49$ and $r_g=0.56$, before and after adjusting covariates respectively), indicating that a large part of covariance between inflammation and depression can be explained by the same genes. **Conclusion**: Current depressive symptoms, but not lifetime history of MD, are significantly correlated with inflammatory markers. Furthermore, the covariation between depressive symptoms and inflammation is due, in large part, to common genes. These genetic variations may be important for CHD risk.

8

Women, Depression, and Outcome of Myocardial Infarction

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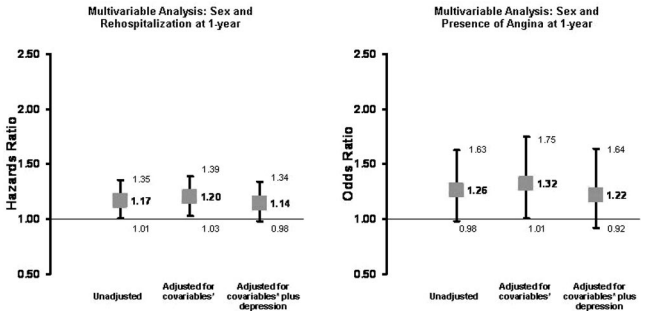
Introduction: Women have an unexplained worse outcome after myocardial infarction (MI) compared with men. Depression predicts adverse outcomes after MI and is far more prevalent among women than men post-MI. We assessed the hypothesis that depression accounts for women's higher rates of adverse outcomes after MI. **Methods**: A total of 2,498 (807 women) MI patients were enrolled from 17 US centers in a prospective registry of MI (PREMIER). Depressive symptoms were assessed with the Patient Health Questionnaire (PHQ). Depression was defined as a PHQ score $\geq$10 (moderate-severe depressive symptoms). Outcomes at 1-year included: rehospitalization, mortality and presence of angina using the Seattle Angina Questionnaire. **Results**: Depression was more prevalent in women compared with men (29% vs 19%, $P<.001$). After adjusting for demographics, comorbidities and MI severity, there was no significant sex difference in 1-year mortality (HR 1.07, 95% CI, 0.77, 1.49)), but sex remained significantly associated with rehospitalization and presence of angina (Figure). After adding depression to the model, however, sex was no longer significantly associated with either rehospitalization or presence of angina (Figure). **Conclusion**: In conclusion, depression explains a portion of the excess risk of adverse events in women at 1-year post-MI, even after adjusting for traditional measures of disease severity. Our results suggest the importance of

early identification of depression post-MI and emphasize the need for a randomized clinical trial to show that treatment of depression decreases sex-disparities in outcome after MI.



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Association of Serotonin Transporter Polymorphism (5-HTTLPR) with Depression, Perceived Stress, and Norepinephrine in Patients with Coronary Disease: The Heart and Soul Study

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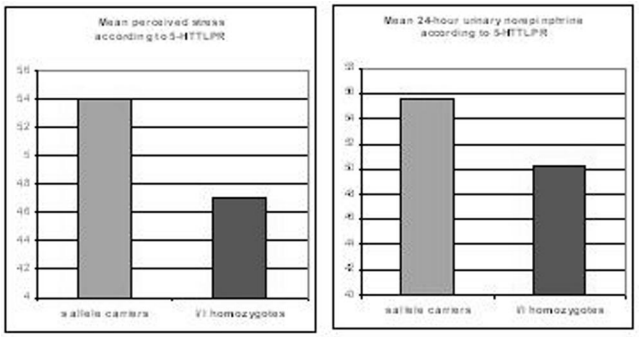
Background: The short allele of a polymorphism in the promoter region of the serotonin transporter gene (5-HTTLPR) interacts with stressful life events to predict depression in otherwise healthy individuals. Whether this allele increases the risk of depression associated with the stress of CAD is unknown. **Methods**: We examined the association of 5-HTTLPR with depression, perceived stress and urinary norepinephrine in a cross-sectional study of 557 Caucasian adults with established CAD. Subjects completed a structured interview for depression, the Perceived Stress Scale, and a 24-hour urine collection. Analyses were adjusted for age and gender. **Results**: Among participants carrying a short allele (SS or SL), 25% (97/383) had current depression, compared with 17% (29/174) of LL homozygotes (OR 1.6, 95% CI 1.0–2.6, p = .04). Participants carrying a short allele had greater mean perceived stress compared with LL homozygotes (5.4±3.4 vs. 4.7±2.9, p = .02) **(Figure)** and a greater odds of high perceived stress (OR 1.6 (1.1–2.3), p = .02). Mean urinary norepinephrine was higher in S allele carriers (55.6±24.0 vs. 50.2±23.8 μg/day, p = .04) **(Figure)** who were also more likely to have norepinephrine values in the highest quartile (OR 1.7 (1.0–2.3), p = .05). **Conclusions**: Among patients with established CAD, carriers of the short allele of 5-HTTLPR are more vulnerable to depression, perceived stress and greater norepinephrine secretion. These factors may contribute to worse cardiovascular outcomes in these patients. **Figure. Mean perceived stress score (panel A) and mean 24-hour urinary norepinephrine concentration (panel B) in short allele carriers (S/S or S/L) compared with LL homozygotes.**



10

Coronary Artery Calcified Plaque in Individuals 38 to 50 Years Old and Cardiovascular Risk Factors Measured 5 Years Earlier: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

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Coronary artery calcified (CAC) plaque, a non-invasive measure of atherosclerosis, predicts near term CVD events independently of traditional CVD risk factors. It is unknown if established CVD risk factors predict the development of CAC plaque in individuals 38–50 years of age. We report on 2183 participants with measured risk factors and CAC from the CARDIA Year 15 and 20 exams. CAC and risk factors at the year 15 exam were dichotomized for analysis (CAC=present, diabetes = fasting blood glucose >=126 or medications, hypertension = SBP>=130 or DBP>=85 or medications, hypercholesterolemia = total chol. >220 or lipid medication, current smoker, BMI>=30 and high school graduate. CAC at the year 20 exam was considered positive if the total Agatston score was >=5 and was incident or prevalent based on a CT exam performed 5 years earlier. Logistic regression was used to determine OR for incident and prevalent CAC adjusted for gender, ethnicity age and simultaneously for all risk factors(see table). At Year 20, prevalence of CAC is 15.4% (337 of 2183) and 5-year incidence is 7.7%(152 of 1982). Among participants with CAC present at the earlier exam, 163 of the 201 (81%) participants progressed by greater than 10 Agatston units over the 5 years. Male gender, older age, diabetes, current smoking and obesity were significantly related to the odds of prevalent and incident CAC, while ethnicity, education and cholesterol were significantly related to prevalent but not incident CAC. All risk factor associations were in the expected directions. Modifiable risk factors significantly increased the odds of having incident and prevalent CAC plaque in adulthood. These data provide further rationale for augmented primary prevention efforts in young adults to improve risk factor profiles, and possibly to prevent the development of subclinical atherosclerosis.

CVD Risk Factors and Coronary Artery Calcified Plaque 5 Years Later

	Incident CAC			Prevalent CAC		
	OR	95% C.I.	P value	OR	95% C.I.	P value
Gender (Male)	3.6	2.5–5.2	<0.0001	3.3	2.6–4.3	<0.0001
Ethnicity (AA)	0.8	0.5–1.1	0.16	0.7	0.5–0.9	0.0056
Age (per 5 yr)	1.1	1.1–1.2	<0.0001	1.2	1.1–1.2	<0.0001
Diabetes (Y/N)	3.4	1.7–6.9	0.0004	3.0	1.6–5.2	0.0002
Hypertension (Y/N)	1.3	0.9–2.0	0.15	1.6	1.2–2.1	0.0006
Current Smoker (Y/N)	2.1	1.4–3.2	0.0002	2.1	1.6–2.8	<0.0001
HS Grad (Y/N)	0.8	0.4–1.8	0.59	0.6	0.3–0.98	0.04
Tot. Chol. >220	1.5	1.0–2.3	0.07	1.9	1.4–2.5	<0.0001
Obese (BMI >= 30)	1.9	1.3–2.8	0.0006	1.4	1.1–1.9	0.01

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Validated Parental History of Premature Cardiovascular Disease as a Risk Factor for Coronary Artery Calcification in the Framingham Third-Generation Cohort

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Objective: Parental history of premature cardiovascular disease (CVD) is a risk factor for offspring coronary heart disease (CHD). We sought to measure the association between a validated parental history of premature CVD and CHD with offspring coronary artery calcification (CAC). **Methods**: We used generalized estimating equations (GEE) to relate validated parental history of premature CVD and CHD (defined as paternal history of CVD/CHD at age <55 years and/or maternal history of CVD/CHD at age <65 years, adjudicated by a three physician endpoint panel) with high CAC (defined as ≥90th%ile cut-point determined from a healthy referent subgroup) in 1244 Framingham Third Generation Cohort participants (mean age 47 years, 53% women). GEE logistic models were chosen to account for sibling correlations between parental history of CVD/CHD and CAC. Covariates included age, sex, total/HDL cholesterol, lipid treatment, systolic blood pressure, antihypertensive medication use, body mass index, diabetes mellitus, current cigarette smoking, hormone replacement therapy use, and menopausal status. The presence and extent of CAC was expressed as a modified Agatston score derived from ECG triggered multidetector computed tomography (performed from 2002–2005). **Results**: A parental history of premature CVD or CHD was noted in 25% and 14% of persons with high CAC (n=176) compared with 13% and 7% of persons without high CAC (n=1068), respectively. In GEE logistic models, a history of premature CVD in at least one parent was significantly associated with high CAC (age-and sex-adjusted OR=1.94, 95%CI 1.23–3.07; multivariable adjusted OR=1.77, 95%CI 1.11–2.80). Similar results were observed for the association between a history of premature CHD in at least one parent and high CAC (age-and sex-adjusted OR=2.02 95%CI 1.13–3.62; multivariable-adjusted OR=1.80 95%CI 1.00–3.26). **Conclusions**: Parental history of premature CVD is associated with high CAC even after accounting for established CVD risk factors. The CHD risk conferred by parental history of premature CVD may be mediated through novel mechanisms which predispose to coronary atherosclerosis.

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Coronary Artery Calcification in Japanese Men in Japan and Hawaii: A Comparison of Prevalence and Risk Factor Relationships

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Background: Although risk of death due to coronary heart disease is higher in the United States than in Japan, it remains unknown whether low susceptibility to atherosclerosis in Japan is due to Japanese ancestry or to differences in modifiable risk factors. The purpose of this report is to compare the prevalence of coronary artery calcification (CAC) and risk factor relationships between Japanese men in Japan and Hawaii. **Methods**: Risk factor and CAC measurements were made in a population-based random sample of 311 Japanese men in Japan and 302 Japanese men in Hawaii. Men were aged 40 to 49 years and free of cardiovascular disease. Based on electron-beam computed tomography, men with a CAC score >0 were defined as having CAC. **Results**: There was a marked excess of CAC in Hawaii (49.3% $^{149}/_{302}$) versus Japan (31.2% $^{97}/_{311}$, p<0.001). Men in Japan were leaner (p<0.001), less likely to have diabetes (p=0.003) and hypercholesterolemia (p<0.001), had lower levels of insulin (p<0.001), triglycerides (p=0.001), and C-reactive protein (p=0.001), and had higher levels

of high-density lipoprotein cholesterol (p=0.004). However, men in Japan were 4-times more likely to smoke cigarettes (49.5% 154/311 vs. 12.6% 38/302, p<0.001). Although there were several risk factor differences, only body mass index (BMI) explained the CAC excess in Hawaii. After adjustment for BMI, the prevalence of CAC in Japan and Hawaii were nearly identical (40.5% and 39.8%, respectively p=0.870). **Conclusion**: Despite higher smoking rates in Japan there is an excess of CAC in Japanese men in Hawaii versus Japan. This is largely explained by higher BMI in Hawaii. While other factors may also be important, weight control in early life could have a role in reducing the risk of subclinical atherosclerosis in middle adulthood. Possible protective factors in smokers in Japan also warrant further study.

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Prevalence and Prognostic Significance of Subclinical Cardiovascular Disease in Individuals with the Metabolic Syndrome

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Background Data are limited regarding the prevalence and prognostic significance of subclinical cardiovascular disease in individuals with the metabolic syndrome (MetS). **Methods**: We investigated the prevalence of subclinical vascular disease and target organ damage in 1949 Framingham Offspring Study participants (mean age, 57.4 years; 59% women) using a panel of five tests, i.e. electrocardiography (left ventricular hypertrophy [LVH]), echocardiography (LVH or LV systolic dysfunction), carotid ultrasound (increased intima-media thickness or stenosis), ankle brachial blood pressure (low index), and urinary albumin excretion (microalbuminuria). We evaluated prospectively the risk of incident cardiovascular disease events (CVD, comprising coronary heart disease, stroke or transient ischemic attack, intermittent claudication and heart failure) in MetS according to the presence versus absence of subclinical disease on any of the five tests. **Results**: Cross-sectionally, 51.5% of the 681 participants with MetS had subclinical disease in at least one test, a rate substantially higher than individuals without MetS (multivariable-adjusted odds ratio, 1.95; 95% confidence interval [CI], 1.58–2.41; p<0.0001). On follow-up (mean 7.2 years), 139 individuals developed CVD, including 59 with MetS (8.7%). In multivariable analyses, MetS was associated with increased CVD risk (adjusted-hazards ratio [HR] 1.62, 95% CI 1.12–2.33). Participants with MetS and subclinical disease experienced an increased CVD risk (HR 2.68, 95% CI 1.63–4.40, compared to those without Mets or subclinical disease), whereas the association of MetS with CVD risk was attenuated in participants without subclinical disease (HR 1.47, 95% CI 0.80–2.71). Subclinical disease was a significant predictor of CVD in participants without MetS at baseline (HR 1.81, 95% CI 1.08–3.02). **Conclusion**: In our large community-based sample, individuals with MetS have a high prevalence of subclinical disease that likely contributes to the increased risk of overt CVD associated with the condition.

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Shared Environmental and Genetic Effects Do Not Confound the Association Between the Mediterranean Diet and Inflammation

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Objectives: The Mediterranean diet (MD) is protective against coronary heart disease (CHD) and the proposed mechanism is to be through a reduction in systemic inflammation. However, the association between MD and inflammation could be due to a shared environmental or genetic effect. We assessed the hypothesis that shared environmental and genetic effects confound the association between MD and inflammation. **Methods**: We studied 345 male twins [88 monozygotic (MZ) pairs and 5 singletons, 77 dizygotic (DZ) pairs and 10 singletons] aged 48–58 yrs, drawn from the Vietnam Era Twin Registry. Dietary habits were measured with the Willet Food Frequency Questionnaire and a score was calculated to measure adherence to the MD based on the published method. Indicators of systemic inflammation included fasting plasma concentrations of interleukin (IL-6), and C-reactive protein (CRP). A mixed-effect regression analysis examined the association between MD and log transformed IL-6 and CRP; models adjusted for total energy intake, other nutritional factors, and known CHD risk factors to assess overall, between- and within-twin pair effects of the MD on inflammation. When examining within-pair effects, twins are matched for demographic, familial and other environmental influences while growing up. MZ pairs are also 100% matched for genetic factors, while DZ pairs share on average 50% of their genes. **Results**: Adherence to the MD is associated with IL-6 (β=-0.05, P<0.001) but not with CRP (β=-0.040, P=0.1) after adjustment. When the overall effect of MD on IL-6 was partitioned into between- and within- pair effects, the between-pair effect was not significant (P=0.9), while the within-pair effect was highly significant (P<0.0001). A 1-unit increment in the within-pair difference in MD score resulted in a 0.10 log units (95% CI, -0.15 to -0.04) decrease in IL-6. The interaction between within-pair score difference and zygosity was not significant (P=0.80), suggesting that shared genetic factors are not important in this association. **Conclusions**: Shared environmental and genetic factors do not confound the association between adherence to MD and systemic inflammation. These results support the notion that the association between MD and reduced inflammation may be causal.

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Delayed Time to Defibrillation and Mortality After In-Hospital Ventricular Tachyarrhythmic Cardiac Arrest

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Background: Although current guidelines recommend defibrillation within 2 minutes of an in-hospital cardiac arrest, clinical data to support this are limited. **Methods**: We identified 6,744 patients with initial cardiac arrests from pulseless ventricular tachycardia or ventricular fibrillation at 369 hospitals in the National Registry of Cardiopulmonary Resuscitation. Using multivariable logistic regression models employing generalized estimating equations to adjust for clustering effects at the hospital level, we assessed whether a time to defibrillation >2 minutes was associated with higher mortality rates immediately post-resuscitation, within 24 hours, and for overall hospitalization. Factors associated with delays to defibrillation were also examined. **Results**: A time to defibrillation >2 minutes (n=2000) was associated with a 30% higher risk of in-hospital mortality (adjusted relative risk [RR], 1.30; 95% CI, 1.26–1.34; p<.0001). This resulted in an absolute increase in mortality rate by 18.2% from 60.7% to 78.9% (95% CI: 15.8% to 20.6%). Other predictors of in-hospital mortality included: age; male sex; non-white race; ventricular fibrillation rhythm; arrest during afterhours; hospital bed location and size; non-cardiac admitting diagnosis; pre-existing congestive heart failure or diabetes mellitus; and central nervous system depression, sepsis, cancer, or respiratory, renal, or hepatic insufficiency at time of cardiac arrest. Delayed defibrillation was also associated with increased mortality risk immediately (RR, 1.48; 95% CI, 1.39–1.58; p<.0001) and within 24 hours post-resuscitation (RR, 1.37; 95% CI, 1.30–1.44; p<.0001). Hospital-level factors associated with delayed defibrillation included: small-sized (<250 beds) hospitals; timing (after hours and weekends) and location (unmonitored hospital units) of cardiac arrest; and a non-cardiac diagnosis on admission. **Conclusion**: Delayed defibrillation times exceeding 2 minutes for in-hospital cardiac arrests amenable to defibrillation are associated with sizable increases in mortality. These findings highlight potential hospital quality improvement areas for resuscitation response and treatment.

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Joint Associations of Obesity and Other Cardiovascular Risk Factors in Relation to Risk of Acute Coronary Syndrome

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Background: Obesity is a well-established risk factor for coronary heart disease (CHD). However, the influence of other lifestyle and clinical risk factors on the association between body-mass index (BMI: weight in kg/height in m^2) and CHD remains uncertain. **Methods and Results**: In the Danish 'Diet, Cancer and Health' study, we followed 29,262 women and 26,088 men, 50 to 64 years of age, who were free of acute coronary syndrome (ACS) and cancer at baseline in 1993–1997. During a mean follow-up of 8 years, we documented 262 female and 845 male cases of ACS. Lifestyle risk factors were categorized as current smoking, <30 min/week of sports activity, below the median for the Mediterranean diet score, and <8 years of education. Clinical risk factors included self-reported hypertension, hypercholesterolemia, and diabetes. Overweight (BMI>25 kg/m^2) and obesity (BMI>30 kg/m^2) were significantly associated with a higher risk of ACS, as were each of the individual lifestyle and clinical risk factors. Joint effects of obesity and each risk factor were close to additive. When all lifestyle factors were summed, obese individuals with the greatest number of lifestyle factors had the highest risk, but no synergism was observed. Similar results were seen for clinical risk factors (**Table**). Of importance, a strong direct association between BMI and ACS was observed even among participants with the lowest number of other risk factors present. **Conclusions**: Our results illustrate that BMI is an important, independent predictor of ACS risk, even among individuals who have few CHD risk factors. BMI and other CHD risk factors appear to work in an additive fashion on risk of ACS.

Table. Joint effects of overweight and obesity and combined categories of modifiable lifestyle and clinical risk factors on risk of ACS among 29,262 women and 26,088 men*

	Women			Men		
	BMI <25 kg/m^2	BMI 25-29.9 kg/m^2	BMI 30+ kg/m^2	BMI <25 kg/m^2	BMI 25-29.9 kg/m^2	BMI 30+ kg/m^2
No. of lifestyle risk factors						
0-1	1 (ref)	1.48 (0.92-2.37)	2.40 (1.39-4.14)	1 (ref)	1.46 (1.11-1.92)	2.50 (1.79-3.48)
	[34/46]	[35/74]	[21/124]	[76/205]	[157/305]	[65/515]
2+	2.91 (1.39-4.14)	4.10 (2.71-6.20)	4.92 (3.10-7.81)	2.30 (1.75-3.03)	2.80 (2.18-3.61)	3.26 (2.44-4.36)
	[66/151]	[67/222]	[39/266]	[157/489]	[279/604]	[114/695]
No. of clinical risk factors						
0	1 (ref)	1.68 (0.99-2.88)	2.84 (1.55-5.21)	1 (ref)	1.51 (1.15-1.97)	1.65 (1.13-2.42)
	[41/60]	[38/98]	[15/103]	[115/245]	[202/358]	[55/416]
1/2	2.71 (1.72-4.27)	3.70 (2.35-5.83)	4.61 (2.81-7.57)	1.42 (1.08-1.86)	1.86 (1.45-2.38)	3.10 (2.40-4.00)
	[59/105]	[64/155]	[45/230]	[118/529]	[234/564]	[124/784]

*Hazard Ratios (95% confidence intervals). [No. of cases/Incidence per 100 000 yrs].

Lifestyle factors: current smoking, < 30 min/week of sports activity, below the sex-specific median for the Mediterranean diet score, < 8 yrs of education.

Clinical risk factors: hypertension, hypercholesterolemia, and diabetes.

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Adiposity-Related Traits and Endothelial Function in the Framingham Offspring Cohort

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Objective: Endothelial dysfunction has been proposed as a possible mechanism linking obesity and cardiovascular disease (CVD). Excess adiposity is related to endothelial dysfunction in small, highly selected samples. We sought to study relate multi-detector computed tomography visceral (VAT) and subcutaneous (SAT) abdominal fat with endothelial function in a large, community cohort. **Methods**: We used multivariable linear regression to assess the relations of VAT and SAT (measured from 2002–2005) as predictors of brachial artery vasodilator function (measured from 1998–2001) in the Framingham Offspring Study. Endothelial function measures included flow-mediated dilation [FMD%] and reactive hyperemia (mean brachial arterial flow velocity after forearm occlusion). Covariates included age, sex, current smoking, systolic and diastolic blood pressure, hypertension treatment, heart rate, total/HDL cholesterol, triglycerides, lipid treatment, aspirin use, moderate-to-high alcohol intake (>7 drinks/week women, >14 in men), diabetes, glucose, menopausal status, hormone replacement therapy, walk test, and prevalent CVD. To facilitate beta coefficient comparison, VAT and SAT were sex standardized (mean 0, standard deviation 1). **Results**: Framingham participants (n=1140), were a mean age=59 yrs, and 52% were women. In age-and sex-adjusted correlations, VAT and SAT were positively associated with brachial artery diameter and baseline mean flow and inversely related to FMD% and hyperemic flow. In multivariable regression models (Table), VAT and SAT were positively related to baseline artery diameter ($p<0.001$). VAT was positively related to baseline mean flow velocity ($p=0.01$). In adjusted models VAT and SAT were not significantly related to FMD% or reactive hyperemia. **Conclusions**: Increasing visceral and subcutaneous adiposity measures are associated with endothelial dysfunction, but the relations appear to be mediated by shared risk factors.

Table: Multivariable-adjusted Regression Models for Adiposity and Endothelial Function

	Brachial artery diameter (mm)mean=4.31	Flow-mediated dilation (%)mean=2.77	Baseline mean flow velocity (cm/s)mean=8.17	Hyperemic mean flow velocity (cm/s)mean=51.0
	β (95%CI)	β (95%CI)	β (95%CI)	β (95%CI)
SAT (cm^3)	0.07(0.03, 0.11) p<0.001	-0.02 (-0.18, 0.13)	0.26 (-0.07, 0.59)	-0.57 (-1.82, 0.67)
VAT (cm^3)	0.11 (0.07, 0.15) p<0.001	-0.002 (-0.17, 0.17)	0.46 (0.10, 0.82) p=0.01	-1.31 (-2.67, 0.05)

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Forecasting the Cardiovascular Disease Epidemic in China

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Background: The adult population of China will be growing and aging in coming decades, resulting in increases in coronary heart disease (CHD) outcomes. We forecasted the epidemic of CHD in China in detail using a computer simulation model. **Methods**: The Coronary Heart Disease (CHD) Policy Model is a validated state-transition, computer simulation of the CHD epidemic in the US. We first calibrated the CHD Policy Model for use in China using data from the Chinese Multiprovincial Cohort Study over 1992–2002. We then entered the population of China aged 35–84 years in 2000, and simulated CHD events 2000–2029. Baseline CHD prevalence was estimated from the China National Hypertension Survey Follow-up Study. Means and distributions of CHD risk factors were entered from the 2000–2001 International Collaborative Study of Cardiovascular Disease in Asia. Risk factor means were assumed constant over time. First CHD events were predicted using a modified Framingham equation. The equation used baseline CHD incidence estimated from the Sino-MONICA Study and risk factor coefficients based on Framingham Study data. Repeat CHD events were predicted based upon data from the US. **Results**: The rates of CHD events and CHD deaths increased with each successive decade during 2000–2029 (Table). The absolute numbers of CHD events and CHD deaths also increased for men and women over the three decades. **Conclusions**: We forecasted that CHD incidence and the absolute number of CHD events and deaths will increase in China over 2000–2029, due to a growing and aging population. Recent data from China suggest that levels of CHD risk factors are overall increasing, and our projections likely underestimate the extent of the dawning CHD epidemic in China. **Summed outcomes for Chinese adults 35–84 years old within three successive decades, 2000–2029, the CHD Policy Model-China.**

		Coronary Heart Disease Events		Coronary Heart Disease Deaths	
Decade	Person-Years, China	Total	Rate*	Total	Rate
2000–2009	Total 5,857,951,655	15,291,860	261	6,890,297	118
	Men 3,018,616,479	9,777,334	324	4,506,248	149
	Women 2,839,335,176	5,514,526	194	2,384,049	84
2010–2019	Total 7,070,754,825	20,529,564	290	8,886,957	126
	Men 3,587,964,288	13,048,913	364	5,737,704	160
	Women 3,482,790,537	7,480,650	215	3,149,253	90
2020–2029	Total 7,953,303,925	26,249,851	330	11,412,797	143
	Men 3,985,610,780	16,369,534	411	7,248,719	182
	Women 3,967,693,145	9,880,317	249	4,164,078	105

*Rate per 100,000 person-years

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The Effects of Functional Foods Enriched with Barley Beta-glucan on CVD Risk Factors in a Population of Generally Healthy Men and Women

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Whole barley foods, like oats, are rich in soluble fibers and particularly β-glucan. However, barley foods are not commonly consumed in the U.S or worldwide. Therefore, we conducted a double-blind, placebo-controlled, 5-group parallel study to determine the effects of extracted barley β-glucan on CVD biomarkers. Treatment groups included either low molecular weight (LMW) or high molecular weight (HMW) β-glucan at both 3 and 5 gram doses. Treatment delivery was both a ready-to-eat cereal and juice. Generally healthy hypercholesterolemic (LDL-C 130–190 mg/dL) men (n = 76) and women (n = 79) between the ages of 25–73 who completed a 4-week diet phase (modified fat diet) were randomly allocated to one of the four treatment groups or control. Additionally, treatment groups were stratified by metabolic syndrome status. Metabolic syndrome participants were identified using the ATP III guidelines definition and/or elevated fasting insulin levels of $\geq$10 μU/L. All subjects consumed treatment or control twice daily for 6 weeks. They were counseled to maintain the study diet and all other lifestyle habits throughout treatment. Three-day food records were collected during week 1 and week 6 of the study. Fasted blood samples were collected pre- and post-intervention, and blood lipids and other CVD biomarkers were determined. Participants in the metabolic stratus also participated in a 4-hour mixed meal challenge where baseline and post-prandial parameters (glucose, insulin, FFA, Tg) were assessed as well as a DEXA scan. Stratified analyses indicated a difference in treatment effect between metabolic and non-metabolic participants for fasted triglycerides and hs-CRP. For these two parameters, metabolic participants had higher baseline values and significant reductions in all treatment groups compared to non-metabolic participants. In conclusion, short-term administration of extracted barley β-glucan significantly improved CVD risk factors.

CVD Risk Factor Results by Treatment Groups:

	Control	3g LMW	3g HMW	5g LMW	5g HMW
TC					
pre	234.0±22.7	235.9±23.0	233.6±22.8	238.0±27.6	235.1±25.3
post	231.3±26.9 *a*	218.8±20.1 **b*	214.5±21.6 **b*	211.6±20.2 **b*	205.9±25.1 **b*
LDL-C					
pre	152.7±13.9	153.9±15.1	152.8±18.1	154.6±19.9	154.5±16.5
post	150.9±24.3 *a*	140.5±15.1 **b*	138.8±20.3 **b*	134.3±12.8 **b*	132.0±11.4 **b*
Apo B					
pre	140.7±15.5	138.0±14.9	135.8±18.6	138.2±20.2	139.9±18.5
post	137.8±28.6 *a*	124.0±13.0 **a*	121.9±21.0 **b*	117.8±13.8 **b*	114.4±14.5 **b*
LDL size					
pre	21.1±1.1	21.0±1.0	21.0±0.9	20.8±1.0	21.0±1.0
post	20.9±1.0 *a*	21.1±0.9 *b*	21.0±1.0 *a*	21.1±1.0 *b*	21.3±1.0 *c*
LDL #					
pre	1248.9±83.7	1233.6±78.3	1210.4±79.6	1228.0±74.3	1248.5±80.3
post	1240.6±82.7 *a*	1186.6±81.8 *b*	1176.0±89.5 *b*	1159.0±97.3 *b*	1126.3±117.3 *c*
HDL-C					
pre	50.5±14.4	49.6±14.8	47.9±10.7	50.4±13.7	50.8±14.2
post	49.9±13.8	50.8±15.8	47.4±11.2	49.7±12.8	51.9±12.7
Tg					
pre	153.9±75.4	154.9±61.7	164.7±88.7	166.7±91.7	158.3±79.2
post	158.8±64.7 *a*	142.2±49.2 **a*	152.5±55.8 *a*	145.7±62.7 **a*	133.7±47.4 **b*
hs-CRP					
pre	2.2±1.3	2.4±1.0	2.1±0.9	2.0±1.1	2.3±1.2
post	2.1±1.3 *a*	1.8±0.9 **a*	1.6±0.6 **b*	1.6±0.7 **b*	1.4±0.7 **b*

*Values given as mean± SD. Different letters indicate statistical differences between groups at p-value >0.05. * indicates statistical differences within groups at p-value <0.05.*

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High Dietary Glycemic Load and Glycemic Index Increase Risk of Cardiovascular Disease: A Population-Based Follow-Up Study

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Background: The associations of dietary glycemic load and glycemic index with risk of cardiovascular disease (CVD) have not been well established, particularly in populations consuming modest glycemic load diets. Moreover, the risk is likely to differ between lean and overweight subjects. **Objective**: To investigate associations of dietary glycemic load and glycemic index with CVD and whether BMI modifies these associations. **Methods**: Associations

of glycemic index and glycemic load with incident CVD were examined in a prospective cohort of 15.714 Dutch women aged 49–70 y without history of diabetes or CVD. Dietary glycemic load and glycemic index were calculated as a function of glycemic index, carbohydrate content and frequency of intake of individual foods, assessed by a validated food-frequency questionnaire. **Results**: During 9 ±2 years of follow-up 556 coronary heart disease (CHD) events and 243 cerebrovascular accident (CVA) events occurred. Energy-adjusted dietary glycemic load (mean 100; SD 17) was associated with increased risk of CVD after adjustment for known risk factors and dietary variables. The hazard ratio comparing the highest with the lowest quartile of dietary glycemic load was 1.47 (95%-CI: 1.04–2.09; $p_{trend} = 0.03$). Similar results were observed for dietary glycemic index with a hazard ratio of 1.33 (95%-CI: 1.07–1.67) for the highest against lowest quartile ($p_{trend} = 0.02$). For glycemic load results were similar for CHD and CVA events, but the association with glycemic index was more pronounced for CHD than CVA events. Particularly among overweight women (BMI >25 kg/m^2), glycemic load was associated with CVD risk (hazard ratio Q4 versus Q1: 1.78 (1.11- 2.85); $p_{trend} = 0.04$), while this association was not present for normal weight women. BMI did not modify the association of glycemic index with CVD risk. In a random sample of 2248 women, the combination of LDL and HDL cholesterol explained ~30% (0.05 of a beta-coefficient of 0.16 ±0.10) of the association between glycemic load and CVD risk. **Conclusion**: In this population of women consuming modest glycemic load diets, high dietary glycemic load and glycemic index increase risk of CVD, particularly among overweight women.

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Dietary Intake and Development of the Metabolic Syndrome: The Atherosclerosis Risk in Communities Study

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Background: The metabolic syndrome (MetSyn) is a constellation of interrelated risk factors, including abdominal obesity, high levels of triglycerides, glucose, systolic blood pressure and low HDL-C concentrations, associated with increased risk of cardiovascular disease morbidity and mortality. Whereas aspects of diet have been linked to individual components of MetSyn, the role of diet in the etiology of MetSyn is not well understood. **Aim**: We sought to evaluate the relationship between incident MetSyn and dietary intake, in terms of both dietary patterns and food groups, using prospective data from 9,514 participants ages 45–64 years enrolled in the ARIC study. **Methods**: Dietary intake was assessed at baseline via a 66-item food frequency questionnaire. We used principal components analysis to derive 'Western' and 'Prudent' dietary patterns from 32 food groups, and also evaluated ten major food groups used in previous studies of the ARIC cohort. MetSyn was defined using ATP III guidelines. Proportional hazards regression was used to evaluate the relation between dietary intake and incident MetSyn. **Results**: Over 9 years of follow-up, 3,782 incident cases of MetSyn were identified. After adjustment for demographic factors, smoking, physical activity, and energy intake, consumption of a 'Western' dietary pattern ($p_{trend} = 0.02$) was adversely associated with incident MetSyn. Following further adjustment for intake of meat, dairy, fruits and vegetables, refined grains, and whole grains, analysis of individual food groups revealed that meat ($p_{trend} = 0.001$) and diet soda ($p_{trend} = 0.01$) were also adversely associated with incident MetSyn, whereas dairy consumption ($p_{trend} = 0.001$) was beneficial. No associations were observed between incident MetSyn and a 'Prudent' dietary pattern, or intakes of whole grains, refined grains, fruits and vegetables, or regular soda. **Conclusions**: As hypothesized, dietary intake was associated with development of MetSyn. These prospective findings suggest that consumption of a 'Western' dietary pattern, and red and processed meat, promote the incidence of MetSyn in adults, while dairy consumption confers some protection. The diet soda association was not as hypothesized and deserves further study.

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Dietary Patterns and Risk of Myocardial Infarction in 52 Countries: Results of the INTERHEART Study

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Introduction: Dietary components are associated with cardiovascular disease. The analysis of dietary patterns has emerged as a promising approach to examining diet-disease relationships. In this study we investigated whether certain food patterns are associated with the risk of acute myocardial infarction (MI) globally. **Design**: INTERHEART is a standardized case-control study of acute MI involving 27, 098 participants. To minimize confounding between diet-disease relationships, this analysis included 6, 530 cases of first MI and 10, 792 controls who did not have previous history of angina, diabetes or hypertension. **Results**: We identified 3 major dietary patterns using factor analysis. The Oriental diet was characterized by high intake of tofu, and green leafy vegetables, the Western diet was high in dairy and fried foods, and the Prudent diet was high in nuts, legumes, fruits & vegetables. The Prudent diet was inversely associated with MI across all quartiles of intake; when compared to the lowest quartile, the OR for the 2nd quartile (0.84, CI 0.75–0.95), 3rd quartile (0.84, CI 0.75–0.95) and the 4th quartile (0.76, CI, 0.67–0.86) after adjustment for age, sex, region, education, physical activity, BMI, WHR, psycho-social factors, alcohol intake, apoB/apoA1, and smoking. Conversely, the Western diet adjusted for the factors noted above was positively associated with MI; comparing the highest to the lowest quartile of intake OR 1.29, CI 1.14- 1.46. The Oriental diet was not associated with MI. Using 7 food items (green leafy vegetables, other raw vegetables, other cooked vegetables, fruits, meats, fried foods and salty foods), we developed a dietary risk score (DRS) for assessment of risk of MI using logistic regression. Compared to the lowest quartile of intake, the 2nd quartile of DRS OR was 1.25, CI 1.14- 1.37, the 3rd quartile 1.55, CI 1.40–1.70, and the 4th quartile 1. 98, CI 1.81–2.17. The adjusted PAR of MI for the top 3 quartiles of the DRS was 29.9% (CI 25.7 -34.1%). **Conclusions**: A Prudent dietary pattern characterized by high fruit & vegetable intake is associated with a lower risk of MI compared to the Western diet, which is associated with an increased risk. Adverse dietary patterns independently account for close to one-third of the PAR of acute MI globally.

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Prospective Association of Serum Selenium and CHD, Stroke, CVD, and All-Cause Mortality: NHANES III Mortality Follow-Up Study

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Background: Selenium is a co-factor for glutathione perioxidase which neutralizes lipid perioxidation and low levels have been associated in ecological and case-control studies with increased rates of coronary heart disease. A limited number of prospective studies have evaluated this association with mixed results. **Methods**: Adult participants in the NHANES III baseline data collection (1988–1994) who had selenium levels were linked using the National Death Index through 2000 to develop a cohort to evaluate prospective associations with CHD, Stroke, CVD and All-Cause mortality. Potential confounders of age, sex, race-ethnicity, geographic location, smoking, BMI, blood pressure, diabetes, total cholesterol, HDL cholesterol, physical activity, alcohol, history of CHD, family history of CHD were evaluated using logistic regression, weighted for the sampling frame using survey procedures within SAS 9.1. **Results**: 16,433 men and women in NHANES III have serum selenium levels with a mean of 123 ng/ml, SD 17.4 with a range from 39–622 ng/dL. The age-adjusted CHD, Stroke, CVD and All-cause mortality rates were 2.46/100, 0.47/100, 3.49/100, 10.20/100 for an average of 9 years of follow-up. Multivariate adjusted logistic regression comparing the participants with the lowest 5th %ile (≤98 ng/dL) of selenium to all others revealed OR=1.57 (95%CI 1.04–2.37) for CHD mortality, OR= 0.74 (95%CI 0.24–2.29) for Stroke mortality, OR=1.46 (95%CI 1.03–2.08) for CVD mortality, and OR=2.10(95% CI 1.53–2.89) for all-cause mortality. **Conclusion**: In this nationally representative U.S.cohort, low levels of selenium are associated with increased risk of CHD, CVD and all-cause mortality but not stroke mortality.

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Impact of Dietary n-3 Fatty Acid and Statins on HDL and Total Cholesterol Levels in US Adults: An Analysis of the 1999–2002 National Health and Nutrition Examination Survey

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Background: While n-3 fatty acid (FA) intake lowers triglycerides, its effect on HDL and total cholesterol (TC) levels is less well established, either taken alone or in combination with statins. There are few large population-based studies that examine the effect of n-3 FA on HDL and TC. **Methods**: We evaluated the 1999–2002 NHANES data on adults with information on n-3 fatty acid intake and with high cholesterol. Using 24-hour dietary recall data, they were categorized into low (<0.75g/day), medium (0.75–1.5g/day), and high (>1.5g/day) dietary n-3 FA intake groups, and further subdivided into statin (S+) and non-statin (S-) groups. After initial descriptive analyses, regression models were used to compare the HDL and TC levels in the six groups. Partial models controlled for age and sex while full models also controlled for race, education, smoking, alcohol use, physical activity, BMI, saturated FA intake, diabetes and CVD. Analyses were performed using SUDAAN to incorporate the sampling design (weights, cluster, and strata variables) in order to obtain population estimates. **Results**: There were 2242 respondents (population estimate = 47,324,872) with high cholesterol and information on dietary n-3 FA intake. When using the partial model with the low n-3 FA S- group as the referent category, we found a higher HDL level [+4.2 (95% CI 1.8, 6.6), $p < 0.002$] and a lower TC/HDL ratio [-0.5 (-0.9, -0.1), $p < 0.03$] in the high n-3 FA S- group. As expected, we found lower TC and TC/HDL in all statin groups. The full model revealed higher HDL in the high n-3 FA S- group [+5.0 (2.5, 7.4), $p < 0.0004$] as well as in the high n-3 FA S+ group [+3.6 (1.1, 6.0), $p < 0.006$] when compared with the low n-3 FA S- group. Although there is a trend towards decreasing TC with increased n-3 FA intake alone, only the statin groups (at any n-3 FA level) had lower TC when compared with the low n-3 FA S- group. Among statin users, we found a lower TC/HDL ratio in adults with high [-0.50 (-0.8, -0.2), $p < 0.004$] as opposed to low n-3 FA intake. **Conclusions**: Our research shows that high dietary n-3 FA intake (> 1.5 g/day) is associated with higher HDL levels in US adults with high cholesterol, even if they are on statin therapy. Adults with high dietary n-3 FA and statin use had lower TC/HDL ratio than those on statin therapy alone.

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20-Year Weight Change Patterns, Obesity, and Subclinical CVD in Young Adults: CARDIA

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Data from NHANES 1999–2004 indicate that the prevalence of obesity continued to increase in men but imply that body weight may be leveling off in women. Moreover, there are relatively few data on longitudinal changes in weight and CVD outcomes, and for subclinical disease which is non-differentially diagnosed by race and/or sex. We examined 20-year trends in weight status and their association with subclinical CVD (coronary artery calcium [CAC] score by CT scan) at the year 20 (Y20) exam in black (B) and white (W) men (M) and women (W) in the longitudinal CARDIA study. Of 5098 young adults aged 18–30 years at baseline (Y0, 1985–6) with body mass index (BMI, kg/m^2) data, 3422 had BMI measured at Y20. Normal weight prevalence decreased while obesity increased (table) during Y0-Y15 follow-up, and continued at a slower rate during Y15-Y20. 20-year mean weight change ranged from +11.9 kg (SD 12.7) in WW to +18.0 kg (14.6) in BW, while Y15-Y0 change ranged from +10.2 (11.7) in WW to +15.9 (13.9) in BW. Overall, 27% with BMI <25 at Y0 and 40% with Y0 BMI 25+ gained 20+ kg over 20 years; 1% and 6% lost >5kg, respectively. Of 2825 participants with CT at Y20, 20% had CAC score>0 (15% CAC>5). Controlling for Y0 risk factors age, physical activity, current smoking, race and sex, baseline obesity (OR 2.9 [95% CI 2.1–3.9]) and

overweight (1.8 [1.5–2.3]) were significantly related to CAC presence vs absence; race-sex specific findings were consistent. Adding obesity related baseline risk factors (blood pressure, lipids, glucose, and hypertension) only partially attenuated relationships with baseline BMI (obesity 1.9 [1.4–2.7]; overweight 1.5 [1.2–1.9] overall). Findings were similar using CAC>5 to define CAC presence. Relationships with weight gain were inconsistent and there were no significant interactions between weight gain and baseline BMI. Weight gain continues in CARDIA through 20 years, and both baseline overweight and obesity are independently related to CAC in black and white young adults.

Prevalence of normal weight (BMI<25) and obesity (BMI 30+) at Y0, Y15, and Y20

	BM (N=624)	WM (N=860)	BW (965)	WW (N=973)
Normal Weight (%)				
Y0	63	64	55	77
Y15	26	29	21	51
Y20	23	24	18	45
Obese (%)				
Y0	10	6	21	7
Y15	37	25	51	24
Y20	42	28	56	27

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Outcomes of a Randomized Controlled Field Trial to Promote Physical Activity in Middle-School Girls: Trial of Activity for Adolescent Girls

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Physical Activity is declining among American youth, particularly in girls. The Trial of Activity for Adolescent Girls (TAAG) was a multi-center group-randomized trial to link schools with community organizations to provide girls with opportunities for physical activity. The primary study hypothesis was that the TAAG intervention would reduce by half the 20% decline in MET-weighted minutes of moderate to vigorous physical activity (MVPA) expected from 6th grade to 8th grade. The study was conducted in 36 middle schools at 6 sites in the United States. The TAAG intervention included four components: Health Education with Activity Challenges; Physical Education; Promotions; and Programs for Physical Activity, a unique feature not included in previous school-based trials. The intent of the latter component was to link school and community agencies to offer physical activity programs for girls before and after school. Physical activity was assessed at baseline (6th grade-spring 2003, N=1603), two years later (8th grade, N=3085), and after an additional year for intervention maintenance (8th grade, N=3378). Girls were chosen at random to represent their schools in the three surveys and participation rates were 80%, 85% and 88% respectively. At each time period, physical activity was assessed using Actigraph accelerometers worn for 6 consecutive days except while bathing, swimming, or sleeping. After two years of intervention, there was no difference in mean MET-weighted minutes of MVPA in girls in intervention schools compared to girls in control schools (mean difference = -0.4, 95% CI: -8.2, 7.4). After the additional year in which the schools and community agencies sustained the intervention, girls in intervention schools were more physically active than girls in control schools (mean difference = 10.9 MET-weighted minutes of MVPA, 95% CI: 0.5, 21.2). Examining MVPA by time of day during this sustainability year, significant differences were noted for 2 - 5pm (after school) with a mean difference = 7.3 MET-weighted minutes, 95% CI: 3.1, 11.5). In conclusion, the hypothesis that a school-based, community-linked intervention can reduce the decline in physical activity in middle school-age girls was supported after three years but not after two years.

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Sex, Race, and Age Differences in the Topography of Visceral Adipose Tissue

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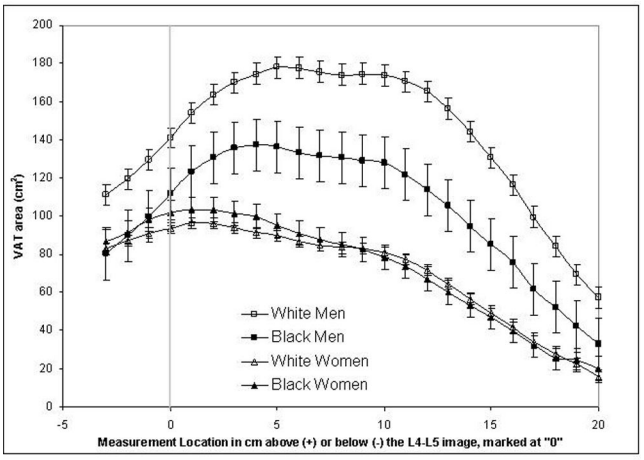
Introduction: Elevated visceral adipose tissue (VAT) is associated with insulin resistance and is an independent risk factor for incident type 2 diabetes, hypertension, and all-cause mortality. To date, both single- and multi-slice imaging studies have focused on VAT area or total VAT volume to examine race, sex, and age differences in VAT, whereas the pattern or topography of VAT deposition in different population subgroups has yet to be characterized. **Objective and Methods**: We used a dataset of 23 contiguous, 1 cm thick abdominal magnetic resonance (MR) images for each of 820 healthy adults (692 whites, 128 non-Hispanic blacks) aged 18–85 years to measure VAT areas and total volume and to test race, sex, and age differences in VAT patterning across the abdomen. The multi-image VAT data were treated as repeated measures in sex-specific mixed effects models testing for race, age, and measurement location effects. **Results**: Peak VAT area occurred higher in the abdomen in men compared to women (see Figure). White males had significantly higher VAT than black males (race p = 0.0045), with the greatest difference in VAT between black and white men occurring in the mid abdomen (race*location p = 0.0019). VAT increased with age, but more so at the location of peak VAT than at other sites (for each sex, age*location p< 0.0001). **Conclusions**: Using a single MR image at the conventional location of the L4-L5 intervertebral space may lead to inaccurate conclusions about the magnitude of sex, race, and age differences in VAT given its highly varied distribution across the abdomen.



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The Impact of Race and Ethnicity on the Association Between Body Mass Index and Inflammatory Markers

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Background The relationship between high body mass index (BMI) and adverse effects such as traditional cardiovascular risk factors and all-cause and cardiovascular mortality appears more striking in Whites than in minority populations such as African Americans (AAs). We hypothesized that the association between BMI and inflammatory markers such as C-reactive protein (CRP) might likewise vary by race and ethnicity. **Methods** We used data from participants age 20 and older with BMI ≥18.5 kg/m^2 in the 1999–2004 National Health and Nutrition Examination Survey. Because CRP was not normally distributed in the sample, we studied the association between BMI and the log transformation of CRP in multivariable models of the overall sample and in Whites, AAs, Mexican Hispanics (MHs), and Non-Mexican Hispanics (NMHs). We used interaction terms to test for racial/ethnic differences in the BMI-CRP relationship. We used sample weights and SUDAAN to account for the complex sampling design. **Results** CRP levels were significantly higher among adults with higher BMI, but this relationship varied across race/ethnicity after adjustment for age, sex, and education (see Table) (p<0.03 for BMI-race/ethnicity interaction). Additional adjustment for smoking, physical activity, and statin or anti-inflammatory medication use did not substantially change results. **Conclusions** The impact of BMI on CRP levels appears to vary by race and ethnicity with the strongest adverse association seen in Non-Mexican Hispanics. Future studies should examine the impact of these differences and their underlying mechanisms.

Table. Adjusted mean CRP levels across BMI in the overall sample and stratified by race/ethnicity.

BMI (kg/m^2)	18.5–24.9	25.0–29.9	30.0–34.9	35.0–39.9	40.0+
Mean CRP±SE(mg/l)					
Overall, n=12393	1.13±0.03	1.94±0.04	2.98±0.08	4.29±0.18	6.94±0.34
Whites, n=6483	1.15±0.04	1.91±0.05	2.91±0.10	4.12±0.19	6.77±0.39
AAs, n=2385	1.11±0.08	2.08±0.10	3.32±0.17	4.69±0.32	7.33±0.71
MH, n=2951	1.05±0.06	2.02±0.09	3.06±0.13	4.72±0.30	6.67±0.57
NMH, n=574	0.97±0.15	2.00±0.14	3.16±0.34	5.17±1.48	10.88±1.40

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Body Size and Blood Pressure: A Collaborative Analysis of 18,072 Participants from Africa and the African Diaspora

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Background. Blood pressure (BP) is directly associated with body mass index (BMI) in populations worldwide. Clinical trials of weight reduction suggest that this is a causal association. Previous data has, however, suggested that the relationship may not be linear across BMI distribution in populations of African origin, likely due to changes in body composition. **Objective**. To determine and compare the relationship between BP and BMI in populations of the African diaspora with a wide range of adiposity. **Methods**. Sample surveys were identified from Africa (Cameroon, Nigeria, two in Ghana, Congo, Tanzania, South Africa and Seychelles), the Caribbean (Barbados, St Lucia, Jamaica), the United Kingdom and the United States. Raw data was provided on individual participants, aged 35–64 for height, weight, BP and treatment of hypertension. Collectively the studies enrolled 18,072 participants (range 249 - 3,702; 43.7% men). Participation rate varied from 54% to >90%. The multivariate regression analysis provided age-specific and age-adjusted estimates of BP, BMI and prevalence of hypertension by country and sex, taking into account the use of anti-hypertensive treatment. **Results**. BP and BMI varied significantly between countries. In every country and in each sex-group, there was a positive relationship between both systolic and diastolic BP and BMI. However, the slopes for systolic BP varied from 0.27 mmHg per unit of BMI [95% CI -0.01 to 0.56] in US to 1.72 [0.92 to 2.53] in Ghana (Kumasi) in men and from 0.08 [-0.54 to 0.72] in South Africa to 1.32 [0.98 to 1.66] in the Republic of Congo in women. Similar trends were seen for diastolic BP. The slopes were significantly shallower, the higher the BMI (p<0.001). Virtually no differences were seen when the analyses were repeated after excluding those on anti-hypertensive medications. **Conclusions**. BP and BMI levels vary substantially among populations of the African diaspora. The effect of BMI on BP levels diminishes as BMI increases. A complex patho-physiological relationship between excess body weight, adiposity and energy

expenditure in populations may underlie these results and their understanding may have important public health implications.

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Sleep Predicts 5-Year Change in Blood Pressure: The CARDIA Sleep Study

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Recent evidence indicates that short sleep is associated with increased risk of hypertension. Most studies, however, rely on self-reported measures of sleep. The aim of this analysis was to determine if a more objective measure of sleep predicted change in blood pressure over 5 years. This is an ancillary study to an ongoing cohort study, the Coronary Artery Risk Development in Young Adults (CARDIA) study. Wrist actigraphy monitors were distributed to participants from the Chicago site of CARDIA twice approximately one year apart. Participants wore the monitor for three sequential days in each year, yielding measures of sleep duration, sleep latency (time to fall asleep) and sleep efficiency (percentage of time in bed spent sleeping). The sleep measurements occurred between Year 15 and Year 20 of CARDIA. Regression models were calculated to predict the 5-year change in systolic (SBP) and diastolic (DBP) blood pressure from each of the three sleep variables. Models included age, race, sex, education, income and current smoking as covariates. We also added the quadratic term for sleep duration to test for curvilinear associations. Participants were aged 38–50 years in 2003 (n=669). Mean 5-year change was 4.2 mmHg for SBP and -2.6 mmHg for DBP. Sleep duration was not significantly associated with change in SBP. However, each additional hour of sleep duration was associated with an additional decline of 1.03 mmHg in DBP over the 5 years (p=.02). The quadratic term for sleep duration was not significant for SBP or DBP. Longer sleep latency was associated with increased SBP (0.05 mmHg per minute of latency, p=.01) and DBP (0.03, p=.05). Greater sleep efficiency was associated with smaller increases in SBP (-0.15 mmHg/% of efficiency, p=.01) and greater decreases in DBP (-0.14, p=.003). Both sleep latency and sleep efficiency, markers of sleep quality and insomnia, are consistently associated with systolic and diastolic blood pressure. Better quality sleep is associated with a smaller increase in blood pressure over a 5-year period. Sleep duration was associated with changes in diastolic blood pressure. Better sleep quality and longer sleep duration is associated with less risk of developing high blood pressure.

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Lipoprotein-Associated Phospholipase A2 and Risk of Ischemic Stroke in Postmenopausal Women: The Women's Health Initiative Observational Study

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Background: Elevated levels of Lipoprotein-associated phospholipase A2 (Lp-PLA2) are an independent risk factor for coronary heart disease. However, few studies evaluated stroke as the endpoint, and these generally have included small numbers of strokes. No study has evaluated the association of Lp-PLA2 and stroke in postmenopausal women. **Methods**: Using a nested case control design, we assessed the relationship between Lp-PLA2 and risk of ischemic stroke in postmenopausal women from the Women's Health Initiative Observational Study. Lp-PLA2 was measured in 929 cases (participants who developed an ischemic stroke) and 935 controls matched on age and race. **Results**: Mean (SD) levels of Lp-PLA2 were significantly higher among cases [309.0 (97.1)] than controls [296.3 (87.3)] P=<0.003). After controlling for age, race, aspirin use, atrial fibrillation, BMI, diabetes treatment, hypertension, systolic and diastolic blood pressure, history of coronary heart disease, smoking, high cholesterol requiring pills and anti-hypertensive medication use, there was a significant increase in the hazard of ischemic stroke, per S.D. increase in Lp-PLA2 (HR 1.07, 95% CI 1.01–1.14). When analyzing stroke type, a significant association was found for large artery strokes (HR 1.34, 95% CI, 1.10–1.64), but not for small vessel strokes (HR 1.02, 95% CI 0.90–1.15). HR per SD of Lp-PLA2 among current users of hormone therapy was 1.05 [0.95–1.17] and among non-users it was 1.10 [1.02–1.19]. There were no differences in association by tertiles of the inflammatory factor C-reactive protein; (HR in tertile 1=1.11 [0.96, 1.27]; in tertile 2=1.06 [0.96, 1.18]; in tertile 3=1.09 [0.99, 1.20]). **Conclusion**: Lp-PLA2 was associated with incident ischemic stroke in this large case-control study of postmenopausal women which was most pronounced for large artery strokes.

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Healthy Lifestyle in Young Adulthood and Markers of Inflammation in Middle Age: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

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Background: Higher levels of inflammatory markers have been associated with lifestyle factors such as smoking and obesity as well as with poorer health and subsequent CVD/CHD morbidity and mortality. However, information is lacking on the relationship of a healthy lifestyle (HL) in younger age and subsequent levels of inflammatory biomarkers. **Objective and Methods**: To assess relations of lifestyle at younger ages with markers of inflammation among 2,707 CARDIA participants (56% women, 46% blacks), ages 18–30 years in 1985–86. Participants were classified into five groups as having *all* 5 (low-risk, LR), any 4, any 3, any 2, or 0–1 of the following HL factors at baseline: non-overweight (BMI 18.5 - <25 kg/m^2), not currently smoking, moderate or no excessive alcohol consumption (≤15 g/day for women or ≤30 g/day for men), moderate-to-heavy physical activity (in the highest race-sex-specific 40%), and a composite healthy diet score (highest 40% for consumption of high fiber, potassium, calcium, and low intake of saturated fat), compared with having any 4, 3, 2, or 0–1 HL. Plasma samples from Year 20 (2005–06) were used to determine levels of inflammatory markers. **Results**: About 9% of the cohort was LR (11.2%, 9.8%, 9.1%, and 7.6% of white women, black men, white men, and black women, respectively). Multivariate-adjusted mean levels of c-reactive protein (CRP) and interleukin-6 (IL-6) were significantly lower for LR persons compared to those with 4, 3, 2, or 0–1 HL (*P*-trends <0.001) (Table). Similar patterns were observed in stratified analyses by gender and race. **Conclusions**: These data demonstrate that practicing healthy lifestyle behaviors in early adulthood is associated with lower levels of inflammatory markers in middle-age. These findings have public health implications for the prevention of CHD/CVD by emphasizing the importance of a healthy lifestyle beginning at younger ages.

Multivariate-Adjusted† Mean Levels (95% CI) of Inflammatory Markers by Healthy Lifestyle

	Baseline HL Status					
	Low Risk (n=254)	Any 4 HL (n=703)	Any 3 HL (n=945)	Any 2 HL (n=634)	0–1 HL (n=171)	
Markers of Inflammation	Mean Levels (95% CI)					*P-trend*
CRP, mg/L	1.1 (1.0–1.1)	1.2 (1.2–1.3)	1.3 (1.2–1.4)	2.0 (1.8–2.1)	2.2 (1.8–2.6)	<0.001
IL-6, pg/mL	1.6 (1.4–1.7)	1.7 (1.6–1.8)	1.8 (1.7–1.9)	2.3 (2.1–2.4)	2.5 (2.2–2.8)	<0.001

†Geometric means adjusted for age, gender, race, and education.

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Perceived Income Inadequacy Is Associated with Incident Cardiovascular Disease in Older Community-Dwelling Women

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Low income is associated with development of cardiovascular disease (CVD), but the relationship between perceived income inadequacy and incident CVD is not well understood. Income inadequacy, a measure of the perceived balance between income and expenses, could be a useful addition to the more traditional socioeconomic measures that are associated with CVD. We examined the association between perceived income inadequacy and incident CVD independent of other socioeconomic factors in 522 community dwelling older women who were CVD free at baseline. These women were participating in companion population-based prospective cohort studies designed to determine the causes and course of disability in community dwelling older women (The Women's Health and Aging Studies I and II). Perceived income inadequacy was based on participant report of more than enough money, just enough money, or not enough money at the end of the month. Other measures of socioeconomic status included income and education. There were 137 new cases of CVD over the 10 year study period. Participants had a mean age of 74 years, average income of $22,400, had 12 years of education, 22% were African American, and 30% reported not having enough or having just enough money at the end of each month to cover expenses. Logistic regression analysis provided odds ratios (ORs) and 95% confidence intervals (CI) for the association between incident CVD and perceived income inadequacy. In univariate analyses, women who perceived their income as inadequate were more likely to develop CVD (OR = 2.35, 95% CI 1.55 - 3.56) than those with more than enough money. Independent of education, race, age, and log-transformed income, the results were essentially the same (OR = 2.36, 95% CI 1.51 -3.70). Interestingly, yearly income was not associated with CVD in unadjusted (OR= 0.91, 95% CI 0.55–1.53) or adjusted (OR = 1.03, 95% CI 0.62 - 1.72) analyses. Our findings suggest that community dwelling older women's perception of their financial resources is a better predictor of incident CVD than annual income. Future research could use perceived income inadequacy as an additional measure of financial resources in older women.

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Consumption of Breakfast Cereals and Risk of Heart Failure: The Physicians' Health Study

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Background: Higher consumption of fiber, fruits, and vegetables has been associated with a lower blood pressure and a lower risk of coronary heart disease. However, little is known about the effects of breakfast cereals on the risk of heart failure (HF) in a community setting. **Objective**: To examine the association between breakfast cereals and incident HF in the Physicians' Health Study. **Methods and Results**: We analyzed prospectively data from 21,410 US male physicians with an average age of 53.7±9.5 years (range; 39.7–85.9 y) at baseline. Frequency of intake of breakfast cereals was obtained through standardized questionnaires, and incident heart failure was ascertained through annual follow-up questionnaires. During a mean follow up of 18.4 years, 898 cases of HF failure occurred. In a Cox regression model adjusting for age, body mass index, smoking (never, past, and current smokers), alcohol consumption (<1, 1–4, 5–6, 7+ drinks/week), vegetable consumption (<3, 3–4, 5–6, 7–13, 14+ servings/week), physical activity (<1, 1+/week), and history of atrial fibrillation and valvular heart disease, relative risks (95% CI) for HF were 1.0 (reference), 0.90 (0.77–1.07), 0.79 (0.66–0.95), and 0.74 (0.61–0.90) for people reporting breakfast cereal consumption of 0, up to 1, 2–6, and 7 or more servings/week, respectively (p for trend 0.002). Additional adjustment for prevalent diabetes and hypertension resulted in a modest attenuation of the relative risks [1.0, 0.93 (0.78–1.11), 0.82 (0.69–0.99), and 0.77 (0.64–0.94), respectively, p for trend 0.007], suggesting that the effects of cereals on HF may partially be mediated by hypertension and diabetes. Furthermore, we observed an inverse association between breakfast cereal consumption and HF without antecedent myocardial infarction. Corresponding multivariable adjusted relative risks were 1.0, 0.95 (0.78–1.15), 0.82 (0.67–0.99), and 0.79 (0.64–0.97), respectively, p for trend 0.02. **Conclusion**: Our data showed an inverse and

graded association between breakfast cereals and incident HF. If confirmed by other studies, breakfast cereals along with other measures may help reduce the risk of HF.

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Vitamin K Epoxide Reductase Complex 1 Variant Influences Warfarin Response in African Americans

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Introduction: Caucasians carrying the Vitamin K Epoxide Reductase Complex 1 (VKORC1) 1173T allele require a lower dose of warfarin compared to Caucasians with the CC genotype. However, no data are available on the influence of this variant in African Americans, nor on its effect on the degree of anticoagulation control in any population. **Aim**: The purpose of this study was to determine whether the VKORC1 1173C/T variant (rs9934438) contributed to the variability in maintenance dose of warfarin and the risk of international normalized ratio (INR) >3 in African Americans and Caucasians. **Methods**: The INR Adherence and Genetics (IN-RANGE) study is a prospective cohort and was conducted from April 2002 through December 2005 at three anticoagulation clinics in Pennsylvania. In total, 317 patients with a target INR of 2.0 to 3.0 participated in this study. Information on warfarin use and potential confounders was obtained prospectively by interviewers using standardized questionnaires. Linear regression analysis was used to test for the differences in maintenance dose and Generalized Estimating Equation logistic regression for the difference in risk of INR >3 between the different genotype groups. All analysis were stratified by race (self-reported Caucasian and African American) and adjusted for cytochrome P450 2C9 *2 or *3 variants, apolipoprotein E4, gender, race, body mass index, and other potential confounders. **Results**: The VKORC1 1173T allele was less common among African Americans (8.0%) than Caucasians (33.5%). The T allele was associated with a lower dose in both African Americans (T-allele=31.3 mg and CC=40.0 mg; $p=0.011$) and Caucasians (T-allele=30.0 mg and CC=42.5 mg; $p<0.001$). Prior to reaching maintenance dose, Caucasians carrying a T allele had a 3.1-fold (95% CI: 1.7–5.6) higher odds of INR >3 compared to Caucasians with the CC genotype. African Americans had no significant risk difference (Odds ratio = 0.6; 95% CI: 0.3–1.2). **Conclusions**: The VKORC1 1173T allele is associated with lower warfarin maintenance dose among African Americans and Caucasians. However, the T allele was associated with increased risk of INR >3 in Caucasians only.

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Heritability of Blood Pressure Responses to Low and High Dietary Sodium Intervention in the GenSalt Study

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The heritability of blood pressure (BP) responses to dietary sodium intake (salt-sensitivity) has not been well studied. We examined the heritability of salt-sensitivity of BP among 1,906 GenSalt study participants. The dietary salt intervention included a 7-day low sodium-feeding (51.3 mmol/day) followed by a 7-day high sodium-feeding (307.8 mmol/day). BP was measured 9 times during the 3-day baseline period preceding the intervention and also during the last 3 days of each intervention phase using a random-zero sphygmomanometer. Percentage changes in the mean of 9 BP measures from baseline to low sodium and from low sodium to high sodium intervention were used for analyses. The data were first adjusted for the effects of age, sex, and other covariates. Univariate and bivariate heritabilities were computed using maximum likelihood methods under a variance components model as implemented in the computer program SOLAR version 2.1.4. Heritability is the % of variance due to familial factors. The heritabilities were all moderately large and significantly different from zero. For example, the heritabilities (standard error) for percentage changes of BP from baseline to low sodium intervention were 0.32 ± 0.05 for mean arterial pressure, 0.27 ± 0.05 for systolic BP, and 0.31 ± 0.05 for diastolic BP. The heritabilities for percentage changes of BP from low to high sodium intervention were 0.37 ± 0.05 for mean arterial pressure, 0.22 ± 0.05 for systolic BP, and 0.38 ± 0.05 for diastolic BP. In the bivariate analysis, genetic correlations ranged from 0.61 to 0.69 (for SBP with DBP under a given intervention) and from -0.35 to -0.62 (for a given BP across the low-sodium and high-sodium interventions). Post hoc tests showed that these correlations were significantly different from 0 and from 1. These data suggest that genetic factors might play an important role in determining individual BP responses to dietary sodium intake. Furthermore, there may be both unique genes affecting BP responses to low and high dietary sodium intake as well as common genes affecting responses to both interventions.

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GSTT1 Genotype Modifies the Effect of Cruciferous Vegetable Intake on Risk of Myocardial Infarction

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Introduction: Cruciferous vegetables are a major dietary source of isothiocyanates (ITCs) that might protect against the development of coronary heart disease, but few studies have examined their association with risk of myocardial infarction (MI). ITCs are inducers of glutathione S-transferases (GSTs), which are a family of polymorphic genes that code for enzymes that conjugate ITCs, as well as mutagens and reactive oxygen species, to make them more readily excretable. **Hypothesis**: We assessed the hypothesis that GST genotypes modify the association between cruciferous vegetable intake and risk of MI. **Methods**: Cases (n=2042) with a first acute non-fatal MI and population-based controls (n=2042) living in Costa Rica, matched for age, sex and area of residence were genotyped for a deletion polymorphism in *GSTM1* and *GSTT1*, and an Ile105Val substitution in *GSTP1*. Cruciferous vegetable intake and smoking status were determined by questionnaire. Odds ratios (ORs) and 95% confidence intervals (95% CI) for MI were estimated by unconditional logistic regression. **Results**: Compared to the lowest tertile of cruciferous vegetable intake, the highest tertile was associated with a lower risk of MI among individuals with the functional *GSTT1*1* genotype [OR (95% CI): 0.70 (0.58–0.84)], but not among those with the *GSTT1*0* genotype [OR (95% CI): 1.23 (0.83–1.82)](P=0.006 for interaction). The protective effect of cruciferous vegetables among those with the *GSTT1*1* genotype was greater for current smokers [OR (95% CI): 0.54 (0.36–0.79)]. *GSTP1* and *GSTM1* did not modify the association between cruciferous vegetable intake and MI. **Conclusions**: In conclusion, consumption of cruciferous vegetables was associated with a lower risk of MI among those with a functional *GSTT1*1* allele suggesting that compounds that are detoxified by this enzyme contribute to risk of MI.

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Genome-Wide Association with Renal Function Traits in the Framingham Heart Study

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Background Chronic kidney disease (CKD) is related to cardiovascular disease (CVD). Glomerular filtration rate (GFR), urinary albumin excretion (UAE), and cystatin-C (cysC) are markers of kidney function that are known to be heritable. We tested for association between the Affymetrix GeneChip Human Mapping 100K single nucleotide polymorphism set and measures of kidney function in the Framingham Heart Study. **Methods** Serum creatinine and cysC were measured on fasting blood samples at the seventh examination cycle (1998–2001) on Framingham Offspring participants. Creatinine was used to estimate GFR via the MDRD equation; UAE was measured on spot urine samples at the sixth examination cycle (1995–1998) and was indexed to urinary creatinine. CVD risk factor-adjusted kidney phenotype residuals were examined in association with the genotype data using additive generalized estimating equations. We evaluated associations with SNPs on autosomes with minor allele frequencies ≥0.10, HWE $p>0.001$, and genotypic call rates$\geq$80%. The study population was composed of 1238 Framingham participants that had both genotype and kidney phenotype measurements. **Results** The lowest p-values for GFR, cysC, and UAE were obtained for the following SNPs: rs2129170 on chromosome 4 associated with GFR (p=3.6E-06); rs1158167 near the *CYS3* gene on chromosome 20 associated with cysC (p=8.5E-09); rs10517612 on chromosome 4 associated with UAE (p=9.3E-08). Two additional SNPs in or near the *CYS3* gene were also associated with cysC levels (p-value 1.0E-05 to 3.0E-04). We found nominal significance between a SNP near the ApoE gene and kidney disease (p=0.04), a gene that has been previously implicated in CKD. **Conclusion** These results suggest that 100K association studies may provide a valuable resource for replication as more genes become identified with renal disease traits.

Poster Presentations

P1

Increases in Systolic Blood Pressure Appear Atherogenic at Any Level and Any Age in CARDIA

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Background: Systolic blood pressure (SBP) elevation is a well-established risk factor for cardiovascular disease, but the consequences of elevations at low levels early in adulthood are unclear. **Methods**: Using repeated measures of SBP in 7 examinations over 20 years in the African-American (AA) and European-American (EA) men and women participating in the Coronary Artery Risk Development in Young Adults (CARDIA) Study, we estimated SBP trajectories using mixed models for each participant. We then devised a measure of *cumulative* SBP exposure in "mmHg-years", similar to "pack-years" of tobacco exposure, to describe the area under the SBP trajectory curve (AUC). AUC was partitioned by age (20–35 vs. 36–50) and by SBP range (110–140, 140+ mmHg, see Table), and used to predict presence of coronary artery calcium (CAC). **Results**: Among 3619 CARDIA participants (44% men, 47% AA, 18% with CAC), cumulative SBP exposure above 110 mmHg, in mmHg-years, was higher in men (141±4) than women (72±3), and in AAs (133±4) than EAs (75±3), and was associated with CAC (OR 1.010/5mmHg-year increase, 95%CI: 1.008–1.013) after adjusting for age, sex, race, pack-years, lipids and glucose intolerance at Year 20. This association was at least as strong at young ages and low levels (AUC I) as at older ages and higher levels (Table). Our model predicts, for example, that having SBP=134 mmHg from age 25 to 35 instead of SBP=110 (excess AUC=240 mmHg-years) would lead to twice the odds of CAC (OR=2.0) independent of SBP later in life. **Conclusions**: SBP exposure appears atherogenic even at low levels in early adulthood, implying that early prevention or treatment may provide important health benefits later in life.

	AUC partitioned by:		Proportion with AUC >0 in given age/SBP range	OR (95%CI) for CAC per 5 mmHg-years of AUC, adjusted for:	
	Age, years	SBP range, mmHg		Other risk factors*	Other risk factors* and other AUC measures
AUC I	20-35	110-140	0.57	1.022 (1.016-1.029)	1.015 (1.006-1.024)
AUC II	36-current**	110-140	0.69	1.018 (1.013-1.024)	1.008 (1.000-1.016)
AUC III	20-current**	>140	0.07	1.027 (1.013-1.043)	1.006 (0.999-1.022)
AUC I+II+III	20-current**	>110	0.75	1.010 (1.008-1.013)	--

* - Age, sex, race, LDL- and HDL-cholesterol, smoking and glucose intolerance. ** - Current age refers to age at the time of the CAC measurement. AUC – Area under the curve; OR – Odds ratio; CI – Confidence interval; CAC – Coronary artery calcium

P2

The Relation of Carotid Arterial Strain to Arterial Pressure Changes Differs Between Men and Women in the Multi-Ethnic Study of Atherosclerosis (MESA)

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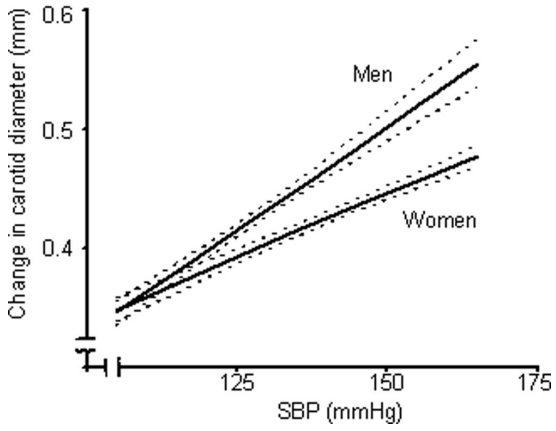
In aging persons, stiffer arteries cause greater cardiac load and failure. Higher pulse pressure implies higher stress on arteries in women than men, but the theory of linear arterial dilatation response has not been tested empirically. We derived the association of carotid artery diameter change (ΔD) with BP in men and women in MESA. **Methods**: At MESA baseline, 3019 men and 3340 women had brachial systolic and diastolic pressure (SBP, DBP) measures and carotid ultrasound for diastolic diameter (DD) and ΔD. In a series of regressions, we derived the relationship among carotid ΔD, DD, SBP and DBP. Variables were untransformed or log-transformed to derive additive and multiplicative relationships, respectively. We tested for heterogeneity by sex, adjusting for age. Further models tested confounding by race, BMI, smoking diabetes, BP medication; and interaction by age decade and ethnicity. **Results**: The mean±SD age was 62±10 years; DD was 6.1±0.8 mm, SBP was 134±20 mmHg and DBP was 74±10 mmHg. The derived relationship between ΔD and BP was a non linear family of curves for every DD and age, which differs by sex. Illustrative curves (with 95% CI, Figure) for men and women with mean age, DD and DBP, plotting change in carotid diameter versus SBP, show that at higher stress (greater SBP at constant DBP), strain (ΔD) is blunted in women vs. men ($p<0.001$). This interaction did not differ by decade or ethnicity, or on covariate adjustment. **Conclusion**: The carotid arteries of women are not as compliant with greater pressure changes during the cardiac cycle, while the arteries of men remain compliant. This may contribute to the greater risk of heart failure with normal systolic function in hypertensive women.

Figure: Carotid diameter change vs. SBP in men and women of mean age, carotid diastolic diameter and DBP in MESA



P3

A Prospective Study of Cigarette Smoking and Risk of Incident Hypertension in Women

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Introduction: Cigarette smoking is an important and well-recognized risk factor for cardiovascular disease. Although smoking appears to have modest effects on blood pressure levels, few cohort studies have examined whether cigarette smoking is associated with an increased risk of developing hypertension. **Hypothesis**: We assessed the hypothesis that cigarette smoking is associated with an increased risk of developing hypertension. **Methods**: We conducted a prospective cohort study among 28,239 women enrolled in the Women's Health Study who were initially free of hypertension, cardiovascular disease and cancer. Detailed risk factor information, including smoking status, was collected from self-reported baseline questionnaires. We used Cox proportional hazard models to calculate the relative risks (RRs) and 95% confidence intervals (CIs) of incident hypertension (defined as either new physician diagnosis, the initiation of anti-hypertensive medication, SBP ≥140 mm Hg or DBP ≥90 mm Hg). **Results**: At baseline, 51% of women were never smokers, 36% were former smokers, 5% smoked 1–14 cigarettes per day, and 8% smoked ≥15 cigarettes per day. During a median follow-up of 9.8 years, there were 8,573 (30.4%) cases of incident hypertension. The age-adjusted RRs (95% CIs) of developing hypertension among never, former, and current smokers of 1–14 and ≥15 cigarettes per day were 1.00 (reference), 1.04 (0.99–1.09), 0.99 (0.90–1.10), and 1.10 (1.02–1.19), respectively. In multivariable models further adjusting for lifestyle, clinical and dietary variables, the corresponding RRs were 1.00 (reference), 1.03 (0.98–1.08), 1.02 (0.92–1.13) and 1.12 (1.04–1.22). Among women who smoked ≥25 cigarettes per day, the multivariable RR of hypertension was 1.23 (95% CI, 1.07–1.40). **Conclusion**: In this large cohort of women, cigarette smoking was modestly associated with an increased risk of developing hypertension, with an effect that was strongest among women smoking at least 15 cigarettes per day. Whether the magnitude of effect is susceptible to confounding or reflects a true association requires an improved understanding of the biological mechanisms through which smoking may lead to the development of hypertension.

P4

Cardiac Risk Factors in Overweight Adolescents Are Reversible with Weight Loss

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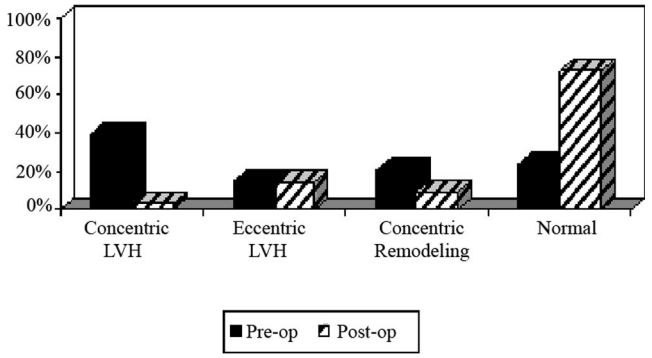
Introduction: Cardiovascular (CV) risk factors are already present in overweight adolescents; however, it is unclear if these are reversible with weight loss. **Hypothesis**: To assess that the CV risk factor, left ventricular hypertrophy (LVH), and its geometric subtypes (concentric LVH, eccentric LVH, concentric remodeling) improves with weight loss. **Methods**: Adolescents (≤ 19 yrs) undergoing bariatric surgery were recruited. Patients were studied at 2 times: pre-operatively (pre-op) & post-operatively (post-op) at least >4 months after bariatric surgery. LV mass (LVM) & geometry subtypes were assessed by echocardiography. Geometry sub-types were based on relative wall thickness (RWT) & indexed LVM (LVMI) (with limits of >0.43 cm & >51 gm/$m^{2.7}$ respectively). **Results**: 33 adolescents (13–19 yrs; 25 females, 8 males, 29 Caucasians, 4 African Americans) were evaluated. Mean follow up was 9±3 months. Weight & BMI dramatically decreased (mean weight loss 56±12 kg, pre-op BMI 60±8.7 kg/m^2 vs follow up BMI 41±8 kg/m^2, $p < 0.0001$). LVMI improved (54±13 to 41±10.6 g/$m^{2.7}$, $p = < 0.0001$). In addition, LV geometry improved with 39% having concentric LVH pre-op & only 3%

having concentric LVH at follow up (p=0.001). The percentage with normal LV geometry improved from 24% pre-op to 73% at follow up (p=0.005). (Figure 1) **Conclusions**: LV mass index significantly improves with weight loss. In addition, the highest risk hypertrophy subtype (concentric LVH) resolved with weight loss in these overweight adolescents. These results support that aggressive weight loss interventions may translate into decreased risk of CV morbidity.



P5

Impact of Metabolic Syndrome on Left Ventricular Mass and Geometry in Young Adults: The Bogalusa Heart Study

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Background: The geometric patterns of left ventricular hypertrophy (LVH) are of incremental importance to the magnitude of left ventricular (LV) mass as a predictor of cardiovascular (CV) risk. However, the role of metabolic syndrome, a constellation of CV risk factors, affecting LV mass and geometry in an otherwise healthy young adult population is unclear. **Methods**: This aspect was examined in 830 asymptomatic individuals (mean age: 36.5 years, 68.5% whites, 41 %males) as a part of the Bogalusa Heart Study. LV parameters were assessed by two-dimensional M-mode echocardiography according to the American Society of Echocardiography recommendations. **Results**: Individuals with metabolic syndrome (as defined by the NECP ATP III) showed significantly higher LV mass, LV mass index, end diastolic posterior wall thickness, septal thickness, relative wall thickness, LV end diastolic diameter, and lower fractional shortening and E/A ratio than individuals without metabolic syndrome. With respect to metabolic syndrome components, individuals with eccentric or concentric hypertrophy showed higher values of metabolic syndrome risk factors compared to individuals with normal geometric pattern but no differences were noted between individuals with normal and concentric remodeling pattern of LVH. Of note, individuals with concentric vs. eccentric hypertrophy showed significantly higher mean arterial blood pressure and HOMA-IR (homeostatic model assessment of insulin resistance). LV mass index and relative wall thickness were significantly correlated to all components of metabolic syndrome. Moreover, after adjusting for age, race, gender and antihypertensive medication use, metabolic syndrome was associated with 6- fold increase in LV mass index and 2.6- fold increase in relative wall thickness; these associations remained significant even after adjusting for individual components of metabolic syndrome. Further, LV mass index and relative wall thickness increased with increasing number of metabolic syndrome risk factors, regardless of age, race, and gender (p for trend, <0.0001). **Conclusion**: Metabolic syndrome is strongly related to LV mass and geometric patterns and exerts more adverse influence on LV structure than each of its components alone.

P6

Fasting Serum Glucose Level and Risk of Ischemic Heart Disease and Stroke: Korea Medical Insurance Corporation Study

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Objective: Diabetes is a well-known risk factor for cardiovascular disease, but the nondiabetic glucose levels are not fully studied in relation with the risk of ischemic heart disease and stroke. We investigated the relation between fasting serum glucose levels and the incidence of ischemic heart disease and stroke in Korean men and women. **Methods**: We measured fasting serum glucose levels and other cardiovascular risk factors in 108,461 men and 64,119 women, aged 35–59 years in 1990 and 1992. Our primary outcomes were hospital admissions and deaths from ischemic heart disease and stroke in 11 year follow-up from 1993 to 2003. Using the Cox proportional hazard model, we estimated the hazard ratios of ischemic heart disease and stroke according to the baseline fasting serum glucose level, after adjustment for age, body mass index, blood pressure, total cholesterol level, cigarette smoking and alcohol consumption. **Results**: During the 11 years, 3,769 ischemic heart disease and 4,422 stroke events occurred. Fasting serum glucose levels of diabetic range (≥126 mg/dL) were positively associated with risk of ischemic heart disease and stroke in men and women. However, Impaired fasting glucose levels (110–125 mg/dL) were not associated with ischemic heart disease in men, but with ischemic heart disease in women and with stroke in men and women. **Conclusions**: Men with impaired fasting glucose levels (≥110mg/dL) had increased risk of stroke, where women with impaired fasting glucose levels had increased risk of both ischemic heart disease and stroke.

Adjusted hazard ratios for ischemic heart disease and stroke by fasting serum glucose levels

	Adjusted Hazard Ratio (95% Confidence Interval)			
	Men		Women	
Fasting Glucose (mg/dL)	Ischemic Heart Disease	Stroke	Ischemic Heart Disease	Stroke
<80	1.00	1.00	1.00	1.00
80–89	0.91 (0.81–1.02)	1.03 (0.92–1.15)	1.07 (0.89–1.30)	1.09 (0.91–1.30)
90–99	0.90 (0.80–1.02)	1.03 (0.92–1.16)	0.99 (0.80–1.23)	0.95 (0.78–1.17)
100–109	0.94 (0.82–1.09)	1.07 (0.94–1.22)	1.21 (0.90–1.63)	0.91 (0.67–1.22)
110–125	1.01 (0.85–1.20)	1.34 (1.15–1.56)	1.67 (1.12–2.50)	1.46 (1.01–2.12)
≥126	1.80 (1.55–2.08)	2.15 (1.87–2.46)	2.93 (2.10–4.09)	1.94 (1.37–2.73)

P7

Path Analysis of the Relationships Among Metabolic Syndrome Components in Black versus White Children, Adolescents, and Adults: The Bogalusa Heart Study

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Introduction: The metabolic syndrome occurs commonly in both children and adults. However, information is scant on the complex relationships among the metabolic syndrome components in black and white populations during periods of childhood, adolescence and adulthood. **Methods**: Path analysis (structural equation modeling) by race was performed on 8203 healthy subjects (35.7% black and 64.3% white) comprised of children (4–11 years), adolescents (12–18 years) and adults (19–44 years) enrolled in the Bogalusa Heart Study. The path diagram was constructed using age and variables of metabolic syndrome (BMI, insulin, glucose, mean arterial pressure, high-density lipoprotein cholesterol (HDLC) and triglycerides). The sample p values were adjusted for multiple comparisons using Bonferroni approach. **Results**: The comparative fit index ranged from 0.927 to 0.985, indicating a good fit of the six models to the data. The direct effect of BMI on insulin was greatest for each age group in both races. In general, path coefficients were greater in whites than in blacks (except for the age-mean arterial pressu path); and in children and adults than in adolescents. Direct age effect on mean arterial pressure was greater in black vs white adults (p=0.010); children and adolescents showed similar but non-significant race differences. The direct effect of BMI on mean arterial pressure was greater in whites vs blacks in children (p=0.007), adolescents (p=0.090) and adults (p=0.022). Whites vs blacks showed a greater direct effect of BMI on triglycerides in childhood (p=0.003); insulin on triglycerides in adulthood (p=0.0005). Other path parameters, including direct and indirect effects, did not show significant racial differences. **Conclusions**: Obesity is of critical importance in the relationships among the components of metabolic syndrome beginning in childhood. The black-white differences in the relationships of obesity and insulin resistance measures to other components, especially regarding BMI to mean arterial pressure and insulin/BMI to triglycerides, may account for the lower prevalence of metabolic syndrome in the black population.

P8

Clustering of Long-Term Trends in Metabolic Syndrome Variables from Childhood to Adulthood in Blacks and Whites: The Bogalusa Heart Study

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Hypothesis. The metabolic syndrome occurs commonly in the general population beginning in childhood. This study tested the hypothesis that the childhood and adulthood metabolic syndrome variables as well as their long-term rates of change since childhood cluster. **Methods**. The longitudinal cohort consisted of 1020 subjects (389 blacks and 631 whites) who were examined 3–6 times both as children (ages 4–17 years) and adults (ages 18–38 years), with 3874 observations, over an average follow-up period of 16 years. The metabolic syndrome variables included body mass index, homeostasis model assessment of insulin resistance, triglycerides/high-density lipoprotein cholesterol ratio and mean arterial pressure. The incremental area under the growth curve was used as a measure of long-term rate of change of risk variables since childhood. **Results**. Intraclass correlations, a measure of the degree of clustering, among four components in childhood and adulthood were significant (p<0.001), as well as their long-term rates of change. The extent of clustering was consistently higher in adulthood than in childhood for both blacks and whites, although the difference was not significant in all cases. Blacks vs whites showed higher degree of clustering of long-term rates of change of four risk variables since childhood. Adjustment for body mass index rather than insulin resistance index reduced the degree of clustering of other three risk variables by about 50%. **Conclusions**. These results show that the metabolic syndrome variables coexist in terms not only of their levels in childhood and adulthood, but also of their long-term rates of change since childhood. Obesity is of critical importance in the development of metabolic syndrome.

P9

The Association of Serum Bioavailable Estradiol with Metabolic Syndrome Components Differs by Years Since Menopause: The PEPI Trial

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Exogenous estrogen has been proposed to be atheroprotective in early menopause, but to have a null or even harmful effect later in menopause. If true, the association of endogenous levels of estrogen with CHD risk factors may differ by years since menopause. We examined the association of serum levels of bioavailable (non-SHBG bound) estradiol (BioE2) with the metabolic syndrome and its components in 592 naturally menopausal women (ages 46 to 64) stratified by years since menopause; 265 were <5 yrs and 327 were 5–10 yrs post-menopause. BioE2 levels were positively correlated with BMI, waist girth, triglycerides and

fasting plasma glucose, and negatively correlated with HDL cholesterol in both groups (all $P<0.01$). BioE2 levels were negatively related to age in the <5 yr group only, and positively correlated with systolic and diastolic blood pressures only in the 5–10 yr group. On average, age-adjusted BioE2 levels were 135% higher in women who fulfilled criteria for the metabolic syndrome (≥3 components) compared to those who did not ($P<0.001$) for both groups. However, in age-adjusted logistic regressions, a 1 SD increase in BioE2 was associated with higher odds for each metabolic syndrome component and 3-fold higher odds of having the metabolic syndrome in women 5–10 yrs versus <5 yrs post menopause (Table 1). In addition, higher BioE2 was significantly associated with hypertension and hyperglycemia only for the 5–10 yr group (p for interaction = 0.01 and 0.10, respectively). Adjustment for BMI reduced, but did not eliminate associations for the 5–10 yr group, whereas only central adiposity remained significantly related to BioE2 in the <5 yr group. Thus, higher levels of endogenous estrogens are associated with adverse CHD risk factors early in menopause, and the association is even stronger 5 to 10 years after menopause.

Table 1. Age-adjusted odds ratio for the metabolic syndrome and each of its components based on a one SD increase in BioE2 by years since menopause.

	<5 yrs (n=265)			5–10 yrs (n=327)		
	% Yes	OR	95% CI	% Yes	OR	95% CI
Blood pressure	16.6	1.36	0.98, 1.89	18.0	2.58	1.71, 3.89
Triglycerides	14.3	1.68	1.19, 2.38	18.3	3.16	2.03, 4.90
HDL cholesterol	19.6	1.75	1.29, 2.38	24.2	3.31	2.20, 4.98
Waist girth	25.3	2.85	2.02, 4.01	26.3	6.20	3.78, 10.17
FPG (>110 mg/dl)	6.4	1.41	0.86, 2.32	8.0	2.41	1.38, 4.22
Metabolic Syndrome	9.8	2.79	1.76, 4.43	13.1	10.20	5.02, 20.72

P10

Effects of Selenium Supplementation on Type 2 Diabetes Incidence: Secondary Analyses in a Randomized Clinical Trial

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Introduction: Oxidative stress is associated with insulin resistance, impaired glucose tolerance, and type 2 diabetes mellitus (DM), and may represent the pathogenic mechanism linking these conditions to cardiovascular disease. Moreover, supplementations with the antioxidant selenium in animal models have produced beneficial effects on glucose metabolism; however, data in humans on the effects of selenium supplementation alone in the prevention of type 2 DM are lacking. **Objective**: As part of the Nutritional Prevention of Cancer (NPC) Trial, the authors examined the effect of a long-term dietary supplementation with 200 μg of selenium daily on type 2 DM incidence (1983–1996). **Methods**: This study was a double-blind, randomized, placebo-controlled trial conducted among 1,312 participants recruited from seven dermatology clinics in low selenium areas of the Eastern United States. Type 2 DM incidence was assessed as secondary end point among participants who were free of type 2 DM at baseline (n = 1,250, mean age 63.2 years±10.0, 74.7% males). Incident type 2 DM was ascertained by a self-reported diagnosis with subsequent evaluation of medical records. Participants were randomly assigned to receive selenium (n = 621) or placebo (n = 629). **Results**: During an average follow-up of 7.6 years, 100 total new cases of type 2 DM were accrued, of which 60 in the selenium group and 40 in the placebo group, for an incidence rate of 12.6 and 8.3 per 1,000 person years, respectively [hazard ratio (HR) = 1.52, 95% confidence interval (CI) = 1.02–2.27]. The lack of benefits of selenium supplementation on the incidence of type 2 DM persisted when analyses were stratified by age, gender, body mass index, or smoking status. Moreover, an exposure-response gradient ($P = 0.026$) was found when analyses were further stratified by tertiles of baseline plasma selenium concentrations, with a significantly increased risk of type 2 DM in the top tertile of baseline plasma selenium (HR = 2.55, 95% CI = 1.25–5.20). **Conclusions**: Overall, these findings indicate no effect of selenium supplementation on the prevention of type 2 DM in this population; moreover, the potential for adverse effects of a long-term supplementation with selenium on glucose metabolism warrants further consideration.

P11

Metabolic Syndrome, Inflammation, and Incidence of Congestive Heart Failure in the Elderly: The Cardiovascular Health Study

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Background: Elevated C-reactive protein (CRP) is associated with the metabolic syndrome (MetS). We evaluated whether the presence of both MetS and elevated CRP increases the risk of incident congestive heart failure (CHF) in the elderly, and if a modified MetS definition incorporating CRP level (CRP-MetS) adds prognostic information on CHF risk. **Methods**: We studied 4017 participants in the Cardiovascular Health Study (a prospective observational study of men and women ≥65 years old) without CHF or diabetes at baseline. Elevated CRP was defined as ≥3 mg/L and MetS was defined by the revised ATPIII criteria. Cox models were used to calculate hazard ratios (HRs) for CHF with 95% confidence intervals (CIs). Rothman's synergy index (SI) was used to assess for additive interaction. "CRP-MetS" was defined as the presence of 3 out of 6 components, with CRP added to ATP III criteria as the 6th component. **Results**: 832 participants developed CHF over 11.6 years of follow-up. Adjusting for age, sex, race, presence or absence of baseline coronary heart disease, LDL, and smoking, both MetS and elevated CRP were risk factors for CHF (HRs; 95% CIs are 1.40; 1.22–1.61 and 1.71; 1.49–1.96, respectively). Elevated CRP and MetS together were more strongly associated with incident CHF than each individually (Table). Considering additive associations of MetS and CRP, there was a 20% relative excess risk than expected under an additive model (95% CI -2%-230%). 18% of subjects without MetS (442/2481) were reclassified as having MetS using the CRP-MetS definition. This group had increased risk of CHF compared to those without either ATPIII or CRP-MetS (adjusted HR 1.71, 95% CI 1.38–2.12). **Conclusion**: We observed an additive effect of MetS and elevated CRP in prediction of incident CHF in this elderly population. The "CRP-modified" MetS definition identified more subjects at risk of incident CHF. Consideration of both CRP and MetS may be useful in risk stratification in clinical and research settings.

Hazard Ratios of incident CHF based on MetS and CRP status

CRP≥3	MetS	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
(-)	(-)	1.00 (ref)	1.00 (ref)
(-)	(+)	1.32 (1.08, 1.61)	1.26 (1.03, 1.54)
(+)	(-)	1.65 (1.37, 1.99)	1.60 (1.33, 1.94)
(+)	(+)	2.15 (1.80, 2.57)	2.11 (1.76, 2.53)

P12

Sleep Predicts 5-Year Change in Glucose, Insulin, and Insulin Sensitivity: The CARDIA Sleep Study

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Epidemiologic studies report that short sleep is associated with increased risk of diabetes, however, those studies rely on self-reported measures of sleep. The aim of this analysis was to determine if an objective measure of sleep predicted changes in glucose, insulin, or insulin sensitivity over 5 years. This is an ancillary study to an ongoing cohort study, Coronary Artery Risk Development in Young Adults (CARDIA). Wrist actigraphy monitors were twice distributed to participants from the Chicago site of CARDIA approximately one year apart. In each year, participants wore the monitor for 3 days yielding measures of sleep duration and sleep efficiency (% of time in bed spent sleeping). Sleep measurements were between Year 15 and 20 of CARDIA. Outcome measures are the 5-year change in fasting glucose levels, fasting insulin levels, and insulin sensitivity derived from homeostatic model assessment (HOMA). Regression models were used to estimate mean outcome measures as a function of each sleep variable, adjusting for age, race, sex, body mass index (BMI), 5-year change in BMI, education, income and current smoking. The quadratic term for sleep duration was added to test for curvilinear associations. Participants were aged 38–50 years in 2003 (n=669). Mean sleep duration was 6.1 hours. Mean change was 13.0 mg/dL for glucose, 1.9 uU/mL for insulin and .95 for HOMA. Results indicated that sleep duration was significantly associated with change in insulin ($p=.02$ for quadratic term) and change in HOMA ($p=.01$ for quadratic term) in a curvilinear fashion such that the shortest and longest sleep durations were associated with reduced insulin sensitivity. The nadir for smallest 5-year change was estimated to be at 5.75 hours of sleep for insulin and 5.5 hours for insulin sensitivity. Sleep duration does not predict change in glucose. Sleep efficiency is negatively associated with changes in glucose (-0.18 mg/dL per %, $p=.05$) and insulin sensitivity (-0.02, $p=.03$). These findings are consistent with prior research suggesting that short sleep increases risk of diabetes. Sleep duration and efficiency both significantly predicted changes in insulin sensitivity. Shortest and longest sleep durations and lower sleep efficiency may increase risk of impaired glucose metabolism.

P13

Individual and Neighborhood Socioeconomic Status Characteristics and Prevalence of Metabolic Syndrome: The ARIC Study

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Metabolic syndrome (MetS), a condition identified as a cluster of disorders related to defects in insulin sensitivity (including dyslipidemia, hypertension, impaired glucose tolerance and central adiposity), is associated with an increased risk of diabetes and cardiovascular disease. While an inverse association between socioeconomic status and components of the MetS has been reported, less is known about the association of individual (iSES) and neighborhood (nSES) socioeconomic characteristics with MetS. We examined iSES and nSES and the prevalence of MetS in the Atherosclerosis Risk in Communities Study, (1987–99). Participants included 2,932 black and 9,777 non-diabetic white men and women ages 45 to 64 years. MetS was identified by 2005 ATP III criteria. Family income [<=$12,000 (L-), $12000-$34,999 (M-), and >=$35,000 (H-)] was used to represent iSES. Six census tract socioeconomic measures were combined into a composite index and categorized as race-specific tertiles (L-, M-, H-). Race-gender specific prevalence ratios (PR) and 95% confidence intervals (CIs) for MetS by (1) iSES, (2) nSES and (3) iSES and nSES were estimated by log-linear regression. Models with nSES were fit with generalized estimating equations to account for the correlation among participants within census tracts. Among black and white men, there was no association between MetS and iSES or nSES. In contrast, black (PR = 1.8, 95% CI=1.4, 2.3) and white (PR =1.5, 95% CI = 1.2, 1.8) women with L-iSES were more likely to have MetS than those with H-iSES after adjusting for age, center, smoking status, alcohol use, physical activity, and LDL cholesterol. Similar but weaker patterns were noted for L-nSES (PR = 1.2, 95% CI=1.0, 1.4 for black women and PR =1.3, 95% CI = 1.1, 1.4 for white women). When nSES and iSES were included in the same model, associations remained similar and statistically significant. In summary, both individual and neighborhood socioeconomic factors were independently associated with an increased prevalence of MetS among women but not men. Insights into the behavioral, social and economic mechanisms related to these gender differences may offer avenues for the prevention of the MetS and its chronic disease sequelae.

P14

Short-Term Variability in Measures of Glycemia and Implications for the Classification of Diabetes and Impaired Glycemic States

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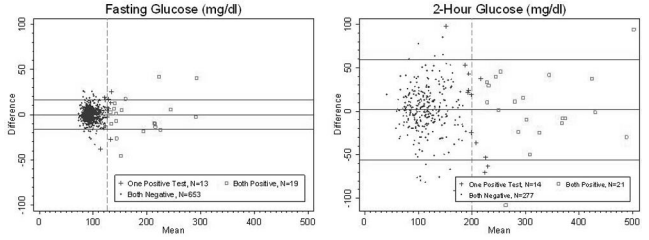
Objective: To characterize the within-person variability in fasting glucose, 2-hour glucose, and hemoglobin A1c (HbA1c) and to assess the impact of using two visits (repeat measurements) for classification of diabetes. **Design and Methods**: The NHANES III Second Exam was a sub-study in which repeat exams were conducted on 2,160 adults ~2 weeks after the original NHANES III exam including 685 fasting participants without diagnosed diabetes. To assess the impact of within-person variability on the classification of diabetes and impaired glycemic states (IFG and IGT), we compared the fasting glucose, 2-hour glucose and HbA1c values obtained during the two visits. **Results**: The within-person CVs for fasting glucose, 2-hour glucose, and HbA1c were 5.7%, 16.7%, and 3.6%, respectively. The overall prevalence of undiagnosed diabetes based on a single fasting glucose ≥126 mg/dl was 3.7%. If a second fasting glucose ≥126 mg/dl was used to confirm a diagnosis of diabetes (American Diabetes Association Guidelines) the prevalence decreased to 2.8% (95%CI, 1.5 to 4.0), a 24% decrease. The impact of using the repeat visit data on prevalence estimates of undiagnosed diabetes is to decrease the current U.S estimate of 5.8 million to 4.4 million individuals. Similarly, the prevalence of IFG would decrease 29% from 54 million to 38 million individuals. **Conclusions**: This analysis documents high variability in fasting and 2-hour glucose relative to HbA1c and our results quantify the impact on prevalence estimates of using a single fasting measurement compared to repeat testing recommended in clinical practice.

Bland Altman plots of fasting and 2-hour glucose comparing repeat measurements (~2 weeks apart), NHANES III



Legend: Solid horizontal lines are mean of the differences +/- 1.96×(SD of the differences). Dotted horizontal lines are drawn at a fasting glucose of 126 mg/dl and 2-hour glucose of 200 mg/dl to indicate cut-points for the diagnosis of diabetes.

P15

Drugs Are Not Enough: Metabolic Syndrome—A Call for Intensive Therapeutic Lifestyle Change

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Background: Recent guidelines have emphasized the need for intensive pharmacologic management of cardiovascular risk factors. It is unknown whether this has impacted the prevalence of the metabolic syndrome (MS) among patients with coronary heart disease (CHD). **Methods**: We compared the prevalence of MS in patients with CHD entering cardiac rehabilitation from 1996–2001 (period 1) with those entering from 2002–2006 (period 2). MS was defined based on ATP III criteria, substituting history of diabetes for the glucose criterion. Medications for secondary prevention (aspirin, angiotensin-converting-enzyme inhibitor or angiotensin receptor blocker, beta-blocker, lipid-lowering agents, and anti-diabetic agents) were counted (one point for each class of agent used with a maximum score of five). Groups were compared by t-test or chi-square as appropriate. **Results**: A total of 1,051 patients with CHD enrolled since 1996, 516 in period 1 and 535 in period 2. Age (60 vs. 61 years), gender (33% vs. 31% women), and ethnicity (32% vs. 34% non-white) were similar in the two periods. Number of medications for secondary prevention increased from 2.75 +/- 1.27 per patient in period 1 to 3.50 +/- 1.02 in period 2 ($p<0.001$). From period 1 to period 2, the prevalence of hypertriglyceridemia decreased from 43% to 34% ($p=0.003$), while the prevalence of low HDL cholesterol (59% vs. 63%), diabetes (37% vs. 38%), and hypertension (81% vs. 81%) were unchanged (all p=ns). However, the proportion of patients meeting MS criteria for waist circumference increased from 50% to 56% from period 1 to period 2 ($p<0.05$). The overall prevalence of MS was unchanged (56% vs. 57%, p=ns). **Conclusions**: Concurrently with more intensive pharmacologic management, fewer patients met the triglyceride criterion for MS, but more patients met the waist circumference criterion resulting in no change in the prevalence of MS between the two periods. While intensive pharmacologic therapy is beneficial and necessary, it was not sufficient to decrease the prevalence of MS in this population. A stronger emphasis on therapeutic lifestyle changes is needed to reduce the prevalence of MS among patients with CHD.

P16

Does Prevalence of the Metabolic Syndrome in Women with Coronary Artery Disease Differ by the ATP III and IDF Criteria?

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Background: The definition of the metabolic syndrome remains controversial. Recent analyses in predominantly healthy populations suggest that the definition proposed by the International Diabetes Federation (IDF), which lowers the waist circumference threshold and makes it an essential component, identifies a greater number of men as having the metabolic syndrome than the Adult Treatment Panel (ATP) III criteria, while there appears to be little increase among women. It is unknown whether the IDF definition identifies a greater prevalence of the metabolic syndrome than the ATP III definition among women with coronary artery disease (CAD). **Methods**: We compared the prevalence of the metabolic syndrome by the two definitions using baseline data from postmenopausal women enrolled in the Women's Angiographic Vitamin and Estrogen Trial (WAVE), all of whom had angiographically documented CAD. We excluded 51 of the 423 women enrolled (12%) who had missing data for components of the metabolic syndrome. **Results**: Of the 372 women, 70% were white, mean age was 65.3+/-8.4 years, mean BMI was 30.5+/-6.0 kg/m^2, mean waist circumference was 96.2+/-12.9 cm, 89% had a history of hypertension or elevated blood pressure, 58% had diabetes or fasting blood glucose ≥100 mg/dl, 54% had HDL-C <50 mg/dL, and 44% had triglycerides ≥150 mg/dL. The overall prevalence of the metabolic syndrome was 70% by ATP III criteria and 74% by IDF criteria; 68% of women met criteria for both definitions. Subgroup analyses by ethnic group and age are shown in the table. **Conclusions**: In this cohort of postmenopausal women with angiographically documented CAD, the metabolic syndrome is very prevalent and a high waist circumference is a common component. Therefore the IDF modification of the ATP III definition results in only a small and clinically insignificant increase in the number of women identified as having the metabolic syndrome, independent of ethnic origin or age.

Prevalence of the metabolic syndrome by subgroup

	MS - IDF Only **N** (%)	MS - ATP III Only **N** (%)	MS - Both **N** (%)	No MS **N** (%)
All women (n = 372)	22 (5.9)	7 (1.9)	253 (68.0)	90 (24.2)
White women (n = 260)	16 (16.2)	6 (2.3)	178 (68.5)	60 (23.1)
Non-white women (n = 112)	6 (5.4)	1 (0.9)	75 (67)	30 (26.8)
Age < 65 years (n = 178)	12 (6.7)	1 (0.6)	124 (69.7)	41 (23.0)
Age ≥65 years (n = 194)	10 (5.2)	6 (3.1)	129 (66.5)	49 (25.3)

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Withdrawn

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Withdrawn

P19

Diabetes Mellitus Is a Risk Factor for New-Onset Atrial Fibrillation

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Introduction: Some studies suggest that diabetes mellitus (DM) is a risk factor for development of atrial fibrillation (AF), but overall, results have been conflicting. In addition, prior studies have not evaluated the impact of glycemic control, nor whether the risk differs by duration and persistence of AF. **Hypotheses**: Diabetes mellitus is associated with increased risk of new-onset AF, and among diabetics, higher risk is associated with worse glycemic control as measured by hemoglobin A1c. **Methods**: This population-based case-control study set in a large health maintenance organization included 437 persons with new-onset AF and 729 controls. Incident ambulatory and hospitalized AF cases were identified through ICD-9 codes and verified by medical record review. Information on DM and other cardiovascular risk factors prior to AF onset came from medical records, while information on hemoglobin A1c levels came from a laboratory database. DM was defined as present if there was a physician diagnosis in the chart. For subjects with DM, we calculated the average hemoglobin A1c level over all years for which laboratory measurements were available (median 7.9 years). Logistic regression was used to obtain adjusted risk estimates. **Results**: Among AF cases, 24% (103/437) had DM, compared to 17% (122/729) of controls. The adjusted odds ratio (OR) for AF in persons with DM, compared to those without DM, was 1.7 (95% confidence interval [CI] 1.3–2.3). Among diabetics, worse glycemic control was associated with higher risk. Across ordered tertiles of average hemoglobin A1c, the ORs compared to persons without DM were 1.2 (95% CI 0.7–2.0), 1.8 (95% CI 1.1–3.0), and 2.4 (95% CI 1.4–3.9) (p for trend <0.05 among diabetics). Diabetes mellitus, compared to no DM, was associated with slightly higher risk of AF that was sustained (OR 2.3, 95% CI 1.3–4.0) as opposed to transitory (OR 1.8, 95% CI 1.1–2.7) or intermittent (OR 1.5, 95% CI 1.0–2.3), but these differences were not statistically significant. **Conclusions**: Diabetes mellitus is associated with increased risk of new-onset AF, and among diabetics, worse glycemic control is associated with higher risk. These findings may shed light on the etiology of AF and also increase understanding of the burden of disease associated with DM.

P20

Metabolic Syndrome and Incident Stroke in Postmenopausal Women: The Women's Health Initiative Observational Study

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Background: The metabolic syndrome (MS) has been associated with subsequent development of diabetes and coronary heart disease, however little research has been conducted on the association between MS and incident ischemic stroke, particularly among women without a history of stroke. **Methods**: In a case-control study of biomarkers and stroke, ancillary to the Women's Health Initiative Observational Study, we assessed the association between MS and incident ischemic stroke among 972 cases and an equal number of controls matched on age and race. MS was defined in two ways: NCEP-ATP III criteria and The European Group for the Study of Insulin Resistance criteria (EGIR). Conditional logistic regression was used to assess the predictive value of each of these definitions, independently of diabetes, controlling for smoking, aspirin use, history of coronary heart disease, atrial fibrillation, and body mass index. **Results**: Under NCEP-ATP III criteria, MS was present in 39.7% of controls (34.4% with MS alone, 3.0% with diabetes alone and 5.3% with both) and 52.8% of cases (41.1% with MS alone, 4.3% with diabetes alone, 11.7% with both). Women with both MS and diabetes were at a greater risk of ischemic stroke (OR=3.04, 95% CI: 2.00, 4.62) than those with either condition alone [diabetes alone (OR=1.97, 95% CI: 1.12, 3.46); MS alone (OR=1.48, 95% CI: 1.17, 1.87)] compared to having neither condition. Under EGIR criteria, MS was present in 25.0% of controls (18.8% with MS alone, 2.1% with diabetes alone and 6.2% with both) and 32.1% of cases (21.4% with MS alone, 5.8% with diabetes alone and 10.7% with both). Women with diabetes alone were at a greater risk of ischemic stroke (OR=3.13, 95% CI: 1.76, 5.56) than women with both MS and diabetes (OR=2.05, 95% CI: 1.38, 3.06) or MS alone (OR=1.32, 95% CI: 1.02, 1.72), compared to having neither condition. **Conclusion**: Results show that both NCEP-ATP III and EGIR defined MS was associated with stroke independent of diabetes.

P21

Cardiovascular Disease Risk Factor Clustering Among US Children and Adolescents, 1999–2002

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Introduction. Because cardiovascular disease (CVD) risk factor clusters tend to track from childhood into adulthood, identifying children with elevated CVD risk factor profiles is of great clinical and public health interest. The objective of our analysis was to determine the national prevalence of CVD risk factor clustering among 8 to 14 year olds by body mass index (BMI) percentile groups using crude and adjusted cut-off values. We hypothesized that as BMI increased in these children, so would the number of CVD risk factors. **Methods**. Combined 1999–2000 and 2001–2002 National Health and Nutrition Examination Surveys (NHANES) data was analyzed among two age groups: 8 to 11 and 12 to 14 year olds (N = 1,698). Clustering of ≥3 CVD risk factors (high waist circumference, fasting blood glucose, triglyceride, and blood pressure, and low HDL cholesterol) were reported using three profiles: (1) a crude profile similar to that used in previous NHANES III analyses that included non-adjusted single cut-off points, (2) an age, sex and ethnicity-adjusted profile with lower threshold values**,** and (3) a more conservative adjusted profile based on higher threshold values. **Results**. Overall rates (~17%) of overweight were similar between the 2 age groups. The prevalence of ≥3 CVD risk factors ranged from 0.24% to 3.79% for 8 to 11 year olds and 3.03% to 8.74% in 12 to 14 year olds. The proportion of 12-to-14 year olds who had ≥3 abnormal risk factors was 8.74% (weighted N = 836,412) using the crude profile, about 6% (weighted N = 587,203) using the less-conservative profile and lower threshold values, and about 3% (weighted N = 289,952) using the more conservative profile and higher threshold values. Among 8 to 11 year olds, the lower CVD risk factor threshold values captured all of those who are at-risk for overweight and who are overweight ($p < 0.01$). **Conclusions**. Adjusted CVD risk factor threshold values can identify at-risk for overweight and overweight 8 to 11 year olds who may be at very early stages of CVD onset. The less conservative profile could be a useful clinical tool among children who are ≥85th percentile for BMI to identify associated CVD risk factors. We found a similar percentage of overweight in both age groups, indicating that problems with overweight start at a young age.

P22

Metabolic Syndrome: Prevalence and Association with Cardiovascular Diseases in the Jackson Heart Study

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Background: The role of metabolic syndrome (MetSyn) in the progression of cardiovascular diseases (CVD) in the African American (AA) population has not been fully investigated. This study examined the prevalence of MetSyn (as defined by NCEP/ATPIII) and assessed its cross-sectional relationship to co-existing Coronary heart disease (CHD), stroke and total CVD in the Jackson Heart Study (JHS) Cohort. **Methods**: The JHS comprises 5302 participants aged ≥21 years who underwent a baseline exam during 2000–2004. The age-gender adjusted odds ratios (AOR) and 95% confidence intervals (CI) were estimated in a logistic regression analysis for a history of CHD and stroke with and without co-existing MetSyn compared with a reference group of cohort members. **Results**: The overall prevalence of the MetSyn was 35.4%. Among ages 35–84 the prevalence was 40.5% in women and 29.2% in men, averaging 36.5%. Elevated BP (70.1%), abdominal obesity (63.2%), and low HDL-C levels (43.3%) were highly prevalent among those with MetSyn. Crude prevalence rates for CVD, CHD and stroke were 10.9%, 7.5%, and 4.6%, respectively. After adjustment for age and gender, the AOR's were high for CVD (AOR = 2.4; 95% CI = 2.0–2.9), CHD (2.6; 2.1–3.3) and stroke (2.3; 1.8–3.1), compared with reference group. The AOR for women vs men ranged from 1.6–1.7. **Conclusion**: The prevalence of MetSyn in the JHS is among the highest reported for population-based cohorts in the US. High rates of Elevated BP, abdominal obesity and low HDL-C levels are the most frequently occurring features of MetSyn in JHS. MetSyn is significantly associated with increased AOR for CVD, CHD and stroke. These baseline data from this large AA cohort point to high levels of risk factor clustering that may contribute significantly to the high prevalence of CVD in AA's living in Mississippi.

P23

Clustered Cardiovascular Risk and Its Association with Cardiorespiratory Fitness in US Adolescents 12 to 19 Years Old: NHANES, 1999–2002

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Introduction: CVD starts in childhood and is accelerated in individuals exhibiting co-occurrence of risk factors. Among adults, low cardiorespiratory fitness (CRF) is an independent correlate of clustered cardiovascular risk (MetS) but limited data exist in adolescents. **Methods**: Complete data on CRF and CVD risk factors were available for 1,247 adolescents between 12 and 19 y (45.7% female, 570 of 1247) as part of the 1999–2000 and 2001–2002 NHANES cohorts. A sub-maximal walking treadmill test was used to estimate CRF, which was then categorized into age and sex-specific quintiles. Height, weight, triceps and subscapular skinfolds, fasting (>6 h) insulin, glucose, lipid profiles and resting systolic blood pressure were measured. Age and sex-specific Z-scores were developed for the sum of skinfolds, the homeostatic model assessment (glucose/insulin * 22.5), systolic blood pressure, triglycerides and total cholesterol/HDL ratio which were used to characterize the MetS. A clustering score was derived by summing the individual risk factor Z-scores (MSz). Mean MSz values across CRF quintiles were calculated and tested for linear trend. Analyses were done using SUDAAN. **Results**: Boys showed significantly higher CRF values (ml/kg/min) compared to girls in both the 12–15 y-old group (47 (8.6) vs. 39.7 (7.5); p<.001) and in the 16–19 y-old group (48.1 (9.5) vs. 38.9 (8.6); p<.001). A graded inverse association between CRF and MSz was detected in both boys and girls. This association remained significant in both weight strata in boys and approached significance among normal weight girls. The steepest decline in clustered cardiovascular risk was observed when comparing the mean MSz values for the 1st and 2nd CRF quintiles. **Conclusion**: Because low cardiorespiratory fitness seems to be associated with the cardiovascular risk factor clustering phenomena, low fitness should be become a specific target for intervention in adolescents, especially in boys.

Clustered Cardiovascular Risk Score by Quintiles of CRF

	Clustered Cardiovascular Risk Score (MSz)											
	BMI<85th percentile				BMI>85th percentile				All			
		Males		Females		Males		Females		Males		Females
CRF	N	Mean (SE)	N	Mean (SE)	N	Mean (SE)	N	Mean (SE)	N	Mean (SE)	N	Mean (SE)
Q1	64	-0.34 (0.35)	69	-0.07 (0.34)	86	3.31 (0.42)	51	2.28 (0.32)	150	1.69 (0.43)	120	0.78 (0.29)
Q2	87	-0.94 (0.32)	75	-0.49 (0.23)	57	2.59 (0.54)	43	2.66 (0.36)	144	0.17 (0.34)	118	0.38 (0.25)
Q3	94	-0.84 (0.18)	76	-0.65 (0.31)	35	2.61 (0.56)	24	1.45 (0.36)	129	0.08 (0.32)	100	-0.34 (0.27)
Q4	97	-1.36 (0.32)	70	-1.10 (0.27)	28	0.94 (0.47)	32	1.60 (0.76)	125	-0.81 (0.29)	102	-1.07 (0.31)
Q5	101	-1.86 (0.21)	98	-0.91 (0.26)	28	2.40 (0.57)	32	2.41 (0.52)	129	-0.49 (0.36)	130	-0.32 (0.20)
P for trend	443	**0.005**	388	0.053	234	**0.01**	182	0.15	677	**<.001**	570	**0.004**

P24

Identification of Insulin Resistance in Asian-Indian Adolescents: Classification and Regression Tree (CART) and Logistic Regression-Based Classification Rules

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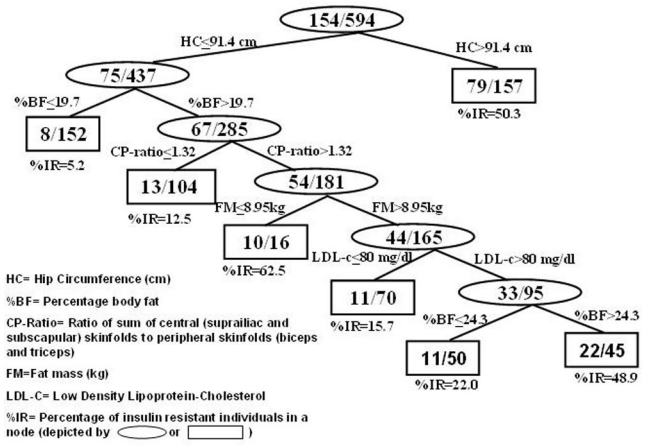
Aims: Biochemical measures for assessment of insulin resistance are not cost-effective in resource-constrained developing countries. Using Classification And Regression Tree (CART) and multivariate logistic regression, we aim to develop simple predictive decision models based on routine clinical and biochemical parameters to identify insulin resistance in apparently healthy Asian Indian adolescents. **Methods**: Data of 793 adolescents (aged 14–19 years) from our previous study have been used. WHO multi-stage cluster sampling design was used. Insulin resistance defined as Homeostasis Model of Assessment (HOMA-IR) value of >4.91 (>75th centile) was the outcome variable. **Results**: Three classification trees and an equation for prediction score were developed and validated. CART I based on anthropometric parameters alone has sensitivity 88.2%, specificity 50.1% and aROC 77.8%. CART II based on anthropometric and routine biochemical parameters has sensitivity 94.5%, specificity 38.3% and aROC 73.6%. CART III based on all anthropometric, biochemical and clinical parameters has sensitivity 70.7%, specificity 79.2% and aROC 77.4%. Prediction Score= 1*(waist circumference) +1.1*(percentage body fat) +1.6*(triceps skin fold thickness) -1.9*(gender). The score has sensitivity 82.4%, specificity 56.7%, aROC 73.4%. **Conclusion**: CART I and CART II can be used for screening insulin resistant individuals in a resource constrained setup.

CART III [Figure 1] can be used as a predictive tool for research purposes. The prediction score can be easily applied in an outpatient setting. These classification rules may be used to predict insulin resistance in Asian Indian adolescents.

Figure 1: CART III (based on anthropometric, biochemical and clinical parameters).



P25

Cereal Consumption and Type 2 Diabetes in the Physicians' Health Study

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Background: While it has been shown that dietary fiber and whole grain intake is associated with improved insulin sensitivity, little is known about the association between cereal intake and the risk of type 2 diabetes (DM). **Methods and Results**: We analyzed prospectively data from 21,195 male participants of the Physicians' Health Study. Cereal intake was self-reported and DM was ascertained through yearly follow-up questionnaires. The average age was 53.6±9.4 years (range 39.7–85.9 years) during the initial assessment of cereal intake (1981–1983). During a mean follow up of 18.0 years, 1,789 cases of DM occurred. The crude incidence rates of DM were 57.7, 53.8, 43.5 and 35.4 cases/10,000 person-years for people reporting breakfast cereal intake of 0, up to 1, 2–6, and 7+ servings/week, respectively. In a Cox regression model adjusting for age, cigarette smoking, body mass index (BMI), physical activity, vegetable consumption, and alcohol intake, relative risks (95% CI) for DM were 1.0 (reference), 0.85 (0.75–0.95), 0.76 (0.67–0.86), and 0.70 (0.61–0.81) from the lowest to the highest category of cereal consumption, respectively (p for trend <0.0001). In secondary analyses, the association between cereal intake and incident DM was observed in individuals with BMI below 25 kg/m2 (RRs: 1.0, 0.83, 0.78, and 0.74 from the lowest to the highest category of cereal intake, respectively) and BMI between 25 and 29.9 kg/m2 (RRs: 1.0, 0.88, 0.74, and 0.73 from the lowest to the highest category of cereal intake, respectively), but not in people with BMI ≥30 kg/m2 (RRs: 1.0, 0.96, 1.04, and 0.97 from the lowest to the highest category of cereal intake, respectively). **Conclusion**: These results suggest that intake of breakfast cereals may confer a lower risk of DM. This potential benefit may be restricted to non-obese individuals.

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High Risk for Abnormal Glucose Tolerance in Overweight Siblings of Children with Type 2 Diabetes Mellitus

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Introduction: The pediatric obesity epidemic has led to increased type 2 diabetes mellitus (T2DM) among U.S. children. Obesity, parental history, race, and insulin resistance are known risk factors. Identifying a high-risk pediatric population is important for screening, and for future prevention trials. Siblings of children with T2DM may be such a population, since they share genetic and environmental risk factors with individuals who developed T2DM early in life. **Hypothesis**: Overweight (≥95%ile BMI) siblings of children with T2DM (exposed group) will have an increased prevalence of impaired glucose tolerance (IGT) and undiagnosed T2DM, in comparison with overweight children without a T2DM sibling (control group). **Methods**: Cross-sectional study of subjects, ages 8–17 yrs, with at least one sibling ≥12 yrs old, with or without T2DM. Primary outcome was IGT/T2DM, as measured by oral glucose tolerance test. Secondary outcomes were insulin resistance by homeostasis model assessment (HOMA), and other cardiovascular risk factors. **Results**: Exposed subjects (n=20) compared to controls (n=38), had similar mean age (both 12.2 yrs), gender, and racial distribution (majority African American) (all p>0.05). The mean BMI±SE was 33.8±1.6 kg/m2 in exposed and 34.1±1.3 kg/m2 in controls (p=0.96). Tanner stage was ≥4 in 60% of exposed and 53% of controls (p=0.78). The prevalence of IGT (n=6) or T2DM (n=2) in the exposed group was 40%, while the prevalence of IGT (n=4) or T2DM (n=0) in the control group was 10.5% (odds ratio=5.7, 95%CI: 1.5–21.1, p= 0.015). This group difference persisted using regression analysis (95%CI: 1.4–22.3, p=0.013), with adjustment for age, gender, and Tanner stage (95%CI: 1.5–29.2, p=0.014). HOMA (based on n= 17 exposed, n= 32 controls) was greater in the exposed (4.27±0.6) than in controls (3.65±0.5), but the difference was not statistically significant (p=0.37). There was no significant difference in mean HgbA1C, lipid profile, or blood pressure between groups. **Conclusions**: Overweight siblings of children diagnosed with T2DM are more than five times more likely to have IGT/T2DM, compared to other overweight children. They may represent a particularly high-risk population to target screening, as well as pediatric T2DM prevention trials.

P27

Engaging Pediatric and Adolescent Populations in Epidemiologic Research: The SEARCH for Diabetes in Youth Study Experience

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SEARCH for Diabetes in Youth is an ongoing multi-center, population-based study of physician-diagnosed diabetes in youth under the age of 20. SEARCH is examining U.S. trends in diabetes incidence, diabetes typology, and factors associated with complications and quality of care. The SEARCH design includes surveillance, and both cross-sectional and longitudinal components. Population-based research presents formidable challenges; surprisingly limited data exist on factors affecting participation among youth. We evaluated the impact of demographic and diagnostic characteristics on participation levels. Cases were identified, validated and then asked to complete a survey and participate in a study visit. Information on age, gender, race/ethnicity, type of diabetes and date of diagnosis was available on virtually all cases from medical records or registries. Participation levels were expressed in percent relative to all ascertained cases and evaluated using multiple logistic regression. A total of 9,932 eligible youth with diabetes were identified, 6,263 prevalent cases in 2001 and 3,669 incident cases (2002–4). Survey-participation (69%, 4,309 of 6,263) and study visit participation (40%, 2,536 of 6,263) was lowest for 2001 cases and highest for 2004 cases; 82% (947 of 1,159) and 60% (698 of 1,159), respectively. Participation levels varied markedly according to characteristics of the youth. Among incident cases occurring in 2002–2004, children younger than 10 years were more than twice as likely to participate in the study visit than young adults aged 18–19 (OR 2.7, 95% CI 1.7–4.3), African Americans were less likely to participate than non-Hispanic whites (OR 0.6, 95% CI 0.4–0.8), and youth with Type 2 diabetes were less likely to participate than those with Type 1 (OR 0.5, 95% CI 0.4–0.7) based on multivariable models adjusting additionally for center and year. Associations with participation in the survey were almost identical to those shown above for study visits. Understanding and describing the relationship between individual and disease characteristics and participation is essential to evaluating the validity of study findings and to promoting increased participation in future studies.

P28

Emerging Risk Factors Improve Prediction of Type 2 Diabetes Mellitus

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Type 2 diabetes mellitus (T2DM) has been characterized as a result of alterations of innate immunity. Biomarkers that signal inflammation, as well as endothelial dysfunction, have been implicated in the etiology of T2DM. Whether knowledge of these emerging risk factors improves the identification of those who will develop diabetes is poorly understood. The Western New York Health Study (WNYHS) assessed whether markers of inflammation and endothelial dysfunction significantly add to the prediction of T2DM, beyond traditional risk factors. The WNYHS is a prospective, community-based population study of 1,455 participants from Erie and Niagara counties, NY who at baseline (1996–2001) were free of diabetes and known cardiovascular disease (mean age 57 years). After a mean follow-up of 5.8 years, 61 persons developed T2DM as defined by self-report of a physician diagnosis and the use anti-diabetic medications or by fasting plasma glucose >125 mg/dl. Cases were matched to nondiabetic controls based upon sex, race/ethnicity, baseline fasting plasma glucose (<110 mg/dl, 110–125 mg/dl), and year of study enrollment (n=61 cases and 158 controls). To examine whether emergent risk factors improved the prediction of T2DM, we obtained Receiver Operating Characteristic curves and estimated the area under the curve (AUC) for two models. A basic model group was obtained using backwards stepwise unconditional logistic regression that included only the traditional risk factors such as, age, sex, family history of diabetes, smoking, alcohol, and obesity. This model identified sex, positive family history of diabetes, and BMI as significant predictors of T2DM ($P < 0.05$). The extended model included these significant traditional risk factors plus leukocyte count, serum albumin, and E-selectin. The results, expressed as AUC (95% CI), were 0.646 (0.562, 0.730) for the basic model, and 0.726 (0.653, 0.798) for the extended model ($P = 0.04$). In conclusion, the addition of the emerging risk factors significantly improved the prediction of T2DM in this study. Whether these findings are useful in clinical practice requires confirmation from other studies.

P29

Trends in Statin Use Rates and Impact on Mortality in Diabetics Referred to a Preventive Cardiology Clinic

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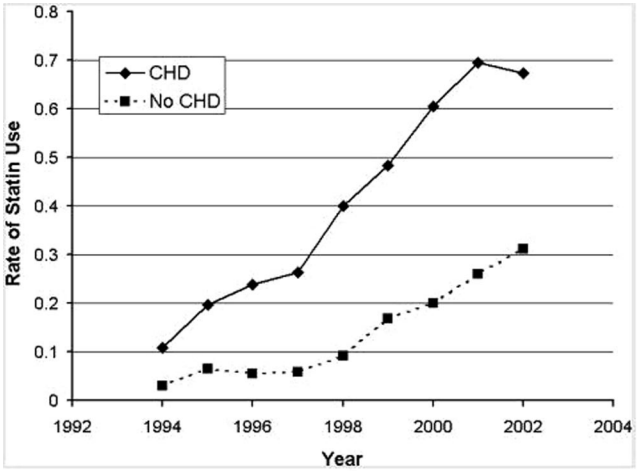
Recent randomized clinic trials have shown that statin treatment improves prognosis in patients with diabetes mellitus (DM), though clinical practice may lag behind the latest research findings or published guidelines. The current study sought to track statin use in diabetic patients referred to a preventive cardiology clinic and the examine effect of clinically-initiated statin treatment on mortality. We queried our preventive cardiology database for diabetic patients seen in the time period 1994 through 6–2003. Diabetes was defined from clinical records at the time of referral. Total morality was determined with the National Death Index through 4–1–05. Cox Proportional Hazards Regression was used to examine the effect of statin treatment on mortality with adjustment for age, gender, baseline coronary heart disease (CHD), hypertension, current smoking, and insulin use. The cohort included 2522 patients of whom 806 had baseline CHD and 632 were women. Age averaged 59±11 years. In the figure, statin use was significantly higher in patients with baseline CHD versus no baseline CHD ($p < .001$)

and increased progressively over the study period. Age and gender did not significantly affect statin use. We were able to determine mortality for 2177 patients (86%) over follow-up of 6.0±2.9 years. Death occurred in 69 of 1369 (5.0%) patients without and 124 of 801 (15.5%) patients with baseline CHD. The adjusted hazard ratio associated with statin treatment was 0.48 ($p<0.0006$). These data suggest that statin use in diabetics in clinical practice has improved progressively over past decade with very favorable outcomes for those treated with statins.



P30

Utility of HbA1c Measurements in Patients Admitted with Chest Pain

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Introduction: HbA1c has been proposed as a useful screening test for diabetes and an independent risk factor for cardiovascular disease and mortality. **Hypothesis**: a) Admission HbA1c may predict size of MI and death and b) patients admitted with MI to a large inner-city hospital may have a large incidence of undiagnosed diabetes. **Methods**: All patients admitted over a six-month period to the Medicine service of Jacobi Medical Center, a large municipal hospital in the Bronx, New York, with the diagnosis of rule-out myocardial infarction or myocardial infarction had admission glucose and an HbA1c within 24 hours of admission. Prior diagnosis of diabetes was confirmed by chart review and personal interview. MI was confirmed by peak troponin ≥0.1 **Results**: Of the 722 admissions for chest pain (mean age 59.5±15.2; 48% male; 37.6% prior diagnosis diabetes), there was no meaningful difference in HbA1c between those with MI (6.8 %±1.8, n=241) and those without MI (6.9 %±2.0, n=481), p=0.35, nor between those who died during the admission (n=30) and those who survived (6.5 %±1.9 vs. 6.9 %±1.9, p=0.32). Furthermore, there was no statistically significant correlation between HbA1c and troponin (r=0.03, p=0.47). In contrast, admission glucose was significantly higher in patients with MI than those without (171 mg/dL ± 107.5 vs. 139 mg/dL ± 81.2, $p<0.001$), and in those who died vs. survivors (228 mg/dL ± 169.9 vs. 146 mg/dL ± 85.9, $p<0.001$). Among the cohort without a prior diagnosis of diabetes, 7.3% had an HbA1c >7%. Among those admitted with a diagnosis of MI and without a prior diagnosis of diabetes, 8.9% had an HbA1c >7%. **Conclusion**: Admission HbA1c, in contrast to serum glucose, does not predict MI outcomes in patients admitted with chest pain. These findings suggest that elevations in serum glucose at time of admission may be a response to "stress" rather than poor short-term control of diabetes, and is unsuitable for diabetes screening. HbA1c testing may, however, be useful as a screening test for diabetes in this population.

P31

Are Nondiabetic Patients with Metabolic Syndrome at Risk for Developing Chronic Kidney Disease? Evidence Based on Data from a Large Cohort Screening Population

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Background. Chronic kidney disease (CKD) is an important health problem in the United States and is associated with significant cardiovascular disease, and premature mortality. Recently, metabolic syndrome (MS), which is present in approximately 20% of the U.S. population, has been highlighted as a CKD risk factor. We were interested in exploring the relationship between the metabolic syndrome and risk of developing of CKD independent of diabetes. **Method**. The study population consisted of 4607 adult (age ≥18) subjects, who were followed for three years, in the Tehran Lipid and Glucose Study, a prospective population based study of cardiovascular risk factors. Metabolic syndrome was defined based on NCEP guidelines and CKD was defined based on the K/DOQI criteria. Creatinin clearance was estimated using the Cockroft-Gault equation. Odds ratio of incident CKD based on metabolic syndrome with adjustment for demographic and confounding factors was defined. **Results**. At baseline 1010 (21.9%) subjects met criteria for metabolic syndrome. Compared to subjects without metabolic syndrome, those with metabolic syndrome were more likely to be males, were older, had higher blood pressure, higher body mass index, as well as worse triglycerides, total cholesterol and LDL cholesterol and lower HDL cholesterol levels. After 3 years of follow-up, 111 subjects (2.4%) from the cohort developed CKD. Of these subjects, 38 patients (3.4% of MS patients) had MS at baseline, while 73 (2.0% of non-MS subjects) subjects did not have MS at baseline CKD, an unadjusted OR= 1.88, 95% CI; 1.26–2.8. After excluding hypertensive people at baseline, in the remaining 3809 people, 406 subjects (10.7%) were defined as having metabolic syndrome and 3403 (89.3%) subjects did not have criteria for metabolic syndrome. After 3 years of follow-up, 70 subjects developed new CKD (1.83%), in which 62 subjects were in metabolic syndrome group (1.82%) and 8 subjects in non metabolic syndrome group (1.98%)(OR=0.925, 95%CI; 0.446–1.917) (p=0.844). **Conclusion**. The result of our study, suggests that metabolic syndrome is a cluster of multiple risk factors and as a cluster it is a significant risk for CKD. The risk of metabolic syndrome for developing CKD is highly impacted by the presence of DM and HTN.

P32

Increased Risk of Cardiovascular Events Among Type 2 Diabetes Patients with Dyslipidemia

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Introduction: Patients with type 2 diabetes (T2D) have an increased cardiovascular (CV) risk compared with the general population. A significant proportion of T2D patients have dyslipidemia in the form of elevated triglyceride (TG) and/or low high-density lipoprotein cholesterol (HDL-C) levels. Little evidence is available about the impact of this diabetic dyslipidemia on the incremental risk of CV events in T2D patients. **Hypothesis**: The study hypothesis tested that T2D patients with diabetic dyslipidemia have an increased CV risk compared with T2D patients without diabetic dyslipidemia. **Methods**: Retrospective study of T2D patients in the Ochsner Health System with TG and HDL-C measurements during 1998–2000 (N=7631) was conducted for occurrence of CV events from 2000–2004, including: 1) coronary heart disease (CHD) events, defined as myocardial infarction, coronary revascularization, and coronary death and 2) cerebrovascular (CRBV) events, defined as fatal and nonfatal stroke. Multivariate logistic regression models assessed 5-yr event rates among patients with and without diabetic dyslipidemia after adjusting for CV risk factors such as age, gender, hypertension, and obesity. Diabetic dyslipidemia was defined in 2 ways: 1) TG>150 mg/dL and HDL-C <40 mg/dL and 2) TG>150 mg/dL or HDL-C <40 mg/dL or TG/HDL-C ratio ≥5. **Results**: Of the 1398 T2D patients with the diabetic dyslipidemia definition of TG>150 mg/dL and HDL-C <40 mg/dL, 5-yr risk was significantly increased for CHD events (OR=1.17, 95%CI=1.02–1.36, rate=30.2) and CRBV events (OR=1.55, 95%CI=1.19–2.02, rate=7.0) compared with T2D patients without diabetic dyslipidemia. The 5-yr CHD risk (OR=1.33, 95%CI=1.16–1.54, rate=29.9) and CRBV risk (OR=1.58, 95%CI=1.20–2.10, rate=6.4) was also significantly increased for 3182 T2D patients with the diabetic dyslipidemia definition of TG>150 mg/dL or HDL-C <40 mg/dL or TG/HDL-C ≥5. **Conclusions**: T2D patients with diabetic dyslipidemia have increased odds of coronary and cerebrovascular events even after adjusting for known CV risk factors when compared with T2D patients without these lipid abnormalities. These findings highlight the need to increase the awareness of the CV risk of diabetic dyslipidemia to improve CV outcomes in T2D patients.

P33

Impact of Optimal Versus Suboptimal Therapy in Diabetic Patients with Acute Coronary Syndromes

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Background: Diabetes mellitus (DM) is one of the major risk factors for cardiovascular diseases and is usually associated with a worse prognosis in acute coronary syndrome (ACS) patients. Many drugs and strategies used to treat ACS can improve this prognosis, but the impact of previous DM treatment on in-hospital (IH) mortality is poorly understood. **Aim**: To evaluate the impact of previous DM treatment in IH mortality in diabetic ACS patients. **Methods**: Retrospective analysis of a database containing 216 patients admitted for ACS in a single coronary intensive care unit between May 2004 and December 2005 that were known to be diabetic at hospital admission. Optimal previous treatment for DM was considered to be insulin, aspirin, ACE inhibitors and statins. We evaluated 2 groups: group A - diabetic patients treated with these 4 drugs (n=19) and group B - diabetic patients treated with ≤3 drugs (n=197). **Results**: In both groups, patients were mainly of male gender (67.6%) with mean age of 70.1±10.1 years. Previous history of hypertension was present in 81% of patients, dyslipidaemia in 77.3%, family history of coronary disease in 12% and smoking habits in 11.1%. Group B patients had an IH mortality rate that was double that of group A (11.2% versus 5.3%). This occurred despite the higher prevalence of previous history of myocardial infarction (77.8% versus 30.8%), catheterization (68.4% versus 34.9%) and percutaneous coronary intervention (38.9% versus 12.8%) in group A. Ejection fraction, either evaluated by echocardiography or left ventriculography, was similar in the 2 groups of patients. **Conclusion**: Our series shows that diabetic patients previously well treated have a better IH outcome. This reinforces the importance of using optimal DM treatment as a mean to prevent ACS and decrease the higher IH mortality rate usually associated with ACS in this group of patients.

P34

Is Inflammatory Expression of Acute Coronary Syndromes Influenced by Abnormal Glucose Regulation?

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Introduction: The relationship between glucose metabolism and C reactive protein (CRP) in patients with acute coronary syndromes (ACS) is not well established. **Aim**: To determine the influence of glucose metabolism and glucometabolic control, evaluated by glycated haemoglobin (HbA1c), in patients with ACS. **Methods**: 199 consecutive patients admitted in the same centre with ACS were prospectively studied; 140 patients who were already diabetic or had done an oral glucose tolerance test (OGTT) and in whom CRP was evaluated were identified.

They were divided in 3 groups according to the glucose metabolism: A - diabetes mellitus (DM) (n=69), B - other glucose metabolism abnormalities (n=34) and C - normal glucose metabolism (n=37). Then we identified 132 patients with evaluations of CRP and HbA1c and divided them according to the level of HbA1c: D - HbA1c >6 mg/dl (n=54) and E - HbA1c <= 6 mg/dl (n=78). CRP level considered was the first one determined and OGTT was performed after day 4. **Results** (table 1): Groups were similar regarding demographics, type of ACS and cardiac enzymes. CRP levels were higher in groups A and D. **Discussion**: The results show a direct relationship between CRP and both abnormal glucose regulation and glucometabolic control level. This occured despite DM patients being older and having lower number of transmural infarctions (conditions generally associated with lower levels of CRP). **Conclusion**: Patients with ACS and DM have higher levels of CRP, which can be related to the poor prognosis presented by these patients. A good metabolic control of DM is, therefore, essential to ameliorate the prognosis after an ACS.

Table 1 - Results

	A (n=69)	**B** (n=34)	**C** (n=37)	**p** (A vs B vs C)	**D** (n=54)	**E** (n=78)	**p** (D vs E)
Age (years)	68.9±1.3	67.9±2.2	64.8±1.8	n.s.	69.5±1.3	66.5±1.4	n.s.
Male (%)	68.1	76.5	78.4	n.s.	66.7	79.5	n.s.
STEMI/NSTEMI/ Unstable angina (%)	43.5/43.5/13.0	50.0/44.1/5.9	37.8/46.0/16.2	n.s.	46.3/46.3/7.4	44.9/43.6/11.5	n.s.
cTn I (ng/ml)	43.2±11.8	32.4±7.2	27.2±6.3	n.s.	27.0±5.7	44.8±10.6	n.s.
CK-MB mass (ng/ml)	137.2±62.5	88.8±20.7	77.6±15.8	n.s.	66.1±16	150.6±55.4	n.s.
PCR (mg/dl)	5.1±0.7	3.2±0.7	2.9±0.5	**0.05**	5.3±0.9	3.5±0.4	**0.045**

P35

Diabetes Control Is Worse in US Compared with Swedish Patients from Similar Populations Despite More Rigorous Intervention

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Objectives: To evaluate diabetes control in regions with similar racial/ethnic mix, infrastructure and physical environment in Pennsylvania served by the Geisinger Health System (GHS), and Skaraborg, Sweden, with a public health service. **Methods**: Using comprehensive longitudinal electronic health records we identified 26,443 GHS patients (12,829 men and 13,614 women) with diabetes seen within the prior 2 years, and 10,391 patients (5,473 men, 4,918 women) in the Skaraborg Primary Care Database (SPCD). Equivalent data on demographics, hemoglobin A1C (A1C), height, weight and medication use were extracted for both populations. We defined Uncontrolled Diabetes (UD) as A1C ≥7.0. **Results**: Mean A1C was 7.54 in GHS (n=17,958) and 6.29 in SPCD (N=9,945). UD among patients with A1C measured within 2 years was more than twice as high in GHS (60%) versus SPCD (25%) patients. Including patients with no A1C in 2 years as UD, the GHS rate increased to 73% and the SPCD rate was unchanged. GHS patients used a mean of 1.6 diabetes drugs compared with 0.9 for SPCD ($p< 0.001$). In logistic regression adjusted for age, sex, BMI, number of diabetes drugs, and insulin dependence, the odds for UD in GHS patients compared with SPCD was 6.9 ($p<0.001$). Further adjustment for type of insurance (including none) changed this minimally to 6.6 ($p<0.001$). Restricting the analysis to patients with similar medical coverage (Geisinger HMO and all SPCD), the odds ratio (OR) was 5.9 ($p<0.001$). Models restricted to users of a specific class of drug demonstrated similarly robust differences. With adjustment for all factors above plus insurance, or all factors above restricted to GHS HMO and SPCD patients, ORs were: Biguanides 5.6 and 5.2, Sulfonylureas 6.1 and 5.5, Insulins 6.2 and 5.5, Glitazons 9.1 and 8.5, Meglitins 4.9 and 4.4, Combinations with Metformin12.4 and 14.1, and other less common drugs 5.3 and 4.8; all $p<0.001$. **Conclusions**: These marked differences in diabetes control between similar populations in the US and Sweden are robust to control for BMI, treatment and access to care. Diet, compliance with treatment, other physical and social environmental factors, or gene-environment interactions may be involved and should be explored.

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Withdrawn

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Clinical Predictors of Glycosylated Hemoglobin Responses to Thiazolidinedione Therapy

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The present investigation was an initial step toward the development of a pharmacogenomic tool for identifying patients who are most likely to respond well to thiazolidinedione (TZD) therapy. To have clinical utility, such a tool should have predictive value beyond that from readily available clinical information. The aim of this investigation was to assess clinical predictors of the HbA_{1C} response after addition of a TZD to a biguanide, a sulfonylurea, or both in subjects with type 2 diabetes. Chart review in the offices of 68 physicians was used to identify consecutive subjects. To qualify, subjects needed to have been treated with pioglitazone (≥4 mg/d) or rosiglitazone (≥30 mg/d) for ≥12 weeks. Clinical characteristics and HbA_{1C} responses were assessed for the purpose of creating an initial predictive model (Study 1). A separate sample from a managed care database was used to independently validate the model (Study 2). Data were collected for 4085 subjects (1365 in Study 1; 2720 in Study 2). In Study 1, subjects were 51% male (696/1365), 75% (1025/1365) non-Hispanic white, had a mean age of 62±0.3 (SEM) years and mean body mass index of 33.4±0.2 kg/m^2. Baseline HbA_{1C} was 8.2±0.1%. Forty-five percent (611/1365) and 55% (754/1365), respectively, were prescribed pioglitazone and rosiglitazone. In multivariate regression, baseline HbA_{1C} (β = -0.693), age (β = -0.006), and use of multiple agents before the addition of a TZD (referent = single agent, β = 0.189) were significant ($p < 0.05$) predictors, explaining 49% of the variance in HbA_{1C} response. This predictive model explained 44% of the variance in HbA_{1C} response in the Study 2 sample. The mean and SD for predicted minus observed response were 0.018% and 1.3%, respectively. The model showed no material evidence of bias across the range of baseline HbA_{1C} values. These results suggest that readily identifiable clinical factors explain a substantial fraction of the variance in HbA_{1C} response to TZD therapy. The most notable finding was the strong effect of baseline HbA_{1C}, with each increment of 1% associated with a 0.69% greater HbA_{1C} response. This suggests that baseline HbA_{1C} should be considered when evaluating TZD responses in clinical practice and when comparing results from clinical trials.

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Waist Is Associated Longitudinally with Adiponectin but Not with Clamp-Derived Insulin Sensitivity in a Cohort of Adolescents

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Studies in adults show that central adiposity is strongly associated with circulating levels of adiponectin and insulin sensitivity, two risk factors for type 2 diabetes. However, the timing of the development of these associations is not well understood. In this study longitudinal associations between waist, adiponectin, and insulin sensitivity were examined in a cohort of adolescents. Participants (n= 206) were recruited from the Minneapolis school system and underwent three clinical research center exams at mean ages 13 (visit 1), 15 (visit 2) and 19 (visit 3). Adiponectin was measured in serum. The euglycemic hyperinsulinemic clamp (EHC) was used to measure insulin sensitivity which was calculated as the amount of glucose needed to maintain euglycemia over the final 40 minutes of the clamp, adjusted by lean body mass (MLBM). Adiponectin measured at age 19 was statistically significantly correlated with waist measured at age 13 (r = -0.23), waist measured at age 15 (r = -0.30) and waist measured at age 19 (r = -0.35). Insulin sensitivity measured at age 19 was not significantly correlated with waist measured at age 13, but was significantly correlated with waist measured at age 15 (r = -0.21) and age 19 (r = -0.16). In linear regression analyses adjusted for sex and ethnicity both waist at age 13 (baseline waist) and change in waist from age 13 to age 19 were predictive of adiponectin measured at age 19. Baseline waist, but not change in waist was also predictive of adiponectin at age 15. Baseline waist and change in waist were not predictive of insulin sensitivity at ages 15 or 19. In conclusion, we found measurements of waist to be predictive of adiponectin but not of insulin sensitivity in this adolescent cohort. The magnitude of the cross sectional and longitudinal associations between waist and adiponectin increased as the participants aged, and, by age 19, was similar in strength to that reported in adults. However, the associations between waist and insulin sensitivity at age 19 were weak or non-significant, unlike associations reported in adults, suggesting the relationship between visceral adiposity and insulin resistance may not develop until later in life.

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Determinants of Plasma Leptin Levels in Hypertensive Adults

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Background: The adipokine leptin has oxidative and inflammatory properties that may influence cardiovascular risk. We investigated determinants of plasma leptin levels, including ethnicity, in hypertensive adults. **Methods**: Subjects included 788 African Americans (AA) from Jackson, MS (mean age 63.8 years; 71.2% women), and 696 non-Hispanic Whites (NWH) from Rochester, MN (mean age 60.5 years; 56.9% women) participating in a community-based study of hypertensive sibships. Plasma leptin was measured by RIA. We assessed whether ethnicity was a significant predictor of leptin concentrations after adjustment for the following risk factors: conventional (age, sex, BMI, total cholesterol, LDL-C, HDL-C, diabetes, smoking and systolic BP), 'novel' (homocysteine, CRP and fibrinogen), 'metabolic' (waist circumference, insulin, glucose and TG), 'lifestyle' (alcohol use and physical activity), and medications (statin and hypertension medications, and estrogen (in women)). Multiple regression analyses were performed using generalized estimating equations to account for intrafamilial correlations. **Results**: In men, plasma leptin levels did not differ

significantly between ethnic groups (11.1 ng/mL AA vs. 11.2 ng/mL NHW, $P = 0.588$). Independent predictors of higher leptin levels were higher BMI, waist circumference, insulin, homocysteine and fibrinogen; and current smoking status. In women, plasma leptin levels were significantly higher in AA compared with NHW (34.4 ng/mL vs. 28.8 ng/mL, $P < 0.0001$). AA ethnicity remained an independent predictor of higher leptin levels after adjustment for other covariates. Additional independent predictors of higher leptin levels in women were higher BMI, HDL-C, insulin and CRP; lower diabetes history and non-smoking status, and decreased alcohol consumption and physical activity. **Conclusion**: In hypertensive adults, determinants of plasma leptin levels differ by sex. In men, adiposity and higher homocysteine levels were independently associated with higher leptin levels. In women, AA ethnicity, inflammation, adiposity, and low physical activity are associated with higher plasma leptin levels.

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Obesity: Role in Middle-Aged Men and Women in Producing Epidemic Rates of the 4 Other Traits Defining the Metabolic Syndrome: The CUORE Project

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Background, Aim: Multiple aspects of the Metabolic Syndrome (MS) remain problematic and require further research assessment. The focus of this population-based study is on in-depth quantification of the role of obesity in producing epidemic occurrence of the four other traits used to define MS. **Methods**: Data from 12 population samples of the Italian CUORE Project; 5,898 men and 11,354 women baseline ages 35–69, free of CVD, followed for 10 years; ATP III definition of MS. **Results**: Age-adjusted MS prevalence was low in the normal weight (BMI 18.5–24.9 kg/m^2): men 6%, women 4%; higher in the overweight (BMI 25.0–29.9 kg/m^2): men 18%, women 15%; and very high in the obese (BMI $>=$30.0 kg/m^2): men 56%, women 40%; 11 times higher in men with waist circumference (W) $>$102 cm than in men with W$<$90; 15 times higher in women with waist W $>$88 cm than in women with W$<$81. (BMI and W were highly correlated – men: r$=$0.83 , women: r$=$0.85). In both genders, there was a continuous, graded, strong relation of BMI (or W) to each of the four other variables included in the MS definition (adverse blood pressure [BP], HDL-cholesterol [HDL-C], triglycerides [TG], glycemia/diabetes [DM]). BMI (or W) was also positively related to TC, non-HDL-C, TC/HDL-C, and non-HDL-C/HDL-C. For both genders, BMI (or W) also related significantly and strongly to prevalence of any four or all five of the five possible combinations of adverse BP, TG, DM, HDL-C, and to all combinations of these four other MS traits. Overall prevalence of these adverse combinations ranged in women from 1.8% with BMI 18.5–24.9 kg/m^2 to 13.1% with BMI$\geq$35.0 kg/m^2. Similar findings prevailed for those with the most common combination, adverse TG$+$HDL-C$+$BP, and for those with all four of these MS traits adverse. **Conclusions**: For middle-aged men and women, both BMI and W relate continuously and strongly to levels of the other traits (adverse BP, TG, HDL-C, glycemia/DM) used to define MS, and to prevalence rates of MS-defining combinations of adverse levels of these traits. MS is rare in people with non-overweight BMI and W levels. Obesity plays a key role in producing epidemic occurrence of the four other traits used to define MS.

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Height and the Waist Circumference Criterion in the Metabolic Syndrome in Japanese Men

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Objective For Japanese men with the metabolic syndrome, waist circumstance must be $\geq$85cm. Whether this criterion needs to be modified according to height is uncertain. The purpose of this report is to assess the association of height and waist circumference with other metabolic syndrome criteria in Japanese men and to determine if the waist circumference criterion in the metabolic syndrome needs to vary according to height. **Methods** A sample of 313 men aged 49–60 years were randomly selected in Kusatsu, Japan. Participants were divided into waist circumference and height strata. Waist circumference strata were defined as $<$80.3, 80.3 to $<$85, and $\geq$85 cm. The value 80.3 is the median waist circumference for those that were $<$85cm. Height strata were defined by tertiles. Within each combination of waist circumference and height stratum, the number of men with $\geq$2 of the following metabolic syndrome criteria was observed: triglyceride $\geq$150mg/dl, HDL-C $<$40 mg/dl, systolic or diastolic blood pressure $\geq$130/85 mmHg, and diabetes or fasting blood glucose $\geq$110 mg/dl. **Results** In the smallest waist circumference strata ($<$80.3 cm), height and the metabolic syndrome criteria were unrelated. In contrast, with the tallest ($>$172.3 cm) and smallest waist circumference ($<$80.3 cm) strata serving as a reference, the relative odds of having $\geq$2 criteria in men with a waist circumference of 80.3 to $<$85 cm declined significantly from 5.0 in the shortest men ($<$168 cm) to 1.7 in the tallest ($>$172.3 cm). The relative odds in the shortest men was the only relative odds that was statistically significant. Using the same reference group, the relative odds of having $\geq$2 criteria in men with a waist circumference $\geq$85cm varied modestly with height. Here, relative odds ranged from 7.0 to 9.5. All were statistically significant. **Conclusions** For men with waist circumstances $\geq$85 cm, current waist circumference guidelines that ignore height appear adequate in identifying other metabolic syndrome criteria. For men with waist circumferences that range from 80.3 to $<$85cm, however, short height ($<$168 cm) tends to be more often associated with metabolic syndrome criteria. Whether the waist circumference criterion in the metabolic syndrome in Japanese men needs to be lowered for short men warrants further study.

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Measurements of Waist Circumference in the 13 Ways Described in Literature, in Relation to Meals, Posture, and Phases of Respiration to Predict the Best Correlate of Body Fat Among Them

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Aims: Waist circumference (WC) is more closely associated with central adiposity than waist-to-hip ratio, BMI or any other anthropometric measurements. Multiple ways to measure WC have been described. We aim to compare the variations in WC measurements in relation to anatomical landmarks, meals, posture and phases of respiration and thus find out the best correlate with body fat amongst them **Methods**: The present study was carried out on 124 apparently healthy individuals visiting the tertiary care hospital as relatives of patients. Person with ascites or any manifested pathology were excluded. The average waist circumferences was measured in thirteen different ways by a single trained person. In addition, percentage body fat (by bio-impedance) and four skin folds were measured. Intra-class correlation coefficient was calculated for each set of measurements separately for males and females. Repeated measures ANOVA and post hoc analysis was done separately for males and females. Linear regression method was used to model the relation between the fat values and WC. **Results**: 124/130 healthy individuals (females $=$48) with mean age $\pm$ SD $=$ 41.89$\pm$14.07; BMI $=$23.85$\pm$4.4 and % body fat$=$28.87$\pm$10.55. Difference in the WC measured in 13 ways is significant in a sex dependent manner. On comparison with % body fat as calculated by regression formula, body fat% found by impedance method correlated best with WC-6 which is the WC measured in erect posture: at midpoint, standing straight, fasting, irrespective of respiratory phase. (REF. TABLE1) **Conclusion**: We propose that WC-6 may be considered as a standard for measuring waist circumference where a surrogate marker to correlate best with body fat% is needed.

Comparison of the waist circumference measured in the thirteen ways and predicted fat percentage.

	Methods of measuring Waist Circumference	Waist Circumference (MALES n= 76)	Waist Circumference (FEMALES n= 48)	Predicted fat percentage (Using Regression Equation)	|D%| = |Absolute - Predicted Fat %|
WC1	Immediately above the iliac crest (NIH)	88.49±16.25	92.71±19.91	28.87±7.98	7.94
WC2	WHO protocol, mid point between iliac crest and sub costal level, end expiration	88.28±16.60	89.56±19.91	28.87±8.02	7.74
WC3	Ideal: at midpoint, erect, fasting, end normal inspiration	87.76±16.62	88.69±14.94	28.87±8.04	7.68
WC4	Normal: at mid point, irrespective of meal or respiratory phase or posture	88.12±16.58	90.72±14.79	28.87±8.00	7.87
WC5	Usual posture: at midpoint, fasting, irrespective of respiratory phase	88.04±16.63	89.70±14.79	28.87±7.99	7.82
WC6	Erect posture: at midpoint, standing straight, fasting, irrespective of respiratory phase	88.87±16.62	88.60+15.00	28.87±8.05	**7.65**
WC7	Erect posture: at midpoint, standing straight, fasting, irrespective of respiratory phase	84.22±16.53	85.79±14.48	28.87±7.74	8.48
WC8	Erect posture: at midpoint, standing straight, fasting, irrespective of respiratory phase	88.11±16.65	90.05±14.94	28.87±7.99	7.87
WC9	End normal expiration: at midpoint, in usual posture, fasting	88.41±16.58	89.58±14.88	28.87±8.02	7.72
WC10	Maximum expiration: at mid point, in usual posture, fasting	89.33±16.72	90.85±14.72	28.87±8.06	7.69
WC11	Measurement at midpoint taken by an unbiased observer.	88.17±16.62	89.69±14.82	28.87±8.01	7.78
WC12	At midpoint, in usual posture, 5–10 minutes post meals	89.77±16.67	91.10±14.96	28.87±8.06	7.66
WC13	At midpoint, in usual posture, 2hrs after meals.	88.93±16.66	90.60±14.80	28.87±5.68	13.31

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Adiponectin Concentration Is a Strong Correlate of Insulin Resistance and the Metabolic Syndrome Among Women with Pregnancy-Induced Disturbances

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Background: Adiponectin is an adipose-tissue specific protein inversely related to insulin resistance (IR) and diabetes incidence. In order to assess its value in identifying women at increased risk of subsequent cardiovascular disease, we compared post-partum adiponectin levels among women with prior pregnancy induced disturbances and assessed its association with HOMA-IR and the metabolic syndrome (MS). **Methods**: Women delivering between 1998 and 2001 and who had gestational diabetes (GDM, n=22), gestational hypertension (GHTN, n=32), or preeclampsia (PE, n=34) were examined 1–2 years after delivery and grouped matched to controls (normal pregnancies, n=29) by age and pre-pregnancy BMI. Adiponectin was measured in citrated plasma and IR was determined by the HOMA-IR equation. The sample was restricted to African American and non-Hispanic white women. **Results**: A higher prevalence of MS was evident in women with GDM and those with PE compared to controls ($p<0.05$). HOMA-IR was increased ($p=0.001$) whereas adiponectin tended to be lower in women with prior GDM compared to all other women ($p=0.08$). Adiponectin was inversely related to HOMA-IR ($r=-0.45$, $p<0.0001$) and a significant trend for decreasing adiponectin with increased number of MS components was noted (p-trend$<$0.0001). In multivariable analyses, adiponectin was strongly, inversely, related to HOMA-IR (beta=-0.28, $p=0.009$), the model explaining 53% of the variation in HOMA-IR (other significant covariates included age, BMI, race, HbA_1, and study group). **Conclusions**: In women with pregnancy-induced disturbances, adiponectin concentration tended to be lower in those with prior GDM and it was a strong correlate of HOMA-IR and the MS.

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Cardiometabolic Risks in US Veterans Health Administration Patients

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The Veterans Health Administration (VA) maintains one of the largest integrated U.S. health care systems, providing care for over 7 million veterans. The VA maintains linked automated medical data on a national level, which we used to study the epidemiology of cardiometabolic risks among VA patients. We used VA laboratory test results and prescription records for selected years from 1998–2004 along with self-reported and clinic measures of weight and height from 1999 and 2000. Patients were classified as having diabetes, hypertension, and dyslipidemia based on prescriptions and ICD-9-CM codes using previously published algorithms. We studied the prevalence of different combinations of risk factors - diabetes or impaired fasting glucose, high blood pressure or antihypertensive medication use, high plasma triglycerides, low HDL, obesity, and microalbuminuria. In addition, patients were classified for metabolic syndrome based on 3 sets of criteria from: the ATP III, the World Health Organization (WHO), and the International Diabetes Federation (IDF). For all 3, BMI was used instead of waist circumference since it was not available. Using the ATP III criteria, we found an overall prevalence of 42.5%. This may be an underestimate since not all patients had results available for all tests; if restricted to the 77% with all tests except for microalbuminuria, the prevalence was 64.2%. Prevalence was highest in patients who were male (43.2%), 60–65 years (51.3%), and white (44.9%) or hispanic (44.4%). If rates are age and sex standardized to the U.S. population, prevalence is still relatively high at 29.0%. Prevalence rates based on WHO or IDF criteria are lower but still high relative to other populations. Among those without a diagnosis of diabetes in 1999, patients meeting these criteria were compared to those who did not and were found to be 6 times more likely to develop diabetes and nearly 50% more likely to die in the subsequent 5 years. Cardiovascular disease events and other outcomes are under investigation. Cardiometabolic risks are relatively common among VA patients and contribute substantially to increased morbidity and mortality. The epidemiology of these conditions and modification of their associated risks deserves further investigation.

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The Implications of Anthropometric, Inflammatory, and Glycemic Control Indices on the Epidemiology of the Metabolic Syndrome Given by Different Definitions: A Classification Analysis

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Background: Individuals with the metabolic syndrome (MS) are at high risk for coronary heart disease. In this work we evaluated the levels of inflammatory, lipidemic and glycemic control markers in people with and without MS, as given by different definitions. **Methods**: During 2001 - 2002, we randomly enrolled 1514 men (18–87 years old) and 1528 women (18–89 years old), without any clinical evidence of cardiovascular disease, from the Attica area, Greece. Among several variables we also measured inflammatory markers, total antioxidant capacity, glucose and insulin levels, and various lipids. The metabolic syndrome was defined according to the NCEP ATP III criteria or the International Diabetes Federation (IDF) Epidemiology Task Force group. In all analyses people with diabetes were excluded. **Results**: The prevalence of the metabolic syndrome was 17.9% according to the NCEP definition and 48.9% according to the IDF definition ($p < 0.001$). The prevalence of metabolic syndrome was higher in males compared to females according to both definitions (p for gender differences $<$ 0.001). Moreover, 3.9% of the total study sample fulfilled only the NCEP criteria, but not the IDF, while 38.6% fulfilled only the IDF criteria. People that were defined as having metabolic syndrome using the IDF criteria were younger, had higher BMI, C-reactive protein, fibrinogen, tumor necrosis factor - α levels, total antioxidant capacity and lower glucose, and insulin. **Conclusions**: Prevalence of the metabolic syndrome is very high among Greek adults when the IDF definition is used, while it is still considerable when we adopt the NCEP criteria. It is evident that subjects who fulfilled the IDF criteria showed increased levels of inflammatory markers compared to those who fulfilled the NCEP ATP III criteria.

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Comparison of 3 Diagnostic Criteria of Metabolic Syndrome in 3 Canadian Populations

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Introduction: The metabolic syndrome (MetS) is a cluster of metabolic abnormalities of which visceral obesity is one of its cornerstones. In a context of global spreading of this syndrome, major world health organisations have formulated definitions still under debate particularly in regards to the visceral obesity cut-off points. The purpose of this study was to compare the definitions of MetS with a special focus on abdominal obesity, and to estimate the prevalence of this syndrome in three ethnic groups residing in one Canadian province, Québec. **Methods**: The study population included adult participants of the extensive cross-sectional health surveys conducted in southern Québec, James Bay and Nunavik between 1990 and 1992. Of these participants, 2,613 adults (18–74 years) were included in the present analysis; 1417 southern Quebecers, 817 Indians Cree and 379 Inuit. **Results** The prevalence between three organisation's criteria varies form 11.9% for the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), 17.7% for the European Group for the Study of Insulin Resistance (EGIR) and 18.6% for the World Health Organisation (WHO). In people with MetS, we observed significant differences in mean waist circumference between the ethnic groups. Indeed, Inuit and Cree individuals with MetS have higher mean waist circumferences than southern Quebecers ($p<0.001$). This was observed in both genders. For waist-to-hip ratio (WHR), the other marker of central obesity, we obtained similar results. Although they have a lower score in abdominal obesity, the southern Quebec population has the highest prevalence of MetS. Moreover, in Inuit and Cree individuals, a decrease of WHR cut-offs increase the crude prevalence of MetS from 22.7 to 24.6%. **Conclusion**: These results support the initiative of the International Diabetes Federation for the inclusion in the MetS definition, of cut-off points adapted to different ethnic susceptibilities.

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Pharmacist-Provided Metabolic Syndrome Screening and Educational Program Reduces Prevalence of Cardiometabolic Risk Factors

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Introduction Recent literature demonstrates evidence of an association between metabolic syndrome and coronary heart disease (CHD). However, there are no published studies describing changes in clinical risk factors and health behaviors after a screening and education program focused on the metabolic syndrome. **Hypothesis** We assessed the hypothesis that a pharmacist-provided clinical screening and educational pilot program will promote positive changes in CHD risk profile and health behaviors. **Methods** Participants were recruited from the employees of a public school system. Participants underwent clinical screening by pharmacists and completed a written survey to assess their health behaviors and knowledge of CHD risk. Fasting blood glucose, lipid profile, waist circumference, and blood pressure were measured. Participants were educated regarding metabolic syndrome and received individualized counseling regarding their CHD risk profile and underwent follow-up screening at 4 months. Changes in CHD risk factors and health behaviors were assessed. **Results** One hundred twelve participants (82% female, mean age 45.1 ± 10.4 years) underwent baseline screening, and 65% (73 of 112) returned for follow-up screening. National Cholesterol Education Program Adult Treatment Panel III diagnostic criteria for metabolic syndrome were met in 31% (35 of 112) at baseline but only 18% (13 of 73) at follow-up ($p=0.04$). Significant reductions in total cholesterol (mean 197.5 ± 40.5 v. 189.6 ± 40.7 mg/dL, $p=0.02$), systolic blood pressure (123.8 ± 13.1 v. 117.3 ± 12.6 mmHg, $p<0.001$), and diastolic blood pressure (79.4 ± 8.6 v. 72.1 ± 10.5, $p<0.001$) were observed. No statistically significant changes in self-reported exercise or dietary habits were reported, but 7% (4 of 61) and 12% (7 of 61) reported initiating drug therapy for hypertension and dyslipidemia, respectively. Ninety-seven percent (59 of 62) found the program "somewhat useful" or "very useful" and 97% (60 of 62) would recommend it to others. **Conclusions** In conclusion, our pharmacist-provided screening and educational pilot program significantly improved total cholesterol and systolic and diastolic blood pressures. Data will be used to design a longer-term, controlled analysis of our program.

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Blood Pressure Control in Patients with Diabetes Better in the US than in Sweden in Similar Populations

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Objectives: Regions in Pennsylvania, USA served by Geisinger Health System (GHS), and Skaraborg, Sweden, with a public health service, have similar rural environments and infrastructure. The populations are homogenous and comparable in ethnic and genetic background. We compared blood pressure (BP) control in patients with diabetes in these two populations. Subjects: We identified 26,443 patients (12,829 men and 13,614 women) with diabetes in the GHS, and 10,391 (5,473 men, 4,918 women) in the Skaraborg Primary Care Database (SPCD), respectively. **Methods**: BP was uncontrolled if at least 140 or at least 90 mmHg. Patients receiving care but missing BP values (n=503, 4.8%) in SPCD and n=0 in GHS were considered uncontrolled. Age was stratified into $<$40 years, 40–59 years 60–79 years, and 80 years and over. **Results**: The prevalence of uncontrolled BP was high in SPCD men

(n=3212, 59%) and women (n=3231, 66%). Rates in GHS were roughly half for both men (n=4052, 32%), and women (n=4350, 32%). BP-lowering medications were used by 60% of SPCD men (n=3263) and 60% of SPCD women (n=2924). Corresponding rates in GHS were 78% for both men (n=10,059) and women (n=10,577). Uncontrolled BP was prevalent in patients treated with antihypertensive medications; in SPCD 64% of men (n=2101) and 71% of women (n=2086), and in GHS 33% of men (n=3289) and 34% of women (n=3577). SPCD patients were more likely than GHS patients to have uncontrolled BP; men OR 3.0 (95% CI 2.8–3.2), women 3.6 (3.4–3.9). This relationship was stronger in patients with BP-lowering medications; 3.7 (3.4–4.0), and 4.5 (4.1–4.9), respectively. There was a consistent pattern in subgroups by age, BMI, being on an ACE-inhibitor or an ARB or no, and being on a thiazide or not. Results were similar when subjects missing BPs were excluded. In a multivariate model with age, BMI, number of BP medications, and presence of ACE or ARB treatment, the association with uncontrolled BP in SPCD increased; men 3.5 (3.2–3.8), women 4.2 (3.9–4.6). **Conclusions**: The striking differences in BP control among similar populations in different countries may be due to differences in medical resources, physical/social environment, clinician /patient performance, or gene-environment interactions.

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The Metabolic Syndrome: Mix of Traits and Utility for Cardiovascular Disease Risk Prediction—Population-Based Data from the CUORE Project

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Objectives: The Metabolic Syndrome (MS) is widely used as a cardiovascular disease (CVD) risk predictor, but questions persist about this. **Methods**: Data from 12 population samples of the Italian CUORE project; 3,195 men and 8,269 women, baseline ages 35–69, free of CVD, followed for 10 years; endpoint: nonfatal/fatal coronary and stroke events; ATP III definition of MS. **Results**: Prevalence of MS was 20% for men, 16% for women. Common MS combinations (16 possible of any 3 or more of the 5 traits defining the MS) were: men, 1. adverse triglycerides (TG), HDL-C, blood pressure (BP) (26% of 646 men with MS); 2. adverse TG, BP, glycemia (DM) (12%); 3. adverse TG, BP, obesity (12%); 4. adverse TG, HDL-C, BP, obesity (12%); 5. adverse BP, DM, obesity (9%); women, 1. adverse HDL-C, BP, obesity (21% of 1,345 women with MS); 2. adverse TG, BP, obesity (21%); 3. adverse TG, HDL-C, BP, obesity (20%); 4. adverse TG, HDL-C, BP (11%); 5. adverse BP, glycemia, obesity (8%). For both genders, BP was the single most common trait identifying people with MS. In age-adjusted Cox models with MS (yes, no) and continuous MS variables, to study if information is lost for CVD risk assessment with dichotomization of MS variables, systolic blood pressure (SBP), HDL-C were independent CVD risk predictors (men); BP (women). TC (or non HDL-C) and smoking were significantly related to CVD in age-adjusted Cox models with MS (yes, no), to study loss of information by non-inclusion of these risk factors. MS as a predictor of CVD was cross-classified (2x2) with adverse risk defined as one or more of TC>=240 mg/dl, SBP>=140 mmHg or DBP>=90 mmHg or antihypertensive drug treatment, diabetes, smoking. MS was rare in both genders not at adverse risk; adverse risk predicted CVD in persons without MS; the sizable numbers with both were at very high CVD risk (relative risk 3.9 for men, 6.9 for women). **Conclusions**: Most with MS were identified by 5 (of the 16) combinations used to define MS. Information for CVD risk assessment is lost due to dichotomization of MS traits, and non-inclusion of TC and smoking. MS is rare people at adverse risk (identified based on classical major risk factors); co presence of adverse risk and MS leads to very high CVD risk. MS as a CVD risk predictor needs re-appraisal.

P50

Serum Concentrations of Uric Acid and the Metabolic Syndrome Among US Children and Adolescents

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The association between concentrations of uric acid and the metabolic syndrome in children and adolescents remains incompletely understood. The objective of this study was to examine how these two were associated in a nationally-representative sample of children and adolescents from the United States. We performed a cross-sectional analysis of 1362 males and females aged 12–17 years using data from the National Health and Nutrition Examination Survey 1999–2002. The prevalence of the metabolic syndrome was <1% among participants in the lowest quartile of serum concentration of uric acid, 3.2% in the second quartile, 9.9% in the third quartile, and 22.3% in the highest quartile. Compared with the lowest two quartiles of uric acid together (≤291.5 micromol/L = 4.9 mg/dl), the odds ratios was 5.67 (95% confidence interval: 3.19, 10.06) for those in the third quartile (>291.5-≤345 micromol/L or >4.9-≤5.8 mg/dl) and 16.12 (95% CI: 8.43, 30.82) for those in the top quartile (>345 micromol/L) after adjusting for age, sex, race or ethnicity, and concentrations of C-reactive protein. Starting with the lowest quartile of concentration of uric acid, mean concentrations of serum insulin were 65.6, 67.3, 80.1, and 90.0 pmol/L for ascending quartiles, respectively. In conclusion, serum concentrations of uric acid among U.S. children and adolescents are strongly associated with the prevalence of the metabolic syndrome. An elevated concentration of uric acid among children and adolescents should alert clinicians to the possible presence of the metabolic syndrome.

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Fish Intake and Metabolic Syndrome in Elderly Coronary Patients

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Background: Metabolic syndrome is associated with an increased risk of coronary heart disease. Whether fish intake could protect against the metabolic syndrome is not yet clear. **Objective**: We examined the association of total, lean and fatty fish intake with the prevalence of metabolic syndrome in elderly Dutch myocardial infarction patients. **Design**: For the present analysis we used baseline data of the Alpha Omega Trial (ClinicalTrials.gov Identifier: NCT00139464). At baseline participants filled out a lifestyle and health and a food frequency questionnaire. Anthropometrics and blood pressure were measured and blood samples were taken. The present analysis comprised 812 men and 235 women aged 60–80 years with a history of a myocardial infarction in the past 10 years. Data were analysed using the Cox proportional hazard model adopted for cross-sectional analysis, with adjustment for age, gender, education level, smoking status, physical activity, and the daily intake of energy, alcohol, fruit and vegetables and saturated fat. **Results**: Metabolic syndrome (according to ATPIII criteria) was present in 42% of the men and 62% of the women. Patterns of fish intake were similar in men and women: 11% never consumed fish, 51% consumed fish less than once a week, and 38% consumed fish once or more per week (mean intake: 15.5 gram per day). Fish intake tended to be inversely associated with metabolic syndrome. The adjusted prevalence ratio for metabolic syndrome in men who consumed no fish was 1.24 (95% CI: 0.86–1.78) compared to men who consumed fish once or more per week. This relation was mainly attributable to fatty fish intake. In women, fish intake was not associated with the metabolic syndrome. However, when analysing the individual components of metabolic syndrome, female participants who consumed no fish had more often a low HDL cholesterol (1.62 (95% CI: 0.82–3.19)). **Conclusion**: Intake of fatty fish may contribute to the prevention of metabolic syndrome, especially in men. However, prospective studies are needed to confirm this relationship.

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Fish Consumption and Risk of Major Chronic Disease in Men

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Background: High fish consumption has been associated with lower risk of chronic disease in several, but not all studies. Other dietary factors may modify the beneficial effects of the long-chain n-3 fatty acids found in fish, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). For example, it is hypothesized that n-6 fatty acids may compete for desaturase enzymes involved in n-3 fatty acid elongation and produce inflammatory eicosanoids. **Methods**: A total of 38,520 men from the Health Professionals Follow-up Study, aged 40–75 and free of major chronic disease at baseline in 1986, were followed for 16 years. Lifestyle and other risk factors were assessed every 2 years and diet every 4 years. During follow-up 7,428 major chronic disease events occurred, including 2,759 cardiovascular events (fatal and non-fatal CHD and stroke), 3,517 new cancers, and 1,152 noncardiovascular deaths (not including accidents or suicides). The men were divided into five groups based on fish consumption (<1 serving/mo, 1–3/mo, 1/wk, 2–4/wk, >=5/wk) or estimated total EPA+DHA intake (<0.05, 0.05-<0.2, 0.2-<0.4, 0.4-<0.6, and >=0.6 g/d). For stratified analyses the three middle groups were combined. Cox proportional hazards models were used to control for potential confounders. **Results**: Overall, neither fish intake nor EPA+DHA consumption were associated with risk of major chronic disease after multivariate adjustments (P for linear trend 0.40 and 0.36, respectively). These associations were modified by intake of n-6 fatty acids (P for interaction 0.03). In the lowest tertile of n-6 fatty acid intake (<10.1 g/day), the relative risk (RR) and 95% confidence interval (CI) for chronic disease was 1.0, 0.90 (0.80–1.01) and 0.82 (0.68–1.00) for fish intake (<1 serving/mo, 1/mo-4/wk and >=5/wk, respectively), P for linear trend 0.04. Similar findings were seen for EPA+DHA in the lowest tertile of n-6 fatty acid intake (P for interaction 0.02). **Conclusions**: Fish or EPA+DHA consumption appears to protect against major chronic disease, but the benefit may be limited to those individuals with lower dietary n-6 fatty acid intake.

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Modification of Lipid Responsiveness by Inflammation and Adiposity

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Introduction: Some studies suggest that greater adiposity and inflammation blunt the beneficial lipid effects of diets low in saturated fat; however, data are sparse. **Methods**: Using data from the DASH-Sodium trial, a multi-center isocaloric feeding study (n=412), we determined if measures of adiposity and inflammation modify the lipid responsiveness to the DASH diet (6% sat fat,13 % mono fat, 8% poly fat) in comparison to a control diet (16% sat fat, 13% mono fat, 8% poly fat). Lipids were measured at baseline and 3 follow-up visits, each separated by ~1 month. Analyses were conducted to examine the impact of the DASH diet, net of control, on serum lipids by mean levels of C-reactive protein (CRP) and baseline levels of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-alpha), waist circumference (WC) and body mass index (BMI). **Results**: The DASH diet had no significant impact, net of control, on any inflammatory marker levels. Reductions in total, LDL and non-HDL cholesterol were significantly more pronounced in those with normal (3 mg/dL) CRP levels. (See table) Changes in HDL-c and triglycerides did not significantly vary by CRP level. There was a general, though not statistically significant, trend towards greater reductions in total, LDL and non-HDL cholesterol in those with lower BMI and WC. The greatest reductions in total (-35.6 mg/dl ± 6.2), LDL (-26.9 mg/dl ± 5.9) and non-HDL cholesterol (-28.6 mg/dl ± 5.6) were seen in normal weight individuals who had normal CRP levels. Serum levels of TNF-alpha and IL-6 did not predict lipid changes. **Conclusions**: In the setting of isocaloric feeding without weight loss, low CRP was associated with significantly improved lipid profiles from consumption of the

DASH diet. The greatest cholesterol reduction occurred in normal weight individuals who also had low CRP levels.

Net Change (± SE) in Lipid Levels (DASH minus Control) According to CRP Level

-	C-reactive Protein (mg/dl)			-
Lipids (mg/dL)	CRP < 1 mg/dl (n=119)	CRP 1–3 mg/dl (n=144)	CRP >3 mg/dl (n=149)	P-trend
Total Cholesterol	-22.3 (3.3)*	-15.2 (3.1)	-13.9 (3.1)	0.033
LDL-c	-17.0 (3.1)*	-11.5 (2.9)	-8.6 (2.7)	0.024
HDL-c	-3.7 (1.0)	-4.2 (0.9)	-3.9 (0.9)	0.880
Non-HDL-c	-18.6 (3.1)*	-11.2 (3.0)	-9.7 (2.8)	0.024
Triglycerides	-5.8 (2.7)	4.2 (4.1)	-4.5 (3.3)	0.720

*p-value for CRP level 3 vs. CRP level 1 < 0.05 Adjusted for BMI (continuous), smoking, age, gender, race, use of lipid-lowering medications, and use of estrogen replacement therapy.

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Withdrawn

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The Confounded Relation Between Coffee Drinking and Coronary Artery Disease

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After decades of conflicting studies, the relation of coffee drinking to coronary artery disease (CAD) risk remains unresolved. Relevant are a correlation of coffee intake with cigarette smoking and evidence of a fat-soluble boiled coffee component which raises LDL cholesterol. We studied 127,212 comprehensive prepaid health plan members who supplied baseline data at examinations in 1978–85. Nondrinkers of coffee composed 27%, with 14%, 42%, 14%, and 4 % reporting <1, 1–3, 4–6, and ≥6 cups per day, respectively. Subsequently, 8,357 persons were hospitalized for CAD. We used Cox proportional hazards models with 5 covariates (age, sex, ethnicity, BMI, and smoking). These yielded relative risk estimates for coffee drinking, which was studied categorically (nondrinkers referent) and as a per cup per day variable. Analyses were for all persons and various subgroups, including smoking strata (see Table). Among 58,888 persons who never smoked, coffee drinking was unrelated to CAD risk, while among 27,448 ex-smokers, 20,520 smokers of <1 ppd and 11,302 smokers of ≥1 ppd, increasing daily coffee intake was associated with progressively higher CAD risk. A model combining ex- & current smokers yielded these RR's for "ever" smokers: 4–6 cups/d = 1.17(1.05–1.29), and ≥6 cups/d = 1.40 (1.24–1.59). The smoking disparity was consistent in subgroups of sex, ethnicity, acute infarction vs other CAD diagnosis, and interval to CAD < 10 vs ≥10 years. Adding education, alcohol or coffee to the models had little effect on the estimates. Control for total cholesterol also had little effect; e.g. among ever smokers RR per cup per day = 1.05(1.04–1.07) without and 1.05 (1.03–1.06) with cholesterol controlled. We conclude that only heavy coffee drinking is related to increased CAD risk only in smokers. Possible explanations include residual confounding by incomplete smoking control, other traits of smokers, or an adverse biological interaction of some coffee ingredient with smoking effect.

Adjusted RR (95% CI) of CAD According to Coffee

Coffee	Never smoked	Ex-smoker	Smoke < 1ppd	Smoke > = 1 ppd
1–3 cups/d	1.05 (0.96–1.15)	0.96 (0.85–1.06)	0.98 (0.83–1.16)	1.01 (0.80–1.28)
4–6 cups/d	0.99 (0.87–1.13)	1.06 (0.91–1.22)	1.13 (0.92–1.38)	1.13 (0.89–1.45)
> 6 cups/d	1.02 (0.82–1.16)	1.23 (1.03–1.49)	1.11 (0.87–1.43)	1.32 (1.02–1.70)
Per cup/d	1.00 (0.98–1.02)	1.03 (1.01–1.05)	1.03 (1.00–1.06)	1.04 (1.02–1.07)

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Association of Television Viewing with Poor Diet Quality in Young Children

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Background: Advertising of unhealthy foods or snacking while watching TV may promote dietary patterns among children that are associated with overweight and cardiovascular risk factors. In previous studies, TV viewing was associated with poor diet quality among adolescents, but few data exist among young children. **Methods**: We performed a cross-sectional study of 1203 3-year-old participants in Project Viva, a study of mothers and children in Massachusetts. Parents reported the number of hours their children watched TV/videos on average weekdays and weekend days in the past month, from which we estimated a daily average of child's TV/video viewing. We collected data on food and nutrient intakes from a validated food frequency questionnaire. Main outcome measures included intakes of selected foods, nutrients, and dietary behaviors. We used multiple linear regression, adjusting for maternal sociodemographic factors and parental BMI as well as child age, gender, breast feeding duration, sleep duration, and BMI z-score, to assess associations between TV/video viewing and diet quality indicators. **Results**: Mean (SD) age of subjects was 3.2 (0.2) years; 322 children (27%) were non-white and 151 (13%) had a household income <$40,000, and 330 mothers (28%) had completed less than a college degree. Mean (SD) TV/video viewing was 1.7 (1.0) hours per day. For each 1-hour increment of TV/video viewing per day, we found higher intakes of sugar-sweetened beverages including juice (1.0 servings/week [95% CI 0.3, 1.6]), fast food (0.3 servings/month [0.2, 0.5]), red and processed meat (0.06 servings/day [0.02, 0.09]), total energy (46.3 kcal/day [16.2, 76.3]), and % energy intake from trans fat (0.05 [0.03, 0.07]) and perhaps saturated fat (0.13 [-0.04, 0.31]). We found lower intakes of fruits and vegetables (-0.2 servings/day [-0.3, -0.1]), calcium (-23.2 mg [-39.6, -6.8]), and dietary fiber (-0.4 g [-0.7, -0.2]). **Conclusions**: Among 3-year-olds, more TV viewing is associated with adverse dietary practices that are related to overweight or cardiovascular disease risk.

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Long-Term Wine Consumption Is Independent of Moderate Alcohol Intake Related to Cardiovascular Mortality and Life Expectancy: The Zutphen Study

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Introduction: Light to moderate alcohol intake lowers the risk of cardiovascular mortality, but whether this protective effect can be attributed to a specific type of beverage remains unclear. Moreover, little is known about the effects of long-term alcohol on life expectancy. **Methods**: The impact of the long-term amount of alcohol and types of alcoholic beverages on mortality and life expectancy was investigated in the Zutphen Study, a cohort of 1,373 men born between 1900 and 1920. Detailed information on the consumption of alcoholic beverages, alcohol intake and potential confounders was collected longitudinally in seven surveys carried out between 1960 and 2000. The participants were followed until death, or censored on June 30th, 2000. Hazard ratios were obtained from time-dependent Cox regression models and (disease-free) life expectancy was calculated from areas under survival curves. **Results**: The adjusted hazard ratios for long-term moderate alcohol intake, i.e. less than or equal to 20 grams per day, compared to no alcohol, were 0.67 (95%CI: 0.57 to 0.79) for all-cause and 0.72 (0.58 to 0.90) for cardiovascular mortality. Independently of total alcohol intake, the consumption of about halve a glass of wine per day was associated with all-cause (HR: 0.62 [0.52 to 0.74]) and cardiovascular (HR: 0.54 [0.42 to 0.69]) mortality. Life expectancy was 3.8 years (0.7 to 6.9 years) higher in those men who consumed wine compared to those who did not use alcoholic beverages. **Conclusions**: The cardioprotective effect of light to moderate consumption of alcoholic beverages is partly due to an effect of absolute alcohol intake and to an additional effect of the consumption of wine. The average wine consumer has a 4 years higher life expectancy compared to those who do not consume alcoholic beverages.

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Dietary Patterns and the Development of Diabetes in the IRAS Population

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Markers of inflammation, adiposity, insulin resistance, lipid metabolism and blood pressure have been associated with development of diabetes, yet little is known about dietary exposures that influence these pathways. We aimed to identify dietary patterns that potentially affect diabetes-related biomarkers in order to provide insight into the relation between diet and the risk of type 2 diabetes. The Insulin Resistance Atherosclerosis Study cohort included 906 middle-aged adults initially free of diabetes, who returned to 5-year follow-up; 148 incident diabetes cases developed based on WHO criteria or use of anti-diabetics. Usual dietary intake was available from an interviewer-administered food frequency questionnaire. Baseline biomarker measurements included fibrinogen, PAI-1, CRP, BMI, waist, percent body fat, SI, AIR, fasting insulin, proinsulin, total cholesterol, LDL, HDL, triglycerides, systolic, diastolic pressure. Dietary patterns were derived by reduced rank regression, which constructs pattern scores through linear functions of predictors (i.e. food groups) by maximizing explained variation in response variables (i.e. biomarkers above). Diabetes risk associated with a pattern was evaluated with multivariable logistic regression. Two dietary patterns were identified, one inversely associated with diabetes (Quartile 4 vs. 1: OR 0.52, 95%CI 0.29–0.94) and one positively (Quartile 4 vs. 1: OR 2.08, 95%CI 1.17–3.72), independent of age, sex, race/center, IGT, diabetes family history, smoking, energy intake and expenditure. The protective pattern was associated with higher intake of green and yellow vegetables, potatoes, fruit juice, pastry, and lower intake of cheese, eggs, high fiber bread/cereal, diet soft drinks and beer and primarily captured variation in cholesterol. The dietary pattern conferring risk was associated with higher intake of salty snacks, cheese, cottage cheese, sweets, cruciferous vegetables, nuts/seeds, and lower intake of wine, beer, tofu and primarily explained variation in inflammatory markers. Both patterns existed in men and women. Further adjustment for obesity had no impact. In conclusion, reduced rank regression proved a useful technique to identify diabetes-related dietary patterns.

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Associations Between Markers of Subclinical Atherosclerosis and Dietary Patterns Derived by Principal Components Analysis and Reduced Rank Regression in the Multi-Ethnic Study of Atherosclerosis (MESA)

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Background: The association of diet with cardiovascular disease (CVD) may be mediated partly through inflammatory processes and reflected by markers of subclinical atherosclerosis. **Objectives**: Our first objective was to determine whether empirically-derived dietary patterns would be associated with coronary calcium (CAC), and common and internal carotid artery intima-media thickness (IMT) in MESA. Our second objective was to determine whether the strength of associations with outcomes would differ between dietary patterns derived by principal components analysis (PCA) and reduced rank regression (RRR). **Methods**: At baseline, diet (food frequency questionnaire), inflammatory biomarkers, CAC, and IMT were measured in 5,089 MESA participants, 45–84 years without clinical CVD or diabetes. Dietary patterns were derived from 47 food groups using PCA and RRR. Dietary patterns created with RRR were derived to maximally explain variation in C-reactive protein, interleukin-6, homocysteine, and fibrinogen. Dietary patterns created with PCA were derived to maximally explain variation in food group intake. **Results**: Primary RRR (RRR 1) and PCA (PCA 1) dietary patterns were characterized by foods high in total and saturated fat and low in fiber and micronutrients.

However, food sources of these nutrients differed between the dietary patterns. RRR 1 was positively associated with CAC presence (Agatston score >0) (OR [95% CI] Q5 vs. Q1: 1.34 [1.05, 1.71]) and marginally associated with high common carotid IMT (≥1.3 mm) (Q5 vs. Q1: 1.33 [0.99, 1.79]) independent of demographic and lifestyle confounders. PCA 1 was not associated with CAC presence or common or internal carotid artery IMT. **Conclusions**: These results suggest that subtle differences in dietary pattern composition due to the method of dietary pattern derivation affect associations with risk of subclinical atherosclerosis. Further research is needed to determine the clinical relevance of these findings.

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Dietary Glycemic Index, Dietary Glycemic Load, and Cardiovascular Disease in Swedish Men

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Introduction: Dietary glycemic index (GI) and dietary glycemic load (GL), measures of the propensity of carbohydrate in the diet to raise blood sugar, have been associated with coronary heart disease in women. However, evidence that dietary GI and GL are associated with cardiovascular disease in men is lacking. **Hypothesis**: We assessed the hypothesis that dietary GI and GL are associated with cardiovascular disease in men. **Methods**: Men aged 45–79 living in 2 counties in Sweden (n = 36,246) completed food-frequency questionnaires that were used to calculate dietary GI and GL. The men were followed from January 1, 1998 until December 31, 2003 for myocardial infarction, ischemic stroke, hemorrhagic stroke, and cardiovascular mortality and until December 31, 2005 for all-cause mortality using the Swedish inpatient registry, cause-of-death registry, and death registry. Relative risks were estimated using age-stratified proportional hazard models adjusted for cigarette smoking, history of hypertension, body mass index, physical activity, demographic, and nutritional factors. **Results**: During follow-up, 1,324 myocardial infarctions, 692 ischemic strokes, 165 hemorrhagic strokes, 785 cardiovascular deaths, and 2,959 deaths occurred. Dietary GI and GL were not associated with myocardial infarction, ischemic stroke, cardiovascular mortality, or all-cause mortality (**Table**). There was a marginally significant association of dietary GL with increased risk of hemorrhagic stroke. The relationships did not vary by body mass index (< 25 kg/m^2 or ≥25 kg/m^2) or waist to hip ratio (< 0.9 or ≥0.9). **Conclusions**: While dietary GI and GL were not associated with ischemic cardiovascular disease in this population, dietary GL was associated with increased risk of hemorrhagic stroke. Discrepancies between these findings and previous studies may be due to differences in dietary contribution to GI and GL or variation of the association by gender.

Relative risks (95% CIs) by quartile of dietary glycemic index and dietary glycemic load

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p for trend
Dietary glycemic index					
Myocardial infarction	1	0.91 (0.77–1.07)	0.96 (0.82–1.13)	0.99 (0.84–1.17)	0.93
Ischemic stroke	1	1.21 (0.97–1.50)	1.12 (0.89–1.41)	1.09 (0.85–1.38)	0.67
Hemorrhagic stroke	1	1.10 (0.70–1.72)	0.99 (0.62–1.59)	1.13 (0.70–1.82)	0.71
Cardiovascular mortality	1	0.98 (0.80–1.21)	0.93 (0.74–1.15)	1.09 (0.88–1.36)	0.46
All-cause mortality	1	1.02 (0.92–1.14)	0.96 (0.86–1.07)	1.06 (0.95–1.19)	0.41
Dietary glycemic load					
Myocardial infarction	1	0.91 (0.77–1.08)	1.02 (0.83–1.25)	1.04 (0.80–1.34)	0.65
Ischemic stroke	1	0.94 (0.74–1.19)	0.95 (0.72–1.26)	1.05 (0.74–1.49)	0.76
Hemorrhagic stroke	1	0.98 (0.60–1.59)	1.57 (1.01–2.44)	1.44 (0.91–2.27)	0.047
Cardiovascular mortality	1	0.93 (0.74–1.17)	1.06 (0.81–1.37)	1.13 (0.81–1.56)	0.39
All-cause mortality	1	0.90 (0.80–1.00)	0.95 (0.83–1.08)	0.94 (0.79–1.11)	0.54

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Trans Fatty Acids Promote Atherosclerotic Lesions and Induce Sudden Cardiac Death

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Epidemiological data indicates that there is a strong correlation between intake of *Trans* fatty acids (TFAs) and sudden cardiac death. TFAs intake cause elevated LDL and reduced HDL levels, which can lead to atherosclerosis. To date, few laboratory studies on TFAs have been conducted and therefore, there is an apparent lack of knowledge about the mechanisms by which TFAs exert harmful effects on the cardiovascular system. This investigation studied the effects of TFAs on atherosclerosis in both *in vivo* and *in vitro* systems. ***In vivo* Studies**: Male rats were subjected to coronary ligation to induce myocardial infarction and were randomly assigned to diets high in omega-3 fatty acids (O3FAs) or TFAs. A diet high in TFAs was associated with a lower 6-month survival rate (50% TFA group, n=30 vs. 80% O3FAs group, n=30) due to sudden cardiac death. Animals on TFA diets also exhibited variable degrees of atherosclerotic lesions in aortas whereas animals on O3FAs diets did not exhibit these lesions. ***In vitro* Studies**: Our *in vitro* study is the first to determine the effects of incorporated TFAs on human arterial endothelial cell (HAEC) functions. Flow cytometric analysis indicated that treatment with C18:2 TFAs significantly increased the expression of endothelial adhesion molecules, including ICAM-1 (CD54) and vitronectin receptor (CD51/CD61). TFAs incorporation increased HAEC adhesion to fibronectin-coated plates by approximately 40% (n=6). Neutrophil adhesion to HAEC monolayers were nearly proportional to CD54 expression, which confirms the physiological relevance of elevated expression of CD54 on HAEC. Furthermore, we examined the role of TFAs on HAEC angiogenesis, a process that involves cell migration and differentiation. Chemotactic migration of TFAs-treated HAECs toward sphingosine-1-phosphate (SPP) was significantly increased over 50% (n=6) compared to controls. Conversely, capillary morphogenesis of TFAs-treated HAECs was significantly inhibited in response to SPP. In conclusion, both *in vivo* and *in vitro* studies demonstrated that TFAs play a role in the induction of atherosclerosis and endothelial dysfunction. Furthermore, *in vivo* studies also demonstared that O3FAs prevent induction of atherosclerosis.

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Fatty Acid Desaturase Activity Is Related to Metabolic Syndrome Risk Factors

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Amount, type, and metabolism of dietary fatty acids are associated with insulin resistance and the metabolic syndrome (MS). Fatty acid desaturase activity (DA) is integral to fatty acid metabolic pathways. High Δ9 DA, characterized by high levels of palmitic (16:0) and palmitoleic (16:1, n7) fatty acids is associated with the MS in adults. High Δ6DA is associated with obesity, while high Δ5DA is related to normal weight and insulin sensitivity. Surrogate measures of DAs are expressed as ratios of plasma fatty acids: Δ9DA= 16:1,n7/16:0; Δ6DA=18:3,n6/18:2,n6; and Δ5DA=20:4,n6/20:3,n6. We assessed the hypotheses that Δ9 and Δ6 DAs are adversely related and Δ5 DA is beneficially related to MS risk factors. The fatty acid composition of plasma cholesterol esters for 265 boys and girls (age 15–17) was determined by gas chromatography. Insulin sensitivity (IS) was measured by the euglycemic insulin clamp. Means of MS risk factors were estimated across tertiles of Δ9, Δ6, and Δ5 DAs, adjusted for age, sex, race, Tanner stage, and physical activity. Waist circumference, triglycerides, insulin, systolic blood pressure, body mass index, and urinary F2 isoprostanes were significantly greater with increasing Δ9 DA, but IS and HDL-cholesterol were not related (Table). Similar patterns were observed for Δ6 DA, but MS risk factors were not related to Δ5 DA (data not shown). These findings support those in adults, showing that DA related to adverse fatty acid patterns are also associated with a MS related cardiovascular risk pattern as early as adolescence. Changing the fatty acid composition of the diet may improve insulin sensitivity, such as substitution of saturated fat with monounsaturated fat. This suggests that dietary intervention should be considered as an intervention strategy for MS prior to adulthood. Adjusted Means* of Metabolic Syndrome Risk Factors across Tertiles of Δ9 Desaturase Activity (16:1/16:0)

Risk Factors	1	2	3	Ptrend
Waist circumference, cm	76.4	78.7	83.5	0.001
Triglycerides, mg/dl	69.8	84.1	113.1	<0.001
HDL-cholesterol, mg/dl	44.3	43.3	42.1	0.68
Systolic BP, mmHg	108	108	111	0.05
Insulin, pmol/l	12.3	14.3	17.9	<0.001
Insulin sensitivity, mg/kg/min	12.3	12.8	12.0	0.46
Body mass index, kg/m^2	21.6	23.4	24.8	<0.001
lnF2-isoprostanes	0.28	0.28	0.35	0.002

*Adjusted for age, gender, race, Tanner stage, and physical activity

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Vitamin E Supplement Use and the Risk of Heart Failure in Men

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Background. Analyses from the initial and extended Heart Outcomes Prevention Evaluation (HOPE) trial have raised concerns that in patients at high risk for cardiovascular events long-term vitamin E supplementation may increase the risk of heart failure. However, no such data are available from observational or community-based epidemiologic studies on low risk populations. **Methods**. We used Cox proportional-hazards regression models to investigate the association between vitamin E supplement use (none [referent], past, and current) and the incidence of heart failure among 22,042 men without known coronary heart disease or cancer at baseline in the Physicians' Health Study (mean age, 53 years). **Results**. During a mean follow-up of 17 years, 799 participants developed new-onset heart failure. After adjustment for age, body-mass index, cigarette smoking, alcohol consumption, vigorous physical activity, presence or absence of history of hypertension, diabetes mellitus, and hypercholesterolemia, and random assignment to aspirin or beta-carotene; as compared with individuals who never used vitamin E supplements, there was no statistically significant increased or decreased risk of heart failure among individuals who used vitamin E supplements in the past or present (Table). **Conclusion**. In this observational prospective cohort of men, vitamin E supplementation was not associated with an increased risk of heart failure.

Table. Hazard Ratio (HR) of Heart Failure According to Baseline Vitamin E Supplement Use

Vitamin E Supplement Use	No. of events/ No. at risk (%)	Multivariable HR (95% CI)
Never	704/19179 (3.7)	1.00 (referent)
Past	50/1126 (4.4)	1.13 (0.85–1.51)
Current	45/1100 (4.1)	0.91 (0.67–1.23)

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Is Obesity Related to the Type of Dietary Fatty Acids? An Ecological Study

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The role of fat intake in obesity and overweight is still controversial. Recently, more attention focuses on the possible relationships between type of fatty acids and risk of obesity since fatty acids are metabolised differently in relation to chain length, degree of saturation and sterioisometric configuration. Animal studies and a few clinical trials lend credibility to the hypothesis that not all fatty acids carry the same potential for weight gain. However, only few studies in epidemiology concerning this issue are currently available and results are conflicting. **Aim**: The purpose of this ecological study is to test the existence of an association between prevalence of obesity and types of fat available in 134 countries. **Methods**: Data on the prevalence of obesity (body mass index (BMI) ≥30 kg/m^2) for women aged 15 years and more were obtained from the World Health Organization (WHO, 2002). Food Balance Sheets for the years 1998 to 2002 were obtained from Food Agriculture Organization Statistics (FAOSTAT).

Five years means for total fat, calories, mono- (MUFA), poly- (PUFA), saturated (SFA) and "other fat" per capita were calculated. All data are presented as mean±SD. Bivariate correlations and multiple linear regression model were used to test for the association between prevalence of obesity and types of fat available in these countries. **Results**: As expected dietary energy supply as well as SFA, PUFA and "other fat" were positively associated with the prevalence of obesity. We also found a strong negative association between MUFA availability and the prevalence of obesity (β=-0,68, p<0,0001). **Conclusion**: Populations with lower prevalence of obesity seem to consume greater amount of MUFA. Considering partial correlations between variables, our results suggest that in countries with higher prevalence of obesity, it is the shift from MUFA to PUFA that appears particularly associated with the risk of obesity. Additional studies on the potential role of MUFA in obesity are needed.

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The Association Between Food Patterns and the Metabolic Syndrome Using Principal Components Analysis: The ATTICA Study

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Background: Dietary habits have been associated with the prevalence of the metabolic syndrome (MS). The associations between foods or food patterns and the characteristics of the MS were evaluated. **Methods**: During 2001 - 2002, 1514 men (18–87 years old) and 1528 women (18–89 years old) without any clinical evidence of cardiovascular disease were randomly enrolled, from the Attica region in Greece. Dietary habits were evaluated using a semi-quantitative, food-frequency questionnaire. Characteristics of the MS (i.e. blood pressure, waist circumference, glucose, triglycerides and High Density Lipoprotein cholesterol) were also measured. Principal Components Analysis was applied to extract dietary patterns from 22 foods or food groups. Multivariate regression analysis evaluated the associations between the extracted dietary patterns and characteristics of the MS. **Results**: Six components were derived explaining 56% of the total variation in intake. Component 1 was characterized by the consumption of cereals, fish, legumes, vegetables and fruits (explained variation 19.7%); component 2, characterized by the intake of potatoes and meat (explained variation 11.7%), component 6, characterized by alcohol intake (explained variation 4.8%), while the other components were mainly characterized by the consumption of dairies and sweets. After adjusting for various confounders, component 1 was inversely associated with waist circumference, systolic blood pressure, triglycerides, positively associated with HDL-cholesterol levels, and inversely with the likelihood of the MS (odds ratio = 0.87, 95% CI 0.79 - 0.97), while components 2 and 6 were positively correlated with the previous indices, and the likelihood of having the MS (odds ratio = 1.13, 95% CI 1.05 - 1.21 and odds ratio = 1.26, 95% CI 1.21 - 1.33). **Conclusions**: A dietary pattern that includes cereals, fish, legumes, vegetables and fruits was independently associated with reduced levels of clinical and biological markers linked to the MS, while meat and alcohol intake showed the opposite results.

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Plasma *Trans* Fatty Acids Are Higher in Men, Lower in Summer, and Decreasing Over Time in Persons with Type 2 Diabetes

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Trans-fatty acids (TFA) increase cardiovascular disease risk. Dietary TFA may vary seasonally and recent changes in snack food formulation suggest a decrease in TFA in the food supply over time. However, the extent to which plasma concentrations of TFA are changing over time and vary seasonally is unknown. We investigated plasma 18-carbon TFA and asked whether concentrations might differ by age or sex, might be lower during spring, summer, or fall compared with winter, and might change over time. Our population (307) included all persons randomized into Look AHEAD, a randomized multi-center, controlled trial of a lifestyle intervention for weight loss in overweight or obese adults (aged 45–75) with type 2 diabetes at two clinics (Baltimore, n=122; Houston, n=185) who also participate in an ancillary study of oxidative stress. Participants were 175 women, 59 African Americans, 24 Hispanics, 210 non Hispanic whites, and 14 others. TFA were measured in plasma collected between December 2002 and April 2004 and before intervention (fall, n=87; winter, n= 94; spring, n=69; summer n=57). In a model including age, sex, race/ethnicity, clinic, season, calendar time, and interaction between clinic and season (R-square 0.129, p<0.0001), log-transformed adjusted fasting plasma TFA was 0.26±0.11 mg/dL lower (p<0.015) in summer compared with winter and decreased with increasing age (-0.0094±0.0047 per year, p<0.05) but did not vary over time. After further adjustment for body mass index, dietary TFA, plasma total fatty acid, total dietary fat, total calories, and serum insulin (R-square 0.45, p<0.0001), log-transformed adjusted fasting plasma TFA was 0.19±0.084 mg/dL lower (p<0.03) in summer compared with winter, 0.104±0.046 higher (p<0.03) in men, decreased over time (-0.14±0.05 per year, p<0.01) while the decrease in TFA with increasing age was attenuated (-0.0047±0.0039). TFA concentrations in each of spring and fall did not differ from that in winter; seasonal variation in TFA concentrations did not differ between clinics in either model. These results might provide additional insight into differences in cardiovascular risk in persons with type 2 diabetes according to sex, and predict decreasing cardiovascular risk as TFA in the food supply are further reduced.

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Alcohol Consumption and Risk of Myocardial Infarction and Coronary Heart Disease Among Chinese Men

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We examined the relationship between alcohol consumption and risk of myocardial infarction (MI) and coronary heart disease (CHD) among Chinese men. We conducted a prospective cohort study of 68,271 Chinese men aged ≥40 years who were free of MI at baseline. Data on frequency and type of alcohol consumed were collected at the baseline examination in 1991 using a standard protocol. Follow-up evaluation was conducted in 1999–2000, and included determining vital status, interviewing participants or proxies and obtaining hospital and medical records for incident and fatal MI and CHD events. Over the course of 523,550 person-years of follow-up, we documented 763 (370 fatal) incident MI and 1017 (570 fatal) incident CHD events. After stratification by province to account for sampling design, and adjustment for age, body mass index, physical activity, urbanization (urban vs. rural), geographic variation (north vs. south), cigarette smoking, history of diabetes, and education, compared to nondrinkers, relative risk (95% confidence interval) of MI was 0.87 (0.65–1.16) for participants consuming 1 to 6 drinks/week, 0.62 (0.51–0.76) for those consuming 7 to 34 drinks/week, and 0.53 (0.38–0.74) for those consuming ≥35 drinks/week (P-value for linear trend<.0001). The corresponding relative risks for CHD events were 0.94 (0.73–1.20), 0.63 (0.53–0.76), and 0.55 (0.41–0.74), respectively (P-value for linear trend<.0001). These results suggest that alcohol consumption may decrease the risk of MI and CHD in Chinese men.

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Cardiovascular Risk Factors and Moderate Alcohol Consumption in the Moli-Sani Project

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Background The association of moderate alcohol consumption with a lower CVD risk might be due to a higher prevalence of CVD risk factors in abstainers. **Aims** To estimate difference in CVD risk factors distribution between abstainers and moderate alcohol drinkers. **Methods** The *Moli-sani* Study is an on-going population-based cohort study of adults in Italy, aged >=35yrs. From March 2005 to July 2006, 6,251 subjects were enrolled. After exclusion of subjects with previous CVD (5%), 5,922 subjects (55±12yrs, 46% males) were analyzed. We found 1,382 abstainers and 2,237 moderate drinkers (defined as intake =<2 (=<1) drinks/day among men (women)). Heavier drinkers (n=2,173) and former drinkers (n=130) were excluded. **Results** Prevalence of diabetes, dyslipidemia, hypertension, high physical activity, LDL-cholesterol and glucose levels was similar in abstainers and moderate drinkers. Higher BMI, CRP, and triglycerides levels and lower percentage of smokers, social status, and adherence to the Mediterranean diet, total and HDL cholesterol levels were more prevalent among abstainers, in age- and sex-adjusted analyses (Poisson regression). These differences were attenuated in fully adjusted analysis: in abstainers a low prevalence of smokers (prevalence ratio for abstention: 0.83, 95%CI: 0.74–0.93, P=0.0016), lower social status (0.94, 0.83–1.06; 0.88, 0.80–0.98; 0.80, 0.71–0.89 for the higher quartiles *vs* the lower, respectively, P<0.0001 for trend) and lower HDL-cholesterol levels (0.88, 0.79–0.99; 0.79, 0.69–0.89; 0.78, 0.68–0.90 persisted for the higher quartiles *vs* the lower, respectively, P<0.0001). **Conclusions**. Abstainers did showed lifestyle characteristicscomparable to moderate drinkers. Association of alcohol consumption with high HDL levels may be related to biological effects of alcohol rather than confounding, whereas lower prevalence of smoking among abstainers may obscure the association of moderate consumption of alcohol with low CVD risk. Our findings strengthen the importance of appropriate selection of reference group, and the need of multivariate analyses controlling for social status in epidemiological studies of alcohol and health. *Supported by Fondazione Pfizer and Italian Research Ministry*

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Omega-3 Index: A Risk Factor for Ventricular Fibrillation in the Early Post–Myocardial Infarction Phase

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Objectives: Several animal studies have demonstrated evidence of an anti-arrhythmic action of marine n-3 fatty acids (FAs). In humans the same mechanism may explain the observed reduction in sudden cardiac death (SCD) associated with an increased intake of fish oil. A direct membrane stabilizing effect of n-3 FAs, through their incorporation into myocardial cellular membranes, has been the most likely hypothesis. Whether n-3 FA levels differ in patients at increased risk for arrhythmias in the early post- myocardial infarction (MI) period is, however, unknown. **Methods**: We measured red blood cell EPA + DHA (expressed as percent of total FAs; the Omega-3 Index) at admission in 464 patients hospitalized with acute coronary

syndrome (ACS). This parameter has recently been found to be a good surrogate for the cardiac content of omega-3 FAs. All episodes of ventricular fibrillation (VF) were recorded from ambulance reports as well as during hospitalization. Patients experiencing VF during the initial 48 hours after the development of symptoms were compared to a control group without VF. The control group (n=58) was matched according to age (55–65 years), sex and TnT level (≥0.06). Differences of the Omega-3 Index were evaluated using non-parametric testing. **Results**: A total of 13 patients suffered a VF during the initial 48 hours, 6 prior to hospital admission Ten VF patients presented with ST-elevation infarction (STEMI), two out of whom had a history of a previous MI. This was the first MI for 11 patients. The two groups were comparable with respect to the majority of other baseline characteristics. The median value of the Omega-3 index in the VF group was 5.36 % as compared to 6.44 % in the control group (p=0.026). **Conclusion**: Our study demonstrates lower levels of n-3 FAs in patients suffering ventricular fibrillation during an acute MI as compared to MI patients without sudden cardiac arrest. This observation supports the hypothesis that n-3 FAs influence the electrical stability of myocardiocyte membranes, resulting in reduced risk for VF.

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Social Cognitive Barriers to the Adoption of Healthy Nutrition Behaviors in Underserved Populations

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Background: Dietary fat intake is a well recognized risk factor for coronary heart disease and modification of nutrition habits is an important strategy to reduce that risk. We examined the impact of physical and psychosocial variables on dietary fat intake among a cohort of inner city and rural underserved patients. **Methods**: Subjects were enrolled in a one-year internet-based telemedicine randomized controlled trial to reduce cardiovascular disease (CVD) risk. All subjects received education and counseling regarding CVD risk factor reduction. At baseline, CVD and nutrition knowledge (multiple-choice questionnaire), outcome expectancies, intentions and nutrition action self-efficacy were assessed. Dietary fat intake was measured utilizing the Medficts (NCEP) questionnaire. **Results**: Baseline data were available for 465 subjects (age= 60.4±10.1 years; mean Framingham risk score = 16.9±9.6 %; 55% rural; 45% inner city; 45% female/55% male; 45% diabetes and 27% smokers). Analysis revealed that rural participants (RP) were more knowledgeable about CVD (70%±13% versus 56%±13%; p<0.001) and nutrition (66%±23% versus 46%±25%; p < 0.001) than inner city participants (ICP). Despite the fact that ICP demonstrated a greater intent to adopt healthy nutrition habits (3.03±0.6 versus 2.90±0.6; P=0.02) and increased outcome expectations (2.8±0.8 versus 2.6±0.7; p=0.03), mean daily dietary fat intake values were higher among the inner city participants (51.3±36.7 versus 39.8±26.2; p < 0.001). Levels of nutrition self-efficacy were similar between the two groups. **Conclusion**: These data suggest that a lack of knowledge regarding prevention, nutrition and CVD may serves as barriers to the adoption of healthy nutrition behaviors despite greater behavioral intention and outcome expectations among inner city populations.

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Relationships Between Dietary and Urinary Amino Acids: The INTERMAP Study

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Background: No population based data exist on relationships between dietary intake and urinary excretion of specific AA. **Objective and Methods**: To assess relationships between dietary intake and urinary excretion of alanine, glutamine, glycine, histidine, lysine, serine, and threonine from the INTERMAP cross-sectional epidemiological study of 4677 persons, ages 40 to 59 years from 17 population samples in 4 countries (China, Japan, UK, USA). Dietary intake was based on two in-depth 24-hour dietary recalls, urinary excretion on one timed 24-hour urine collection. Urinary concentrations of AA were determined chromatographically (*Biochrom 20 Plus AA Analyzer)* and converted to mmol/24-hour. **Results**: Age-adjusted correlations between specific dietary-urinary AA ranged from 0.19 to 0.32 (p-values <0.0001), with the exception of glycine (*r*=0.07; p<0.001). In general, gender specific dietary-urinary AA correlations were lower (*r's* from 0.08 to 0.28; p-values <0.001). With further adjustment for BMI and physical activity, correlations were unchanged. Sensitivity analyses with exclusion of diabetics (n= 241) or people on special diets (n=628) showed lower associations; correlations ranged from 0.05 to 0.28, p-values <0.006, except for glycine (p=0.35) and serine (p=0.26). **Conclusions**: There are moderate correlations between dietary and urinary amino acids. These data permit detailed assessment as to whether urinary AA excretion adds meaningfully to dietary data on relationships of individual amino acids to variables such as blood pressure.

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Variability of Cholesterol and Saturated Fat Content in Dietary Supplements

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Background: Omacor (omega-3 acid ethyl esters) is the first FDA-approved omega-3 fatty acid (FA) indicated, as an adjunct to diet, to lower very high triglycerides in adults. The approved dose is 4 g/d (3.4 gr of EPA and DHA omega-3 FA). Omega-3 dietary dietary supplements (DS) are widely available and may require up to 16 capsules/d to reach a therapeutic dose equivalent of Omacor. In addition to EPA and DHA, many omega-3 capsules contain cholesterol, saturated, monostaturated and trans fats. These components can have a negative impact on the Therapeutic Lifestyle Change (TLC) diet recommended to patients with dyslipidemia. DS are regulated as food; not being tightly monitored for content and quality control and having limited labeling requirements. Thus the variability of fatty acid and cholesterol content across different DS is unknown. **Objective**: Assess the variability of omega-3 DS contents at therapeutic doses to reduce triglycerides by measuring cholesterol, saturated, monounsaturated and trans fats, key components of the TLC diet recommended to dyslipidemic patients. **Samples**: Prescription Omacor was compared to 12 omega-3 DS selected as an industry representative range of omega-3 DS (20% to 50% EPA/DHA). **Measurements**: Samples were tested for cholesterol, saturated, monounsaturated fats and trans-fat (1 lot tested in triplicate). **Results**: Cholesterol content/DS capsule ranged from 0.82 to 9.0 mg. 3 of 12 DS had higher cholesterol content than claimed on their nutrition label. At a therapeutic dose (3.4 g EPA/DHA), cholesterol ranged from 10.4 to 98.4 mg/dose (Omacor = 5.6 mg) with half the DS measuring between 60 mg - 100 mg of cholesterol/dose. Saturated fats ranged from 22 mg to 316 mg/capsule or from 0.15 to 3.25 g at therapeutic dose (Omacor = 0.01 g). All DS had very low levels of trans fat. **Discussion**: Omega-3 dietary DS have a wide range of cholesterol and saturated fat content. At a therapeutic dose, half the omega-3 DS tested provided 30% to 50% of recommended daily cholesterol intake (maximum intake is 200 mg/day). Eight of the 12 DS provided at least 2.5 grams of saturated fats. Increasing omega-3 dietary DS capsule count to achieve therapeutic levels of EPA and DHA may significantly increase cholesterol and saturated fats into a patient's diet.

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Fish Consumption and Risk of Myocardial Infarction in the Physicians' Health Study I

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Background: Data on the association between fish consumption and cardiovascular disease remain controversial. **Objective**: To assess whether fish consumption is associated with a decreased risk of myocardial infarction (MI) among participants of the Physicians' Health Study. **Methods and Results**: We analyzed prospectively data from 20,210 US male physicians who provided information on fish intake on the 12-month questionnaire. Incident MI was assessed through annual follow-up questionnaires. We used direct standardization to estimate age-adjusted rates of MI across categories of fish consumption. The average age of participants during the assessment of fish intake was 54.5±9.4 years (range 40.7 to 87.1 years). During a mean follow up of 19.5 years, 1,407 cases of incident MI occurred. The age-standardized incidence rates of MI were 40.3, 36.4, 35.1, 35.1, and 31.0 cases/ 10,000 person-years for people reporting fish consumption of less than once per week; 1 to less that 2 times per week; 2 to less than 4 times per week; 4 to less than 6 times per week; and daily, respectively. In a multivariable Cox regression model adjusting for age, alcohol consumption, cigarette smoking, body mass index, physical activity, and history of hypertension and diabetes, corresponding hazard ratios (95% CI) for MI were 1 (reference); 0.94 (0.78; 1.14); 0.82 (0.77; 1.11); 0.95 (0.76; 1.19), and 0.78 (0.59; 1.04), respectively. **Conclusion**: These data do not provide strong evidence for an inverse association between fish consumption and incident MI in this cohort. Additional studies are warranted to clarify whether fish consumption confers a lower risk of MI.

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Dietary Patterns Are Associated with Antioxidant Biomarkers in the Diet and Physical Activity Substudy (DPASS) of the Jackson Heart Study (JHS)

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Background: Intake and biochemical status of antioxidant nutrients like carotenoids and tocopherols are associated with cardiovascular disease. **Objective**: To describe the dietary patterns of a subset of JHS participants using dietary data obtained from the Delta NIRI Adult FFQ-Long Form and to investigate the associations between these patterns with biochemical measurements of antioxidant nutrients. **Design**: Cross-sectional study using data from the DPASS of the JHS. **Subjects**: 373 African American men and women (aged 35–84 y) from three counties surrounding Jackson, MS. **Statistical Analysis**: Dietary patterns were generated using cluster analysis. Descriptive analysis was used to describe each cluster. For each cluster, means±SEMs were calculated for antioxidant nutrients after adjusting for several covariates. Using regression analyses, associations between each cluster and serum antioxidant nutrients was examined. **Results**: Four dietary patterns were identified:1) Soft drinks, Snacks & Fast Food, 2) Cereal, Milk, Fruit & Vegetables, 3) Corn products & Bread and 4) Fruit Juice, based on relative contributions to energy by food groups to each cluster. In multivariate-adjusted regression models, participants in the Cereal, Milk, Fruit & Vegetables cluster had higher serum alpha and beta carotene (P<0.05), beta cryptoxanthin (P<0.001), lutein and zeaxanthin (P<0.01) concentrations relative to Soft drinks, Snacks & Fast Food cluster. Similarly, the Fruit Juice cluster was associated with higher alpha and beta carotene (P<0.05), beta cryptoxanthin (P<0.01), lutein and zeaxanthin (P<0.05) concentrations; and the Corn products and Bread cluster was associated with higher serum lutein and zeaxanthin concentrations (P<0.05). No associations were seen with tocopherols. **Conclusions**: Carotenoid status varies by dietary pattern. Diets high in soft drinks, snacks and fast food are associated with lower concentrations while those high in cereal, milk, fruit and vegetable intake are associated with higher concentrations of these important antioxidants. In this population sample, participants were most likely to be classified into the poor quality dietary pattern. This may help explain the extensive health disparities seen in this region.

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Refinement and Validation of a Food Frequency Questionnaire to Estimate Nutrient Intake in South Indians

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Introduction The potential sources of errors in nutrient estimation with Food Frequency Questionnaires (FFQ) include inaccurate or biased recall, overestimation of intake due to too many items on the FFQ and underestimation due to too few items. Here we report the refinement of an FFQ that overestimated nutrient intake and validate the refined FFQ (RFFQ) against multiple 24-hour recalls. **Methods** Data on 1867 participants in South India (Trivandrum) were available for the original FFQ (OFFQ) that consisted of 132 food items and overestimated nutrient intake. We shortened the OFFQ by stepwise regression analyses with nutrients as the outcome and foods as predictors, and estimated food intake using average portion sizes and grouped intake categories. We evaluated its validity by comparing it with 2–24 hour recalls, and reliability by comparing two administrations of the RFFQ among 100 participants. **Results** The OFFQ over estimated nutrient intake (Energy 2619±634 kcal, Protein 77.9±22.2 g, Fat 96.0±33.5g). In stepwise analyses 57 food items, explained 90% of the variance in nutrient 13 food items were consumed more than twice/month, and 12 food items were kept on the suggestions of local nutritionists. Nutrient estimates from the RFFQ (82 food items) were (Energy 1897±489 kcal, Protein 54.5±16.0g, Fat 62.0±23.8). The correlations between mean 24 hour recall and RFFQ1 ranged between 0.11 for Vitamin A to 0.44 for protein intake; the de-attenuated correlations ranged from 0.25 for Vitamin A to 0.82 for fat intake. **Conclusions** We refined an FFQ that overestimated nutrient intake by shortening it, and redesigning the questionnaire to minimize erroneous recall. This strategy could be used by others to correct for overestimation of nutrient intake evaluated by FFQs.

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Food Insecurity in Head Start Families

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Objective: To examine the associations between household food insecurity and fruit and vegetable intake, child weight status, and mother's affect in a geographically and ethnically diverse sample of Head Start Families. **Methods**: Data were collected from 722 parent-child dyads (mean age: parent, 31.6±8.2 years; child, 4.5±0.6 years) of African Americans (AAB; n=174) and Whites (WB; n=198) from Alabama, and African Americans (AAH; n=139) and Hispanics (HH; n=211) from Houston, TX enrolled in Head Start. Household food insecurity was determined using the USDA 6-item Short Form of the 12-month Food Security Scale. Three 24-hr dietary recalls were collected for parent and child using the Nutrition Data System for Research (NDS-R). Child BMI was determined from measured height and weight. Mother's affect was assessed using the Positive Affect and Negative Affect Scale (PANAS). Logistic regression was used to determine the associations between food insecurity and child weight status (gender-specific BMI for age $\geq 85^{th}$ percentile), fruit and vegetable intake (FVI), and mother's affect. **Results**: Some degree of food insecurity was experienced by 50.2% (106/211) of HH households, 34.5% (60/174) of AAB households, 33.8% (67/198) WB households, and 12.9% (18/139) of AAH households. Mothers in food insecure households for all ethnicity/geographic groups, except the AAH group were more likely to report high negative affect than those in food secure households ($p<0.001$). There was no association between food insecurity and FVI in parent or child. The percent of children BMI $\geq 85^{th}$ percentile was 51.0 % (101/198) in WB, 37.4% (79/211) in HH, 33.9% (59/174) in AAB, and 29.5% (41/139) in AAH. In Head Start Families from Houston, children in households experiencing food insecurity were less likely to be at risk for overweight or above compared to children in food secure households (AAH: OR 0.12, 95% CI 0.02, 0.93; HH: OR 0.54, 95% CI 0.30, 0.94). **Conclusions**: Low income families with young children are characterized by high prevalence of food insecurity and psychological distress of mothers. This research suggests that interventions are needed to reduce food insecurity among low income families with young children.

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Betaine Intake from Dietary Sources Is Not Associated with Higher Plasma LDL Cholesterol

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Background: Betaine supplementation up to 6 g/day lowers plasma homocysteine (tHcy) concentration, a potential risk factor for cardiovascular disease. Betaine, and its dietary precursor choline, also plays a role in VLDL metabolism. In high dose trials up to 6g/day, there is a positive dose-response relation between betaine supplementation (1.5 to 6 g/day) and LDL-cholesterol (LDL-C). Thus, the adverse effect of betaine supplementation on LDL-C may counterbalance any beneficial effect of tHcy lowering on cardiovascular risk. The association between betaine intake within the range consumed in the diet (approximately 200 mg/day) in relation to plasma lipid concentrations has not been assessed. **Methods**: A cross sectional analysis among 809 women from the Nurses' Health Study I and II. Adjusted means for LDL-C, total cholesterol (TC), HDL-cholesterol (HDL-C) and triglycerides (TG) were calculated using multiple linear regression models. **Results**: Betaine intake was estimated from a 131 item semi quantitative food frequency questionnaire and ranged from 122 to 312 mg/day from the median of the lowest to highest quintiles, 10 to 20 fold lower than the dose of betaine used in the clinical trials. For increasing quintiles of betaine intake, adjusted mean (±SE) LDL-C concentrations were 118.0 (±2.8), 118.1 (±2.5), 116.5 (±2.1), 120.1 (±2.1) and 124.1 (±2.7) mg/dl. The difference between the highest and lowest quintiles was not significant ($p=0.14$). There was a suggestion of a positive trend across increasing quintiles of betaine intake (p-trend =0.08). There was no significant difference between the highest and lowest quintiles of betaine intake for concentrations of TC, HDL-C or TG. TC was 4.7 mg/dl higher (2%) ($p=0.35$), HDL-C was 0.7 mg/dl higher (1%) ($p=0.73$) and TG was 0.02 mg/dl lower (0%) ($p=0.99$). There were no significant associations between choline intake and plasma lipids. **Conclusions**: Betaine intake in the range consumed from dietary sources is not associated with higher concentrations LDL-C. However, the suggestion of a trend towards higher LDL-C warrants further studies to assess the effect of betaine at higher doses, such as those used in clinical trials (6 g/day).

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Body Mass Index, Waist Circumference, and Waist-to-Hip Ratio on the Risk of Total and Type-Specific Stroke

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Background: Obesity is an established risk factor for cardiovascular disease, but the relationship of obesity with the risk of cerebrovascular disease is still to some extent unclear. **Aim**: To investigate the association of different indicators of obesity (body mass index, waist circumference, and waist-to-hip ratio) with total and type-specific stroke incidence. **Methods**: Study cohorts included 23 967 Finnish men and 26 029 women who were 25 to 74 years of age and free of coronary heart disease and stroke at baseline. Incidence of total, ischemic, and hemorrhagic stroke was obtained through computerized register linkage from national hospital discharge and mortality registers. **Results**: During 19.5-year follow-up period, 1673 men and 1555 women developed an incident stroke event (674 hemorrhage and 2554 ischemic). After adjustment for age, study year, smoking, physical activity, education, family history of stroke, and alcohol consumption, there was a statistically significant trend for increased risk of total and ischemic stroke across 7 body mass index categories in both men and women. A significantly U-shaped association between body mass index and the risk of hemorrhagic stroke was found among women but not men. Using World Health Organization criteria, men who were obese (body mass index >=30) had hazard ratios of 1.59 (95% CI 1.37–1.83) for total stroke, and 1.70 (95% CI 1.45–2.00) for ischemic stroke, compared with men with body mass index <25. Among women the hazard ratios were 1.29 (95% CI 1.12–1.47) and 1.39 (95% CI 1.19–1.62), respectively. Abdominal obesity, defined as highest quartile of waist circumference or waist-to-hip ratio, was associated with a greater risk of total and ischemic stroke in men but not in women. Additional control for systolic blood pressure, total cholesterol and history of diabetes slightly attenuated these associations. **Conclusions**: Body mass index was an independent risk factor for total and ischemic stroke in both men and women. Both low and high body mass index increased the risk of hemorrhagic stroke in women. Abdominal obesity was an independent risk factor for total and ischemic stroke in men only.

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Effect of Obesity on Platelet Function and Response to Low-Dose Aspirin

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Background: Cardiovascular disease is more prevalent in obese persons. Low dose aspirin (ASA) is often prescribed for primary prevention, although the effect of obesity on platelet function and response to aspirin related to obesity remains poorly characterized. **Objective**: To evaluate the impact of obesity on platelet function prior to, and after, low dose aspirin in a high risk population. **Methods**: Platelet function was measured by whole blood (WB) aggregometry and thromboxane release (TxB2) after in vitro stimulation of platelets with arachidonic acid (AA) and collagen (COL), respectively. Platelet activation in vivo was measured by urinary 11-dehydrothromboxane B2 (TxM). Assays were performed before and after 14 days of aspirin 81 mg as part of the ongoing GeneSTAR Study in unaffected family members of probands with premature coronary disease. Participants refrained from antiplatelet agents two weeks before and during the study. Height and weight were measured, and body mass index (BMI) was calculated as weight in kg/height in m^2; obesity was defined as BMI >= 30. Multivariate analyses predicting pre- and post-ASA platelet function tests were adjusted for age, race, sex and nonindependence of families using the generalized estimating equation. **Results**: Participants (N=2014) had a mean age of 44 years, 57% were female, 41% were black. Obese individuals were older (46 vs. 44 years), and more likely to be female (63% vs. 54%) and black (52% vs. 32%), all $p<0.001$. Obese individuals showed greater platelet reactivity at baseline for most parameters (Table) and remained significantly more reactive following ASA. **Conclusions**: Obese individuals from high risk families do not appear to achieve the same degree of platelet inhibition as those who are not obese. This has putative implications for the effectiveness of antiplatelet regimens in primary prevention of cardiovascular disease in obese people.

Table. Platelet Function Tests

	Nonobese* (n=1184)	Obese* (n=830)	p Adjusted
WB aggregation to AA			
Pre-ASA (ohms)	15.5 (6.5)	16.5 (6.5)	<0.0001
Post-ASA (% nonzero aggregation)	4.9	8.3	0.001
WB aggregation to COL			
Pre-ASA (ohms)	19.6 (5.5)	20.2 (6.0)	0.04
Post-ASA (ohms)	6.1 (5.2)	6.7 (5.5)	0.2
WB TxB2			
Pre-ASA (ng/10^8 platelets)	67.7 (117)	63.4 (115)	0.2
Post-ASA (ng/10^8 platelets)	0.87 (3.56)	1.02 (3.78)	0.02
TxM			
Pre-ASA (ng/mmol creatinine)	235.5 (581.5)	254.6 (530.2)	0.02
Post-ASA (ng/mmol creatinine)	49.9 (97.3)	54.4 (102.0)	0.01
% ASA resistant (upper quartile TxM)	20.5	26.4	0.008

* Mean (SD)

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The Effect of Low-Dose Aspirin on hs-CRP and IL-6 in Normal, Overweight, and Obese Individuals at High Risk of Coronary Artery Disease

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Background: Obese individuals have an increased risk of cardiovascular disease (CVD). While aspirin (ASA) is often used for primary prevention and has potent antiplatelet effects, there is little information on its impact on high-risk inflammatory markers, such as high sensitivity CRP (hs-CRP) and interleukin-6 (IL-6). **Objective**: To evaluate the impact of obesity on markers of inflammation before and after low dose ASA in a high-risk population. **Methods**: Serum hs-CRP and IL-6 were measured prior to and following two weeks of ASA 81 mg/day in apparently healthy relatives of index cases with documented premature CVD. Participants were excluded if they had serious comorbidity (e.g. cancer or AIDS) and refrained from taking anti-inflammatory medications 14 days prior to and during the study. Body mass index (BMI) was calculated as weight in kg/height in m^2 from direct measurements. BMI was categorized as normal (18.5–24.9), overweight (25–29.9), obese I (30–34.9), obese II (35–39.9) and obese III (>=40). Multivariable linear regression analyses predicting pre- and post-ASA levels of hs-CRP and IL-6 were adjusted for age, race, and sex and intrafamilial correlations using the generalized estimating equation. **Results**: Participants (N=1866) had a mean age of 45 years, 57% were female, 40% were black. Obese individuals were older (46 vs. 44 years), and more likely to be female (63% vs. 53%) and black (52% vs. 32%), all p<0.01. Although hs-CRP and IL-6 steadily increased with BMI, there was no reduction in inflammation following ASA use in any BMI group (Table). **Conclusions**: Although there was a significant increase in hs-CRP and IL-6 across BMI categories, ASA had no impact on either marker. Thus, low dose ASA is not associated with any short-term anti-inflammatory benefits in individuals with an increased risk of CVD. Higher ASA doses or a longer treatment duration may be required to demonstrate a reduction in pro-inflammatory profiles associated with obesity.

Inflammatory Markers Pre- and Post-ASA

	Normal (n=486)*	Overweight (n=616)*	Obese I (n=394)*	Obese II (n=210)*	Obese III (n=160)*	P Adjusted
hs-CRP pre-ASA	1.4 (2.2)	2.1 (2.6)	3.2 (3.0)	4.4 (3.7)	6.1 (3.7)	<0.0001
hs-CRP post-ASA	1.3 (2.1)	2.2 (2.8)	3.2 (3.1)	4.1 (3.5)	6.4 (3.7)	<0.0001
hs-CRP difference	-0.1 (1.9)	0.1 (2.4)	0.2 (2.3)	-0.3 (2.1)	0.3 (2.3)	0.05
IL-6 pre-ASA	5.9 (10.4)	7.3 (14.9)	8.1 (13.1)	11.2 (24.9)	12.9 (16.7)	<0.0001
IL-6 post-ASA	6.4 (14.8)	7.0 (11.8)	7.8 (15.8)	11.7 (32.6)	12.8 (17.2)	<0.0001
IL-6 difference	0.3 (10.7)	-0.4 (11.8)	0.04 (11.7)	0.6 (16.1)	-0.2 (6.2)	0.9

* Mean (SD)

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Structural and Functional Changes in Left and Right Ventricle After Major Weight Loss in Morbid Obesity

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Background: Although obesity has been associated with changes in ventricular performance and structure, there are no data assessing changes after significant long-term weight loss, independent of changes in blood pressure and other obesity-associated comorbidities. **Methods**: We included 57 patients who underwent gastric bypass surgery for morbid obesity [body mass index (BMI) >40 kg/m^2 or >35 kg/m^2 with comorbidities] and had at least one echocardiogram before and after the surgery. A control group was frequency-matched for body mass index (BMI) ±2 kg/m^2, sex, age (±2 yr), and follow-up (±6 mo). We measured (LV) mass, ejection fraction (EF), LV and right ventricular (RV) myocardial performance index (MPI), LV and RV fractional area change (FAC). Analyses were adjusted for potential confounders. **Results**: Main results shown in table. Overall, there was a positive correlation between rate of weight loss and reduction in ventricular septum thickness (R=0.31, p<0.01), posterior LV wall thickness (R=0.22, p=0.02) and LV mass (R=0.27, p<0.01) that remained significant after adjusting for potential confounders. **Conclusions**: Weight loss is associated with decrease in LV mass independent of changes in blood pressure and other obesity-associated comorbidities. Ventricular systolic function was not affected by long-term significant weight loss.

	Cases (n=57)	Controls (n=57)	p-value for difference	P for Multivariate analysis§
Male sex, N (%)	22 (38.6)	22 (38.6)	0.99	–
Age at enrollment, yr	51.1±9	51.8±9.7	0.71	–
Follow-up, months	45±24.9	41.3±21.4	0.4	–
Change in weight, kg	-42.4±25	-3.5±17.4	**<0.0001**	–
Changes in Echocardiographic Parameters (Follow Up - Baseline Values)				
Ventricular septum thickness, mm	- 1.4±2.03‡	0.11±2.12	**0.0002**	0.002
Posterior wall thickness, mm	- 1.24±1.36‡	0.42±1.88	**<0.0001**	<0.0001
Left ventricular mass, g	- 31.68±65.4†	7.73±69.72	**0.002**	0.0006
LV mass index, g/m^2	- 0.18±0.38†	0.05±0.41	**0.002**	0.0005
LV end-diastolic dimension, mm	1.07±6.74	0.09±7.55	0.46	0.79
RV end-diastolic area, m^2	0.92±5.11	2.11±4.41†	0.21	0.12
LV MPI	-0.07±0.3	0.01±0.3	0.18	0.13
RV MPI	0.02±0.1	0.05±0.2	0.49	0.27
LV FAC (%)	0.86±9.7	0.8±8.9	0.97	0.87
RV FAC (%)	0.21±14.3	1.85±10.8	0.51	0.65

Values represent mean±SD.*p<0.05;† p<0.001;‡ p<0.0001 for intragroup comparison§ Adjusting for age, sex, hypertension, diabetes mellitus, coronary artery disease, change in blood pressure, obstructive sleep apnea

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Relationship of Body Mass Index in Young Adulthood and Health-Related Quality of Life (HRQoL) in Later Years: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

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Background: A BMI in the overweight/obese range is associated with a greater risk of developing diabetes, hypertension and CVD as compared to normal weight. It is unknown whether obesity in young adulthood is associated with lower HRQoL years later. **Methods**: The sample includes 3160 black and white males and females from the CARDIA Study, ages 18–34 at baseline examination in 1985–86. Baseline BMI was classified as normal (18.5 - <25.0), overweight (25.0 - <30.0), and obese (≥30). HRQoL (physical, mental, social well-being) was assessed using the Medical Outcomes Study Short Form-12 (SF-12) in 2000–01. The SF-12 yields two summary scales: Physical Component Summary (PCS) and Mental Component Summary (MCS). Linear tests of trend were conducted using multivariate regression models. **Results**: Approximately 34% of the sample was overweight or obese. Multivariate-adjusted association of BMI with HRQoL in the sample was inverse and significant for the physical component summary score (PCS) in all gender-race groups (Table). The higher the BMI the lower (worse) the score (all p-trends <0.001 for all women and white men). **Conclusion**: These findings suggest a long-term relationship between obesity in young adulthood with impaired self-reported physical health.

Table. Adjusted^ Mean Summary Scores After 15 Years of Follow-Up According to BMI‡

	PCS	MCS
Black Men		
Normal weight	332.8	309.8
Overweight	340.4	319.3
Obese	315.3	304.6
P for trend	0.05	0.84
Black Women		
Normal weight	326.5	285.5
Overweight	308.1	281.6
Obese	297.5	280.3
P for trend	<0.001	0.25
White Men		
Normal weight	355.1	312.8
Overweight	349.3	309.5
Obese	300.8	288.3
P for trend	<0.001	0.07
White Women		
Normal weight	348.9	300.7
Overweight	314.7	293.4
Obese	298.0	274.5
P for trend	<0.001	0.002

^Adjusted for age, education, marital status, alcohol use, smoking, physical activity, diabetes, hypertension, antidepressant use, and BMI in 1990–91 ‡Using the Rand SF-12 percentage scoring method

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Waist–Hip Ratio as a Predictor of Incident Hospitalized Heart Failure: The ARIC Study

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Background: Obesity measured by BMI was associated with incident heart failure (HF) in a large population based study but less data exist on the role of central adiposity in the prediction of HF. **Methods**: The ARIC cohort is a bi-racial population-based sample of those aged 45–64 years from 4 U.S. communities with ongoing follow-up starting in 1987 (N=15,792). After exclusion of prevalent HF, missing anthropometry, and poorly represented race groups, there were N=8,129 women and N=6,788 men. Waist girth was measured at the umbilicus and hip girth at the level of maximal protrusion of the gluteal muscles. Waist-hip ratio (WHR) was analyzed as gender-specific tertiles: cut points were WHR less than 0.86, 0.86–0.93, and greater than 0.93 for women; less than 0.94, 0.94–0.98, and greater than 0.98 for men. Incident HF was ascertained through annual contacts and review of medical record and death certificate codes. A first occurrence of either ICD-9-CM discharge code 428 ("heart failure", n=1,200) or heart failure from a death certificate (underlying cause of death, 428 or I50, n=6) was considered an incident event. Gender-specific multivariable Cox proportional hazard regression was used to estimate incidence of HF by tertiles of WHR, adjusted for history of CHD, established CHD risk factors, demographics and BMI. **Results**: There were 1,206 incident HF cases over 13 years of follow-up. After adjustment for covariates the hazard ratio (HR) contrasting the 3rd and 1st tertiles of WHR was 1.94 (95 % CI = 1.46, 2.56) for women and 2.06 (95 % CI = 1.65, 2.58) for men. These estimates remained statistically significant after additional adjustment for BMI: HR = 1.63 (95 % CI = 1.21, 2.18) for women and HR = 1.66 (95 % CI = 1.29, 2.13) for men. **Conclusion**: High WHR is associated with incident HF in men and women in this middle-aged cohort, even after adjustment for BMI. These results suggest that central adiposity - a correlate of impaired insulin sensitivity - be studied as an upstream predictor of HF. If replicated, these findings have implications for prevention.

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The Impact of the Obesity Epidemic on Framingham Risk Score: Results from 20 Years of the Coronary Artery Risk Development in Young Adults Study

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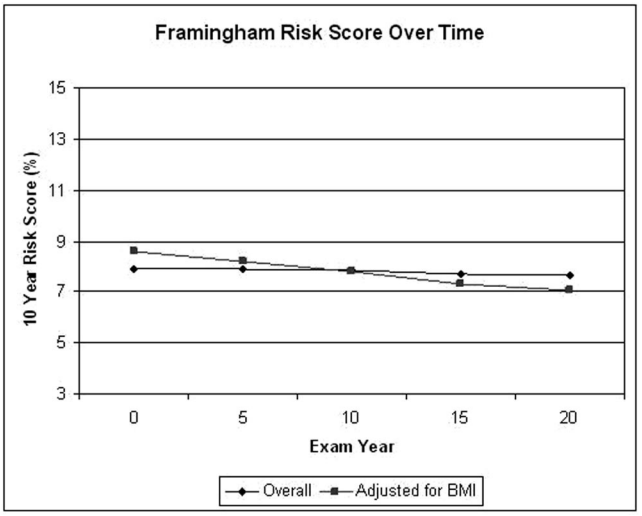
Introduction: While cardiovascular (CV) mortality has decreased, with secular improvements in some risk factors, we lack estimates of combined risk factor change. **Methods**: We examined

the 10-year Framingham risk scores (FRS) over 20 years of follow-up in CARDIA, a cohort of 5,115 African American and white men and women from 4 U.S. cities, ages 18–30 at baseline (1985); we report data on 2882 participants attending each of the 0, 5, 10, 15, and 20 exams. Data on age, tobacco use, fasting blood glucose, blood pressure, HDL, LDL (Friedewald equation), BMI, and physical activity were collected and FRS calculated at each exam. Using repeated measures regression with a compound symmetry covariance structure, we modeled trends in FRS first as a function of time and then with BMI added. **Results**: The mean age (SD) of the cohort was 25.3 (3.6) at year 0 and 45.3 (3.6) at year 20. Mean BMI (SD) and the prevalence of diabetes increased from 24.4 (4.8) kg/m^2 to 29.3 (6.9) kg/m^2 and 0.6% to 6.6%, respectively, while tobacco use decreased from 24.6% to 17.8%. Over 20 years, the mean FRS remained stable (Figure). Adjusting for BMI, FRS decreased from year 0 to year 20. Neither adjustment for physical activity nor stratification by both race and gender changed these trends. **Conclusions**: Concurrent changes in the component risk factors create the impression of stable longitudinal trends in 10-year FRS. However, rising BMI may mask improvements being made in CV risk factor control. Our findings offer an estimate of the countervailing effect of the rising obesity epidemic to population-based improvements in CV risk over time.



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Body Mass Index Over the Life Course and Incidence of Hypertension in Men

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The risk of hypertension associated with BMI assessed over the life-course has not been well characterized. We assessed BMI and risk of incident hypertension in a cohort of 1177 male former medical students at the Johns Hopkins School of Medicine followed from a mean age 22 to 69 years, a median of 45 years. Body weight, height and blood pressure (BP) were measured in medical school and assessed by questionnaire after graduation for a median of 17 times and 13 times, respectively. These self reports have been validated in this cohort. Hypertension was defined as BP $\geq$160/95 mmHg on 1 annual questionnaire, $\geq$140/90 mmHg on $\geq$2 annual questionnaires, or hypertension requiring drug therapy. Self reports of hypertension were confirmed by an endpoint committee review of annual questionnaires, medical records and death certificates. The average BMI at ages 20–29 was 23.1(SD 2.5); 30–39, 23.9(SD 2.5); 40–49, 24.3(SD 2.7); 50–59, 24.7 kg/m^2 (SD 3.1). Cumulative incidence of hypertension by Kaplan Meier analysis at age 60 for the 20–29 age group was 24% for normal weight (BMI $<$25.0), 37% for overweight (BMI 25.0–30.0) and 68% for obese (BMI $\geq$30.0). In Cox proportional hazards analysis, persons who were overweight or obese, at age 20–29 had a significantly higher risk of developing hypertension (Hazards Ratio (HR)1.6; 95% CI 1.3 -1.9) and (HR 3.5; 95% CI 1.9 - 6.6) respectively compared to normals. Results were similar for age 30–39 (HR 1.6; 95% CI 1.3 - 2.0): (HR 1.9; 1.0 -3.6), 40–49 (HR 1.7; 95% CI 1.4 - 2.1): (HR 2.9; 95% CI 1.7 - 5.0) and 50–59 (HR 1.7; 95% CI 1.3 - 2.3): (HR 2.5; 95% CI 1.3 -5.0). After adjusting for smoking, coffee consumption, alcohol use and physical activity, results were similar. Compared to persons with normal BMI at both ages 20–29 and 40–49, those who became (HR 1.6; 95% CI 1.2–2.0) or remained (HR 2.0; 95% CI 1.5–2.6) overweight/obese had an elevated risk of hypertension. Those who were overweight/obese at 20–29 but whose BMI fell to $<$25 kg/m^2 at 40–49 did not have a higher risk (HR 0.7; 95% CI 0.4–1.4). Overweight, obesity and weight gain throughout young adulthood and midlife are associated with an increased risk of incident hypertension. These results emphasize the importance of prevention of overweight and obesity in the prevention of hypertension.

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Subcutaneous and Visceral Adipose Tissue and Their Association with Coronary and Aortic Artery Calcification: The Framingham Heart Study

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Background Abdominal adipose tissue compartments confer differential metabolic risk. We examined whether subcutaneous (SAT) and visceral adipose tissue are associated with either coronary (CAC) or aortic artery calcification (AAC). **Methods** Participants from the Framingham Heart Study Offspring and Third Generation cohorts (n=3130, 49% women, mean age 52 years), free of CVD, underwent computed tomography assessment of SAT, VAT, CAC, and AAC between 2002–2005. TOBIT models were constructed to examine the relation between SAT or VAT per 1 standard deviation (SD) in relation to log-transformed CAC or AAC; models were age-sex adjusted and multivariable adjusted for systolic blood pressure, hypertension treatment, total/HDL cholesterol, triglycerides, lipid treatment, or diabetes. **Results** SAT (per 1 SD increase) was related to CAC in age-sex (0.34 increase in log CAC per 1 SD of SAT, $p<0.001$) and multivariable-adjusted models (0.15 increase in log CAC per 1 SD of SAT, $p=0.03$). SAT (per 1 SD increase) was also related to AAC in age-sex (0.52 increase in log AAC per 1 SD of SAT, $p<0.001$) and multivariable-adjusted models (0.27 increase in log AAC per 1 SD of SAT, $p<0.001$). VAT (per 1 SD increase) was related to CAC in age-sex (0.42 increase in log CAC per 1 SD of VAT, $p<0.001$) but not MV-adjusted models (0.09 per 1 SD of VAT, $p=0.23$), whereas VAT was associated with AAC in both age-sex (0.80 per 1 SD of VAT, $p<0.001$) and MV-adjusted models (0.39 per 1 SD of VAT, $p<0.001$). **Conclusions** Measures of regional adiposity are related to CAC and AAC, even after adjusting for traditional CVD risk factors.

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Genome-Wide Association with Adiposity-Related Traits: The Framingham Heart Study 100K Project

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Background Obesity is related to multiple cardiovascular disease (CVD) risk factors as well as CVD and has a strong familial component. We tested for association between the Affymetrix 100k SNP GeneChip and measures of adiposity in the Framingham Heart Study. **Methods** A total of 1341 Framingham Heart Study participants genotyped with the Affymetrix 100k SNP GeneChip had adiposity traits measured over 30 years of follow up. Body mass index (BMI) and waist circumference (WC) were measured at multiple examination cycles. BMI was averaged over 7 original cohort examinations (10, 16, 18, 20, 22, 24, 26) and 7 offspring examinations (1–7); WC was averaged over 4 offspring examinations (4–7). Sex-specific multivariable-adjusted residuals were created, adjusting for age, age-squared, smoking, and menopausal status. Residuals were evaluated in association with the genotype data using additive GEE and FBAT models. We evaluated associations with SNPs on autosomes with minor allele frequencies of at least 0.10, HWE $p>0.001$, and genotypic call rates of at least 80%. **Results** The top SNPs in GEE models were rs110683 (p-value=1.22E-07) for BMI and rs4471028 (p-values=1.96E-07) for WC, located near the GDAP1 gene. In FBAT models, the top SNPs were rs10503776 (p-value=3.81E-05) for BMI, located in the SEC8L1 gene, and rs10488165 (p-value=2.64E-06), located in the EBF2 gene, for WC. We were able to validate SNPs in known genes that have been related to BMI or other adiposity traits, including 4 SNPs in the INSIG2 gene, 5 SNPs in the ESR1 gene, 6 SNPs in the PPARG gene, and 1 SNP in the ADIPOQ gene. **Conclusions** Adiposity traits are associated with SNPs on the Affymetrix 100k SNP GeneChip. These data will serve as a resource for replication as more genes become identified with BMI and WC.

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Does Active Commuting to Work Influence Adult Fitness, Body Weight, and Obesity in Adults? The CARDIA Fitness Study

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Background: There is little research on the role of active commuting to work and its association with obesity and fitness in population-based, ethnically diverse cohorts. **Hypothesis**: We aimed to understand the patterning of active commuting, defined as walking or biking to work, hypothesizing that active commuting is inversely associated with body weight, obesity, and fitness. **Methods**: Black and white adults initially aged 18–30 years (1985–86) in the CARDIA study and followed into Year 20 (2005–06), self-reported time, distance, and mode of commuting to work, age, leisure-time non-walking physical activity (PA), smoking, and education. Height and weight were measured and obesity defined as BMI$>$/=30 kg/m^2. Fitness was measured using graded exercise treadmill testing (GXT) duration. Associations between walking or biking to work and body weight, obesity and fitness were separately assessed by sex- and race-stratified multivariate linear (or logistic) regression modeling after adjustment for age, years of education, smoking, and non-walking PA score. **Results**: Of the 1926 respondents who worked outside of the home, 18.7% of the sample (whites: males: 21.2%; females: 19.9%; blacks: males: 18.7%; females: 14.6%) actively commuted to work, for an average of 6.32 minutes and 1.68 miles. Among white males, any active commuting (versus none) was associated with lower body weight pounds (β=-14.9; $p<0.0001$), longer GXT duration in seconds (β=76.40; $p<0.0001$), and reduced likelihood of obesity (OR=0.40; 95% CI 0.22–0.73), controlling for age, education, smoking, and non-walking PA. For white

females, active commuting was associated with higher GXT duration (β=51.22; p<0.001). Associations for females were weaker than males, and in the same direction for black as white males, although not statistically significant. Results were similar when considering those living within a two-mile distance from workplace. **Conclusion**: A small proportion of adults in this cohort walked or biked to work. Yet active commuting was inversely associated with body weight, obesity, and fitness for white males (who had highest levels of active commuting). Our findings suggest that increasing the proportion of adults who bike or walk to work may have a positive impact on health.

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Subjective and Objective Sleep Measures Have Different Associations with BMI: The CARDIA Sleep Study

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Recent epidemiologic studies have found an inverse or quadratic association between sleep and obesity based on self-reports of usual sleep duration; studies that stratified by sex have found sex-specific associations. However, subjective reports of usual sleep hours may not be very accurate. Here we ask whether we see similar associations between sleep duration and BMI if we use an objective measure of sleep. This is an ancillary study to CARDIA, an ongoing cohort study whose participants were aged 38–50 years in 2003. Wrist actigraphy monitors were twice distributed to participants from the Chicago site of CARDIA approximately one year apart. Participants (n=669) wore the monitor for three sequential days in each year. The sleep measurements occurred between Year 15 and Year 20 of CARDIA. Participants were also asked how many hours of actual sleep they got on average over the past month. Outcomes were BMI in Year 20 (cross-sectional analysis) and change in BMI from Year 15 to Year 20 (longitudinal analysis). Primary predictors were average of actigraph sleep duration (6 nights), and subjective habitual sleep duration. Sex-stratified linear regression models were adjusted for education, income, age, race and smoking. In cross-section, there were similar weak inverse associations for men between BMI and both subjective sleep (-0.61 kg/m2 per hour, p=0.08) and objective sleep (-0.61, p=0.08). For women, the association was much stronger for subjective (-1.05, p=0.002) than objective sleep (-0.50, p=0.28). Quadratic terms were not significant. The association between change in BMI and objective sleep was not significant for men (-0.21, p=0.12) or women (0.16, p=0.46). There was a highly significant quadratic association between change in BMI and subjective sleep for men (p<0.001), but not for women. This study confirms cross-sectional associations between weight and subjective sleep found in other studies, but finds no significant associations with objective sleep either in cross-section or longitudinally. Since we found in earlier analyses that only 17% of the variation in subjective sleep was explained by measured sleep, one possible explanation is that other determinants of how people perceive their sleep hours, such as sleepiness, correlate with weight.

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Association of High Leptin with History of Myocardial Infarction and Stroke: Findings from NHANES III

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Background: Leptin, an adipose tissue-derived hormone, has been linked to cardiovascular outcomes; however data are limited due to small sample sizes, especially in women. The aim of this paper was to assess the association between leptin concentrations and myocardial infarction (MI) and stroke, independently of traditional cardiovascular risk factors, in the United States population using NHANES data. **Methods and Results**: We analyzed data from 6,239 subjects (mean age 47 years; 3,336 women) with measurements of serum leptin and full assessment of traditional cardiovascular risk factors from the National Health and Nutrition Examination Survey (NHANES) III performed from 1988 to 1994. Logistic regression was used to estimate the cross-sectional association of leptin concentrations (highest quartile versus lowest quartile) and history of MI, stroke and the composite endpoint of MI or stroke (MI/stroke). Sex-specific models of leptin were adjusted for age, race, dyslipidemia, hypertension, diabetes, smoking, and body mass index. MI and stroke were self-reported according to the NHANES methodology. A composite endpoint (MI/stroke) was created based on the presence of self-reported MI and/or stroke. There were 212 men with MI/stroke (adjusted prevalence 5.4%), 154 with MI (adjusted prevalence 4.1%), and 82 with stroke (adjusted prevalence 1.7%). There were 135 women with MI/stroke (adjusted prevalence 2.6%), 74 with MI (adjusted prevalence 1.5%), and 78 with stroke (adjusted prevalence 1.4%). In multivariate analysis, high leptin was significantly and independently associated with MI/stroke in both men (OR, 2.29; 95% CI, 1.16 to 4.65) and women (OR, 3.05; 95% CI, 1.47–6.51); with MI in men (OR, 2.54; 95% CI, 1.16 to 5.84); and with stroke in women (OR, 3.17; 95% CI, 1.27–8.26). **Conclusion**: In the US population, high serum leptin is significantly associated with MI or stroke in men and women, independently of traditional cardiovascular risk factors.

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Endothelin-1 Vasoconstrictor Activity Contributes to Impaired Acetylcholine-Mediated Vasodilation in Obesity

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Obesity is associated with impairments in vascular endothelial function, particularly endothelium-dependent vasodilation. However, the mechanisms responsible for diminished endothelial vasodilator function with obesity are largely unknown. Endothelin-1 (ET-1), a potent vasoconstrictor peptide released by the endothelium, plays an important role in vasomotor regulation and has been linked to the pathogenesis of atherosclerotic vascular disease. We and others have reported that obesity is associated with increased endogenous ET-1 vasoconstrictor tone. The aim of this study was to determine whether the obesity-related reduction in forearm endothelium-dependent vasodilation to acetylcholine is due, at least in part, to ET-1 vasoconstrictor activity. To address this aim, we studied 33 sedentary, middle-aged adults: 17 normal weight (NW: age: 57±2 yr; 7 M/10 F; BMI: 23.4±0.4 kg/m^2) and 16 obese (O: 58±2 yr; 9M/7 F; 30.2±0.8 kg/m^2). Forearm blood flow (FBF) responses to intra-arterial infusions of acetylcholine (ACh: 8.0–32.0 μg/min), sodium nitroprusside (SNP: 2.0–8.0 μg/min) and BQ-123 (a selective ETA receptor antagonist; 100 nmol/min) were measured by plethysmography. FBF responses to ACh were determined in the absence and presence of ETA receptor blockade. As expected, forearm vasodilator responses to ACh were lower (25%; P=0.01) in O (from 4.8±0.2 to 11.5 mL/100 mL tissue/min) vs NW (4.6±0.2 to 15.5±1.0 mL/100 mL tissue/min) subjects. FBF responses to SNP were comparable between the groups. In response to BQ-123, FBF was not significantly changed from baseline in NW, however, O demonstrated a marked (~20%; P<0.05) vasodilator response. ACh in combination with BQ-123 resulted in an ~25% increase in vasodilation in O compared with saline. Interestingly, the obesity-related difference in ACh-mediated vasodilation was largely negated by ETA receptor blockade. Indeed, ETA receptor blockade resulted in ACh vasodilation (4.4±0.2 to 14.5±0.7 mL/100 mL tissue/min) similar to that of normal weight adults. These results suggest that the obesity-related impairment in forearm ACh-mediated vasodilation is due, in large part, to increased ET-1 vasoconstrictor activity.

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The National Rates of Morbid Obesity Among US Children and Adolescents

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Background: Morbid obesity among children and adolescents is not clearly defined. Recommended selection criteria for bariatric surgery in obese adolescents start with a BMI ≥40. The extent to which morbid obesity affects American youth is unknown. **Hypothesis**: We hypothesize that morbid obesity, defined by BMI percentiles and absolute BMI values, is more common among ethnic minorities and is also associated with poverty status in U.S. adolescents. **Methods**: We analyzed measurements from 12,384 U.S. children and adolescents from the National Health and Nutrition Examination Survey 1999–2004. Outcome variables were the proportion of subjects with BMI ≥99th percentile for age/sex and the proportion with absolute BMI ≥30, 40 and 50. Covariates include age, gender, race and poverty-income ratio (PIR). We used SUDAAN for bivariate and multivariate analyses. **Results**: Currently 3.8% of U.S. children 2–19 yr have a BMI ≥99th percentile, with boys, 4.6%, more than girls, 2.9% (p<0.001). This is more common among Blacks, 5.7%, then Mexican-Americans, 5.3%, Other race, 3.6%, and then Whites 3.1% (p< 0.001). The rate of morbid obesity decreased with increasing income by PIR, from 4.3% for those below poverty and with PIR of 1–3, to only 2.5% for those in the highest category (PIR >3), p = 0.002. Among adolescents, 1.3% had a BMI ≥40, with no difference by sex. Blacks were most affected, 3.4%, then Mexican Americans, 1.4%, then Whites, 0.9% and Other, 0.6% (p < 0.001). Teens below the poverty level were more affected, 2%, than teens in the highest PIR category, 0.8% (p=0.002). Only 1.8% of children 6–11yrs had BMI ≥30 and only 0.2% of 12–19 yr olds had BMI ≥50. **Conclusion**: Almost 4% (2.7 million) U.S. children have a BMI ≥99th percentile for age/sex, with significant differences by race, sex and poverty. In addition, over 1% of U.S. teens have a BMI ≥40. (418,000 teens), a level of obesity which may qualify for bariatric surgery.

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Global Burden of Obesity

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Background Obesity is a major preventable cause for morbidity and premature deaths. We aimed to estimate the overall prevalence and absolute number of overweight and obesity worldwide in 2000 and to project the global burden in 2025. **Methods** We searched the published literature from January 1990 through July 2006, using MEDLINE and other computerized databases, supplemented by a manual search of references from retrieved articles. Sex- and age-specific prevalence of overweight and obesity from representative population samples were applied to the 2000 population and the 2025 population projections to estimate the number of overweight and obese persons in each country. The total numbers of overweight and obese persons in each country were summed to provide an estimate of the total numbers of overweight and obese individuals for each region and the entire world. **Results** Overweight and obesity prevalence data were collected from 89 countries, covering approximately 80% of the world population. Overall, 23.1% (95% confidence interval 22.9 -23.4%) of the world's adult population in 2000 was overweight (24.0% in men [23.6–24.3%] and 22.3% in women [22.0–22.7%]), and 9.7% (9.5–9.8%) was obese (7.7% in men [7.5–7.9%] and 11.6% in women [11.4–11.9%]). The estimated total number of overweight and obese adults in 2000 was 857 million (848–866 million), and 358 million (353–364 million), respectively. By 2025, the number of overweight and obese adults was projected to increase by 54% and 55%, respectively, totaling 1.32 billion (1.31–1.34 billion) overweight and 556 million (548–563 million) obese individuals. **Conclusions** Overweight and obesity is an important public health burden worldwide. National programs for the prevention and treatment of overweight, obesity, and related co-morbidity and mortality should be a public health priority.

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Predictors of Body Fatness and Cardiovascular Risk in Pediatric Cancer Survivors

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Background: Body composition and CV risk factors of survivors of childhood cancer have been compared rarely to appropriate sibling controls. **Methods**: We prospectively studied body

composition (using DXA) and BMI in pediatric cancer survivors >5 yrs from dx and sibling controls. We evaluated age, race, gender, yrs since dx, age at dx, chemotherapy, radiation, lipids, hsCRP, sex hormones, insulin, IGF-1, and TSH at DXA testing to determine correlation with and effects on body fat and BMI. **Results**: 170 survivors and 71 siblings were evaluated. Siblings were younger (p=0.004) than the survivors (16.1 yrs [se=.88] vs 19.4 yrs [se=.62] with an equal distribution of males and females. Survivors were a mean of 11.9 yrs since dx. 57% had a past dx of leukemia/lymphoma. In an age-adjusted analysis, BMIs were similar between survivors and controls. Total body fat was greater in male survivors (25.7% [se 1.05]) vs male controls (21.5% [se 1.70]) (p=0.04), yet there were no differences among females. Male survivors had greater trunk fat% than controls (26.6% [1.13] vs 22.0% [1.79]; p=0.03). There were no differences in females. CV risk factors (insulin, cholesterol, trigylcerides, HDL, LDL, and CRP) were all significantly increased (except decreased HDL) in male survivors compared to controls, yet no differences were found among females. Multivariate models to ascertain predictors of BMI, total body fat, and trunk fat were developed for both male and female survivors. For males, cytoxan treament (-2.84, p=.009), and IGF-1 (0.01, p=.01) were independently associated with BMI and for females, cytoxan treament (-3.34, p=.01) was associated with BMI. In addition to age, cranial irradiation in both males (6.18, p=.003) and females (6.16, p=0.004) was associated with increased total body fat. Similar results were found for trunk fat. Increasing doses of cranial radiation were associated with both increased total body fat (33.7% with none vs 40% with 1–20 Gy and >20 Gy [females]; 21.6% none, 27.1% 1–20 Gy, 32.6% >20 Gy [males]; p<0.05 all analyses). **Conclusion**: Compared to siblings, male pediatric cancer survivors have greater body fat and CV risk factors than siblings. Cranial irradiation is an important risk factor for body fatness in both male and female pediatric cancer survivors.

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Waist Circumference in Viennese School Children Is Closely Related to Inflammatory, Endothelial, and Oxidation Markers

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Abdominal obesity and its associated pathophysiology is an increasing health concern in Western societies. In juveniles assessment of waist circumference is better than BMI and has a high predictive value for the later development of abnormal lipid profile and cardiovascular disease. We assessed parameters of abdominal obesity in Viennese juveniles (aged 10 - 18 years) in 3 schools together with biochemical parameters of inflammation, endothelial dysfunction and oxidation injury. Parameters assessed were history, risk factors, height, weight, BMI, waist-circumference (WC), cholesterol, triglycerides, LDL, HDL, CRP, 8-epi-$PGF_{2\alpha}$ as marker of oxidative stress, circulating endothelial cells (CEC), and circulating endothelial progenitor cells (CEPC). In 1995 a school screening in juveniles (aged 10 - 18 years; n = 984; 481 boys/503 girls) was performed. Ten years later in the same 3 schools 997 juveniles (495 boys/502 girls) were investigated. Mean WC at age 10 was 66.3 cm (boys) and 65.4 cm (girls), at age 14 for boys 75.1 and for girls 73.4 cm. Mean totals was 78.7 and 77.5 cm, respectively. In 46% (girls) and 51% (boys) WC was >70 cm (the upper limit for juveniles according to ACCC). Cigarette smoking was associated with significantly ($p < 0.01$) higher 8-epi-$PGF_{2\alpha}$ > CEC > CEPC and lower HDL. Separate evaluation for smokers and non-smokers revealed comparable findings. WC was significantly ($p < 0.01$) correlated with 8-epi-$PGF_{2\alpha}$ (IP) > CRP > CEPC > CEC. Correlation of BMI to these parameters was less pronounced. IP was negatively correlated with HDL ($r = -0.5681$; $p < 0.005$), positively with WC (0.6984; $p < 0.0001$), active ($r = 0.8371$; $p < 0.0001$) and passive ($r = 0.6135$; $p < 0.0001$) cigarette smoking. Within the 10 years interval mean WC increased by 1.34 cm; in parallel, 8-epi-$PGF_{2\alpha}$, CRP and CEPC changed significantly ($p < 0.01$). These data clearly show that WC in Viennese juveniles is too high. The increase in WC over a decade is significantly correlated to parameters of inflammation, endothelial dysfunction and oxidation injury.

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Does Weight Loss Maintenance Differ for Minorities Compared to Non-Minorities?

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Background: Overweight and obesity have reached epidemic proportions, and racial minorities are affected disproportionately. In 2003–2004, the obesity prevalence rate for non-Hispanic black adults in the US was 45% compared to 31% among non-Hispanic white adults. The foremost issue in weight loss treatment is determining how to promote lifestyle changes that support the maintenance of a lower weight after the initial loss. **Objective**: The purpose of this study was to examine if there were differences between minorities and non-minorities in weight loss maintenance during the final 6-month maintenance phase of the PREFER study, an 18-month randomized clinical trial of behavioral weight loss treatment. **Methods**: The PREFER trial randomized participants to either receive their dietary treatment preference or not, and secondly to standard behavioral therapy plus a *standard* reduced calorie and fat diet or a reduced calorie and fat *lacto-ovo-vegetarian* diet. Participants attended weekly group sessions for months 1–6, biweekly months 7–9, and monthly for months 10–12; the final 6 months was a no-contact, maintenance phase. Assessment of weight occurred at baseline, 6, 12, and 18 months. We examined the percent weight change between the 12- and 18-month maintenance period, without regard to treatment assignment, to determine if there were differences in weight maintenance between minorities and non-minorities. **Results**: The sample (N = 124, non-minorities n = 87, minorities n = 37) was mostly female (86%, 106 of 124) with a mean age of 44.8 years (SD = 8.4) and 15.4 (SD = 2.6) years of formal education. Sociodemographic variables (age, gender, education and income) as well as baseline weight were not different between minorities and non-minorities (p's > .05), and there was no significant difference in percent weight change between the two groups during the 12 to 18 month maintenance phase ($p = .82$). Minorities regained 3.6%±4.0% of their 12 month weight at 18 months, while non-minorities regained 3.4%±4.1%. **Conclusions**: These findings suggest that there is no difference in weight loss maintenance between minority and non-minority participants, and in fact, support the use of the same strategies to promote maintenance of lost weight for individuals of all ethnicities.

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The Association Between Attained Educational Level and Changes in Body Mass Index Over 20 Years: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

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Objective: There is a paucity of data on the association of education with long-term changes in BMI from young adulthood to early middle age. This study examines the association of attained educational level and 20 year changes in BMI in a biracial cohort of men and women in CARDIA. **Methods**: Analyses include 2658 participants with complete data for BMI and education at years 0 and 20 (2005–06). Exclusions were made for: missing data, pregnancy, misreported education, and changed gender. Repeated measures analyses were used to compare changes in BMI (years 0 to 20) for three education groups as determined at year 20: <12 years (n=120); 12–15 years (n=1477); and ≥16 years (n=1061). All models were age adjusted using the PROC MIXED procedure. **Results**: Although there was a significant increase in BMI for each race-gender and education group the pattern of increase by education was different between Blacks and Whites. The least educated (<12 years) Black Men (BM) increased their BMI by 4.2 units versus a 5.2 increase among the highest educated (≥16 years). White Men (WM) with the least education increased their BMI by 4.5 compared with an increase of 3.5 among the highest educated. Black Women (BW) with 12–15 years of education had the greatest increase in their BMI, 6.8 units compared with 5.5 units in the least educated. White Women (WW) with the least education increased their BMI by 6.1 versus a 3.5 increase among the highest educated. **Conclusion**: These findings suggest that prevention efforts need to address differences in the relationship between educational attainment and BMI among ethnic groups.

Age-adjusted Means for Changes in BMI (years 0 to 20) by Attained Education Level

	Years of Attained Education								
	<12	<12		12–15	12–15		≥16	≥16	
	Year 0	Year 20	Change$^{\Psi}$	Year 0	Year 20	Change$^{\Psi}$	Year 0	Year 20	Change$^{\Psi}$
BMI (kg/m^2)									
BM	25.6	29.7	4.2	24.6	29.8	5.2	25.7	30.9	5.2
WM	24.0	28.6	4.5	24.8	29.3	4.5	24.3	27.8	3.5† *
BW	26.6	32.1	5.5	26.0	32.8	6.8	25.2	30.7	5.5† **
WW	24.8	30.9	6.1	24.1	29.4	5.3	22.4	25.9	3.5† **

$^{\Psi}$All changes are significantly different from 0 ($p<0.01$) †For comparing changes in BMI among education groups; *$p<0.05$ and **$p<0.001$

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Adiponectin and Nutrient Intakes Among Japanese in Japan and Hawaii: The INTERLIPID Study

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Aim Investigate whether dietary factors explain higher average serum adiponectin in Japanese in Japan compared with Japanese-Americans living a Western lifestyle in Hawaii. **Methods and Results** Serum adiponectin and nutrient intakes were examined by standardized methods in population samples (ages 40 to 59 years) of Japanese-Americans in Hawaii (99 men, 104 women) and Japanese in Japan (124 men and 125 women). Mean adiponectin was signicantly higher in Japan than Hawaii (10.5±5.5 vs 8.1±4.0 μg/ml, $p < 0.0001$). Mean body mass index (BMI) was lower in Japan than Hawaii (23.4 vs 26.9 kg/m^2, P<0.0001), as was dietary total protein (15.7 vs 16.8 %kcal, P<0.0001) and arachidonic acid (0.07 vs 0.08 %kcal, P<0.0001) intake; moderate or heavy physical activity (5.1 vs 1.7 h/day, P<0.0001) and omega-3 polyunsaturated fatty acids (PFA) intake (1.22 vs 0.88 %kcal, P<0.0001) were higher in Japan. In multiple linear regression analyses with each dietary, lifestyle variable considered separately, BMI reduced the Hawaii-Japan adiponectin difference by 50.7% and physical activity by 15.4%. The combination BMI, physical activity, energy-adjusted dietary total protein, omega-3 PFA, and arachidonic acid further reduced the coefficient (by 78.3% total), and the difference was statistically nonsignificant. Total energy intake, Keys dietary lipid score, alcohol intake, hours postprandial, smoking were not related to adiponectin. **Conclusions** Adiponectin concentrations were positively associated with nutrients/lifestyles implicated in preventing atherosclerosis, and inversely associated with nutrients/lifestyles implicated in promoting atherosclerosis. Higher adiponectin concentration in Japanese in Japan compared to Japanese-Americans in Hawaii disappeared after adjustment for specific nutrients, BMI, and physical activity.

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The Change in Central Obesity Over Time Is Associated with Sex Hormones at Baseline in the Multi-Ethnic Study of Atherosclerosis (MESA)

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We have previously shown cross sectionally in the MESA study that estradiol (E2) levels are associated with greater central obesity, and dehydroepiandrostenedione (DHEA) and sex

hormone (SH) binding globulin (SHBG) with lesser central obesity, while bioavailable testosterone (BioT) is associated with lesser central obesity in men but greater central obesity in women. We analyzed associations of endogenous SH with longitudinal changes in waist circumference (WC) or waist to hip ratio (WHR) in MESA. **Methods**: Analyses included 2959 men and 1859 postmenopausal women who were not on hormone therapy at MESA baseline (45–84 years, 37% white, 13% Chinese, 27% African-American, 23% Hispanic), with at least one follow-up visit (median follow-up from baseline to visit 2 : 578 days, visit 3 : 1135 days; 91% had both visits). WC (or WHR) at follow-up was regressed simultaneously on all log-transformed SH adjusted for baseline WC (or WHR), age, race, systolic BP, smoking, fasting glucose, and follow-up time using Generalized Estimating Equations accounting for intrasubject correlations. Interaction by sex, ethnicity, and baseline diabetes (ADA 2003 criteria or medication) were studied. **Results**: Adjusting only for baseline WC (or WHR), per year of follow-up, WC increased 3.4±0.6 mm in men vs. 1.5±0.8 mm in women (p=0.065), and WHR increased 0.25% in men vs. 0.45% in women (p=0.015). In adjusted models (Table), E2 was associated with greater increase, while DHEA and SHBG were associated with decreases in central obesity. For SHBG, decreases were more marked in women (p for interaction: WC, 0.040, WHR, 0.014). There were no other interactions by sex, ethnicity, or baseline diabetes. **Conclusions**: Similar to their cross sectional associations, E2 was associated with a small increase, while DHEA and SHBG were associated with a small decrease in central obesity. In contrast to our cross sectional data, BioT was not significantly associated with longitudinal increases in central obesity.

Table: Longitudinal Association of WC and WHR with Baseline SH in MESA

Hormone (typical doubling range: 1x-2x geometric mean)	Adjusted WC regression coefficients in mm per 2-fold sex hormones, (p-value)		Adjusted WHR regression coefficients in % per 2-fold sex hormones, (p-value)	
BioT (1.6 to 3.2 nmol)	-1.74 (0.081)		-0.11 (0.149)	
E2 (0.1 to 0.2 nmol)	-1.74 (0.081)		0.33 (<0.001)	
DHEA (12 to 23 nmol)	-2.13 (0.069)		-0.27 (0.003)	
SHBG (44 to 88 nmol)	Men: -2.49 (0.118)	Women: -7.79 (0.002)	Men: -0.79 (<0.001)	Women: -1.26 (<0.001)

P100

Risk of Mortality Following Hospitalization for Heart Failure Is Lower in Obese Patients: 2-Year Findings from the Minnesota Heart Survey

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Background. The epidemiological evidence on the effects of obesity on mortality has been controversial in the heart failure (HF) population. We examined whether this paradox persists in a community-based population of patients hospitalized for HF. **Methods**. The Minnesota Heart Survey Community Surveillance of Congestive Heart Failure for 1995 and 2000 hospital discharge years studied residents of the Minneapolis-St. Paul area (35–84 years old) hospitalized with an eligible ICD-9 discharge code for HF. Cases of HF were classified as "HF" or "advanced HF" (AHF) according to the Minnesota Heart Failure Criteria, based on dyspnea at rest or on exertion, pulmonary rales, cardiomegaly, interstitial or pulmonary edema, S3 gallop, tachycardia and LVEF. Ascertainment of 2-year mortality was performed using a state-wide death registry. Adiposity was defined using BMI: thin (BMI < 18 kg/m^2; 116/5451=2%), normal (18 kg/m^2 BMI < 25 kg/m^2; 1185/5451=22%), overweight (25 kg/m^2 BMI < 30 kg/m^2; 1160/5451=21%), obese (30 kg/m^2 BMI < 35 kg/m^2; 658/5451=12%), morbidly obese (BMI >35 kg/m^2; 529/5451=10%), and BMI missing (1803/5451=33%). Multivariable adjusted absolute risk (AR) of 2-year mortality was obtained via linear regression adjusting for sex, smoking, Charlson Comorbidity Index, LVEF, cardiac drug use and CVD risk factors. **Results**. Of the 5451 cases, 4661 (85%) had HF and 790 (15%) had AHF, a symptom constellation with higher mortality risk. Obese cases were more likely to have AHF than thinner cases: thin (27/116=23%), normal (228/1185=19%), overweight (117/1160=15%), obese (100/658=15%), morbidly obese (49/529=9%), and BMI missing (209/1803=12%). By the end of 2-year follow-up, 2360 cases (43%) died. Obese cases of HF had a lower multivariable adjusted risk of death than thinner cases (p-value for linear trend < 0.0001): thin (AR: 61%, 95%CI: 53%–70%); normal (AR: 49%, 95%CI: 46%, 51%); overweight (AR: 37%, 95%CI 34%–39%); obese (AR: 37%, 95%CI: 33%–40%); morbidly obese (AR: 34%,95%CI 30%–38%). **Conclusion**. In a large community-based sample of patients hospitalized for HF, obese individuals are more likely to have a milder form of disease compared to thinner individuals, which translates into improved survival following hospital discharge.

P101

CRP Levels Correspondingly Increased with Body Weight Gain and Decreased with Body Weight Loss During 2 Years in 3620 Healthy Japanese Adults

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Background: Traditional risk factors for cardiovascular diseases (CVD) are thought to progress atherosclerosis by mediating inflammatory reaction. Obesity is one of the important risk factors and body weight gain may exacerbate inflammatory reaction. However, whether body weight gain increases serum CRP levels and whether body weigh loss decreases serum CRP levels have not been fully examined in the general population. **Methods**: A total of 3,620 healthy participants (men, 2,227 aged 27 to 86 years; women, 1,393 aged 22 to 88 years) who underwent both thorough medical examinations in 2001 and 2003 in our institute were enrolled. Participants were divided into three groups according to body weight change during two years (weight gain group, WG group: the highest quartile group according to body weight change; no changed group, NC group: the middle two quartile groups; weight loss group, WL group: the lowest quartile group) in both sexes. Serum high-sensitivity CRP (hsCRP) levels (mg/L) were measured in all participants and multivariate adjusted logarithm-transformed hsCRP levels were compared between in 2001 and 2003 after adjusting for risk factors that were independently associated with serum CRP levels in a multiple regression analysis. **Results**: Adjusted mean CRP levels significantly increased in the WG group and significantly decreased in the WL group and did not change in the NC group during two years (see table). **Conclusion**: Body weight gain exacerbates inflammatory reaction and may contribute to an increase in CVD morbidity and mortality, while weight loss attenuates inflammatory reaction and may prevent future CVD development.

Table. Crude mean and adjusted mean CRP level by the groups according to delta body weight

Men 2,227	Crude CRP (mg/L)	Adjusted geometric mean CRP (mg/L)		Women 1,393	Crude CRP (mg/L)	Adjusted geometric mean CRP (mg/L)	
WL group (delta BW -9~-2 kg/ 2 years)				WL group (delta BW -9~-2 kg/ 2 years)			
2001	0.85	0.55	] *	2001	0.73	0.40	] *
2003	0.84	0.49		2003	0.70	0.34	
NC group (delta BW -1~+1 kg/ 2 years)				NC group (delta BW -1~+1 kg/ 2 years)			
2001	0.88	0.51		2001	0.70	0.40	
2003	0.91	0.50		2003	0.69	0.38	
WG group (delta BW +2~+9 kg/ 2 years)				WG group (delta BW +2~+9 kg/ 2 years)			
2001	0.83	0.51	] *	2001	0.54	0.37	] *
2003	0.98	0.58		2003	0.72	0.45	

*, p < 0.05 by ANCOVA

P102

Excess Weight and Impaired Quality of Life (QOL) in a Diverse Cohort of Women: Results from the Women's Health Initiative (WHI)

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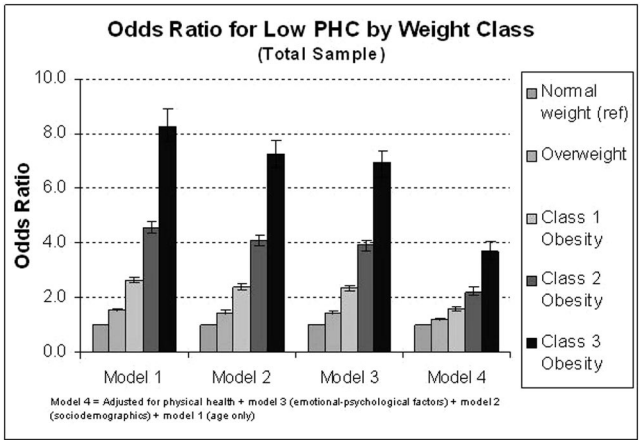
Objective: To examine the relationship between obesity and QOL or physical well-being in older women. **Methods**: We did a cross-sectional study of baseline data (collected 1993–1998) from the WHI cohort (n=161,393). Covariates were sociodemographic and physical health (obesity-related diseases, pain, self-rated health) data plus emotional-psychological factors (mood disorder history, social support, religious affiliation, living situation, life events). We looked at weight class (standard BMI categories) and QOL (SF-36 physical health component, PHC, score). Bivariate analyses of racial/ethnic differences for predictors were done using chi-squared tests. We also used odds ratios (OR) from logistic regression models to examine the link between BMI and PHC score. **Results**: The sample comprised 133,534 non-Hispanic White, 14,627 African American, 6,512 Hispanic/Latino, 4,192 Asian/Pacific Islander, and 715 American Indian women. The prevalence of poor physical well-being (i.e., PHC score 40; p<0.001). A linear increase of poor physical well-being occurred with increasing weight class even after adjustment for covariates, including weight-related diseases (OR 3.71, 95% CI 3.41 to 4.04; trend p-value <.001) for Class 3 obesity compared to normal weight. The increased risk of poor physical well-being with increasing BMI category was generally similar in each racial/ethnic cohort. **Conclusions**: Overweight and obesity have a profound effect on physical well-being of older women; this is only partially explained by the major weight-related diseases. Adverse effects on physical well-being and performance may be one of the most important consequences of excess weight.



P103

Predictive Value of Weight-for-Age Percentiles to Identify Overweight Children and Adolescents

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Objective: To assess the predictive value of weight-for-age to identify overweight children and adolescents in the atypical research or public health situations where height is not available to calculate body mass index (BMI). **Methods**: Data from the National Health and Nutrition

Examination Survey (NHANES) 1999–2004 were used to calculate the sensitivity, specificity, positive, and negative predictive value of selected weight-for-age cutoff points to identify overweight children and adolescents (as defined by BMI at or above the 95th percentile of the reference population). **Findings**: The 50th and 75th weight-for-age percentiles had good sensitivity (100% and 99.6%, respectively), but poor positive predictive value (23.7% and 37.0%, respectively), while the 95th and 97th had reasonable positive predictive value (80.3% and 91.5%, respectively), but limited sensitivity (82.0% and 66.7%, respectively) to identify overweight subjects. The properties of weight-for-age percentiles to identify overweight subjects differed between sex, age, and ethnicity/race, but remain within a relatively narrow range. **Conclusions**: No single weight-for-age cutoff point was found to identify overweight children and adolescents with acceptable values for all properties: sensitivity, specificity, positive and negative predictive values. Thus weight-for-age cannot be used in the clinical setting instead of BMI-for-age to identify overweight children and adolescents. However, in atypical research or public health situations where height is not routinely or easily available (emergency care, existing database, telephone surveys), some of the weight-for-age percentile cutoffs may provide useful screening tools to target limited resources, including formal BMI assessment, to groups more likely to include overweight children and adolescents than the general population.

P104

Diet Alone Does Not Improve Endothelial Function in Overweight Children

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Background: Obese children exhibit vascular endothelial dysfunction compared to normal weight peers. Recently we demonstrated that an 8-week aerobic exercise program results in significant improvement in endothelial function in overweight children. To date no studies have been conducted in children examining the benefit of decreasing body mass and percent fat on endothelial function via dietary intervention alone. **Hypothesis**: We hypothesized that body mass and percent fat loss in overweight children due to dietary changes would be associated with an increase in endothelial function. **Methods**: Participants were overweight children (BMI $>85^{th}$ percentile, 12 male, 11 female, age = 11.5±0.7 yrs, Tanner stage=1.8±0.9) who were randomized to either a 5 month dietary modification program (Diet; N = 12) (Shapedown®) or a control period (Control; N = 11) in which no dietary counsel was provided. Body composition was assessed before and after the 5-month period by dual-energy x-ray absorptiometry system. Endothelial function was evaluated by ultrasound imaging of the brachial artery during flow-mediated dilation (FMD). Fifteen minutes following the measurement of FMD, 0.3 mg sublingual nitroglycerin was administered and the brachial artery was imaged in order to assess endothelium-independent dilation (EID). **Results**: During the 5 month period a significant change between groups over time for body weight (Diet = 62.3±3.1 to 61.0±3.2 kg vs. Control = 78.8±4.8 to 82.1±5.1 kg; $P < 0.0001$) and body fat % (Diet = 42.8±1.7 to 39.9±2.1 % vs. Control = 47.5±1.3 to 48.0±1.4 %; $P = 0.008$) was observed. Although there was a significant change in body weight and fat mass in the Diet group there was no change between groups over time for peak FMD (Diet = 6.06±0.61 to 6.91±0.68% vs. Control = 5.28±0 .58 to 5.40±0.56%, $P = 0.8893$) or peak EID (Diet = 24.47±2.52 to 25.48±1.69 vs. 21.79±2.23 to 21.62±1.45%, $P = 0.7210$) **Conclusion**: In conclusion, the data from this study indicates that changes in body mass and percent fat in overweight children due to dietary modification do not result in improved endothelial function. The data would also suggest that dietary modification must be combined with aerobic exercise to improve endothelial function in overweight children.

P105

Patterns of Adherence to Standard Behavioral Weight Loss Treatment

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Adherence to a weight loss treatment protocol is essential for initial weight loss and maintenance of that loss. We examined adherence to the treatment protocol among participants who were randomized to a standard calorie- and fat-restricted diet (STD) or a calorie- and fat-restricted lacto-ovo-vegetarian diet (LOV) by their dietary preference (Preference-Yes and Preference-No). A cognitive behavioral intervention of 33 group sessions was delivered over 12 months; a 6-month, no-contact maintenance period followed. The five intervention components were: (1) attending group sessions, (2) following a daily calorie goal, (3) following a daily fat gram goal, (4) engaging in at least 150 minutes of physical activity per week, and (5) recording foods eaten and minutes of physical activity in a paper-and-pencil diary (self-monitoring). We used objective measures of adherence (attendance and turning in a diary at each session) and self-report measures of following the daily dietary goals and weekly exercise goals. The PREFER trial sample included 176 participants (age 44.1±8.6 years; 87% females; 70% Caucasian). Using a mixed model analysis, we found a significant decline in adherence to attendance ($p = .01$), self-monitoring ($p < .0001$), and weekly exercise goal ($p < .0001$) across the four treatment groups over time. Adherence to the daily fat gram goal declined over time ($p = .01$) and was also significantly different by diet ($p = .05$), indicating better adherence in the LOV diet group ($p = .01$). We found a similar significant decline in adherence to the daily calorie intake over time ($p = .0002$) and also by diet ($p = .05$), again revealing better adherence in the LOV diet group. A significant interaction among preference, diet and time was also observed in adherence to the calorie goal ($p = .01$). The findings demonstrate that even during active treatment, adherence begins to decline across all components of the intervention protocol and emphasize the need to develop strategies that can help sustain and improve adherence. The results also suggest that adherence to the daily calorie and fat gram goals may be more easily achieved among those who are following an LOV eating plan.

P106

Significance of Anthropometric Indicators of Obesity in Determining Coronary Heart Disease Risk Among Males and Females

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Objectives: This study compares gender-specific waist circumference (WC) and body mass index (BMI) in their associations with obesity-related-CHD risk factors and estimates their optimal risk thresholds for identifying the 'obesity-related-CHD risk' amongst males and females. **Methods**: A community based cross-sectional study on 515 adults (262 males) aged 20–64 years, residing in the district of Colombo, Sri Lanka selected by a multi-stage, stratified, probability-sampling method. Demographic and lifestyle factors, CHD events and smoking were assessed by questionnaires. Obesity-related-CHD risk factors [hypertension, diabetes, triglycerides, low-density (LDL) and high-density (HDL) lipoproteins] were identified by diagnosis cards, blood pressure (BP) readings or bio-chemical assessments. WC and BMI measurements were also obtained. **Results**: In both males and females, systolic BP, diastolic BP and triglycerides correlated significantly with WC and BMI ($p<0.01$). Plasma glucose did not associate with either measurement among females nor did HDL among either sex. Of the two anthropometric measurements, WC was a stronger correlate of systolic BP (Pearson correlation co-efficient (r)= Males(M): 0.29; females(F): 0.32), diastolic BP (r= M: 0.30; F: 0.27) and triglycerides (r= M: 0.30; F: 0.31) compared to BMI. WC was also an independent predictor of 'obesity-related-CHD risk' (defined by ≥ one condition of obesity-related-CHD risk factors) amongst both males (Adjusted odds ratio (OR): 1.05; 95% confidence interval (CI):1.02, 1.07) and females (OR: 1.02; 95% CI:1.00–1.05), when adjusted by confounding effects in the logistic regression models. In contrast, BMI was significant as an independent predictor only among males (OR: 1.15; 95% CI: 1.07–1.23). At the same risk threshold of 25 and 30 kg/m^2 of BMI, WC corresponded with 90.5 and 105.5 cm among males and with 100 and 129 cm among females, respectively. The optimal risk threshold of WC that predicted the presence of 'obesity-related-CHD risk' was 88.5 cm in the receiver-operator-characteristic (ROC) curve. It was lower than the universal cutoff value of 90 cm among Asian males. **Conclusions**: WC is a better anthropometric indicator than BMI in identifying males at risk of obesity-related-CHD.

P107

Evaluation of Coronary Artery Disease: Characterizing the Unique Pattern of Symptoms in the Obese and Morbidly Obese

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Background: The impact of obesity on long-term outcomes in patients with coronary artery disease (CAD) has been reported in several studies. We sought to determine if obese and morbidly obese patients present with unique baseline symptoms in the initial evaluation of CAD. **Methods**: A prospective cohort study was initiated in six countries (France, Germany, Italy, Spain, UK, US). Three hundred and twenty cardiologists participated and each site enrolled up to 5 consecutive patients (N= 1,608): Europe (n=1,264), US (n=344). Cardiologists were asked to select from a list of symptoms that were exhibited at first presentation: chest pains, shortness of breath, pain on inside of left arm, general pain in arms/shoulders, dizziness, nausea, fatigue, pain in lower jaw, GI issues, or None. **Results**: Age distribution <50 (13.9%), 51–60 (28.8%); 61–70 (31.2%), 71–80 (19.8%), 80+ (5.5%) and gender (67.1% male) did not vary significantly across the six countries. The baseline cardiovascular risk profile for the entire cohort was low (11.5%), intermediate (55.7%), and high (32.1%). The population was stratified according to BMI: Underweight (BMI<18.5, n=3); Normal weight (BMI 18.5–24.9, n=335); Overweight (BMI 25–29.9, n=974) Obese (BMI 30–35, n=283); Morbidly Obese (> 35, n=13). Compared to normal weight patients, Morbidly obese patients were more likely to exhibit chest pains (92% vs. 63%, P<0.05) and pain on inside of left arm (54% vs. 13%, P<0.05). Compared to normal weight patients, obese patients were more likely to exhibit fatigue (31% vs. 20%, P<0.05). **Conclusion**: In the diagnostic evaluation of CAD, variations exist in the presenting symptoms of normal weight, obese, and morbidly obese patients.

P108

Withdrawn

P109

Obesity Predisposition Predicts Waist Circumference and Its Tracking in Children

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Objective: Waist circumference (WC) may reflect cardiovascular disease (CVD) risk in children. Our first aim was to assess the hypothesis that elevated WC would be more common among children born at high-risk (HR) compared to those at low-risk (LR) for obesity. Our second hypothesis was that the WC of these groups would "track" during ages 3 to 8 years. **Method/Design**: A prospective cohort study examined the waist circumference of children, ages 3 to 8 years, who were born at HR (n=34) or LR (n=37) for obesity, based on maternal pre-pregnancy body weight. Children were classified as being "high" or "normal" in WC using both (1) national normative cutoffs (ie, $<85^{th}$ or $\geq 85^{th}$ percentile for WC using age-gender specific cutoffs from NHANES) and (2) CVD-risk status cutoffs, defined from the literature as either 71 cm or 50.6 cm - 80.4 cm (depending on child age/gender). Additionally, based on BMI at age 6, HR children were subclassified as normal weight (HRNW, n=24) or overweight (HROW, n=10). Tracking was defined as the percentage of children who remained in the same group, either normal or elevated WC, in adjacent years. **Results**: The proportion of children with elevated WC, using normative cutoffs, was significantly greater among HR than LR children at

ages 4 to 8 years (p= 0.002 - 0.04). When using CVD-risk cutoffs, the proportion of children with elevated WC was significantly greater among HR than LR children at all ages, except for yr 5 (p= 0.057), but only when using the 71 cm criterion (p= 0.001 - 0.03). For all cutoffs, the proportion of children with elevated WC was significantly greater among HROW than HRNW or LR children at most years. The average percentage of children who tracked across adjacent years was 95 percent (LR children) and 90 percent (HR children). Interestingly, 67 percent (6 of 9) of HROW transitioned from a WC $<85^{th}$ percentile at age 3 (national norms) to $\geq 85^{th}$ percentile at age 4. After age 4, 80% to 100% of these children tracked their WC in subsequent years. **Conclusion**: In conclusion, obesity predisposition predicts elevated child WC, when using normative or select CVD-risk cutoffs. WC tracks over time, although a transition from normal to elevated WC between ages 3 to 4 years may foreshadow subsequent childhood obesity.

P110

How Do Barriers to Healthy Eating Impact Weight Loss?

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Background: A variety of issues, such as resisting temptation, meal planning, portion control, and affordability of food, may thwart weight loss and weight maintenance efforts. Identification of such factors and understanding their effect on success in weight loss programs may help improve future treatment protocols. Participants in PREFER, a randomized clinical trial, received standard behavioral therapy for weight loss while following one of two calorie- and fat-restricted diets: standard or lacto-ovo-vegetarian. Dietary treatment assignment was made with or without regard to the participant's preference (Preference-Yes vs. Preference-No). Intervention sessions were held weekly for 6 months, biweekly and monthly the second 6 months followed by a 6-month maintenance phase. **Objective**: The present study assessed whether participants' perceived barriers to healthy eating differed by treatment and/or preference group and how reported barriers were related to weight loss. **Methods**: The Barriers to Healthy Eating (BHE) Questionnaire has established psychometric properties and consists of three subscales: emotions, daily mechanics, and social support. The BHE was administered and body weight measured at baseline, 6, 12, and 18 months. **Results**: Participants (N=176) were 44.0±8.8 years old with 15.2±2.5 years of education and were predominantly Caucasian (70%), female (87%), employed (93%) and married (63%). Across all groups, participants' overall perceptions of barriers decreased significantly (P<.01) from baseline to 6 months with nonsignificant increases in BHE scores from 6–12 and 12–18 months. The reported barriers were a consistent predictor of change in weight at all time points (Baseline–6 and 6–12 months, P<.01; 12–18 months, P=.014). The emotions and daily mechanics subscales followed patterns similar to the total score with a significant decrease in barriers from baseline to 6 months and nonsignificant increases between later time points; nonsignificant differences were seen in reported social support across time and between groups. **Conclusions**: These findings suggest that continual emphasis on how to overcome the identified emotional and logistical barriers for the long-term may improve weight loss maintenance.

P111

Waist Circumference Is More Strongly Associated with Cardiometabolic and Global Cardiac Risk Among Women than Body Mass Index

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Background: To determine if waist circumference (WC) or body mass index (BMI) is more strongly associated with major cardiometabolic risk factors in free living women stratified by race/ethnicity and to evaluate inter- and intra-rater reliability of WC measurements taken by trained health professionals and participants. **Methods**: Weight, WC, BMI, blood pressure (BP), total cholesterol (TC) and high density lipoprotein (HDL)-cholesterol were systematically measured among 846 women (mean age 53 years, 32% white) who attended a free public health outreach event in February 2006. Height was self-reported. Global risk was calculated using the Framingham function. **Results**: The prevalence of risk factors by WC and BMI levels is shown in Table 1. White women (n=199) with a WC>35 inches were more likely to have low HDL (OR=1.98, p=0.03) compared to those with a WC≤35. Black and Hispanic women (n=389) with a WC>35 were more likely to have hypertension (OR=3.62, p<0.01) and global risk >20% (OR=2.91, p=0.01) vs those with a WC≤35. Multivariable regression analysis adjusted for age, race/ethnicity, education, personal history of heart disease/risk equivalent, medication use and smoking showed WC to be a stronger correlate of hypertension (OR=2.35, p<0.01) and low HDL (OR=1.62, p=0.01) compared to BMI. WC was also a stronger correlate of a global risk >20% vs BMI in a model adjusted for race/ethnicity and education (OR=2.60, p<0.01). Having both a WC>35 and BMI≥25 kg/m^2 had the strongest association with cardiometabolic risk. Inter- (r≥0.97, p<0.01) and intra- (r>0.99, p<0.01) rater reliability was high. **Conclusions**: Increased WC was a stronger indicator of cardiometabolic risk than BMI and specific risk factors associated with WC varied by race/ethnicity. WC is a simple, reliable and inexpensive index that should be more widely utilized to identify persons at increased cardiometabolic risk.

Table 1.

	Smoking	BP≥140/90 mmHg	TC≥200 mg/dL	HDL<50 mg/dL	Cardiac Risk*>20%
WC (>35 in)	6%	60%	46%	36%	2%
BMI (≥25 kg/m^2)	4%	50%	45%	32%	2%
BMI (≥30 kg/m^2)	7%	63%	45%	37%	2%
Both WC>35 and BMI ≥25 kg/m^2	6%	60%	47%	37%	2%

Note: *=Framingham score >20% or personal history of heart disease/diabetes.

P112

The Impact of the Obesity Epidemic on Access to Diagnostic Medical Imaging for United States Adults

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The prevalence of obesity (body mass index ≥30 kg/m^2) in the United States has increased tremendously over the past several decades, with 31.1% of men and 33.2% of women being obese in 2003–2004. The radiological cradle weight limit is 300 pounds for several diagnostic imaging procedures including computed tomography, nuclear stress test equipment, dual energy x-ray absortiometry, and magnetic resonance imaging. Data from the National Health and Nutrition Examination Surveys in 1988–1994 and 1999–2004 were used to determine trends in the prevalence and number of US adults with a body weight 300 pounds or greater, and thus ineligible for many imaging procedures. Additionally, the prevalence of hypertension, diabetes mellitus, and elevated LDL cholesterol among this group was determined. The percentage of US adults who weigh 300 pounds or greater increased from 0.79% to 1.54% between 1988–1994 and 1999–2004 (p<0.001). This represents an increase of 1.63 million US adults (from 1.39 to 3.02 million US adults). A majority of adults weighing more than 300 pounds had at least one additional major cardiovascular disease risk factor. Specifically, 60.8% had hypertension, 35.0% had diabetes, and 27.3% had an LDL cholesterol ≥130 mg/dL. In addition to higher cardiovascular disease, cancer and mortality risk, the obesity epidemic is precluding a large segment of US adults from receiving useful diagnostic imaging tests. The inability of diagnostic equipment to accommodate adults with body weights above 300 pounds may limit the ability of these high risk individuals to receive optimal medical care.

P113

A Family-Based Intervention to Promote Healthy Lifestyles in an Aboriginal Community in Canada

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Context: Obesity is a major public health problem among aboriginal people. We hypothesized that a culturally sensitive household-based intervention designed to improve dietary intake and increase physical activity may help prevent weight gain. **Objective**: To determine the feasibility of household-based lifestyle interventions designed to reduce energy intake and increase energy expenditure compared to usual care in a high-risk community. **Design, Setting, and Participants**: Randomized open trial of 57 Aboriginal households recruited between May/04–April/05 from Six Nations Reserve in Ohsweken, Canada. **Intervention**: A 6 month household-based intervention in which Health Counsellors made regular home visits assisting families in setting dietary and physical activity goals. Filtered water was provided to each intervention household weekly, an after-school physical activity program was available for children/adolescents, and events to learn about meal preparation and grocery shopping were organized. **Main Outcome Measures**: The primary outcomes were change in energy intake, macronutrient composition, dietary components, and leisure time physical activity. Dietary intake and physical activity were assessed at baseline and after 6 months. **Results**: 57 households involving 174 individuals were randomized 1:1 to intervention or usual care between April/04-March/05. Intervention household's decreased consumption of fats, oils and sweets compared to usual care households (-4.9 svgs/d vs-3 svgs/d P=0.006), and reduced trans fatty acids intake (-0.2 vs+0.6 g/d, P=0.02). Water consumption increased (+0.3 vs-0.1 svgs/d, P<0.04), soda pop consumption decreased (-0.3 vs-0.1, P=0.02) in intervention families compared to usual care. No changes in energy intake or leisure activity was observed, although sedentary behaviours such as television or computer use decreased in intervention compared to usual care households (-0.6 hrs/day vs-0.1 hrs/day; P=0.01). **Conclusions**: A household-based intervention to improve lifestyle practices is feasible, and is associated with some positive changes in dietary practices and activity patterns. Larger and longer term studies are needed to determine the impact on body weight.

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School-Based Early Prevention Interventions Improve Body Mass Index Percentiles: Preliminary Results of the HOPS Study

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Introduction: The Healthier Options for Public Schoolchildren (HOPS) Study aims to understand the efficacy of prevention efforts that address nutrition and physical activity implemented in the elementary school setting. **Hypothesis**: We assessed the hypothesis that HOPS Study interventions reduce obesity rates more so than traditional school-based dietary and physical activities. **Methods**: The HOPS Study was implemented in fall 2004 and includes approximately 3,200 children (48% Hispanic; 1,549 out of 3,247) attending six elementary schools (4 intervention; 2 control). Data are collected at baseline/fall and follow-up/spring (demographic information, height, weight, BMI percentiles, sedentary behavior and food consumption data). HOPS Study interventions include modified dietary offerings, nutrition and lifestyle educational curricula, school gardens, and other school-based wellness projects, with the goal of reducing childhood obesity rates in a manner that is replicable in other public school settings. **Results**: Overall, 2005–2006 data show statistically significant differences between treatment groups with respect to changes in BMI age- and gender-specific z-scores. Analyses of subgroups show statistically significant differences between intervention groups for BMI risk groups as well as some quintiles, when controlling for one control school with a particularly rigorous physical activity program. **Conclusions**: Early results show HOPS Study interventions improve BMI percentiles of elementary-aged children. Additional data collection and analyses, over time, will provide important data to inform school-based obesity prevention strategies.

	Changes in BMI Z-Scores mean (SD)
Intervention (n=2,135)	.07 (.64)
Control (n=1,112)	.02 (.44)
p-value	.004*

	Changes in BMI Z-Scores by Risk Group mean (SD)			Changes in BMI Z-Scores by Quintile mean (SD)				
	Normal (<85%)	At Risk (>= 85% - <95%)	Overweight (>=95%)	1st Quintile	2nd Quintile	3rd Quintile	4th Quintile	5th Quintile
Intervention (n=2,135)	.03 (.77)	.14 (.44)	.13 (.34)	-.14 (1.00)	.095 (.58)	.13 (.58)	.15 (.48)	.13 (.26)
Control (n=559)	-.08 (.39)	.02 (.29)	.04 (.20)	-.23 (.44)	-.01 (.34)	.002 (.34)	.01 (.28)	.05 (.20)
p-value	.001*	.001*	.003*	.388	.016*	.018*	.000*	.002*

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Prediction of the Framingham Risk Score and Coronary Heart Disease Risk in Extremely Obese Individuals

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The Framingham Risk Score (FRS) is widely used as a 10-year estimate of an individual's risk of death due to myocardial infarction (MI) and coronary heart disease (CHD). The variables in the FRS include age, total cholesterol (TC), HDL cholesterol (HDL), systolic blood pressure (SBP), treatment for hypertension, and cigarette smoking. Current thinking alludes to the development of CHD through risk factors associated with the Metabolic Syndrome (MetS), i.e., elevated triglycerides (TG), waist circumference (WC), blood pressure (BP), glucose (BG) and decreased HDL. In addition to the FRS, the ratio of TC to HDL cholesterol has been validated to estimate 10-year coronary heart disease risk (CHDR). The purpose of this study was to explore the relationship between MetS risk factors, FRS, and CHDR in individuals classified as extremely obese (EO). Seventy-three EO individuals (Age = 48±9 yr; BMI = 40.7±8.8) randomly selected to participate in a weight loss program were used in this study. Multiple biometric measures, including those variables for MS and FRS were measured or calculated. The data were analysed by multiple stepwise regression. Triglyceride (TG) was the best predictor of FRS from a subset of MetS variables (Model 1; $F_{1,70} = 40.41$, $p < 0.00$), however, it was a poor fit ($R^2_{adj} = 36\%$). The inclusion of HDL, TG, and WC produced the best fit for CHDR (Model 2; $F_{3,68} = 26.35$, $p < 0.00$) from the subset of MetS variables and accounted for slightly half of the variance ($R^2_{adj} = 52\%$). Although both Model 1 and Model 2 were highly significant, they were not able to explain 64% and 48% of the model variance, respectively. Despite the MetS risk factors being implicated in the development of CVD and CHD, these results suggest that using MetS variables to predict the 10-year risk of dying from MI and CHD is not warranted.

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Baseline Associations Between Aortic Pulse Wave Velocity and Adiponectin, Leptin, Ghrelin, and CRP: The Woman on the Move Through Activity and Nutrition (WOMAN) Study

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Background: Ghrelin, C-reactive protein (CRP) and the adipocytokines, adiponectin and leptin, are associated with obesity and insulin resistance - important predictors of arterial stiffness- and may have vascular effects. Therefore, we hypothesized that adiponectin, leptin and ghrelin would be inversely associated and CRP would be positively associated with aortic pulse wave velocity (aPWV), a validated marker of arterial stiffness, among postmenopausal women aged 52–62, with a BMI of 25–40 kg/m^2. **Methods**: At baseline, adiponectin, leptin, ghrelin, and CRP were measured with standard methods on a subset (n=201) of 508 overweight postmenopausal women enrolled in a randomized clinical trial of weight reduction on cardiovascular risk factors. aPWV was measured using the carotid and femoral arteries. All measures were available for n=190. **Results**: At baseline, the women were predominantly white (86%), on hormone therapy (HT:80%); mean age: 57 years, mean waist circumference (WC): 106 cm (86–139), and 26% were using anti-hypertensive medications (htnmeds). Mean aPWV was 879 cm/sec (S.D.=205) and was higher among black women. Higher aortic PWV was correlated with higher age (spearman rho (ρ)= .11), systolic BP (ρ=.20), heart rate (ρ=0.16), BMI (ρ=.10), and fasting insulin (ρ=.14), and lower adiponectin (ρ= -.15) and ghrelin (ρ= -.23), p<0.05 for all. In this sample of overweight, large-waisted women, aPWV was not significantly associated with WC, weight, leptin or CRP. With linear regression, ln(adiponectin) and ln(ghrelin) were each significantly associated with lower aPWV after adjustment for age, race, BMI, WC, ln(HOMA), SBP, heart rate, HT use, and htnmeds. An increase of 1 standard deviation in adiponectin (8.75 ng/ml), or ghrelin (340 pg/ml), was associated with a decrease in aPWV = 40 or 44 cm/sec, respectively. Race interactions were not significant, and results were similar for HT only or no htnmeds analyses. **Conclusion**: Among overweight, large-waisted postmenopausal women, adiponectin and ghrelin were significantly associated with aPWV independent of body size, insulin sensitivity, and CVD risk factors, suggesting that these hormones may have direct vascular effects that contribute to arterial stiffening in obesity.

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Influences of Age and Gender on Cardiovascular Disease Risk Factor–Associated Inflammation

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Epidemiologic evidence indicates the rising prevalence of obesity & other cardiovascular disease risk factors (CVDRF) in nearly all segments of society, while growing evidence suggests the association of traditional CVDRF with a chronic, sub-acute inflammatory state. It is unclear how such an inflammation changes between traditional CVDRF or across age & gender boundaries.To better evaluate these relationships, plasma samples from 245 human participants in a community-based study were analysed using multi-plexed assay technology.In addition to anthropometric measurements (incl. height, weight, blood pressure, estimate of % body adiposity (%BA) using body impedance analysis), multiple markers of inflammation were obtained from blood plasma.Table 1 summarizes results from univariate analysis.Leptin, fibrinogen, and haptoglobin were consistently different across phenotypic groups, with other markers differing depending upon the stratification.To better understand variable interactions & *ceteris paribus* effects, a series of multiple linear regression analyses were performed modelling the inflammatory marker as a function of %BA, total cholesterol (TC), gender, & age; results shown in Table 2.After accounting for simultaneous effects, age, %BA, and TC but not gender were important predictors of multiple markers.These results suggest future work to understand the effects of aging on CVDRF-related inflammation, & highlight the importance of more complex statistical modeling. table {7D3A9C72–4E2D-4A46-A242-B914345F7925}$$

Table 1. Summary of Univariate Results (ANOVA, p<0.05)

Type of Marker	Differs Across Adiposity Groups	Differs Across Total Cholesterol Groups	Differs Across Age Groups	Differs by Gender Category	Differs by Age & Gender Category
	< OR >= 30 %BA	*< OR >= 240 mg/dl*	*<16 OR 16–50 OR >=50*	*Male OR Female*	*Age X Gender Groups*
Endocrine	c-Peptide Leptin	NONE	GLP-1 Leptin	Leptin	GLP-1 Leptin
Adipokine	MCP-1	tPAI-1	MCP-1 Resistin tPAI-1	NONE	MCP-1
Cytokine	NONE	NONE	NONE	NONE	EGF IFN-g IL-13 IL-1a MIP-1b
CVD / Other	CRP Fibrinogen Haptoglobin sVCAM-1	Fibrinogen Haptoglobin MMP-9 MPO	sE-Selectin Fibrinogen Haptoglobin MMP-9	Fibrinogen Haptoglobin	Fibrinogen Haptoglobin sVCAM-1

Table 2. Results of Regression Analysis

Predicted Marker	Model Significant	Gender	Age	Total Cholesterol	% BA
	F Statistic p<0.05	*NS: p>0.05 s: p<=0.05*	*p>0.05 s: p<=0.05*	*p>0.05 s: p<=0.05*	*p>0.05 s: p<=0.05*
c-Peptide	Yes	NS	NS	S	NS
CRP	Yes	NS	NS	NS	S
MMP-9	Yes	NS	NS	S	NS
tPAI-1	Yes	NS	S	NS	p=0.059
Fibrinogen	Yes	NS	NS	S	p=0.068
GLP-1	Yes	NS	S	NS	NS
Haptoglobin	Yes	NS	S	S	S

Models Not Significant: IFN-g, sE-Selectin, EGF. IL-10, IL-13, IL-1a, MIP-1b, MPO, sVCAM-1

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Impact of Overweight on Linear Growth in Children and Adolescents

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Background: Overweight in childhood has been associated with accelerated linear growth in pre-puberal children. Childhood obesity increases the risk for adult short stature. **Objectives**: To compare stature in a group of overweight children and adolescents with CDC 2000 growth charts for normal weight. **Methods**: This study includes baseline anthropometric data from 416 patients with a body mass index ≥95th, in good health except for their obesity, referred to our lifestyle modification program. Study population was divided in two age groups, A: 8 to 11 years, and B: 12 to 16 years. Stature-for-age z-score (zstatage) from CDC 2000 charts was used for comparisons. **Results**: Group A was composed of 206 subjects, mean age: 10.2±1.1 years, and group B of 210 subjects; both groups were similar in ethnic distribution (Hispanic: 53%, Caucasian: 24%, African-American: 11% and other races: 12%). Boys and girls from group A were significantly taller than their normal weight peers. In group B only boys were significantly taller than their normal weight peers. Data are summarized in table. **Conclusion**: In these overweight pediatric patients the mean stature-for-age z-score for height was statistically higher in all sub-groups except in girls 12 to 16 years, suggesting that body mass index is not negatively impacting the linear growth.

	8 to 11 years		12 to 16 years	
	Girls	Boys	Girls	Boys
	n = 92	n = 114	n = 90	n =120
BMI-Zscore	2.33±0.29	2.34±0.25	2.32±0.30	2.46±0.29
zstatage	1.15±0.83 *	1.14±0.91 *	0.18±0.91	0.53±1.06 *

* p < 0.001

P119

Elevated BMI Does Not Discriminate Between Body Fat and Lean Mass in the US Population

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Background: The association between body mass index (BMI) with mortality and cardiovascular events is not linear, suggesting a high noise-signal ratio in the normal-mildly elevated BMI ranges. We hypothesized that BMI does not adequately discriminate between body fat percent (BF %) and lean mass (LM), especially in the normal-mildly elevated BMI ranges. **Methods**: This

was a cross-sectional analysis of 13,601 subjects (20–79.9 yr; 48 % men) from the National Health and Nutrition Examination Survey III. Bioelectrical impedance was used to estimate BF % (calculated as (weight - fat free mass)/ weight x 100) and LM (calculated as 100 - BF % * weight). We constructed Pearson correlation coefficients between BMI and both, BF % and LM by sex, age groups and BMI ranges. We calculated the diagnostic performance of BMI to detect excess BF %, as defined by the World Health Organization (BF % >25 in men and >35 in women). **Results**: Mean BMI was 26.6±6 in men and 27.6±6 in women, while BF % was 24.8±6 in men and 36.7±7 in women. The correlations between BMI and BF % and between BMI and LM were very similar. Data are presented in the Table. The correlation between BMI and BF % was poor-moderate in the BMI range from 25–29.9 (r = 0.22 in men and 0.40 in women). Obesity diagnosed by BMI (≥30) was present in 20.8 % of men and 30.7 % of women, while obesity diagnosed by BF % was present in 50 % of men and 62 % of women. A BMI ≥30 had poor sensitivity to detect BF %-defined obesity (36 % in men and 49 % in women) but high specificity (95 % in men and 99 % in women). **Conclusions**: Despite a good overall correlation between BMI and BF %, BMI failed to discriminate between BF % and LM in the adult US population, especially in the elderly and in men. BMI had poor-moderate correlations with BF % in normal-mildly elevated BMI. In addition, a BMI cut-off of ≥30 has a good specificity but misses more than half of people with excess fat. These results help to explain the non-linear association between BMI and outcomes.

Correlation coefficients (r) between BMI and both, BF% and LM by sex and age groups

Age (years)	20–29.9 (M=1,514) (F=1,487)	30–39.9 (M=1,353) (F=1,589)	40–49.9 (M=1,120) (F=1,204)	50–59.9 (M=773) (F=884)	60–69.9 (M=1,026) (F=995)	70–79.9 (M=700) (F=779)
BMI/BF%						
Male	0.70	0.67	0.66	0.64	0.60	0.60
Female	0.86	0.86	0.82	0.83	0.81	0.78
BMI/LM						
Male	0.72	0.72	0.72	0.75	0.72	0.73
Female	0.70	0.75	0.76	0.77	0.71	0.73

P120

Management of Obesity: A Challenge for Medical Education and Practice

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Background: Excess weight is a public health problem influencing health status and life expectancy. Physicians are in a unique position to provide counseling to prevent the health conditions associated with excess weight; however, it is not clear to what extent this is implemented. **Methods**: An adapted Behavioral Risk Factor Reduction Surveillance (BRFRSS) survey was employed to determine patterns and prevalence of weight loss counseling in a general medical clinic at an academic medical institution, Columbia University Medical Center. **Results**: There were 255 subjects (34% male and 66% female) who completed the survey: mean age 54.8 +/- 14.3 yrs; mean BMI 30.9 +/- 7.5. Regarding advice: 54% (43/79) of overweight and 76% (94/124) of obese subjects received weight advice in the last year ($p<0.0001$). Overweight (27% (21/78)) and obese (65% (80/124)) subjects were specifically advised to lose weight ($p<0.0001$). Seventeen percent (13/78) of overweight and 47% (58/123) of obese subjects were given a weight loss referral ($p<0.0001$). Fifty percent (81/162) of HTN subjects reported receiving weight loss counseling compared to 24% (22/92) of subjects without HTN ($p<0.02$). HTN subjects were more likely to be counseled even after controlling for BMI (odds ratio 2.36, 95% CI 1.34–4.18). Smokers were less likely to be counseled (66% (106/161) vs. 52% (49/94), $p=0.0340$) and there was a decreasing trend of counseling with an increasing level of current smoking ($p=0.0216$). Smokers were less likely to be counseled even when controlling for BMI (odds ratio 0.412, 95% CI 0.20–0.85). Subjects who received weight loss counseling were more likely to attempt to lose weight (67% (92/138) vs. 33% (46/138), $p<0.0001$) and a weight loss referral were more likely to report weight loss attempts compared to counseling alone (90% (56/62) vs. 62% (53/85), $p=0.0001$). **Conclusion**: Significant physician differences in counseling occur even among overweight and obese subjects with CV risk factors such as HTN and smoking. Patients advised to lose weight and referred to weight loss specialists are more likely to attempt to lose weight. Since counseling is a factor enhancing weight loss attempts, physician education and training should emphasize obesity as an independent risk factor for poor health.

P121

Cardioprotective Effects of Antihypertensive Therapy with Orlistat Treatment and Hypocaloric Diet in Combination in Obese Hypertensive Patients

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Background: Obesity is associated with increased risk of cardiovascular complications of hypertension. In present study we evaluated the probability of the association of angiotension II receptor antagonist losartan (L) and diuretic hydrochlorothiazide (HCT) with lipase inhibitor orlistat (O) and hypocaloric diet for decrease the left ventricular mass index (LVMI) in obese hypertensive patients (pts). **Design and Methods**: Forty two obese non diabetic mild to moderate essential hypertensives (24 males and 18 females, mean body mass index (BMI) = 38,9 kg/m^2, mean age = 47 years, office blood pressure (BP) = 154/98 mm Hg) with left ventricular (LV) hypertrophy were randomly assigned to L 50 mg once a day and HCT 12,5 mg once a day (group I - 21pts), L 50mg once a day and HCT 12,5mg once a day with O 120 mg three times a day and hypocaloric diet in combination (group II -21 pts). Echocardiography was performed at baseline and after 9 months of therapy. LVMI was calculated by Devereux formula. **Results**: BP fell under 140/90 mm Hg in both groups. BMI significantly reduced only in group II (-5,3±0,09kg/m^2, $p<0,001$). Echocardiographic parameters significantly reduced at the end of the study. LV end diastolic diameter decreased from 5,38±0,11 to 5,08±0,09 cm in group I ($p<0,01$) and from 5,41±0,12 to 4,91±0,08 cm in group II ($p<0,001$). LV posterior wall thickness reduced from 1,26±0,04 to 1,12±0,02 cm in group I ($p<0,01$) and from 1,27±0,03 to 1,04±0,01 cm in group II ($p<0,001$), Interventricular septal thickness decreased from 1,31±0,04 to 1,16±0,03 cm in group I ($p<0,01$) and from1,32±0,03 to 1,08±0,02 cm in group II ($p<0,001$). LVMI reduced from 154,8±10,1 to 125,5±9,6 g/m^2 in group I ($p<0,01$) and from 156,5±11,8 to 112,1±6,5 g/m^2 in group II ($p<0,001$). **Conclusions**: Antihypertensive treatment significantly improves the echocardiographic parameters of LV hypertrophy in obese hypertensive pts. The association of antihypertensive therapy with lipase inhibitor and hypocaloric diet can decrease the parietal stress and improve the cardioprotective effects of drugs.

P122

Early Life and Parental Influences on Timing of Adiposity Rebound

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Adiposity rebound (AR) has been proposed as a critical period for the development of obesity. AR is defined as the age at which body mass index (BMI) starts to increase after reaching its nadir in childhood, occurring usually between 3 and 8 years. Little is known about factors influencing AR timing. The aim of this study was to evaluate early life, demographic and parental characteristics and their association with timing of AR. The Dortmund Nutritional and Anthropometrical Longitudinally Designed Study (DONALD) is a prospective birth cohort study conducted in Dortmund, Germany. DONALD collects extensive data on perinatal, nutritional and lifestyle factors. Anthropometric assessments including height and weight are conducted starting at 3 months up to 18 years. Serial BMI values were evaluated for each child born between 1984 and 1996 and AR was determined with a statistical program implementing the visual approach. Timing of AR was categorized as early (<5 years), intermediate (5–6.5 years) and late (≥7 years). Complete data on 344 children were available. We used generalized logistic regression models to study the association between early life, demographic and parental characteristics and timing of AR. Mean age at rebound was 5.5 years, 5.2±1.8 in girls and 5.8±1.6 in boys. Among girls, 35% (60 of 171) had early AR, compared with 20% of boys (34 of 173). Early AR was positively associated with female gender (OR 2.43, 95% CI 1.29–4.58), higher maternal BMI (OR 1.11, 95% CI 1.01–1.21), and with more recent year of birth (OR 1.10, 95% CI 1.01–1.20) in multivariable analysis compared to late AR. Early AR was also inversely associated with high birth weight (≥4,000 g, OR 0.40, 95% CI 0.16–1.02) and higher parental education (OR 0.40, 95% CI 0.21–0.76). Early AR was not associated with breast feeding (exclusive or ever) or with exposure to smoking in the household. A similar direction of association for all factors was observed with intermediate vs. late AR, however statistical significance was reached for only parental education and year of birth. In conclusion, several early life and parental characteristics seem to play an important role in the timing of adiposity rebound, which in turn may be related to development of overweight and obesity in childhood and adolescence.

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Twenty-Year Change in Graded Exercise Treadmill Test Performance in Young Adults: CARDIA Fitness Study

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Background: Physical fitness is inversely associated with risk of total and cardiovascular disease mortality. Most studies reporting longitudinal change in fitness were conducted in smaller, select samples with relatively brief followup. **Hypothesis**: We aimed to evaluate 20-year change in fitness in a population sample of black and white men and women, hypothesizing that mean change in fitness is inversely associated with body weight and BMI change and directly associated with self-reported physical activity (PA) score change. **Methods**: Black and white adults initially aged 18–30 years (1985–86) in the CARDIA study underwent symptom-limited graded exercise treadmill testing at baseline and year 20 (2005 - 06). We calculated change in fitness among participants who reached 85% of age-predicted heart rate (220 - age) at both exams (N = 2083). **Results**: Mean test duration decreased 176 seconds (28%) over 20 years (black men, 33% decrease; white men, 26%; black women, 32%; white women, 26%) as did mean time to heart rate 130, a measure of submaximal fitness. Mean BMI increased 19% from 23.9 to 28.5 kg/m^2 and mean PA score decreased 18% from 444 to 366 units. 20-year change in BMI and PA score predicted duration change in all race-gender groups in the predicted direction ($p< 0.001$). Baseline BMI and physical activity score were not associated with duration change. Weight change of >30 lbs (45% of cohort; 937 of 2083) was associated with nearly twice the decline in duration (216 v. 116 second decline, $p< 0.001$) as weight loss or weight gain <10 lbs (21% of cohort, 445 of 2037). For the 148 (7% of cohort) whose test duration remained stable or increased, mean physical activity score increased 97 units while mean weight increased 10 lbs. **Conclusion**: Fitness declined substantially in this cohort and was associated with large adverse changes in BMI and physical activity. Increasing physical activity while losing or maintaining body weight may preserve fitness level with aging in young adults.

Mean baseline and 20-year change in test duration and time to heart rate 130 (mean, sd)

Race/gender	Baseline test duration (seconds)	Change in test duration (seconds)	Percent change	Baseline time to heart rate 130(seconds)	Change in time to heart rate 130 (seconds)	Percent change
All (N=2083)	630 (161)	-176 (115)	-27.9	272 (123)	-46 (93)	-16.8
Black men (N=334)	707 (113)	-231 (122)	-32.7	341 (108)	-97 (105)	-28.5
White men (N=610)	758 (120)	-194 (111)	-25.6	353 (112)	-58 (98)	-16.5
Black women (N=470)	464 (98)	-148 (105)	-31.9	180 (78)	-30 (71)	-16.9
White women (N=669)	592 (124)	-151 (111)	-25.5	229 (99)	-19 (83)	-8.5

P124

Longitudinal Changes in Cardiorespiratory Fitness and Pulmonary Function Over 20 Years: The CARDIA Study

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Background: Cross sectional studies demonstrate that pulmonary function, measured by forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1), is inversely correlated with cardiorespiratory fitness (fitness) in young adults. However, the longitudinal relationship between fitness and pulmonary function in this age group has not been explored. **Methods**: Black and white adults ages 18–30 in the CARDIA Study, an NHLBI sponsored multi-center longitudinal study, underwent spirometry at exam years 0,2,5,10, and 20 (n=3546). Fitness was assessed using a graded exercise treadmill test (GXT) at exam year 0. Generalized Estimating Equation models were used to estimate the relation of baseline quintiles of fitness to average yearly changes in FEV_1 and FVC over 20 years. **Results**: After adjustments for baseline age, gender, race, and height^2; time-dependent measures of BMI and smoking status; and asthma diagnosis, high fitness was associated with better pulmonary function at baseline. Declines in pulmonary function over 20 years were significantly smaller in participants with higher baseline fitness. **Conclusion**: High fitness in young adults at baseline appears to benefit pulmonary function through higher FEV_1 and FVC at baseline and this benefit is maintained through smaller declines in pulmonary function over time.

Association of Fitness Level at Baseline with Baseline Pulmonary Function and Adjusted* Average Annual Changes in Pulmonary Function over 20 Years

Fitness (Treadmill Time) at Year 0		Baseline	Change in	Baseline	Change in
Quintile (n)	Range, minutes	FEV_1 (L)	FEV_1	FVC (L)	FVC (L)
Q1 (678)	0–6.2 (women) 0–9.9 (men)	3.581	-0.030‡	4.365	-0.029‡
Q2 (736)	6.3–7.64 (women) 10–11.44 (men)	3.575	-0.027‡	4.354	-0.024‡
Q3 (711)	7.65–8.87 (women) 11.45–12.42 (men)	3.601	-0.025‡	4.387	-0.020‡
Q4 (707)	8.88–10.01 (women) 12.43–13.62 (men)	3.622	-0.022	4.387	-0.014†
Q5 (714)	10.02–18.0 (women) 13.63–18.0 (men)	3.617‡	-0.020‡	4.377‡	-0.010‡
p-trend	—	<0.001	<0.001	<0.001	<0.001

*Adjusted for baseline age, gender, race, and height^2; time dependent body mass index and smoking; and asthma diagnosis
Abbreviations: FEV_1-forced expiratory volume in one second, FVC-forced vital capacity † $p<0.05$, ‡ $p<0.01$

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Cardiorespiratory Fitness and 20-Year Risk of Dyslipidemia: The CARDIA Fitness Study

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Background: Cross-sectional studies show fitness related inversely to low density lipoprotein cholesterol (LDL) and triglycerides (TG) and directly to high density lipoprotein cholesterol (HDL), but exercise training studies show benefits mostly for HDL. **Hypothesis**: Higher fitness in young adults is related to decreased 20-year incidence of dyslipidemia (by NCEP ATP III criteria or reported lipid lowering medication); larger 20-year declines in fitness are related to increased prevalence of dyslipidemia in middle age. **Methods**: Black and white men and women ages 18–30 in 1985–86 in the CARDIA study who had HDL ≥40 mg/dl, LDL <160 mg/dl, or TG ≤200 at baseline, and achieved 85% predicted maximum heart rate (HRmax) on a baseline graded exercise treadmill (GXT) test (N=2299) were followed for incident dyslipidemia. Fitness is defined as GXT duration and change in fitness, examined only in those who reached 85% predicted HRmax at Year 20 also, as the difference in duration. **Results**: By Year 20, the incidence of low HDL, high LDL, and high TG was 26.5% (N=609), 11.0% (N=253), and 11.1% (N=254), respectively, and was lowest among participants in the highest quartile of baseline fitness (low HDL = 19.3%, p<.0001; high LDL = 8.1%, p=.03; and high TG =7.8%, p=.006). After adjustment for body mass index (BMI) and demographic factors, the risk ratios for incident low HDL, high LDL, and high TG in the lowest vs. highest baseline fitness quartiles were 1.72 (95% CI: 1.38–2.14), 1.56 (1.10–2.23), and 1.76 (1.24–2.50), respectively. By Year 20, fitness had declined by 32% (176 seconds, sd=115), and BMI increased by 19% (23.9 to 28.5). Fitness declined most in participants who, at Year 20, had low HDL (34.0% vs. 28.0%, p=.001), high LDL (35.6% vs. 28.4% p=.02), and high TG (36.7% vs. 28.2%, p=.0005). The odds ratios for low HDL and high TG at Year 20 were 1.49 (95% CI: 1.00–2.21) and 2.74 (1.24–6.03), respectively, comparing participants with the greatest declines in fitness to those with the least, adjusted for baseline fitness, BMI, % change in BMI, and other covariates. **Conclusion**: These findings suggest that higher fitness in young adulthood and better maintenance of fitness over time are both associated with a decreased risk of dyslipidemia in middle age, despite increases in BMI.

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Dose–Response Association of Physical Activity with Acute Myocardial Infarction Risk: Do Amount and Intensity Matter?

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Background: Physical inactivity is an independent risk factor for coronary heart disease. However, the dose-response curve for physical activity practice, taking into account different intensities, and myocardial infarction (MI) risk is not properly defined. The aim of this study were: a) to analyze the dose-response association between leisure time physical activity practice and MI risk taking into account not only the amount of total physical activity practice but also levels of intensity; and, b) to determine whether these associations were modulated by age or sex. **Methods**: A large population-based age- and sex-matched case-control study was conducted in Spain. All first acute MI patients aged 25 to 74 years admitted to participating hospitals were prospectively registered. Controls were randomly recruited from the same population origin of the cases. The Minnesota leisure time physical activity questionnaire was administered to assess total energy expenditure in physical activity and energy expenditure in light (<4 METs), moderate (4.5–5.5 METs), and high intensity (≥6 METs) physical activities. Conditional logistic regression and non-parametric regression were used for statistical analyses. **Results**: Finally, 1341 cases and 1341 controls were recruited. The association between physical activity practice and MI risk was exponential, with significant risk reductions at low practice levels (500 kcal/week), maximum benefit around 2,000 kcal/week, and a posterior plateau. Light (at least in subjects older than 64 years), moderate, and high intensity physical activities reported similar benefits. **Conclusions**: Low levels of physical activity practice are associated with significant MI risk reduction. This level of physical activity could be achieved by most of the population.

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Not published at the request of the authors.

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Associations Between Walking Performance, Physical Activity, and Subclinical Cardiovascular Disease

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Background: Currently, there are no standardized methods for measuring physical activity in a clinical population. The use of an objective measure of walking performance could have several potential applications in clinical settings particularly among women at risk for cardiovascular disease (CVD). **Methods**: The Woman On the Move through Activity and Nutrition (WOMAN) study is a 5 year randomized clinical trial designed to test whether a lifestyle intervention will reduce measures of subclinical CVD. The cross-sectional relationships between total walk time from the long distance corridor walk (LDCW), physical activity levels, and subclinical CVD measures were examined prior to group randomization in 492 [57.0 (2.9) years] women. The LDCW is a 400 meter course consisting of 10 laps along a hallway with cones set 20 meters apart. Cardiovascular response measures, including heart rate (HR) and systolic blood pressure (SBP) response and 2 minute HR recovery were also obtained during the LDCW. **Results**: The study participants completed the LDCW protocol in 301.2 (range: 211.2 - 454.2) seconds. Mean HR and SBP increased from resting by 36.8 bpm and 4.3 mmHg, respectively (range: -15 - 78 bpm and -32 - 52 bpm, respectively). At the end of the 2 minute recovery period, HR decreased by 20.4 (range: -28 - 52) bpm. Longer walk times were significantly associated with higher body mass index (BMI) (rho = 0.36, p<0.0001) and waist circumference (WC) (rho = 0.29, p<0.0001) and lower self-reported past-year and past-week leisure physical activity estimates (rho = -0.23 and -0.18, respectively; both p<0.0001). The proportion of detectable coronary artery calcification (CAC) and median aortic pulse wave velocity (aPWV) levels, both subclinical measures of CVD, were significantly higher among those with slower walk times (% detectable CAC: 40.8% vs. 62.4%, p<0.002 and median aPWV: 834.0 vs. 916.3 cm/sec, p<0.001). **Conclusions**: Total walk time from the LDCW was inversely associated with physical activity levels and positively associated with measures of subclinical CVD. These findings support the potential utility of the LDCW to identify women at higher risk for CVD who may be candidates for further cardiovascular testing or intensive lifestyle intervention.

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Lifestyle Bias? Exercise Effects on Risk Factors in an Observational Study (Obs) vs a Randomized Controlled Trial (RCT)

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This study compared the results of an Obs and RCT regarding effects of exercise on cardiovascular risk factors, conducted at the same institution employing the same program. **Methods**. Our institution (public) offers health exam and its fitness club membership as an inexpensive package to the citizens of Sapporo. In the Obs subjects had health exam and lifestyle recommendations (HELR). They were advised to exercise at the facility. Yet, one group, did not exercise, but returned for recheck after one year (Obs-Cont, n=303). Another group exercised at the facility >=once/week (Obs-Ex, n=229). Exercise consisted of about 90 minutes of mainly aerobic exercises. Based on the data of those in high-risk, a RCT sample size was calculated. The RCT was completed in 6 months. The same protocol as used for the Obs was employed for exercise and HELR. With 10% dropouts, 252 controls (RCT-Cont) and 249 exercise participants (RCT-Ex) completed the trial. Obs and RCT subjects did not overlap. PeakVO2 was estimated from the symtom-limited maximal exercise test. **Results**. Tables shows that in the RCT subjects, despite a higher baseline risk profile in which greater intervention effects are expected, the effects of exercise was greatly attenuated. The adjustments for age, sex and observation period did not explain the difference. **Conclusion**. A large unexplained difference in exercise effects on risk factors was observed between an observation study and a randomized controlled trial which were conducted by the same research team, by using the same methodology, and recruiting subjects from the same area. It is suspected that a "lifestyle bias" played a major role in causing discrepancy.

Table 1. Baseline values (mean(SD)

Group	N	Age	Female (%)	BMI	Systolic blood pressure (mmHg)	LDL-cholesterol (mg/dl)	HbA1c (%)	Estimated peakVO2 (ml/min/kg)
Obs	532	51 (14)	80	23.5 (3.6)	122 (19)	127 (32)	5.2 (0.6)	25.6 (5.9)
RCT	503	67 (7)	56	26.5 (2)	140 (17)	135 (26)	5.6 (0.6)	20.9 (3.7)

Table 2. The mean difference (follow-up minus baseline) between Cont and Ex (* <0.05)

Group	Body weight (kg)	Systolic blood pressure (mmHg)	LDL-cholesterol (mg/dl)	HbA1c (%)	Estimated peak VO2 (ml/kg/min)	Visits to exercise facility (/week)
Obs	-1.2*	-3.2*	-5.3*	-0.14*	1.8*	1.8
RCT	-1.6*	-2.1*	-2.3	-0.07	2.1*	2.6

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Results of a Lifestyle Modification Program on Exercise Capacity in Overweight Children

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Background Physical inactivity and decrease exercise capacity has been associated with long-term poor prognosis in terms of morbidity and mortality in overweight children. **Objectives** To assess changes in exercise capacity in overweight children attending a 12-week lifestyle modification program. **Methods** This study includes data from 121 children with body mass index (BMI) $\geq 95^{th}$ percentile who completes a 12-weeks lifestyle modification program. The program consists of nutrition counseling and medically supervised exercise. BMIs were assessed using the 2000 CDC growth charts. Exercise capacity was estimate by the amount of the exercise load (Rockport walking test) and the energy cost of exercise (metabolic equivalents -METs-). All measurements were taken at entry and at the end of the program. Each individual served as its own control. **Results** Group was composed of 50 girls and 73 boys, mean age: 11.2 years (range: 6 -17 years), ethnic distribution: Hispanic 43 %, Caucasian: 33%, Afro-American: 7 %, and other races: 13 %. By the end of the program there was significant increase in Rockport test (19.5$\pm$11.9 vs. 29.2$\pm$9.3, $p < 0.001$) and METs (3.0$\pm$0.6 vs. 3.5$\pm$0.5, $p < 0.001$). There was also a significant decrease in BMI Z-score (2.4 $\pm$0.3 vs. 2.3 $\pm$0.3, $p < 0.001$). **Conclusions** This group of children was successful in achieving a significant improvement in their exercise capacity and BMI Z-score, after participation in a 12-week lifestyle modification program.

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Lifestyle Physical Activity in Hypertensive Rural Elders: Association with Self-Efficacy Related Constructs

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Hypertension is often amenable to secondary prevention through health behaviors such as regular exercise or increased levels of lifestyle physical activity (LPA), yet many hypertensives, especially elders, continue sedentary lifestyles. Self-efficacy (SE) is a salient cognitive factor in health behavior change & maintenance, however, most research is limited to the effects on exercise & not LPA behaviors. This study examined relationships among LPA, SE, outcome expectations (OE), physical health (PH), mental health (MH), & social support (SS) in a sample of rural, hypertensive elders. **Methods**: A correlational design was used. Subjects were rural dwelling hypertensive elders (n=99), 83.8% female, 94.9% Caucasian, 57% married, 66.7% retired with mean age 70.19$\pm$6.95 years. Variables & measures were LPA (Physical Activity Scale for the Elderly; PASE), SE (SE for LPA scale), OE (OE for LPA scale), SS (Family & Friend SS for LPA scales), PH & MH (SF-36v2), Body Mass Index (BMI), perceived exertion (RPE), & Work/Volunteer time commitments. Multiple linear regression was used to determine the multivariate relationships of the variables with LPA & evaluate relationships with SE for LPA. Logistic regression was used to evaluate relationships with OE for LPA. **Results**: PASE scores suggested the sample was sedentary. In univariate analysis, LPA scores were higher in participants with a lower BMI (r=-.27, p=.007) & lower RPE (r=-.35, p=.001). The proposed model predicted a small portion of variance (17%) in LPA. Perceived PH (p=.000) was the only independent predictor of LPA in the multivariate model. Greater perceived PH (p=.001) & MH (p=.012) were significantly associated with increased SE for LPA. Greater perceived PH (6%) & MH (8%) were significantly associated with increased odds of having high OE for LPA. Elders with full- or part-time work/volunteer commitments were significantly more active than those who were retired. DISCUSSION: SE was not as important an influence on LPA as perceived PH in this rural sample of elderly hypertensives. To improve LPA in older adults, clinicians should focus on developing interventions for those with lower PH & MH, increased BMI & increased RPE. Further research is required to understand the complex behavior of LPA in rural elders.

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Physical Activity Is Related to Insulin Sensitivity and the Metabolic Syndrome in Adolescents

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The metabolic syndrome (MS), which is related to insulin sensitivity (IS), predicts the occurrence of cardiovascular disease (CVD) and type II diabetes in adults. Strategies, such as physical activity (PA), that improve IS and MS in children are likely to reduce adult CVD risk. Our prior study in a cohort of children, average age 13 years, reported a direct relation between PA and IS. This report extends the hypothesis in our cohort study to determine whether the effect of PA is directly related to IS in adolescents six years later. A physical activity questionnaire was administered to 217 youth (127 boys and 90 girls) at average age 19$\pm$0.9 years and a PA score was created using the Godin PA algorithm. IS was measured using a euglycemic insulin clamp as part of a protocol evaluating the influence of insulin resistance on the development of cardiovascular risk factors. A MS score (the mean of z-scores for waist, HDL-C, triglycerides, glucose, systolic blood pressure) was used to represent MS. In cross-sectional analysis, linear regression models were used to assess the relation of PA with IS, MS score, and CVD risk factors, adjusting for age, gender, race, and energy intake. As shown in the table, IS increased significantly across increasing tertiles of PA scores while the MS score was inversely, but marginally, related to PA. We found that PA continues to be related to IS in adolescence and suggests that PA may be an important strategy to increase IS.

Tertiles of Godin Physical Activity Score

Characteristic	1	2	3	p-value
PA Score, range	0–0.6	0.7–3.7	>3.8	
Waist (cm)	85.2 (1.6)	81.5 (1.6)	81.5 (1.6)	0.18
HDL Chol (mg/dl)	42.8 (1.1)	42.6 (1.1)	44.8 (1.1)	0.30
Trig (mg/dl)	106.3 (6.0)	88.6 (6.1)	90.5 (5.9)	0.07
SBP (mmHg)	110 (1.0)	112 (1.0)	111 (1.0)	0.68
Fasting Glucose (mg/dl)	88 (1.0)	88 (1.0)	86 (0.7)	0.36
Insulin Sensitivity (mg/kg/min)	10 (0.4)	10.7 (0.4)	12 (0.4)	0.003
MS Cluster Score	0.1 (0.06)	-0.002 (0.06)	-0.9 (0.06)	0.08

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Home-Based Exercise Improves Outcomes in Patients with Type 2 Diabetes: A Feasibility Trial

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Background: Limited research has investigated how to increase physical activity in people with type 2 diabetes. This feasibility trial evaluated short-term benefits of a home-based exercise supplement to education designed to increase physical activity among adults with type 2 diabetes. **Methods**: From June 2004 through August 2005, participants with type 2 diabetes in a multispecialty group practice were recruited and randomly assigned to the home-based exercise intervention or usual care. All participants were given diabetes self-management education and were followed monthly for 3 months. Theoretically based in Health Belief Model and self-efficacy, the home-based exercise videotape intervention contained 3 distinct exercise routines of 10, 20 and 30 minute duration. Aerobic and resistance exercises were included. The main outcome measures included changes from baseline at 3 months between groups in body mass index (BMI), quality of life, A1C, blood pressure, and program satisfaction. **Results**: Seventy-six sedentary adults with type 2 diabetes completed the study (81%, 76/94): 49% (37/76) were randomized to intervention, 68% (52/76) were women, 47% (36/76) were black, and mean age was 56.6$\pm$9.6 years. Intervention group participants used the videotape approximately 4 times per week for an average of 85 minutes per week over the study period. Improvements from baseline at 3 months between groups for BMI (mean change -0.4 versus 0.1, respectively; p=0.06) and quality of life (mean change 8.1 versus -0.9, respectively; p=0.11) were identified. No other differences were detected between groups. **Conclusions**: Home-based exercise video interventions have potential to enhance the care and reduce cardiovascular risk factors in patients with diabetes. Larger studies of longer duration are needed to confirm these findings.

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Physical Activity and Risk Factors for Cardiovascular Disease in a Southern Italy Population: The Moli-sani Study

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Background: There is evidence that physical activity is involved in protection for CVD. However, it is controversial whether the beneficial effect of vigorous physical activity and walking on risk factors is different. **Aims**: To explore the association between physical activity and CVD risk factors and differences in walking compared with vigorous physical activity. **Methods**: The Moli-sani Study is an on-going epidemiological cohort study, on male and female subjects, aged $\geq$35 years, randomly recruited from the general population of a Southern Italian region. From March 2005 to July 2006, 6,251 subjects have been enrolled. After exclusion of subjects with CVD at baseline (5%) and incomplete questionnaires (8%), 2,917 females and 2,521 males (55$\pm$12yrs) were cross-sectionally analyzed. Physical activity was assessed by a structured questionnaire (24 questions on working and leisure time). Weekly energy expenditure in metabolic equivalent task-hours (MET-h) was calculated and analysed in quintiles. In separate analysis walking (>1hr/week, MET-h=6.4$\pm$4.8) was compared with vigorous physical activity (sport>1hr/week, MET-h=96$\pm$175) **Results**: The univariate linear regression analysis showed significant association between quintiles of physical activity and all risk factors for CVD both in males and females (<0.001). After adjustment, physical activity remained positively associated with pulse rate (PR) (<0.0001) and negatively with age (<0.0001) and CRP (0.04) in males,while it was negatively associated with age (<0.0001), glucose (0.0002) and PR (0.0004) in females. Overall, performing vigorous physical exercise as compared to walking was associated with male sex (<0.0001) younger age (<0.0001) and lower BMI (<0.02), WHR (<0.0001), and PR(<0.0001), in multivariate analysis. **Conclusions**: Physical activity is overall associated with a better metabolic profile, although a different pattern was found in males and females. Vigorous activity versus walking is associated with decreased anthropometric index and pulse rate, without a significant benefit on metabolic variables and BP. *Supported by Fondazione Pfizer and Italian Research Ministry*

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Physical Activity at Baseline in African Americans in the Jackson Heart Study

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Background: Low levels of physical activity (PA) increase risk for CVD and other chronic disease. Surveys report lower levels of PA among U.S. racial minorities but many studies rely only on self-reported PA. The Jackson Heart Study (JHS) is an ongoing observational study of CVD in African Americans. We examined PA assessed by interview in the cohort of more than 5000 35–85 year old participants completing the first examination of the JHS; 397 of these participants also wore an Actigraph accelerometer for 24 hours. **Methods**: Responses from a 30-item interview based on the Baecke PA survey were used to compute 4 PA index scores: Active Living (ACL), Work (WRK), Sport (SPT), Home Family Life (HFL), and Total Activity (TOT). The time in light, moderate, and vigorous intensity activity was estimated from accelerometer data using published cutpoints. **Results**: The sample was 64% women and 36% men; 32% were overweight, 54% were obese, and 13% were smokers. Self-reported PA scores declined with age and increased with education (p's $<.0001$) except for WRK, which was inversely related to education and income (p's$<.001$). Men and women with greater ACL and SPT PA scores had lower waist circumference. PA scores were generally highest in overweight and lower in obese men and women. For men and women, TOT PA was lower in participants with prevalent heart disease, diabetes, and hypertension (p's<0001). These results were consistent with accelerometer data, and ACL and SPT scores were significantly correlated with minutes of moderate and vigorous activity. On average, participants had less than 10 minutes of moderate activity during the 24 hour monitoring period. **Conclusion**: Demographic and health correlates of PA in the JHS cohort were generally consistent with previous studies. Examination of the diversity of demographic and health attributes and their relationships to different PA domains in the predominantly overweight and obese JHS cohort will contribute to a richer understanding of PA and CVD in African American men and women.

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A Review of Increased Physical Activity in Physical Education: Benefits for Cardiovascular Risk Reduction

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Purpose: Two risk factors for cardiovascular disease (CVD), obesity and sedentariness, are increasing in prevalence among United States (US) children. School-based physical education (PE) provides an opportunity to engage children in physical activity towards physical fitness and healthy behaviors. However, in traditional school-based PE, most children are active less than 15 minutes during a 45 minute class. Enhanced PE focuses on physical activity, fitness and health education. The purpose of this project was to evaluate traditional vs. enhanced school-based PE on CVD risk factors: physical fitness (VO_2max, blood pressure, heart rate), body composition (BMI, percent body fat, waist circumference), blood values (total serum cholesterol, fasting insulin, fasting glucose), and cardiac knowledge. **Methods**: A search of CINAHL, PubMed, HealthSource, and Medline used the keywords: physical education, physical fitness, children and school-based, and resulted in 43 articles. Inclusion criteria were: peer-reviewed journal, controlled trial conducted within the past 10 years, school-based PE education, an intervention to increase physical activity and health education, CVD risk factor data, and English language. Data extracted from the 9 articles that met the criteria included: sample characteristics, risk factors measured, types and duration of PE interventions and results. **Findings**: Participants included children of both genders, and different races, ethnicities, and regions of the US. Across studies, improvements were greater for intervention vs. control groups on: VO_2max (1.48 mL/kg/min), body fat percent (1.01%), waist circumference (1.11cm), heart rate (0.4 b/min), total serum cholesterol (6.36 mg/dL), fasting insulin level (6.7 μIU/mL) and heart health knowledge (9.14% correct). **Discussion**: Results suggest that improving upon traditional PE curricula, through a marked enhancement of physical activity and the inclusion of health and fitness education may improve CVD risk factors. PE curricula modified in these ways will need further systematic evaluation to determine whether they optimize the time devoted to school-based PE time in ways that contribute to CVD risk factor reduction.

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Aging, Exercise, and Endothelial Progenitor Cell Apoptosis

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Clinical interest in bone marrow-derived circulating vascular progenitor cells, specifically endothelial progenitor cells (EPCs), has increased due to their importance in reendothelialization and neovascularization processes as well as their emerging role as a biomarker of cardiovascular risk. Circulating EPCs home to sites of ischemia and vascular injury as a repair mechanism to denuded or dysfunctional endothelium. Declines in circulating EPC function has been suggested to contribute etiologically to age-related vascular dysfunction and disease. The activation of the cellular suicide pathway leading to apoptosis of mature endothelial cells heightens with age and plays a role in vascular damage and dysfunction. However, it is currently unknown whether aging is associated with increased EPC susceptibility to apoptosis. If so, this may underlie the impaired vascular repair capacity with aging. We tested the hypothesis that: 1) aging is associated with increased EPC caspase-3 activation; and 2) regular aerobic exercise (EX) will reduce EPC caspase-3 activation in previously sedentary older adults. Caspase-3 is an important initiating protease in the apoptotic signaling pathway. EPCs were isolated from peripheral blood samples collected from 40 healthy sedentary men: 14 young (Y: age 26 ± 1 yr), 20 middle-aged (MA: 47 ± 1 yr) and 16 older (O: 63 ± 1 yr). EPCs were treated with the apoptotic stimulant staurosporine (1 μM) and active intracellular caspase-3 concentrations were determined by enzyme immunoassay. There were no age-related differences in basal EPC caspase-3 activity. However, in response to staurosporine active caspase-3 concentrations were significantly higher ($\sim$50%) in O (3.1 ± 0.5 ng/mL) compared with MA (2.1 ± 0.3 ng/mL) and Y (2.0 ± 0.2 ng/mL). To date, 5 sedentary O men have completed a 3-month EX intervention (walking 5.1 d/wk, 56 min/d @ 72% of maximal heart rate). EX training resulted in a 20% reduction in stimulated active caspase-3 concentrations (from 3.0 ± 0.6 to 2.4 ± 0.5 ng/mL) in EPCs. These results suggest that EPC susceptibility to apoptosis increases with age. Importantly, regular aerobic exercise appears to be an effective strategy for improving EPC resistance to apoptosis in previously sedentary older men.

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Exclusion of Secondary-Listed Discharge Diagnoses of Acute Myocardial Infarction Can Bias Selection of Cases: The Multiethnic Cohort

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Background: Criteria to select cases of acute myocardial infarction (AMI) using hospital discharge diagnoses vary widely. Validation studies show high predictive values for ICD-9-CM code 410 (AMI). However, it is not established whether hospitalizations should be selected using principal diagnosis alone or in combination with secondary-listed diagnoses, nor whether co-diagnoses or treatments can confirm AMI within all ethnic groups. **Methods**: The California portion of the Multiethnic Cohort (MEC) consists of a large representative sample of African-Americans and Latinos and a smaller sample of Japanese-Americans and Whites, aged 45–75 at cohort entry, who reside in Los Angeles County. We identified hospitalizations with any discharge diagnosis of AMI by linking to California Hospital Discharge Data files. **Results**: A majority of the 5,251 cases had AMI coded as the principal diagnosis (77%) or first-listed other diagnosis (11%); there were no significant differences by ethnicity in the position of the AMI code within the hierarchy of diagnosis variables. Lower hierarchical position of AMI code was associated with decreased frequencies of comorbidities ($p < 0.0001$) and revascularization procedures ($p < 0.0001$) but increased frequencies of complications ($p < 0.0001$). These results were not confounded by gender, ethnicity, or age. The overall frequency of complications was significantly higher in women than men ($p < 0.05$), in African-Americans and Whites than Latinos and Japanese-Americans ($p < 0.05$), and in individuals aged 71 years or older ($p < 0.0001$) whereas the overall frequency of revascularization procedures was significantly higher in men than women ($p < 0.0001$), in Japanese-Americans and Whites than Latinos and African-Americans ($p < 0.0001$), and in individuals aged 70 years or younger ($p < 0.0001$). **Conclusions**: Hospitalizations with AMI coded as a secondary-listed diagnosis may include more complicated cases that present later and are less likely to undergo revascularization. Exclusion of such cases would introduce selection bias and reduce generalizability of an AMI study. Moreover, varying frequencies of complications and procedures by gender, ethnicity, and age suggest that neither criteria can be used to confirm cases of AMI.

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Elevated Leukocyte Count Is Associated with Adverse Mortality, Morbidity, and Healthcare Cost Outcomes in Acute Heart Failure

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Background. Elevated white blood cell count (WBC) is associated with development of heart failure (HF) in the general population, and WBC is an independent predictor of in-hospital death and new-onset HF after myocardial infarction. The prognostic and economic significance of WBC level in acutely decompensated HF remains unknown. We tested the hypothesis that WBC is predictive of adverse in-hospital outcomes during HF exacerbation. **Methods**. We studied 333 consecutive patients admitted for acute HF exacerbation over a 16-month period. Based on admission WBC, subjects were categorized into 4 groups: WBC <5, WBC $= 5$–10, WBC $= 10$–15, and WBC >15. Demographic profile, clinical variables, and laboratory data were measured. Rates of in-hospital mortality and ICU admission, length of hospital and ICU stay, and cost of hospitalization were assessed as outcomes. ANOVA and multivariate regression were used in statistical analysis. **Results**. The 4 groups were homogenous in terms of demographic and clinical profile. Compared with subjects with low/normal WBC, those in the higher WBC groups had significantly higher mortality, ICU admission rate, and hospitalization cost, and had longer hospital and ICU length of stay. In multivariate regression analysis, controlling for possible confounding factors, WBC was predictive of mortality ($P<0.001$, 95% CI), length of stay ($P<0.001$, 95% CI), and ICU admission ($P=0.05$, 95% CI), independent of age, sex, functional class, illness severity score, ejection fraction, BMI , creatinine, hemoglobin, troponin, BNP, myocardial infarction, renal failure, liver failure, cerebrovascular disease, and major infections. **Conclusion**. In patients hospitalized for acute HF exacerbation, WBC elevation was associated with worse mortality, morbidity and healthcare cost outcomes. This suggests that WBC is a readily-available marker which provides clinically important prognostic information in acutely decompensated HF.

	WBC <5	WBC 5–10	WBC 10–15	WBC >15	P-Value
Sample Size (n=333)	9 (3%)	201 (60%)	75 (23%)	48 (14%)	ANOVA 95% CI
Mortality Rate	0 (0%)	3 (1.5%)	8 (3%)	25 (6%)	<0.001
Mean Hospital Length of Stay (Days)	4.7 +/-2.5	5 +/-4	5 +/-4.5	9 +/-5	<0.001
ICU Admission Rate	0 (0%)	33 (16%)	15 (20%)	24 (50%)	<0.001
Mean ICU Length of Stay (Days)	0	3.5 +/-2	3.6 +/-2	5.5 +/-4	0.01
Mean Cost of Hospitalization ($)	10,343.13	25,237.86	34,717.64	42,201.89	0.05

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Obesity Affects Outcomes Post Coronary Artery Bypass Grafting Differently Depending on Patient Gender

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Introduction The impact of obesity on outcomes post-coronary artery bypass grafting (CABG) is controversial, in particular as it relates to gender. **Hypothesis** We assessed the hypothesis that there is an association between obesity and outcomes post-CABG and that this association varies by gender. **Methods** Peri-operative data was prospectively collected on all patients who underwent isolated CABG between 1995 and 2003. Follow-up was available until 2004 for all. For

univariate comparisons subjects were stratified by BMI (<25; 25–29.9; 30–34.9; ≥35), and then by gender. Short-term adverse events were defined as a composite including in-hospital death, stroke, infarction, renal failure, wound infection, sepsis or return to operating room. Intermediate adverse events were defined as hospital readmission for any cardiac disease or late mortality. Logistic regression and Cox proportional hazard models were used to adjust for differences in age, acuity, and comorbidities. Models were constructed for the group as a whole and stratified by gender. **Results** A total of 6338 patients (4718 male, 1620 female) were included. For the entire group, gender was not a significant predictor of short term adverse events (OR 1.05, 95%CI 0.87–1.26), but BMI 30–34.9 (OR1.39, 95%CI1.31–1.70) and ≥35 were (OR 1.82, 95%CI1.40–2.38). When stratified by gender, BMI 30–34.9 (OR=1.52, 95%CI 1.20–1.93) and ≥35 (OR=2.10, 95%CI 1.51–2.93) were predictors of adverse events for males, but not females (BMI 30–34.9 OR=1.06, 95%CI 0.71, 1.59; BMI ≥35, OR=1.34, 95%CI 0.85,2.10). For intermediate outcomes in the whole population, female gender was a predictor of poor outcome (HR=1.12, 95%CI=1.02–1.24). When stratified by gender, BMI did not emerge as a significant predictor of poor intermediate outcomes. **Conclusion** Obesity was a risk factor for poor in-hospital outcomes for the population as a whole. However, when stratified by gender, obesity was found to have a negative impact on in-hospital outcomes in males only. Obesity had no impact upon intermediate outcomes for either gender. The effect of obesity may not be direct: it may indirectly impact outcomes through a synergistic effect upon other risk factors such as hypertension and diabetes.

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Cardiometabolic Risk Factor Clusters Represent a Major Economic Burden to Payers in the US

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Objective: The burden of cardiovascular disease is enormous. Risk factors tend to cluster together in individuals and may be preventable. The prevalence of cardiovascular risk factor clusters is increasing significantly for all demographic groups, but little is known about their economic impact. The hypothesis of the current study is that cardiometabolic risk factor clusters result in an economic burden to all major payers in the US. **Research Design and Methods**: The Medical Expenditure Panel Survey (MEPS) is a nationally representative survey of the U.S. population with detailed information on sociodemographic characteristics, medical conditions, utilization and expenditures. From 2000–2002, detailed information was collected for 44,841 adults (age 18 and older). The current study estimated 1) the marginal cost of cardiometabolic risk factor clusters per person using a Heckman selection model with Smearing retransformation; 2) the national cost in the US; and 3) the cost for all major payers. Cardiometabolic risk factor clusters included BMI greater than or equal to 25 and two of the following three: diabetes, hyperlipidemia and/or hypertension. All analyses incorporated MEPS sampling and variance adjustment weights to ensure nationally representative estimates. **Results**: For each individual, $5,640 in medical expenditures was attributable to cardiometabolic risk factor clusters, of which $1,842 was for prescription drugs. The majority was paid by third-party insurance with each individual spending $1,991 out-of-pocket on attributable medical expenses, of which $835 was spent on prescription drugs. National medical expenditures attributable to cardiometabolic risk factor clusters in the US totaled $143 billion, of which $47 billion was spent on prescription drugs. Among third-party insurers, private insurance paid the largest amount ($50.6 billion), followed by Medicare ($20 billion), Medicaid ($10 billion) and the VA ($7 billion); while individuals paid $50.4 billion out-of-pocket. **Conclusions**: The current study provides evidence of the negative economic impact of cardiometabolic risk factor clusters on the US economy.

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Predictors of and Barriers to Medication Adherence in a Minority Population

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Background: Long term adherence to pharmacotherapy proven to prevent cardiovascular disease (CVD) has been shown to be suboptimal, yet reasons for non-adherence are poorly understood, especially among high risk racial and ethnic minorities. The purpose of this study was to investigate barriers to medication adherence and to compare characteristics of individuals reporting non-adherence to those adherent to prescription therapy in a racial and ethnic minority population. **Methods**: Ambulatory care center visitors to Harlem Hospital in New York in May and August 2006 were systematically interviewed and screened for CVD risk factors (n = 214; 63% African American, 29% Hispanic; 70% female). Demographic data, education level, medication use, medication adherence, and barriers to medication adherence were obtained from each participant using a standardized questionnaire. Medication non-adherence was defined using a standard definition of self-reported intake of medications as prescribed <80% of the time. Associations between participant characteristics/barriers and non-adherence were assessed using logistic regression to adjust for age, sex, race/ethnicity, and education. **Results**: Among study participants, 39% were prescribed therapy for blood pressure and/or lipid management (11% dual therapy). Among these, 14% reported non-adherence that did not vary by gender or race/ethnicity. One in three (29%) believed that combining medications into one pill would make it easier to take medications more regularly. Compared to adherent participants, those who reported non-adherence were more likely to be hypertensive (73% vs 53%) and hyperlipidemic (36% vs 26%). In logistic regression models, predictors of medication non-adherence were 1) being less than 45 years old (p=.004), 2) not having health insurance (p=.01), 3) not believing one needs medication (p = .001), and 4) not feeling well when taking medication (p=.004). **Conclusion**: These data suggest educational efforts regarding the benefit of adherence to chronic preventive therapy are needed, especially in younger, disadvantaged racial and ethnic minorities. Improved adherence to pharmacotherapy has the potential to reduce CVD risk in racial and ethnic minority populations.

P143

Differences in Episode-Based Costs of Coronary Computed Tomographic Angiography vs Myocardial Perfusion Imaging for the Diagnosis of Coronary Artery Disease

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Background: Cardiac computed tomographic angiography (CTA) and myocardial perfusion imaging (MPI) are diagnostic modalities used to identify patients (pts) with coronary artery disease (CAD). We used Symmetry's Episode Treatment Groups™ (ETG) software (which is widely used and considered an industry standard for combining healthcare billing information into specific episodes of care) to identify and compare costs related to CAD and cardiac risk related episodes of care in a U.S. private payer population. **Methods**: Administrative claims with complete facility, physician and pharmacy data from 2 large health plans for 2003–2005 were employed. Pts were separated into either CTA or MPI cohorts based on their initial diagnostic screen for CAD (no prior screen within six months was required). All claims for the study population were then grouped into episodes of care using the ETG methodology. Total costs, defined as the amount allowed by the health plan for a particular service, were summed for CAD, diabetes, hyperlipidemia, or hypertension related episodes of care during 1-year prior and subsequent to screen. Log transform regression was used to model cost endpoints, controlling for pt demographics, health status, screen year, pre-screen costs, and baseline cardiac risk level. Bootstrapping techniques were then used to estimate whether the cost difference between cohorts was significant. **Results**: CTA pts (N=638) were younger (55 vs. 58 yrs, p= <.0001), included a different proportion of women (63% vs. 45%, p=<.0001), had more comorbidities (1.75 vs. 1.34, p= 0.0015), and higher cardiac risk scores (0.47 vs. 0.29, p= <.0001) compared to MPI (N=17,851) pts. After adjusting for baseline factors, 1-year cardiac-related episode costs incurred post screen were significantly lower for the CTA cohort ($4,764) as compared to the MPI cohort ($5,544) (p<0.05), with an average difference of $800 (95% Confidence Interval: $39 to $1394). **Conclusion**: Pts who receive CTA as an initial diagnostic screen for CAD incurred lower costs for CAD and cardiac related episodes of care compared to MPI during follow-up. These results suggest that CTA may be a reasonable alternative to MPI for the evaluation of CAD.

P144

The Burden of Comorbid Medical Conditions and Diabetes Performance Measures: Too Much Testing, Too Little, or Just Right?

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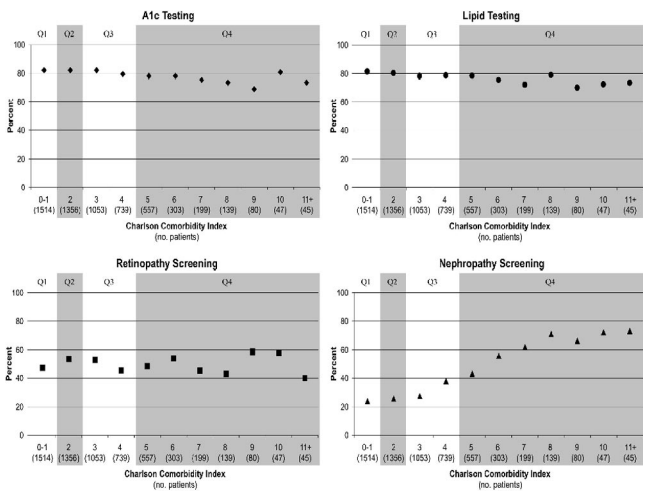
Introduction: With growing demands for accountability in patient care, the forces of quality measurement, performance-based reimbursement, and increasing comorbidity dramatically converge for patients with diabetes mellitus (DM). For complex patients with multiple comorbidities, most quality measurement systems treat each condition in isolation. We assessed the hypothesis that increasing comorbidity would be associated with lower performance on diabetes measures. **Methods**: In a cross-sectional study of 6,032 patients with DM enrolled in a Medicare managed care organization, we determined the association between medical comorbidity, measured by the Charlson Comorbidity Index (CCI), and hemoglobin A1c (A1c), lipid, retinopathy, and nephropathy screening. Logistic regression models adjusted for patient age and demographics. **Results**: Compared to patients in the 1st quartile of CCI, patients in the 2nd and 3rd quartiles received similar A1c, lipid, and retinopathy screening. However, patients in the 4th quartile, received less screening (odds ratio, 95% confidence interval) for A1c (0.67, 0.55 - 0.82), lipid (0.75, 0.62 - 0.91), and retinopathy (0.82, 0.70 - 0.96). Nephropathy screening was low in all quartiles but increased with increasing CCI. **Conclusions**: For A1c testing, lipid testing, and retinopathy screening, performance rates remained stable with increasing comorbidity until reaching an inflection point at the fourth quartile, at which screening decreased. Physicians may be appropriately foregoing preventive screening in very sick patients. Our findings call for renewed emphasis on incorporating patient comorbidity into performance measures.



P145

Prevalence of Mixed Dyslipidemia and Predictors of Lipid Abnormalities in Patients Treated with Statins in General Practice

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Introduction: Determining predictors of elevated total cholesterol (TC), elevated low density lipoprotein cholesterol (LDL-C), low high density lipoprotein cholesterol (HDL-C) and elevated triglycerides (TG) in statin users may help identify patients in need of additional treatment. **Objective**: To identify the prevalence and clinical/sociodemographic predictors of lipid abnormalities among statin users in the UK general practice. **Methods**: A retrospective cohort study using the UK General Practice Research Database included patients aged >35 if they received a first-ever statin prescription between Jan-2000 and Dec-2004, used statins for at least 6 weeks, had >2 years of pre- and 1-year of post-statin database history, received no concomitant lipid lowering drugs and had ≥1 complete lipid profile within one year before and after the statin initiation. Complete lipid profile was defined as TC, LDL-C, HDL-C and TG readings recorded on the same day. Predictors of elevated TC (≥5.0 mmol/L), low HDL-C (<1.0 mmol/L for men and <1.2 mmol/L for women) and elevated TG (≥1.7 mmol/L) were determined for each lipid using random effects logistic regression. High cardiovascular (CV) risk patients were those with diabetes, ischemic heart disease or cerebrovascular disease, or those with a 10-year coronary heart disease risk ≥30%. **Results**: Within 1-year of statin initiation, 35%, 68% and 58% of patients did not reach optimal levels of TC, HDL-C and TG respectively. Failure to attain TC goal was explained by smoking (Odds Ratio=1.17, 95% Conf. Int. [1.06–1.30]) and baseline TC>6.2 mmol/L (4.31 [3.96 - 4.69]). Low follow-up HDL-C was associated with a baseline HDL-C level of ≤0.9 mmol/L in both men (4.17 [3.18–5.47]) and women (4.61 [3.16–6.73]), and with high CV risk in women only (1.75 [1.38 - 2.23]). Elevated follow-up TG was associated with smoking (1.27 [1.12–1.43]), hypertension (1.11 [1.01–1.21]), baseline TG≥2.2 to <5.6 mmol/L (4.15 [3.78–4.55]) and baseline TG≥5.6 mmol/L (14.81 [3.40–64.44]). **Conclusion**: Comprehensive lipid management remains inadequate in the UK. Physicians should more closely monitor statin-treated patients with high pre-treatment lipid levels and cardiovascular risk factors which may help improve control of key lipid parameters.

P146

The Role of the Framingham Risk Score in Symptomatic Women: A Report from the NHLBI-Sponsored Women's Ischemia Study and the St James Women Take Heart Project

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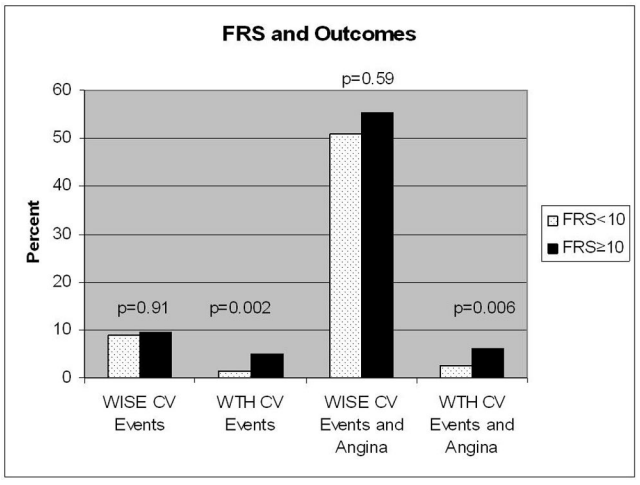
Introduction: The Framingham Risk Score (FRS) was developed to estimate 10 year risk of cardiovascular (CV) events in asymptomatic populations. We evaluated its role in predicting CV events in women with symptoms of ischemia. **Methods**: We studied 544 women with chest pain but without angiographically documented CAD enrolled in the Women Ischemia Syndrome Evaluation (WISE) and an asymptomatic community based cohort of 929 women from the Women Take Heart (WTH) Project. Women were categorized as low risk (FRS <10%) or intermediate/high risk (FRS ≥10%). The 10 year rates (actual for WTH, projected for WISE) of CV events (CV death or non-fatal MI) and CV events + hospitalization for angina were stratified by FRS risk category. **Results**: In the WISE, 66.4% were categorized as low risk by FRS compared to 67.4% of the WTH population, suggesting similar risk profiles, albeit WISE women were significantly older (56 vs. 54), had higher BMI (29 vs. 26), and more hypertension [53% vs. 17%] and diabetes [19% vs. 5%]). WTH women had significantly higher total cholesterol (217 vs. 190) and lower HDL (51 vs. 53). In WISE women with FRS <10, the 10 year rate of CV events was 8.9% and CV events + angina was 51.0%, compared to 1.4% and 2.4% in WTH. In WISE women with an FRS ≥10, the 10 year risk of CV events was 9.3% and the risk of CV events + angina was 55.2%, compared to 5.0% and 6.0% in WTH (figure). **Conclusions**: Consistent with its design, the FRS accurately estimated CV risk in an asymptomatic cohort of women but not in women referred for coronary angiography. Even when characterized as low risk, WISE women had a high rate of CV events. The FRS should not be utilized to characterize risk in women with signs and symptoms of ischemia.



P147

Does Timely Access to Medical Care Partially Explain Excess Heart Disease Mortality Among Unmarried Men?

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Background: The protective effect of marriage on heart disease mortality among men has been well established. We tested the hypothesis that part of the excess risk of heart disease mortality for unmarried vs. married men is explained by timely access to medical care. We used death occurring prior to transport to hospital as a marker of lack of timely access to medical care. Therefore, we hypothesized that relative risks of heart disease mortality for unmarried vs. married men would be higher for "no transport deaths" vs. "transported deaths." **Methods**: Our study included men aged 35 years and older who resided in an ethnically diverse metropolitan population during the years 1998–2000. Population estimates were calculated using the 2000 U.S. Census Public Use Microdata Sample (PUMS). Death data were obtained from the Florida Office of Vital Statistics. Deaths with underlying cause coded to "diseases of the heart" or "ill-defined conditions" were included, resulting in a total of 23,101 deaths analyzed. We calculated age-adjusted heart disease death rates separately by marital status, transport status prior to death (obtained from the death certificate), 15-year age group, and race/ethnicity. All relative risks (RRs) were calculated for unmarried vs. married men. **Results**: Our hypothesis was supported by results for white men of all age groups. For men aged 35–49 years, the RR of heart disease mortality for unmarried vs. married men dropped from 3.5 for "no transport" deaths to 1.5 for deaths after transport. Comparable RRs for white men in other age groups were: ages 50–64: 3.4 vs. 1.5; ages 65–79: 1.9 vs. 1.2; and ages 80+: 2.0 vs. 1.5. For Blacks, results supported our hypothesis among men aged 35–64 years and 80+ years. Results for Hispanics showed no consistent pattern. **Conclusions**: Our study confirmed the excess risk of heart disease mortality among unmarried men of all ages. Part of this disparity is explained by high death rates for unmarried men outside of hospital and prior to transport. Further research is needed to investigate whether social isolation (e.g. living alone), socioeconomic status, or other factors explain this phenomenon.

P148

Angiotensin-Converting Enzyme Inhibitor/Angiotensin Receptor Blockade Therapy in Subjects with Symptomatic Hypotension: Experience of a Community Disease Management Program for Heart Failure

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Background: Heart failure (HF) is a disease with high rates of mortality and hospitalizations. Failure to receive recommended medications increases mortality. Patients with hypotension are often denied Angiotensin Converting Enzyme Inhibitor/Angiotensin Receptor Blockade (ACEI/ARB) therapy and suffer poor outcomes. **Objective**: Evaluate the ability to successfully treat subjects referred to a HF clinic with symptomatic hypotension, and examine long-term outcomes. **Methods**: Retrospective study of patients admitted to a HF clinic from10/01/00–9/30/01. Patients excluded for ejection fraction (EF) >45%; bypass, valve replacement, or myocardial infarction within 3 months; death within one month; and those referred for consult only. Subjects receive aggressive management coupled with education on medication and self-management. Patients are referred back to primary physicians with follow-up in the HF clinic. Hypotension defined as systolic blood pressure (SBP) <100 mm/Hg at enrollment. Endpoints were all cause mortality and hospitalization. **Results**: Study criteria was met by 154 subjects (hypotensive n=24 [Group 1]; normo-tensive n=130; [Group 2]). At enrollment, EF and SBP for Group 1 was 16±6% and 92±8 mm Hg vs. 23±9% and 130±18 mm Hg for Group 2 ($p<0.001$ and $p=0.008$, respectively). Other variables were similar between groups. At enrollment, 94% of subjects with hypotension were successfully placed on ACEI/ARB. At one year, 81% were successfully maintained on ACEI/ARB, with 50% tolerating maximal doses. After median follow-up of 61 months for surviving patients, Kaplan-Meier analysis showed no significant differences in all cause mortality for Group 1 vs. Group 2 ($p=0.086$). All cause hospitalization, however, was significantly more frequent for Group 1 vs. Group 2 ($p<0.001$). **Conclusion**: Many HF patients with initial symptomatic hypotension can be managed with ACEI/ARB in a dedicated HF program. When patients were initiated with life-saving medications by a dedicated HF team prior to returning to primary physicians, 81% maintained medications at one year with 50% on maximal doses. Subjects with symptomatic hypotension that are aggressively managed achieve survival benefit that is not different compared to normo-tensive patients.

P149

Inability of High-Intensity Statin Therapy Alone to Optimize Lipid Values in a Coronary Heart Disease or Risk-Equivalent Population

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Background: Treatment guidelines and trials support the initial use of statin monotherapy to lower LDL-C in CHD or risk equivalent (CHD/RE) patients; however, residual CHD event risk remains high and may be due in part to persistent dyslipidemia. **Methods**: Patients were selected from a 2.1M record managed care database with a baseline (BL) lipid panel between 1/1/00–12/31/01, no concomitant lipid therapy, and continuous eligibility for 24 months; and those with a diagnosis/procedure of CHD/RE were retained for analysis. Each patient's lipids were assessed for achievement of guideline defined optimal values for LDL-C, HDL-C, triglycerides (TG), nonHDL-C, and combined LDL-C+HDL-C+TG at untreated BL and after modeled treatment with simvastatin 40/80mg, atorvastatin 40/80mg, and rosuvastatin 20/40mg using product labeling. Primary measures were the % of patients with non-optimal values at BL and after statins, and mean actual lipid values after statins. **Results**: Analysis included 20,948 patients: 49% female, mean(±SD) age 65±14 yrs, hypertension 44%, diabetes 34%. Lipids at BL (mg/dL): TC 208±41; LDL-C 128±35; HDL-C 49±15; TG 152±76; nonHDL-C 159±39. **Conclusions**: In a CHD/RE population, dyslipidemia was highly prevalent

and persisted despite high-intensity statins. These data support a strong population-based need for the addition of one or more drug(s) with substantial effects on HDL-C (≥ +11%) and TG (≥ -32%) as well as LDL-C (≥ -20%-38%), and proven efficacy and safety when added to a statin.

Non-optimal Lipid Values in 20,948 CHD/RE Patients

	LDL-C		HDL-C	TG	NonHDL-C		LDL-C, HDL-C, TG combined	
Threshold (mg/dL):	*>100*	*>70*	*<40M/50F*	*>150*	*>130*	*>100*	*>100**	*>70**
Baseline	79%	86%	43%	42%	77%	82%	92%	93%
Medium-intensity statin								
Simvastatin 40mg	34%	46%	14%	34%	36%	47%	59%	65%
Atorvastatin 40mg	25%	36%	23%	30%	33% [F]	45% [F]	55% [A]	60% [A]
Rosuvastatin 20mg	21%	32%	17% [A]	32% [A]	29% [D]	40%	51% [C]	56% [G]
Mean value on statin (mg/dL)	124	112	37 M 46 F	220	159	147		
High-intensity statin								
Simvastatin 80mg	28%	39%	17%	32%	32%	44%	55%	61%
Atorvastatin 80mg	17%	27%	26%	27%	27%	38%	50%	55%
Rosuvastatin 40mg	15%	25%	12%	30% [B,E]	22%	33%	44%	49%
Mean value on statin (mg/dL)	123	109	37 M 46 F	219	158	145		

*LDL-C threshold, HDL-C and TG per table; All statin percentages $p<0.001$ vs Baseline; All within and between statin dose comparisons $p<0.001$ except: p=NS [A] vs simvastatin 80mg, [B] vs atorvastatin 40mg,and [C] vs atorvastatin 80mg; p=0.001 [D] vs atorvastatin 80mg and [E] vs simvastatin 80mg; [F] p=0.03 vs simvastatin 80mg; [G] p=0.04 vs atorvastatin 80mg

P150

Differences in Real-World Cardiovascular Event Rates Between Leading Atorvastatin and Simvastatin Among New Users When LDL-Lowering Is Controlled

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Introduction. Recent clinical trials and observational studies have suggested that reduction in low-density lipoproteins (LDL) does not account for all differences among statins' effects on CV events. This study provides further evidence in this area using a large managed care dataset. **Hypothesis**. We assessed whether a difference in inpatient CV event rates could be observed between new atorvastatin (A) and simvastatin (S) users when prior risk factors and dose-related LDL-lowering are well-controlled. **Methods**. Using the Ingenix LabRx dataset for 2002–04, we identified patients who received a prescription for A or S following at least 6 months of no statin use. Patients were required to maintain 80% compliance for the first 3 months, and at least 60% compliance thereafter, with no statin switching, which qualified 61,324 A users and 19,585 S users. The primary endpoint was the first inpatient admission after 3 months of statin use with a primary diagnosis of myocardial infarction, ischemic stroke, transient ischemic attack, angina, coronary artery disease, peripheral or CNS vascular disease, or a revascularization procedure. Actual event rate and multivariate Cox regression time to event analyses were conducted. Control variables used were age, gender, prior CV event, prior medical costs, hypertension, diabetes, clopidigrel use, compliance, # baseline medications, labeled LDL reduction of dosage used, and statin type. **Results**. Actual event rates during the analysis period (median time: 177 days) were 11.6 (A) vs.16.5 (S) per 1000 patients/year; 8.4 (A) vs. 9.8 (S) for patients with no prior CV event, and 61.5 (A) vs. 63.6 (S) for those with prior events. S users had more prior events than A users, possibly due to hospital contracting policies. Among A users, 91% (55864 of 61324) took 10–20 mg doses; 84% (16427 of 19585) of S users took 20–40 mg doses. In the Cox analysis, the any-event hazard rate for A was 0.856 (p=0.03) vs S. The effect of dose-related LDL-lowering was positive, reflecting higher risk patients being prescribed more potent doses. **Conclusions**. Observational data are consistent with lower CV event rates within 6 months for new atorvastatin users than for new simvastatin users, even after controlling for the effects of LDL reduction and prior risk.

P151

The Accuracy of Self-Reported Hypertension in Middle-Aged and Older Women and Men

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During follow-up in large cohort studies, researchers commonly rely upon self-reports for "soft" endpoints like hypertension. Only a few studies have evaluated the accuracy of self-reported incident hypertension, which remains a major public health burden. We therefore assessed the accuracy of self-reported incident hypertension in the Women's Health Study (WHS) and the Physicians' Health Study (PHS). From each study, we randomly chose 50 initially normotensive subjects who recently reported a new hypertension diagnosis (women) or antihypertensive treatment (men). We also randomly selected 50 women in WHS and 50 men in PHS who never reported a hypertension diagnosis, antihypertensive medication use, SBP ≥140, or DBP ≥90 mmHg. A brief standardized telephone interview sought to confirm their self-reported information for the presence or absence of a hypertension diagnosis, antihypertensive treatment, and elevated BP levels. We found high sensitivity and specificity for self-reported hypertension in women and men. Incident cases of hypertension identified from follow-up questionnaires were confirmed in 48 (96%) of 50 women and 46 (92%) of 50 men on the basis of a new diagnosis, antihypertensive treatment, or elevations in BP without a diagnosis or treatment. Meanwhile, the absence of hypertension was confirmed in 45 (90%) of 50 women and 46 (92%) of 50 men. Among 5 women incorrectly classified as not having hypertension, 4 had transient elevations of BP in the past, but not present, suggesting that up to 49 (98%) of 50 women in fact confirmed their absence of hypertension. Finally, self-reported BP screening rates were similar for cases and non-cases of hypertension, indicating that the likelihood of surveillance bias should be low. In conclusion, we found confirmation rates of 96% in women and 90% in men for self-reported hypertension. In addition, at least 90% of WHS and 92% of PHS participants reporting no hypertension throughout decades of follow-up were confirmed to be normotensive. Because hypertension status can be accurately determined from self-reports, any misclassification would only slightly bias our risk estimates for hypertension.

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Gender Difference in Blood Pressure Responses to Low and High Dietary Sodium Intervention in the GenSalt Study

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Identifying individuals who are more sensitive to dietary sodium intake is useful for developing targeted dietary interventions. We examined factors related to blood pressure (BP) responses to a dietary sodium intervention among 1,010 adult male and 896 adult female GenSalt study participants in rural China. The dietary salt intervention included a 7-day low sodium-feeding (51.3 mmol/day) followed by a 7-day high sodium-feeding (307.8 mmol/day). BP was measured 9 times during the 3-day baseline preceding the intervention and also during the last 3 days of each intervention phase using a random-zero sphygmomanometer, and the mean of 9 measures from each phase was used for analyses. Multiple linear regression analysis was used to compare BP response to the dietary sodium intervention by study variables. On average, mean age (year), body mass index (kg/m^2), systolic BP and diastolic BP (mm Hg) at baseline among study participants were 38.7, 23.3, 116.9, and 73.7, respectively. Both systolic and diastolic BP responses to the dietary sodium intervention were significantly greater in women and in those with pre-hypertension and hypertension (all $p<0.001$). Systolic BP responses to the sodium intervention were greater in older age groups. These results suggest that female gender, older age, and hypertension increase sensitivity to dietary sodium intervention. Therefore, low dietary sodium intake may be more effective in reducing BP among these sub-groups.

	Low Sodium		High Sodium	
	ΔSBP	ΔDBP	ΔSBP	ΔDBP
Gender				
Men	-7.0	-3.4	5.2	1.7
Women	-8.1	-4.5	6.4	3.1
p value	0.0004	<0.0001	<0.0001	<0.0001
Age, yrs				
<35	-6.0	-4.1	4.3	2.0
35 - 44	-7.6	-4.0	5.7	2.6
≥45	-9.0	-3.8	7.4	2.7
p value	<0.0001	0.66	<0.0001	0.08
BP, mm Hg				
<120/80	-3.3	-1.5	4.1	1.4
<140/90	-7.6	-4.0	5.5	2.4
≥140/90	-11.8	-6.4	7.7	3.4
p value	<0.0001	<0.0001	<0.0001	<0.0001

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Mortality and Hypertension in China: A Prospective Study of 169,871 Men and Women

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We studied the cause-specific mortality attributable to hypertension in a nationally representative cohort of 169,871 men and women aged 40 years and older in China. Data on demographic profile, lifestyle risk factors, medical history, and blood pressure (BP) were obtained at a baseline examination in 1991 by trained observers using a standard protocol. Follow-up was conducted in 1999–2000 with a response rate of 93.4%. Hypertension was defined as a systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg or use of antihypertensive medication. The relative risk (RR) was estimated using the Cox proportional hazard model after adjustment for age, education, physical activity, cigarette smoking, alcohol consumption, obesity, diabetes, geographic region (north vs. south) and urbanization (urban vs. rural). The absolute number of deaths attributable to hypertension was calculated using population attributable risk (PAR %), cause-specific mortality, and the size of the general population of China in 2000. RR (95% confidence interval) and PAR for all-cause mortality were 1.57 (1.49, 1.65) and 15.4% in men, and 1.56 (1.47, 1.65) and 15.1% in women, respectively. The annual absolute number of deaths attributable to hypertension in Chinese men and women, 40 years or older, was 464,284 and 355,800, respectively. The majority of the hypertension-related deaths were from vascular diseases (427,871 in men and 334,556 in women). In addition, an extra 154,288 vascular deaths in men and 117,966 vascular deaths in women were attributable to pre-hypertension (systolic BP 120–139 mm Hg or diastolic BP 80–89 mm Hg). Our study indicates that hypertension is the leading preventable cause of death in the Chinese general adult population. These data suggest that prevention, detection, evaluation, and treatment of hypertension should be the most important public health priority in China.

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Hyperuricemia and the Risk for Incident Hypertension Among Middle-Aged Men

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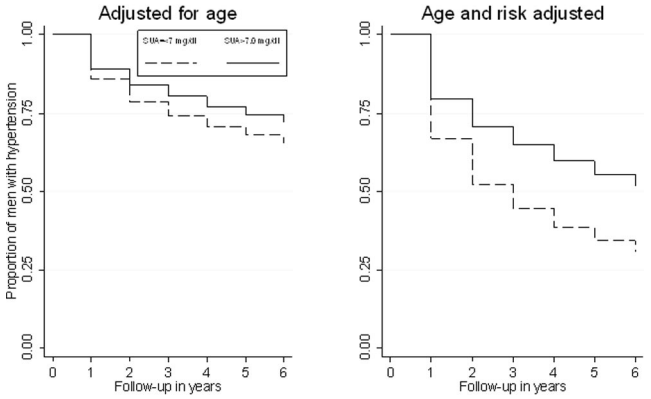
Previous studies on the relationship between elevated serum uric acid and the future risk for hypertension have been clouded by the potential for confounding of coexistent insulin resistance and/or metabolic syndrome. The aim of this project was to study the risk of developing hypertension over a 6-year follow-up in normotensive men with baseline hyperuricemia (serum uric acid >7.0 mg/dL), but without diabetes/glucose intolerance or metabolic syndrome. We analyzed the data on men without metabolic syndrome or hypertension at baseline from the Multiple Risk Factor Intervention Trial. These men (n=3073; age 35–57 years) were followed for an average of 6 years by annual examinations. Follow-up blood pressure among those with baseline was consistently higher among those with hyperuricemia than among those with normal serum uric acid concentration. We used Cox regression models for adjustment for the effects of serum creatinine, body mass index, age, blood pressure, proteinuria, serum cholesterol and triglycerides, alcohol and tobacco use, risk factor interventions. In these models, normotensive men with baseline hyperuricemia had an 80% excess risk for incident hypertension (hazard ratio 1.81, 95% confidence interval 1.59 - 2.07) compared to those who did not (Figure). Each unit increase in serum uric acid was associated with a 9% increase in the risk for incident hypertension (risk adjusted hazard ratio 1.09, 95% confidence interval 1.02 - 1.17). We conclude that the hyperuricemia-hypertension risk relationship is present among normotensive middle-aged men without diabetes/glucose intolerance or metabolic syndrome.

Baseline hyperuricemia and risk of future hypertension



Log rank p <0.001 for both adjusted and unadjusted survivor functions

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Risk Factors for Hypertension in Lean and Overweight/Obese Individuals: The CARDIA Study

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Background: Some studies suggest that lean hypertensive subjects are at greater risk of ischemic heart disease or CVD mortality than obese hypertensive subjects. We examined the relationship between hypertension and sociodemographic, health, and lifestyle factors in lean and overweight/obese CARDIA participants at Year 20 when participants were aged 38 to 50 years. **Methods**: Hypertension is defined as SBP ≥130 or DBP ≥85 or currently taking antihypertensive medication. Logistic regression was used to assess the associations of risk factors with hypertension within lean (BMI <25) and overweight/obese (BMI ≥25) groups. **Results**: Among 968 lean participants, 135 (14%) had hypertension, whereas among 2418 overweight/obese participants, 837 (25%) did. In age-, gender-, race-adjusted analysis, male gender was positively associated with hypertension for the lean group only, whereas black race, age, diabetes, total cholesterol >220 mg/dl, and taking anti-depressants were positively associated for both BMI groups. Education was inversely associated in both BMI groups. Income, physical activity, and cardiorespiratory fitness had inverse associations and insomnia had a positive association in the overweight/obese group only. In multivariable analysis, factors that remained significantly associated with hypertension in both BMI groups were black race, age, diabetes, and high cholesterol. In the overweight/obese group only, physical activity and cardiorespiratory fitness remained significant, and in the lean group, alcohol intake became significant. **Conclusion**: Although lean and overweight/obese subjects have some demographic and health related risk factors in common, physical activity and fitness have a protective role for the overweight/obese and alcohol intake has an adverse role for the lean. Age-, race-, and gender-adjusted and multivariable-adjusted odds ratios for prevalent hypertension at Year 20.

	BMI <25		BMI ≥25	
	Age, race, gender adjusted OR	Multivariable adjusted OR	Age, race, gender adjusted OR	Multivariable adjusted OR
Male gender	1.9**	1.5+	1.0	1.0
Black race	4.7***	3.8***	2.5***	2.4***
Age (per 5 years)	2.0***	2.0***	1.4***	1.4***
Diabetes	7.2**	6.9**	3.5***	2.9***
Cholesterol >220 mg/dl	2.5**	2.6***	2.1***	1.9***
On anti-depressants	1.9*	1.6	1.4*	1.2
Years education (per 1 year)	0.9*	0.9	0.9***	1.0+
Income (7 levels)	1.0	1.1	0.9**	1.0
Total physical activity (per 100 units)	1.0	1.0	0.9***	0.9**
Cardiorespiratory fitness (per 1 minute)	0.9+	1.0	0.8***	0.8***
Insomnia	1.3	1.0	1.4**	1.2+
Current smoker	1.5+	1.1	1.1	1.0
Alcohol intake (per 10 ml)	1.1+	1.1**	1.0	1.0

+p<0.10, *p<0.05, **p<0.01, ***p<0.001

P156

Effects of a Disaster: Medication Adherence in Older Adults with Hypertension

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Background: In post disaster situations, new barriers may reduce medication adherence, contributing to lower rates of hypertension control. **Methods**: Between November 2005 and August 2006, 215 patients receiving care at a multi-specialty group practice in New Orleans with a diagnosis of hypertension completed a validated questionnaire. Hypertensive medication adherence was measured through the 9 item Hill-Bone medication adherence subscale. In a subset of patients, difficulties filling prescriptions and medication changes post disaster were collected. **Results**: Overall, only 55 % (119/215) of patients reported perfect medication adherence. Seventy-five percent of patients reported damage to their residence (157/208). In the subset of patients responding to post disaster questions related to medications, 10% (8/78) did not bring their medications with them when they evacuated, 32% (25/78) ran out of medications when they evacuated, 15% (12/78) reported difficulties getting medications filled post disaster, and 30% (23/78) reported a medication change post disaster. After Hurricane Katrina, whites were 2.66 (95% CI 1.71–4.14) time more likely to report perfect medication adherence compared to blacks. However, no significant differences in adherence were noted between males and females and participants older than, compared to less than 65 years of age. After adjustment for age, race, and sex, participants who reported their houses to be completely damaged were 1.97 (95% CI: 0.69, 5.61) times more likely to report not achieving perfect medication adherence. **Conclusions**: The current study indicates that new barriers to antihypertensive medication adherence are present post disasters. Opportunities exist to improve disaster planning and prescription refill processes to increase medication adherence and hypertension control post disasters in older adults.

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Trends in the Prevalence of Hypertension in Chinese Adults: 1990–1991 to 1999–2000

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China is undergoing a rapid westernization of dietary and physical activity behaviors. We evaluated trends in blood pressure and the prevalence of prehypertension and hypertension between 1990–1991 and 1999–2000, using two population-based samples of Chinese adults aged 45–80 years (n=11,942 for the 1990–1991 time period and n=12,195 for the 1999–2000 time period), selected to be comparable with respect to age, gender, degree of urbanization, and region (North/South). For each time period, seated blood pressure was measured three times following the American Heart Association protocol. Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg and/or current antihypertensive medication use, while prehypertension was defined as SBP 120–139.9 mmHg and/or DBP 80–89.9 mmHg. Between 1990–1991 and 1999–2000, systolic and diastolic blood pressure increased 5.7 and 4.0 mmHg, respectively, among males and 3.6 and 3.2 mmHg, respectively, among females (all p<0.001). In the overall population, the prevalence of hypertension increased from 24.9% to 30.4% (P<0.001). While an increase (p<0.001) in hypertension was noted in all age groups, among both men and women, and in both rural and urban areas (32.8% increase in rural, and 23.4% increase in urban), a greater increase was noted in adults in South China (68.5% increase) compared to North China (13.9% increase) (p-interaction<0.001). In addition to increased hypertension prevalence over the 9-year time period, there was also a substantial increase in the prevalence of prehypertension, from 43.6% to 57.6%. These serial population-based data show large increases in the prevalence of hypertension during the 1990's in the overall population and each sub-population examined. By 1999–2000, nearly one third of both men and women were hypertensive, with an additional 58% having prehypertension. Given the continuing rapid pace of economic development in China, these data underscore the need for enhanced hypertension prevention, detection, treatment, and control programs in China.

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Treatment-Associated Decline in Diastolic Blood Pressure Is Not Associated with Poorer Outcomes in Older Patients: The Geisinger Clinic Population

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Introduction: Prior work has suggested that higher rather than lower diastolic blood pressure (DBP) is associated with better survival in older men and that treatment associated declines carry a strong risk for events. **Hypothesis**: A treatment-associated decline in DBP is associated with greater risk of events in the elderly, with an effect in men at earlier ages than women. **Methods**: Using a comprehensive longitudinal ambulatory electronic health record fully established in 2001, we identified 59,196 women and 48,651 men aged 55 years and older who had at least 3 BP measurements at different encounters receiving care from the Geisinger Health System (GHS). GHS is an integrated system providing care to a geographically defined rural population of approximately 2.5 million in central Pennsylvania. DBP change (DBPChg) was assessed by calculating change in mmHg from the earliest visit to the last visit before 1/1/2004. Events were death, incident MI, coronary disease, stroke, or congestive heart failure occurring on or after 1/1/2004, and >2 years after baseline. Age groups were defined as 55 - 74, and 75–100 years. **Results**: Antihypertensive medications (BPmeds) were used by 56% of women and 59% of men aged 55–74, and 78% of women and 76% of men aged 75–100. Mean baseline DBP, DBPChg, and baseline SBP for these same groups were: 78.7, -2.8, 134.4; 79.7, -3.3, 134.3; 79.6, -3.1, 141.5; and 74.5, -3.5, 136.4. Whether categorized as any decline versus no change or increase, or in clinically useful strata of no change or increase, decrease of not more than 5 mm, decrease in excess of 5 mm, all four age/sex groups demonstrated similar results with modestly poorer outcomes for those with a decline in DBP. In sex and age-group specific Cox proportional hazards models for DBP decline of 5 mm or more vs no change/increase adjusted for age, earliest DBP and earliest SBP, hazard ratios (HRs) for patients on BPmeds were between 1.21 and 1.24 (p-values <0.01), except in women 55–74 in whom results were non-significant. HRs in patients not taking BPmeds were only significant in men aged 55–74 (1.9, $p<0.01$). **Conclusions**: There was no increased hazard with a medication-associated decline in DBP in older men. Better management, cohort differences, or too short a follow-up interval may be factors.

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Relationship of Poverty Status to Diuretic Use Only Among Mexican-American Hypertensives: NHANES, 1999–2002

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Objectives: JNC 7 guidelines recommend diuretics as first-line pharmacologic therapy for treatment of uncomplicated hypertension. Clinicians are also advised to minimize cost of therapy to improve patient adherence. This study assessed the relationship of poverty status to diuretic use among hypertensives receiving pharmacologic treatment in non-Hispanic whites (NHW), non-Hispanic blacks (NHB), and Mexican-Americans (MA). **Methods**: Logistic regression analyses (adjusting for gender, age, and waist circumference) assessed the association of diuretic use with poverty status among US participants aged ≥20 years in the 1999–2002 National Health and Nutrition Examination Survey who reported receiving pharmacologic treatment for hypertension. Diuretic use was defined by either monotherapy or combination therapy. Poverty status (poverty income ratio) was calculated based on the ratio of family income to the federal poverty threshold (poor: <1.00, near poor: 1.01–1.99, not poor: ≥2.00). **Results**: Among 3,257 adults with hypertension, 60.7% were treated with antihypertensives (61.5% of poor, 59.2% of near poor, 61.0% of not poor; and 61.4% of NHW, 66.5% of NHB, 42.4% of MA). Prevalence of diuretic use among those 1,885 adults treated with antihypertensives was 46.5% (42.6% for poor, 52.3% for near poor, and 45.8% for not poor; and 47.6% for NHW, 52.1% for NHB, and 31.7% for MA). Among MA using an antihypertensive, those who were poor or near poor were less likely to use diuretics (OR=0.38, 95%CI=0.22,0.66 and OR=0.32, 95%CI=0.15,0.68 respectively) than those who were not poor. There was no relationship of poverty status to diuretic use among NHW and NHB who were taking antihypertensives. **Conclusions**: Clinicians seem to prescribe diuretics to almost half of patients taking antihypertensives. However, MA with hypertension were less likely to report taking antihypertensives and among those taking antihypertensives, to report the use of diuretics than NHW and NHB. Whether use of higher cost drugs in lower income MA reflects greater hypertension severity or comorbidities remains to be clarified.

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Patterns of Antihypertensive Therapy in the Jackson Heart Study Cohort

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Evidence suggests that adequate pharmacologic control of blood pressure (BP) could improve hypertension-related morbidity and mortality in African-Americans (AAs). Certain regimens have been identified as more effective in specific clinical situations and populations, yet little is known about the actual treatment patterns in large groups of AAs. Participants in the Jackson Heart Study (JHS) were asked to bring all currently prescribed medications to their initial clinic visit. Of 5,302 participants (age range 21–95), 2640 were treated with anti-hypertensive medications (HRX). This report describes HRX use by various drug classes (strategy) and drug combinations (intensity) as well as general medication adherence behavior assessed by an eleven item instrument. Of the treated hypertensives, 37%, 38%, and 25% received one, two, or ≥ three HRX, with the corresponding BP control (140/90 mmHg) rates of 68%, 68%, and 63%. Among mono therapies, diuretics were used most often (34%) followed by calcium channel blockers (CCB) and ACE inhibitors (ACEI), at 23% and 19%, respectively. Diuretic combinations were the most frequent dual treatment regimens, with control rates ranging from 68–73%. Lower control rates were observed in diabetics when using ADA target BP (130/80). Control rates in men were found to be significantly lower for both mono and poly therapy. Non-adherence was reported by 75% of the treated hypertensives. Among the most common reasons for non-adherence, "no money to purchase it" (reported by 22%), was the only response significantly associated with lower control ($p<0.01$). The results indicate that diuretics were used more frequently than any other class as either mono or dual therapy, thus showing adherence to JNCVII diuretic use recommendations. The observation that AA men have significantly lower control rates, despite higher reported adherence, suggests that therapeutic strategy and intensity may need gender-specific refinements. Policy implications for medication affordability are suggested by lower BP control rate in those citing finances as a reason for non-adherence.

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Ventricular Repolarization, Systolic Hypertension, and Ambient Particulate Air Pollution: The Environmental Epidemiology of Arrhythmogenesis in WHI (EEAWHI), 1999–2002

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The joint effects of systolic blood pressure (SBP) and air pollution on measures of ventricular repolarization have not been studied. We examined them in EEAWHI, an ancillary study of Women's Health Initiative clinical trial participants. We used data from EPA Air Quality System monitors and national-scale, log-normal kriging to spatially interpolate daily mean, residence-specific concentrations of ambient particulate matter <10 μm in diameter (PM_{10}) at geocoded addresses of 58,705 participants in 1999–2002. We estimated the duration of ventricular repolarization from rate-corrected QT intervals on the 1st-recorded, resting, standard 12-lead ECG among participants (52–87 yr; 84% non-Hispanic White) examined at 57 clinic sites during this period. We excluded 1,977 women with low quality ECGs, electronic pacemakers or addresses outside the contiguous U.S. Hypertension (history, BP ≥140/90 or treatment with antihypertensives) was present in 51% of women. Mean QT (ms) increased with JNC-VII SBP stage (normal [409]; pre [412]; I [414]; II [416]), number of antihypertensives used (0 [410]; 1 [413]; 2 [415]; ≥3 [417]) and PM_{10} quintile (1–2 [411]; 3–5 [412]). We used center-specific linear models adjusted for demographic, clinical, temporal and climatic factors to estimate associations between QT and PM_{10} on exam days and random-effects meta-regression to combine center-specific regression coefficients and test for interactions. Associations differed by hypertension severity: 25 $\mu g/m^3$ increases in PM_{10} (1/6th of the 24-hr National Ambient Air Quality Standard) were associated with -0.5% (95% CI: -1.0%, -0.1%) vs. +0.1% (0.0%, +0.2%) changes in QT among women with vs. without stage II disease ($p=0.01$) and -0.2% (-0.7%, +0.2%) vs. +0.1% (0.0%, +0.3%) changes in QT among women using ≥ vs. < 3 antihypertensives, although the latter interaction did not reach statistical significance ($p=0.11$). We obtained similar findings for $PM_{2.5}$ and after excluding normotensives, adjusting for left ventricular mass, conduction defects, drugs associated with torsades and socioeconomic status. **Conclusion**: The modest QT-prolonging effect of ambient particulate air pollution is detectable in the absence of factors with strong effects on ventricular repolarization.

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Beliefs Related to High Blood Pressure in African Americans Scale: Preliminary Reliabilty and Construct Validity

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Background & Purpose: African Americans (AA) have unique cultural beliefs regarding hypertension (HTN) that influence health behaviors, increasing the risk for poor HTN outcomes. Few reliable and valid culturally-sensitive measures to assess HTN-related health beliefs are available. This study examined the reliability and construct validity of the newly devised Beliefs Related to High Blood Pressure in African Americans (BRHBPAA) Scale which was developed based on the Health Belief Model. **Methods**: A cross-sectional design was used to enroll a community sample of 167 AA women aged 18 to 45 years with no history of HTN. Subjects completed the BRHBPAA Scale, a 65-item self-report measure with seven subscales: susceptibility, actions to reduce susceptibility, seriousness, benefits of physical activity, benefits of nutrition, barriers to physical activity and barriers to nutrition. Demographic (age, SES and family history of HTN), clinical (SBP, DBP and waist circumference), sociopsychological (stress and HTN knowledge) and behavioral (daily physical activity and daily caloric intake) data were also obtained. Data were analyzed for internal consistency reliability using Cronbach's alpha and for construct validity using a priori hypotheses-testing to assess correlations among the variables, total BRHBPAA Scale and subscales. **Results**: Mean (sd) age was 31.3 (7.0) years with SES (Hollingshead) = 34.7 (17.2), SBP = 114 (12.0), DBP = 87 (9.0) and BMI = 29.7 (7.9). Cronbach's alphas ranged from 0.71 to 0.87. HTN knowledge was significantly related to susceptibility ($r = 0.242$, $p = 0.002$), actions to reduce susceptibility ($r = 0.165$, $p = 0.035$), seriousness (0.337, $p = 0.000$), benefits of physical activity ($r = 0.183$, 0.019) and the BRHBPAA total score ($r = 0.269$, $p = 0.001$). SBP ($r = 0.313$, $p = 0.000$) and DBP ($r = 0.342$, $p = 0.000$) significantly correlated with susceptibility. Other significant correlations supported the construct validity of the BRHBPAA scale and five of the subscales. **Conclusion**: Study results support the reliability and validity of the BRHBPAA Scale. Refinement of the benefits of nutrition and barriers to physical activity subscales and further psychometric testing in a larger and more diverse population is warranted.

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Predictive Utility of Pulse Pressure and Other Blood Pressure Measures for Stroke and Heart Failure

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Background: The association between pulse pressure (PP) and coronary heart disease has been well described, but less is known about PP in association with stroke and heart failure (HF) events, and data are sparse regarding actual predictive utility. We sought to compare the predictive utility of PP with other blood pressure (BP) measures for stroke and HF. **Methods**: We included all participants from the Chicago Heart Association Detection Project in Industry who were free of CVD and not receiving BP treatment at baseline in 1967–1973. Baseline BP measures were assessed for predictive utility for fatal and non-fatal stroke and HF over 33 years of follow up. **Results**: Among 36,314 participants (mean age 39±13 years, 43.4% women), there were 11,452 deaths, of which 745 (2.1% of cohort; 6.5% of decedents) were attributed to stroke and 599 (1.7% and 5.2%, respectively) were attributed to HF. Of 16,393 participants who attained Medicare eligibility and enrolled, 3050 (18.6%) had ≥1 hospitalization for stroke, and 2207 (13.5%) had ≥1 hospitalization for HF. As shown in the Table, in univariate analyses, PP was associated with both stroke and HF death, but SBP and DBP had significantly larger hazards ratios (HR). Furthermore, the χ^2 values, Akeke (AIC) and Bayes' (BIC) information criteria and areas under the receiver-operating characteristic curves (AUC) suggested better predictive utility for SBP and DBP compared with PP for stroke or HF death. When PP was combined with SBP or DBP in two-component models, PP was consistently a weaker predictor of stroke or HF death. Results for the outcomes of stroke or HF hospitalization were similar. Summary measures of mid-BP and mean arterial pressure were also better than PP in prediction of stroke and HF. **Conclusions**: In this large cohort study, PP had predictive utility for stroke and HF events that was clearly inferior to SBP or DBP. These findings support the approach of current guidelines in use of SBP and DBP to assess risk and need for BP treatment.

Predictive Utility of Blood Pressure Measures for Stroke and Heart Failure Death

BP Measure	Unadjusted HR (95% CI) per SD	P value	Likelihood Ratio χ^2	AIC	BIC	AUC
Stroke Death, N=745						
SBP	1.75 (1.66–1.85)	<0.001	302.0	14966.14	14974.64	0.64
DBP	1.71 (1.60–1.82)	<0.001	232.6	15035.51	15044.01	0.63
PP	1.49 (1.40–1.59)	<0.001	134.3	15133.85	15142.35	0.59
Heart Failure Death, N=599						
SBP	1.82 (1.71–1.93)	<0.001	294.6	12111.77	12120.27	0.67
DBP	1.74 (1.62–1.87)	<0.001	210.1	12196.30	12204.80	0.65
PP	1.57 (1.47–1.68)	<0.001	146.5	12259.95	12268.45	0.62

Abbreviations: AIC = Akeke information criterion; AUC = area under the receiver-operating-characteristic curve; BIC = Bayes' information criterion; CI = confidence interval; HR = hazards ratio; SD = standard deviation

P164

Young Adults with "Spurious" Systolic Hypertension Have an Increased Risk of Coronary Heart Disease

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Background: Spurious systolic hypertension (SSH), i.e. high brachial systolic blood pressure and low central systolic pressure, is a condition predominantly found among young adult men. There is a discussion whether this phenomenon should be seen as a benign condition, or if these individuals are at a significantly increased cardiovascular risk. **Objective**: To estimate the 20-year risk of coronary heart disease in young men with SSH and evaluate the effect of differences in the chosen cut-off points of central systolic pressure on the Framingham systolic pressure risk scores. **Methods**: We studied 352 men, aged 26–31 years, from the Atherosclerosis Risk in Young Adults study. Blood pressure levels were measured twice and central (aortic) pressures were derived by applanation tonometry on the radial artery using a generalized transfer function. SSH was defined as brachial systolic blood pressure (SBP) > or = 140 mmHg, brachial diastolic blood pressure <90 mmHg, and central SBP <124 mmHg (90th percentile). The Framingham risk score was calculated. **Results**: SSH was diagnosed in 57 men (16.1%, 57 of 352; 95% confidence interval, 12.3–20.0). Based on brachial SBP, SSH individuals had a significantly higher Framingham risk score compared with the normotensive group (mean 3.95 versus 2.90%, P < 0.05). The risk was lower when compared with hypertensive subjects, but this difference was not statistically significant. When the cut-off point of central systolic pressure was set lower, with a shift of SSH patients towards the hypertension group, the estimated Framingham risk declined in the hypertensive group (Table). The risk in the SSH group remained constant. **Conclusion**: SSH individuals are at increased risk of developing coronary heart disease within 20 years after diagnosis compared to normotensive subjects. This finding seems to remain also when central systolic pressure is below 110 mmHg.

Table: Prevalence of 'spurious' hypertension and hypertension, and mean Framingham risk score (by level of central systolic pressure as cut-off point), in men aged 28 years.

Central systolic pressure cut-off point	'Spurious' hypertension	Hypertension	Normotension
	Prevalence (%)*		
<124 mmHg	57 (16%)	29 (8%)	266
<120 mmHg	38 (11%)	48 (14%)	266
<115 mmHg	20 (6%)	66 (19%)	266
<110 mmHg	4 (1%)	78 (22%)	266
	Framingham risk score (%)**		
<124 mmHg	3.95	4.97	2.90
<120 mmHg	4.08	4.47	2.90
<115 mmHg	3.74	4.45	2.90
<110 mmHg	3.69	4.32	2.90

* Values are the absolute number with percentages in parentheses. Normotension is defined as a systolic pressure <140 mmHg and a diastolic pressure <90 mmHg. Hypertension is defined as a systolic pressure >= 140 mmHg or a diastolic pressure >= 90 mmHg. 'Spurious' systolic hypertension is defined as hypertension but with a central blood pressure lower than used cut-off points. ** Framingham risk score reflects the estimated 20-year risk of coronary heart disease.

P165

Hemoglobin A_{1c} Concentrations and the Risk of Developing Hypertension in Nondiabetic Middle-Aged and Older Women

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Hemoglobin A_{1c} (HbA1c) measures glycemic control and reflects average glucose levels over several months, and has been associated with insulin resistance, hyperinsulinemia, and CVD. Though hyperinsulinemia is implicated in the pathogenesis of hypertension, scant epidemiologic evidence supports this claim. We tested whether baseline HbA1c concentrations were prospectively associated with hypertension in the Women's Health Study. We analyzed 19,664 women initially free of CVD, cancer, diabetes, and hypertension who provided baseline blood samples from which we measured HbA1c concentrations. Extensive information on baseline behavioral and clinical variables was collected. We considered quintiles and clinical cutpoints of HbA1c for the risk of incident hypertension, defined as either a new physician diagnosis, the initiation of antihypertensive treatment, SBP ≥140 mmHg, or DBP ≥90 mmHg. During 10.9 years of follow-up, 5,823 (29.6%) women developed hypertension. In age-adjusted models, the RRs of hypertension from the lowest (<4.79%, referent) to the highest (≥5.19%) quintile of HbA1c were 1.00 (ref), 0.96, 1.04, 1.11, and 1.25 (p, linear trend <0.0001). Multivariate adjustment for traditional coronary risk factors greatly reduced the RRs of hypertension to 1.00 (ref), 0.93, 1.01, 0.97, and 1.01 (p, linear trend 0.44), primarily due to confounding by BMI. However, a stronger association with hypertension emerged when higher levels of HbA1c concentrations were assessed. For clinical cutpoints across a wider range of HbA1c concentrations (<5.0, 5.0-<5.5, 5.5-<6.0, and ≥6.0%), there was a strong age-adjusted positive association with hypertension (p, linear trend <0.0001) that persisted in multivariate models (p, linear trend = 0.02), driven by a RR (95% CI) of hypertension of 1.35 (1.03–1.76) for 130 women with HbA1c values ≥6.0%. Excluding 2,429 obese (BMI ≥30 kg/m^2) subjects, this significant RR increased to 1.85. Finally, additional adjustment for dietary factors or C-reactive protein did not alter the RRs. HbA1c concentrations were not associated with the risk of hypertension across the nondiabetic spectrum. However, at higher HbA1c levels where undiagnosed diabetes is common, an increased risk of hypertension emerges.

P166

Cardiovascular Risk Factor Awareness in a Racial and Ethnic Minority Population

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Introduction: Cardiovascular disease (CVD) is the leading cause of the death in the US and disproportionately affects racial and ethnic minorities. The purpose of this study was to assess personal awareness of CVD risk and knowledge of goals for hypertension (HTN) and dyslipidemia among minorities. **Methods**: This was a cross-sectional study of 214 individuals >20 yrs (mean age 49, 71%females, 63% Black, 30% Hispanic) of visitors to Harlem Hospital in NYC. Standardized information was collected including demographics, education level, medical history, CVD awareness, perceived risk and knowledge of risk factors. Standard measurements were obtained for blood pressure (BP) and lipid sub fractions. The main outcome measure was % of participants unaware that they had HTN, dyslipidemia or both (BP≥140/90, total cholesterol (TC) ≥200mg/dL or HDL<40 in men or <50 in women) who screened positive for either condition and did not report a prior diagnosis by a health care provider. Knowledge of risk factor goals was defined as correctly identifying optimal levels of BP (<120/80) and TC (<200). **Results**: Among the 37% of participants documented to have BP≥140/90 on screening, 34% were unaware they had HTN. Similarly, of the 62% found to have dyslipidemia, 48% were unaware they were at risk. Both HTN and dyslipidemia were present in 24% of participants and 63% were unaware of their conditions. Individuals <55 yrs were more likely to be unaware they had HTN than those ≥55 yrs (OR 8.5, 95% CI=2.6–28.1). Participants who perceived themselves to be low or moderate risk for CVD were more likely to be unaware they had HTN compared to those who perceived their risk to be high (OR 3.2, 95% CI=1.2–9.0). More than half of participants lacked knowledge of CVD as the leading cause of death (59%) and did not know optimal BP (52%) and TC goals (60%). Lack of health insurance (OR 2.1, 95% CI=1.0–4.5) and ≤ high school education (OR 2.0, 95% CI=1.02–3.87) were associated with lack of knowledge of optimal BP goals. **Conclusion**: Young, uneducated racial and ethnic minorities without health insurance were least aware they had major CVD risk factors and lacked knowledge about optimal risk factors. Targeting these individuals for education and appropriate intervention may help reduce disparities in CVD.

P167

Population Effect of Extended-Release Niacin/Lovastatin Versus Atorvastatin in Patients with Hypertension and Multiple Lipid Abnormalities at High Risk for Cardiovascular Events

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Background: Current interest in the management of patients with dyslipidemia and hypertension (HTN) is centered primarily on LDL-C lowering with statin monotherapy. Since HTN clusters with low HDL-C and high triglycerides (TG), alternate therapeutic strategies may be of value, but haven't been comparatively evaluated. We examined the effects of extended release niacin/lovastatin (ERN/L) and atorvastatin (ATORVA) in a dyslipidemic population with HTN. **Methods**: Patients were selected from a 2.1 M record managed care database based on the following criteria: lipid panel present between 1/1/00 and 12/31/01, no concomitant dyslipidemia therapy, ≥24 months of continuous plan eligibility; those with HTN (ICD-9 code and HTN therapy) and CHD/risk equivalent (by diagnosis/procedure code) were evaluated. Initial lipid values from each patient were assessed for combined LDL-C, HDL-C and TG optimal value attainment based on guidelines, and treatment effects were modeled using product labeling. **Results**: We analyzed 28,854 patients; 53% female, age 67±13 years, and baseline (BL) lipid

values (mg/dL): TC 211±40; LDL-C 131±35; HDL-C 50±15 ; TG 155±75; Non-HDL 162±39. **Conclusions**: In the total HTN population and all subgroups except for males and females ≥65 yrs, modeled ERN/L dosing (1g/40mg & 2g/40mg) yielded combined optimal lipid values significantly more often than ATORVA (40 & 80), ERN (2g) or lovastatin (LOVA) (40mg). In males and females ≥65 yrs, ERN/L (1g/40 mg) was equivalent to A (80 mg).

		Combined Optimal Lipid Value Attainment*						
	N	BL (%)	ATORVA 40 mg (%)	ATORVA 80 mg (%)	ERN/LOVA 1g/40 mg (%)	ERN/LOVA 2g/40 mg (%)	ERN 2 g (%)	LOVA 40mg (%)
Overall	28,854	13.1	49.1	52.0	53.9	59.1	38.9[a]	39.2[a]
CHD/Risk Equivalent Population								
Female								
<65 years	5,284	8.6 12.2	40.6[b] 50.2	42.4[b] 53.8[c]	51.0 53.5[c]	56.9 58.8	37.7 38.2[d]	37.3 33.1[d]
≥65 yrs	10,002							
Males								
<65 years	5,735	7.1 12.0	45.7 56.1	48.4 58.8[f]	50.3 59.2[f]	54.6 64.2	35.9[e] 42.7	36.1[e] 45.1
≥65 yrs	7,833							

*Optimal Values: LDL <100 mg/dL for CHD Prevention or Diabetes; HDL >40 mg/dL in males or >50 mg/dL in females; TG <150 mg/dL All groups are significantly different from baseline by chi-squared for goal achievement. [a,b,c,d,e,f] = groups with the same letter ***are NOT*** significantly different p> 0.05.

P168

Blood Pressure <120/80 mm Hg Is Risky in Elderly CAD Patients: Findings from the INternational VErapamil SR-Trandolapril STudy (INVEST)

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Background: Blood pressure (BP) has been categorized as normal (SBP and DBP <120/80mmHg), pre-hypertensive (SBP 120–139 or DBP 80–89mmHg) and hypertensive (SBP or DBP ≥140/90mmHg) for primary prevention. The effect of these categories on progression to cardiovascular outcomes in hypertensive CAD patients treated for secondary prevention is not known. **Methods**: INVEST, a prospective, randomized trial comparing two antihypertensive strategies, assessed incidence of death, nonfatal MI or nonfatal stroke (primary outcome, PO) in 22,576 patients with hypertension and CAD followed for a mean 2.7 years. BP was measured at baseline, every 6 weeks for 6 months, and every 6 months thereafter. Mean follow-up BP was calculated by averaging each BP component, weighted by time between visits. Mean BP was categorized according to <120/80 mmHg, 120–139/80–89mmHg and ≥140/90mmHg. Cox regression was used to compare the hazard for the PO between these BP categories. Time of follow-up was used as a weight in the model to reduce the contribution of patients with shorter compared with longer follow-up. **Results**: Patients are characterized in the Table. We observed the PO in 10.9% of those with BP <120/80 mmHg, 7.1% of those with BP 120–139/80–89mmHg and 15.2% of those with BP ≥140/90 mmHg. Compared to those with mean follow-up BP in the 120–139/80–89mmHg group, the <120/80 mmHg BP group had a 41% increase and the ≥140/90mmHg BP group had a 62% increase in the risk for the PO. **Conclusions**: Mean follow-up BP in the <120/80 mmHg and ≥140/90 mmHg categories was associated with significantly higher PO rates than in the 120–139/80–89mmHg category. Further investigation as to causality is warranted, however until further data are available, our findings suggests BP reduction in elderly hypertensive CAD patients is important but care should be taken to avoid excessive BP lowering in this population.

	Follow-up Blood Pressure Category			
BASELINE CHARACTERISTICS	<120/80 mmHg (n=1,535)	120–139 or 80–89 mmHg(n=13,586)	≥140/90 mmHg (n=7,455)	p value
Mean Age yrs (SD)	64.7 (9.8)	65.6 (9.6)	67.1 (10.0)	<0.001
Female (%)	46	51	55	<0.001
Caucasian (%)	47	47	52	<0.001
Black (%)	9	11	19	<0.001
Hispanic (%)	41	40	26	<0.001
Diabetes (%)	27	27	31	<0.001
Prior MI (%)	42	31	32	<0.001
Smoking (%)	57	46	45	<0.001
Systolic BP mmHg (SD)	135 (19)	148 (18)	160 (19)	<0.001
Diastolic BP mmHg (SD)	82 (13)	87 (12)	89 (12)	<0.001
FOLLOW-UP INFORMATION				
Primary Outcome Rate n (%)	167 (10.9)	968 (7.1)	1134 (15.2)	<0.001
HR (95% CI) for risk of Primary Outcome*	1.41 (1.14–1.76)	1.0 (reference)	1.62 (1.44–1.82)	

* adjusted for age, gender, race, baseline risk factors, treatment strategy, baseline SBP and DBP and follow-up time.

P169

Health Food Stores and Recommendations for Hypertension Management

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Introduction: Patients choose dietary supplements for various reasons and there is evidence of benefit for particular supplements in the management of hypertension (HTN). What are less clear are the recommendations made by health food store (HFS) employees for HTN and how consistent these recommendations are with evidence. Our objective was to conduct a telephone survey to further define these issues. **Methods**: A telephone survey was conducted among Southeastern US (AL, FL, GA, LA, MS) HFSs. An internet search (www.yellowpages.com, "nutrition" "health and diet food stores") was used to select a convenient sample, 150 HFSs per state. The survey used a conversational format with the surveyor posing as a HTN patient. Data collected included supplement recommendation, and product contents, actions, warnings, interactions, and cost. Other responses identified were additional recommendations for management, whether prescription drugs could be discontinued after beginning supplements and references suggested for supplemental information. **Results**: There were 426 recommendations from 711 successful calls. Garlic was the most recommended generic product. "Blood Pressure Factor" (garlic, cheyenne, hawthorne roots, herbs, vitamins) was the most recommended brand name. Product monthly costs ranged from $5 to $150. Only in 56% (398/711) of calls did an employee recommend talking to a healthcare provider about either potential adverse effects or discontinuation of prescription drugs. Even fewer employees, 42% (298/711), recommended talking to a healthcare provider in general. **Conclusions**: Because supplements are easily accessible and the frequent misinterpretation that all natural products are safe, patients may choose these for blood pressure control. We observed questionable reliability and much inconsistency in the information provided by HFS employees when asked for recommendations for HTN management. It is imperative that healthcare providers question patients regarding use of supplements and help them understand the importance of reviewing these in the context of their management. All HFS employees should recommend consulting a healthcare provider when confronted with questions concerning the treatment of a medical condition such as HTN.

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Cardiovascular Disease Health Awareness and Self-Reported Behaviors in Patients with Hypertension

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Introduction: Lack of medication and lifestyle adherence is a common barrier to blood pressure (BP) control. The purpose of this study was to further develop effective patient education and adherence among patients managed in a hypertension referral center. **Methods**: A convenient sample of patients were asked by students to complete a survey; providers/clinic staff were not involved in any way. The survey contained questions ("yes/no" responses, multiple choice, fill-in-blank) on a 5th grade reading level addressing awareness of heart attack/stroke symptoms, risk factors, and optimal BP. Also included was self-assessment of overall health, diet and exercise, compliance with treatment and evaluation of provider/clinic methods regarding HTN management. **Results**: A total of 84 patients participated, in whole or part. All identified HTN leads to heart disease/stroke, BP reduction reduces risk and BP reduction occurs with regular physical activity (84/84). Most (83%, 62/75) identified optimal BP. The majority reported daily low-fat dairy foods, unsalted nuts, and fruits/vegetables as part of a healthy diet (89–99%, 75–83/84). For these participants, average fruit/vegetable servings/day was 3. Participants identified nutrition labels help determine salt content, serving size, fat content and calories (95–100%, 80–84/84) though only 45% (38/84) routinely use labels to make food decisions. Most rated the clinic "excellent" (41%, 28/69) or "very good" to "good" (51%, 35/69) when asked how well information is provided about foods to eat or avoid. The majority reported not missing medication doses over the previous week (80%, 55/72), 19% (14/72) missed 1–2 doses and 1% (1/72) missed 5 or more doses. Of these, 81% (58/72) check BP at home and most felt the clinic provided information needed to properly take medications. Most (90%, 68/76) reported being advised to exercise regularly though less than half reported following this recommendation. **Results**: Overall the multidisciplinary method of education and patient-provider communication appears effective in this clinic. Increased focus needs to be placed on reinforcing dietary and exercise adherence. Patient group sessions are being formed as another method to address this issue and improve patient care.

P171

Lack of Blood Pressure-Lowering Effect of a 12-Week Monitored Exercise Program for African-American Women with Hypertension: Results of the African-American Women's Study of Moderate Exercise

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Few randomized trials assessing the blood pressure lowering effects of exercise have included African-American women. We conducted a randomized controlled trial including 132 African-American women with diagnosed hypertension. Participants were randomized to a monitored physical activity intervention (n=66) or usual care (n=66). The intervention included exercise sessions on a resistance bicycle, three to five times per week, using a heart rate monitor and a perceived exertion scale, at exertion levels consistent with American College of Sports Medicine (ACSM) guidelines. Six blood pressure measurements were obtained by trained observers using random-zero sphygmomanometers, over two visits, at the baseline, six- and twelve-week visits of the trial. At baseline, participants in each randomization group were similar with respect to all characteristics assessed. Women in the active intervention group participated in an average of two exercise sessions per week; 28 women participated in 36 or more sessions, 12 participated in 30 to 35 sessions, 9 participated in 20 to 29 sessions, and 17 participants completed fewer than 20 sessions. At the end of the intervention period, VO2 max had increased from 17.8 to 18.8 ml/kg/min among those randomized to the exercise program and decreased from 17.6 to 17.2 ml/kg/min among their usual care counterparts (p-value comparing the change=0.014). After six-weeks of intervention, the net decrease in systolic blood pressure was -2.83 mmHg greater (95% CI: -6.00 mmHg to +0.33 mmHg; p=0.08) among the intervention group compared to control group. In contrast, after 12 weeks of intervention, systolic blood pressure increased +1.25 mmHg (-2.37 mmHg to +4.87 mmHg; p=0.49) in the exercise group compared to their control counterparts. The six- and twelve-week change in diastolic blood pressure, comparing the exercise intervention and usual care groups, was -0.13 mmHg (95% -2.15 mmHg to +1.89 mmHg; p=0.90) and -1.37 (95%: -3.67 mmHg to 0.93 mmHg; p=0.24), respectively. This intervention failed to show a substantial blood pressure lowering effect. The current level of exercise exertion recommended by the ACSM guidelines may not be sufficient to reduce blood pressure among African-American women with hypertension.

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High Blood Pressure in Pregnancy and Coronary Calcification

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Abstract Purpose: A considerable proportion of pregnant women develop high blood pressure in pregnancy. Although it is generally assumed that this condition subsides after pregnancy,

many of these women develop the metabolic syndrome later in life and are at increased risk to develop coronary heart disease. Therefore, we set out to study the relation of high blood pressure during pregnancy with risk of coronary artery calcification (CAC) later in life. **Design**: Cross-sectional study. **Materials and Methods**: The study population comprised 491 healthy postmenopausal women selected from a population based cohort study. Information on high blood pressure during pregnancy was obtained using a questionnaire. Between 2004 and 2005, the women underwent a multi slice computed tomography (MSCT) (Philips Mx 8000 IDT 16) to assess coronary calcium. The Agatston score, a volume measurement and a mass measurement were used to quantify coronary calcium. **Results**: 30.7% of the women reported to have had high blood pressure in pregnancy. Body mass index (BMI) (OR=1.05, 95% CI 1.01, 1.09) and diastolic blood pressure (DBP) (OR=1.03, 95% CI 1.01, 1.05) were significantly related to a history of high blood pressure in pregnancy. Age was significantly related to increased coronary calcification. Women with a history of high blood pressure during pregnancy had a 57% increased risk of having CAC compared to those women without high blood pressure during pregnancy (OR=1.57, 95% CI 1.04, 2.37). After adjusting for age, the relation did not change (OR=1.64, 95% CI 1.07, 2.53). **Conclusion**: High blood pressure during pregnancy is associated with an increased risk of coronary calcification later in life.

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Prevalence, Treatment, and Control of Hypertension in the Moli-sani Study

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Introduction. Blood pressure (BP) control is required for the prevention of cardiovascular events. **Aims**. To estimate prevalence, treatment and control of hypertension (HTN) in a general Italian population. **Methods**. The Moli-sani Study is an on-going cohort study on males and females, aged ≥35yrs, randomly recruited from the general population of a Southern Italian region. From March 2005 to July 2006, 6,251 subjects were enrolled. After exclusion of subjects with diabetes or previous CVD (9%), 5,661 subjects (55 ±12yrs, 45% males) were analyzed. BP was measured according to the *'British Society of Hypertension (BSH)' guidelines,* by using an automatic device (OMRON-HEM-705CP). HTN was defined as SBP ≥140 mmHg and/or DBP ≥90 mmHg and/or current anti-hypertensive treatment, *Gold Standard* BP control as SBP<140 mmHg and DBP <85 mmHg. **Results**. Overall, 59% of subjects was hypertensive; the prevalence of HTN increased with age, in both sexes (P<0.0001). Only 40% of hypertensive subjects was under anti-hypertensive treatment, 20% was also following a low-salt diet. Male hypertensive subjects were more frequent than females (65% *vs* 54%, P<0.0001), but females were more treated than males (45% *vs* 34%, P<0.0001). Forty-four % of subjects received a single drug therapy, 56% a combined treatment. The most frequently used drugs in mono-therapy were ACE-inhibitors (33%), Ag.II receptor blockers (22%), β-blockers (21%) and calcium channel antagonists (16%). Among treated hypertensives, only 16% reached the *Gold Standard*. After exclusion of subjects who had started the therapy within one year from the recruitment (8%), the percentage of subjects under control was similar. In multiple logistic regression analysis, *Gold Standard* BP control was negatively associated with glucose (P=0.028) and stop smoking from at least one year (P=0.019) but positively with the use of combined therapy (P=0.013) and high social status (P=0.018) in males. No similar association was found in females. **Conclusions**. A high proportion of subjects treated for HTN is still out of control. Antihypertensive therapy appears under-used and poorly successful. Targeted interventions are necessary to improve this therapy. *Supported by Fondazione Pfizer and Italian Research Ministry*

P174

Olmesartan, Monotherapy, and Combination Diuretic Therapy for Treatment of Hypertension: Findings from a Large Cross-Regional Study

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Background: Large cross-regional studies on the effectiveness of olmesartan (a selective angiotensin II receptor blocker), alone or in combination with a diuretic, are lacking–particularly in Asian populations. **Method**: This 16-week, open label, dose titration, treat-to-target study carried out in 10 countries throughout Asia (7), Latin America (2) and Turkey included outpatients with mild to moderate hypertension. The primary measure was the proportion of subjects who achieved pre-specified JNC VII blood pressure (BP) targets: <140/90 mmHg (<130/80 mmHg for diabetes mellitus/renal disease). Subjects received olmesartan 20 mg/day for the first 4 weeks. At goal status was assessed at Weeks 4, 8 and 12; if BP targets were achieved, subjects remained on 20 mg/day; if BP targets were not achieved, the dose was increased to 40 mg/day or hydrochlorothiazide (HCTZ) (12.5 or 25 mg/day) was added. Safety was assessed throughout the study. **Results**: In total, 483 subjects were treated and 449 (93%) completed the study. The proportion of males and females was similar and the mean age was 50 years (range 23 to 68). Subjects had hypertension for an average of 4 years (range 0 to 34) and 99 subjects (21%) also had diabetes mellitus or renal disease. At Week 16, 82% (n=394) of subjects achieved BP targets. Of the 99 subjects with diabetes or renal disease, 57% (n=56) achieved the more stringent BP goals. Fifty-three percent (n=255) of subjects were maintained on olmesartan 20 mg/day monotherapy throughout the study–93% (n=238) of these were at goal at Week 16. Overall, 23% (n=109) subjects were assigned combination HCTZ; and 7% (n=32) were up-titrated at every visit (ie, all dosage options prescribed), of which 50% (n=16) reached goal. Adverse events were generally mild in nature; the most frequent were dizziness (8%), headache (5%) and upper respiratory tract infection (5%). There were 6 serious adverse events, none of which were treatment-related. In total, 12 (2.5%) subjects discontinued as a result of treatment-related events. **Conclusion**: These data will provide valuable information for local clinicians in their management of hypertensive patients with or without concomitant diabetes/renal disease, particularly with respect to JNC VII recommended BP targets.

P174-A

Methodologic Challenges in Studying Incident Hypertension: Lessions from TROPHY

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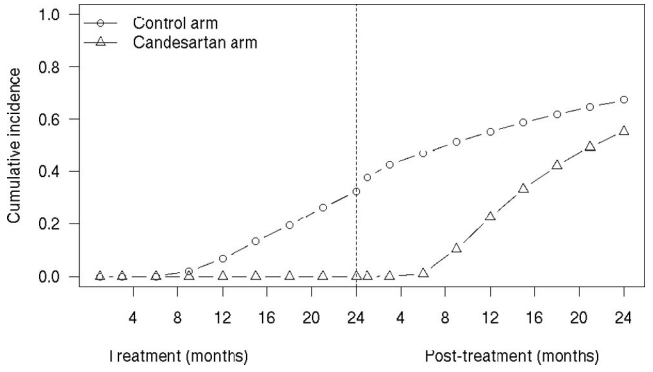
Prevention and treatment of hypertension is a major component of strategies to prevent heart disease. Because blood pressure has substantial day-to-day variability, the incidence rate for diagnosed hypertension is sensitive to the number of blood pressure measurements made and the number of over-threshold measurements used to define incident hypertension. TROPHY (N Engl J Med 2006; 354: 1685–97) randomized prehypertensive subjects to two years of candesartan vs placebo and two years of untreated followup, with the primary aim of preventing the onset of hypertension. TROPHY reported a 10% difference in cumulative incidence two years after stopping treatment, and concluded that candesartan delayed onset of hypertension for up to two years after the discontinuation of treatment. We explored whether measurement error might offer an alternative explanation for the findings of TROPHY. We simulated the TROPHY study design assuming that candesartan reduced blood pressure by 8/6mmHg during treatment, but had no carryover effect after treatment stopped. We simulated individual true blood pressures in the TROPHY-eligible range 130–140mmHg SBP and 80–90mmHg DBP and added individual measurement variability. Figure 1 shows incidence based on measurement standard deviation of 3/2.5 mmHg (SBP/DBP) and an annual blood pressure increase of 1/0.5 mmHg(SBP/DBP). Measurement variability in blood pressure, rather than suppression of the development of hypertension, offers an alternative explanation for the results of TROPHY. Studies of incident hypertension should report within-individual variability in blood pressure and consider the impact of measurement schedules in the design.



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The Incidence, Prevalence, and Case Fatality of Stroke in American Indians: The Strong Heart Study

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Background There are few published data regarding the incidence of fatal and non-fatal stroke in American Indians during systematic follow-up. The aims of this observational study were: (1) to examine the prevalence, incidence and age of onset of stroke in American Indians, (2) to examine 30-day and one-year case-fatality and the age of onset for patients with first ever stroke. **Methods and Results** This report is based on 4549 participants aged 45–74 at enrolment in the Strong Heart Study, the largest longitudinal, population-based study of cardiovascular disease and its risk factors in a diverse group of American Indians. At baseline examination in 1989–1992, 42 participants (923/100,000) had prevalent stroke. Among the 4507 without prior stroke, 292 (6.5%) suffered a first stroke, at a mean age of 66.3 years, through December 2003. The unadjusted incidence of stroke was 589/100, 000 person-years and that adjusted to the age and gender distribution of the U.S. adult population in 1990 was 679/100, 000 person-years (1989–2003). There is no obvious trend of incidence by period of follow-up (1989–94, 1995–1999, and 2000–2003) among participants 65–74 years old, who had the highest stroke incidence and allowed the most stable comparison among time periods. Non-hemorrhagic cerebral infarction was the predominant type of stroke, occurring in 86.9% (206/237) of participants; 13.1% (31/237) suffered hemorrhagic stroke. Overall 30-day case-fatality from first stroke was 20% (57/290), with a one-year case-fatality of 32% (66/205). **Conclusions** Compared to U.S. white and black populations, American Indians have higher prevalence and incidence of stroke. The case-fatality rate for first stroke is also higher in American Indians than in the U.S. white or black population with the same age range. Cerebral infarction is the most common type of stroke in this population. Prevention focus on the risk factors in this population such as diabetes, hypertension is suggested.

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Trust in the Patient-Physician Relationship Is Related to Care-Seeking Behavior Following Stroke Symptoms: The REasons for Geographic and Racial Differences in Stroke (REGARDS) Study

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Background. Individuals with stroke symptoms may not seek medical attention but few studies examine potential reasons. Previously, we found increased income and past cigarette smoking

were associated with more care seeking. We hypothesized that adults with greater trust in their doctor were more likely to seek medical care following stroke symptoms. **Methods**. We used telephone interview, in-home evaluation, and self-administered questionnaire data from REGARDS (REasons for Geographic and Racial Differences in Stroke), a national, population-based, longitudinal study of African Americans (AA) and whites ≥45 years old. Participants were asked 6 questions on level of trust with usual source of medical care (5-point scale, range "strongly agree"-"strongly disagree"). New physician-diagnosed stroke or TIA (P-Dx-S) and stroke symptoms were asked at 6-month telephone follow-ups. Care-seeking was defined as seeking medical care following reported symptoms or reporting a P-Dx-S since the last contact. For each trust question, we estimated age, race, and sex adjusted odds ratios (with 95% confidence limits) for care seeking as a trend with increasing trust, using logistic regression. As of September 1, 2006 follow-up was available on 5322 participants enrolled since February 2005. **Results**. There were 415 participants who had P-Dx-S (54) or stroke symptoms without P-Dx-S (361). Of these, 177 (42.6%) did not seek medical care for symptoms, with no difference ($p = 0.95$) between whites (42.9%) and AAs (42.6%), however, after control for age, gender, income, and cigarette smoking, AAs but not whites with greater trust on 2 domains were more likely to seek care (table). **Conclusions**. These preliminary data suggest that building trust between patient and physician, particularly for AA, may encourage care-seeking following stroke symptoms. Further attention to these factors in REGARDS may provide additional insights to removing barriers and ensuring appropriate acute care.

	OR (95% CI) for Seeking Care Following Symptoms per category of increasing trust			p-value effect modification by race
	Entire cohort	AA	White	
My doctor would always tell me the truth, even if bad news	1.52 (1.06,2.19)	1.93 (1.21, 3.09)	0.97 (0.52, 1.81)	0.084
I completely trust my doctor's judgment about my medical care	1.20 (0.90, 1.61)	1.53 (1.07, 2.19)	0.67 (0.38, 1.18)	0.015
I can tell my doctor anything	1.12 (0.83,1.51)	1.37 (0.97, 1.95)	0.62 (.34, 1.15)	0.029
How much do you agree going to doctor will keep you healthy	1.00 (0.76,1.31)	0.98 (0.70, 1.37)	1.03 (0.65, 1.64)	0.87
My doctor cares more about holding costs down than doing what is needed for my health	1.13 (0.91, 1.40)	1.16 (0.90,1.49)	1.07 (0.71, 1.60)	0.74
If mistake were made in my treatment, my doctor would try to hide it from me	1.19 (0.92,1.55	1.16 (0.83, 1.62)	1.25 (0.81, 1.93)	0.78

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Predictors of Time to Initial Brain Imaging Among Patients in the North Carolina Collaborative Stroke Registry

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While the literature on factors influencing delay from onset of stroke symptoms to hospital arrival is growing, there has been little focus on factors influencing the timing of the receipt of stroke care after hospital arrival. We examined predictors of delay in time from hospital arrival to initial brain imaging among patients in the North Carolina Collaborative Stroke Registry (NCCSR). The NCCSR is one of four Paul Coverdell National Acute Stroke Registries designed to measure and improve the quality of key indicators of acute stroke care. Among 5943 patients prospectively enrolled from December 2004 and September 2006, time (hours) from hospital arrival until imaging varied greatly (Mean = 1.9, Median = 1.3, 1st to 99th percentile = 0.2 to 16.0). Because imaging delay time was not normally distributed, values were log transformed prior to analysis. In unadjusted models, there was no significant variation in imaging delay time by insurance status or prior history of stroke. In contrast, imaging delay time was greater in women than men ($p < 0.03$); greater in blacks than whites ($p < .002$); less among those arriving by EMS than by other modes of transportation ($p < .0001$); less among certified primary stroke centers than hospitals without primary stroke center certification ($p < .0002$); less among those independently ambulating than those who were not ($p < .02$); and less among those who arrived within 2 hours of symptom onset than those with an unknown time of symptom onset or who arrived at the hospital more than 2 hours after symptom onset ($p < 0.0001$). Delay time also varied by discharge diagnosis. Compared to those presenting with stroke symptoms but not discharged with a stroke-related diagnosis, delay times were shorter among those with a stroke-related discharge diagnosis ($p < 0.0001$), and least for those with a hemorrhagic stroke diagnosis. In multivariate regression analyses, significant differences in delay time persisted. In the NCCSR, we identified factors contributing to delay in initial brain imaging among patients with stroke symptoms. Additional studies of factors influencing delay in receipt of stroke care after hospital arrival are warranted to help inform the development of interventions aimed at assuring the timely receipt of stroke care.

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Short- and Long-Term Prognosis After Cerebrovascular Disease and Acute Myocardial Infarction in the Netherlands

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Objective Comparison of mortality risk of patients after a first acute myocardial infarction (AMI) with patients after a first cerebrovascular disease (CVA) by age and gender. **Methods** Two nationwide cohorts, one of 22.475 patients with a first hospitalized CVA and one cohort of 21.565 patients with a first hospitalized AMI were identified through linkage of the national hospital discharge register and the Dutch population register. Patients were followed through linkage of the Dutch population register and the Dutch cause of death register. Follow-up for mortality lasted 5 years. **Results** The CVA cohort consisted of 11.333 men (69 yr) and 11.142 women (72 yr). At the end of the follow-up period 57% (12.746 of 22.475) of the patient had died. CVA was a frequent (45%, 5.625 of 12.746) cause of death. In 36% (4.488 of 12.746) cause of death was other than cardiovascular origin. The AMI cohort consisted of 14.463 men (64 yr) and 7.102 women (72 yr). At the end of the follow-up period 38% (8.147 of 21.565) of the patient had died. AMI was a frequent (46%, 3.747 of 8.147) cause of death. In 27% (2.167 of 8.147) cause of death was other than cardiovascular origin. Mortality risks at 28 days and 5 years after a first hospital admission with the diagnosis of CVA, Subarachnoid haemorrhage (SAH), Intracerebral haemorrhage (ICH), ischemic stroke or AMI are presented by age and gender in figure 1 and 2. **Conclusion** Short- and long-term mortality after CVA or AMI is high. In particular mortality risk for SAB and ICH. The mortality risks for ischemic stroke and AMI are quite similar.

Figure 1: Mortality risk at 28 days and 5 years after a first hospital admission with the diagnosis of CVA, SAH, ICH, Stroke or AMI, by age. Men.

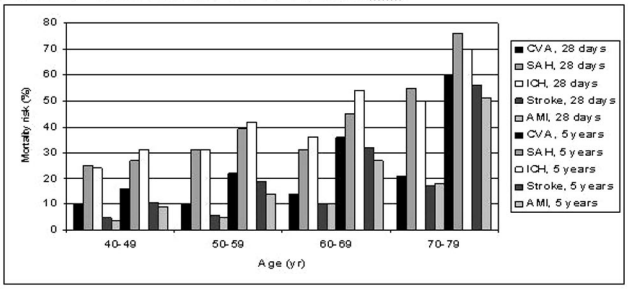
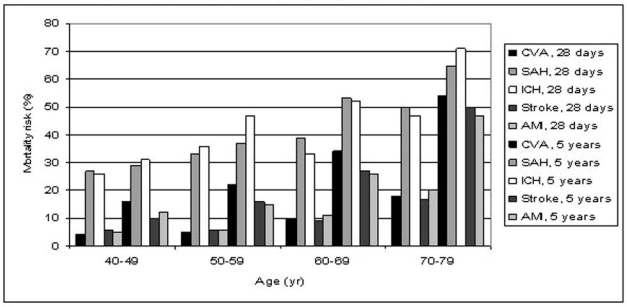


Figure 2: Mortality risk at 28 days and 5 years after a first hospital admission with the diagnosis of CVA, SAH, ICH, Stroke or AMI, by age. Women.



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Effects of Eicosapentaenoic Acid-Ethyl Ester on the Occurrence of Stroke: JELIS Subanalysis

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Background: The Japan EPA Lipid Intervention Study (JELIS) employed a PROBE design to examine the preventive effect of eicosapentaenoic acid-ethyl ester (EPA-E) against coronary artery diseases. Major analytical results, presented at the American Heart Association Scientific Sessions 2005 showed EPA significantly suppressed the occurrence of coronary artery diseases by 19%. This sub-analysis examined the effects of EPA-E on occurrence of stroke. **Methods**: Hypercholesterolemic patients, TC 250 mg/dl or higher, received statin only (control group: n=9,319), or statin with EPA of 1,800 mg/day (EPA group: n=9,326). Plasma EPA concentrations were measured in all subjects. Analyses were conducted by intention to treat. **Results**: With a study follow-up rate of 91% and a mean duration of 4.6 years, stroke occurred in 162 (1.7%) patients in the control group and 166 (1.8%) in the EPA group. There were no statistically significant differences between the two groups in total stroke incidence (multi adjusted hazard ratio, 1.01; 95% confidence interval, 0.90 - 1.12; P=0.907) and again no significant differences between the groups in ischemic stroke and hemorrhagic stroke incidences. In 942 patients who had history of a stroke (control group; n= 457; EPA group, n=485), stroke recurrence occurred in 33 (6.8%) patients in the EPA group as compared with 48 (10.5%) patients in the control group, which represented a significant 20% relative reduction by EPA (95% confidence interval, 0.64 - 1.00; P=0.047). The mean EPA concentrations on treatment in all subjects were divided into 3 groups (≤3mol% group, 3< to ≤5mol% group, >5mol% group). When the ≤3mol% group was taken as the standard, incidence of stroke was significantly lower for the >5mol% group (multi adjusted hazard ratio, 0.86; 95% confidence interval, 0.75 - 0.99; P=0.042) **Conclusions**: Whereas EPA did not decrease the incidence of stroke in the total study population, it significantly suppressed the recurrence of stroke in patients with a history of stroke. Further, EPA concentrations of >5 mol% significantly suppressed the incidence of stroke compared with concentrations of ≤3mol%.

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Mortality and Cause of Death After Hospital Discharge in Patients with Stroke: Analysis of a Nationwide Sample

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Background: Although stroke is the most common cause of death in Korea, no national representative data is available on the prognosis of stroke patients in Korea. The aim of this study was to examine the 4-year mortality and cause of death, and to identify the predictive factors for death after hospital discharge in stroke patients with a nation wide sample. **Methods**: We identified 8,334 hospital discharges between January 2000 and March 2000, which were presumed due to stroke, from 152 hospitals of nationwide sample. Trained medical doctors and nurses abstracted data required to verify the diagnosis. Based-on the findings of imaging studies (computed tomography and/or magnetic resonance imaging) and neurologic examinations, 5,238 cases were confirmed to stroke (excluding transient ischemic attack). Eventually 4,154 patients (2,142 men and 2,012 women) with valid identification number, date of birth and date of symptom onset, were followed until December 2003. Date and causes of deaths were obtained from the death certificate data of the National Statistical Office. **Results**: Ischemic stroke was the most common subtype (n=2,611), which were followed by intracerebral hemorrhage (ICH, n=923), unknown subtype (n=342) and subarachnoid hemorrhage (SAH, n=278). During the 4 years after discharge 1,185 (28.5%) patients died. Common causes of deaths were stroke (61.9%), malignancies (7.0%), diabetic complications (4.5%), ischemic heart disease (2.7%), pneumonia (0.9%) and renal failure (0.8%). Mortality was similar between ischemic and hemorrhagic subtypes before adjustment for age, but hemorrhagic stroke showed significantly higher mortality after adjustment. Multivariate analysis suggested that age at onset (RR=1.06 per year; 95%CI 1.05–1.06), male gender (RR=1.22; 95%CI 1.09–1.37), subtypes of ICH (RR=1.34; 95%CI 1.17–1.54) and SAH (RR=1.69; 95%CI 1.34–2.14), longer hospital stay (RR=1.01 per week; 95%CI 1.00–1.02) were independent predictors of death during the follow-up period. **Conclusions**: In a national representative samples of stoke patients in Korea, 4-year mortality after hospital discharge was 28.5% and associated age, gender, subtypes of stroke and initial length of stay in hospital.

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Primary Stroke Center Certification: Does It Make a Difference?

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The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) launched a certification program for Primary Stroke Centers (PSC) in 2004. Part of the certification process involves monitoring of key quality of care indicators. There are only limited data reflecting the quality of stroke care at JCAHO certified PSCs as compared to non-primary stroke center (NPSC) hospitals. As part of the Coverdell National Stroke Registry, the North Carolina Collaborative Stroke Registry (NCCSR) monitors the documentation of key quality indicators at 36 hospitals including 5 of the 6 state's PSCs. We compared performance on 10 quality indicators between PSC (n=5) and NPSC hospitals (n=15) with at least 6 months of data collected between January 2005 and July 2006. During this period, 1611 patients in PSC hospitals and 3758 at NPSC hospitals were enrolled. PSC patients tended to be younger ($p < .0001$), more often black ($p < .0001$), and male ($p < .03$). On average, compared to NPSC hospitals, PSC hospitals more often administered thrombolytic therapy for ischemic stroke patients arriving within 2 hours of symptom onset (26% vs. 20%, $p < .10$), measured lipid profiles for ischemic stroke and transient ischemic attacks (TIA) patients (73% vs. 68%, $p < .01$), and provided stroke education materials to all stroke or TIA patients (62% vs. 54%, $p < .0001$). PSC hospitals were less likely to document smoking cessation counseling (60% vs. 71%, $p < .0001$), or indicate a rehabilitation plan (84% vs. 92%, $p < .0001$) than NPSC hospitals. Deep vein thrombosis prophylaxis, use of anti-thrombotics at discharge, and anticoagulation therapy for patients with atrial fibrillation were used in the majority of eligible patients in both PSC and NPSC hospitals. PSC hospitals did not significantly differ from NPSC hospitals in dysphagia screening before oral intake (59% vs. 62%, $p < .11$). Analysis of time trends indicated that on average NPSC hospitals improved over time in thrombolytic therapy use, lipid management, and distribution of stroke education materials, yet lagged behind the PSCs. As a group, PSCs had better performance than NPSCs for several quality indicators. Future studies will need to adjust these types of analyses for stroke severity and other factors that might affect the process of care.

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The Joint Effect of Oxidative Stress and Antioxidants and the Risk of an Aneurysmal Rupture Subarachnoid Hemorrhage in Women: A Case–Control Study in Japan

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Several studies have examined the independent effect of those factors on SAH, but few studies have examined the synergic effect of oxidants and antioxidants on the risk of SAH. We reported that smoking was associated with an increased SAH risk, and soy products were inversely associated with SAH risk. We therefore conducted a case-control study to explore the relationship between the joint effect of smoking as oxidative stress and soy products as antioxidant defenses system and the risk of SAH, using a relatively large number of newly diagnosed patients in Japan. This is the first epidemiological finding that the combined effect of high psychological stress and less frequent intake of soy products was strongly associated with an increased risk of SAH Case subjects included were women aged 30 to 79 years and those who experienced the first spontaneous onset of SAH. SAH was diagnosed by aneurismal bleeding pattern on CT, with the additional condition that the presence of 1 or more aneurysms was confirmed by cerebral angiography. We set up community control subjects with no past history of SAH, matching to each patient for age (±2 years) and gender randomly selected from among general population in the same district as case subjects based on the basic register of residents. Conditional logistic regression models was used to compute odds ratio adjusted for smoking and drinking habit, history of hypertension, and family history of SAH. A total of 124 consecutive female SAH patients and 248 matched controls were identified in the study period (mean age, 60.0 10.0 years and 60.3 10.5 years, respectively). In this study, smoking was used as an index of oxidative stress, and soy products as that of antioxidants. The greatest effect on risk for SAH was the combination of psychological stress and less frequent intake of soy products (adjusted OR = 6.8; 95% CI, 2.9 to 16.1), and less frequent intake of soy products alone and high smoking alone were not associated with increased risk. The present study clearly suggest that imbalances between excessive productions of oxidants coming from patient-specific and the decrease or lack of antioxidant defense in cerebral vessels may increase the risk of SAH.

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20-Year Secular Trends in LDL-Cholesterol in CARDIA: Down After Accounting for Weight Gain

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Background: National data suggest that LDL-cholesterol (LDL) may be decreasing, despite increases in mean weight and decreases in physical activity. **Methods**: We examined trends in LDL over 20 years of follow-up in CARDIA, an observational cohort study of African-American (AA) and white men and women ages 18–30 years in 1985. At baseline, 5,115 participants were recruited from 4 U.S. cities, with follow-up exams 5, 7, 10, 15 and 20 years after baseline, and 3,478 attending the year 20 exam (72% of the surviving cohort). LDL was estimated by the Friedewald equation, and age, BMI, smoking and drinking habits, physical activity and antihyperlipidemic medication use were collected by standardized protocol at each exam. Trends in LDL were assessed using repeated measures regression with a compound symmetry covariance structure, and adjusted for current age to estimate secular trend. **Results**: Over 20 years, unadjusted mean LDL remained relatively constant for the cohort: 109.0, 108.5, 107.6, 109.2, 112.9 and 109.8 mg/dL for years 0, 5, 7, 10, 15 and 20, respectively. After excluding those who used any type of antihyperlipidemic medication, these means were 109.0, 108.2, 107.4, 109.2, 113.3, and 112.9 mg/dL, reflecting the low prevalence of use in this young cohort. Mean BMI increased from 24.5 to 29.4 kg/m^2, while smoking prevalence and physical activity both decreased as the cohort aged. However, mean LDL showed a downward secular trend in all race and sex groups after adjustment at each exam for age, age^2, BMI, and study center among those not using antihyperlipidemics (Table), suggesting strong confounding of unadjusted time trends in LDL. Further adjustment for smoking, physical activity, and alcohol consumption at each exam minimally altered these trends. **Conclusion**: In this healthy population, strong decreasing secular trends exist in LDL after accounting for weight gain and aging that are consistent in all race and sex groups.

Secular trends in mean LDL by race-sex group, adjusted for age, age2, BMI, center: CARDIA, 1985–2006

	AA men	AA women	White men	White women
Year 0	120.9	118.2	123.7	113.7
Year 5	112.6	109.9	117.5	107.9
Year 7	108.6	106.7	114.1	105.1
Year 10	107.6	105.4	112.2	104.0
Year 15	105.7	102.8	113.7	101.2
Year 20	99.7	98.1	109.5	96.6
p-trend	<0.0001	<0.0001	<0.0001	<0.0001

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Statin Use and Platelet Activation in Families at High Risk of Coronary Artery Disease

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Few studies have examined the impact of statin therapy on platelet function. A recent large statin stroke prevention trial showed that statin use was associated with hemorrhagic stroke, raising the question of the impact of statins and goal LDL-C levels on platelet function. We thus examined a panel of platelet activation tests, statin use, and LDL-C levels in an apparently healthy group at increased risk for atherosclerotic vascular disease by virtue of family history of premature coronary disease. **Methods**: In vivo platelet activation was measured by urinary 11- dehydro thromboxane B2 (TxM) excretion; ex vivo platelet activation was measured in platelet rich plasma using 1 mmol collagen (COL), 10 mmol epinephrine (Epi) and 10 mmol ADP as agonists in 2015 subjects. Lipids were measured with the subjects in the fasting state. Statin use was assessed by self report and all subjects were taking aspirin 81 mg/day for primary prevention. Adjusted association analyses* examining platelet activation by strata of LDL-C and statin use were analyzed using Generalized Estimating Equation models accounting for intra-familial correlations. **Results**: The sample was 58% female, 41% Black, with 13% using statins. As per the table, in general, there were no differences in platelet activation measures by statin use across the range of LDL-C levels except in the lowest LDL-C group, where statin users showed a trend to lower levels of platelet activation compared to nonusers. **Conclusion**: Decreased platelet activation was observed consistently only in people with the lowest LDL-C level. Thus, it is possible that individuals who are most responsive to statins as demonstrated by the very low LDL-C levels achieved, may have greater platelet inhibition. Further research is necessary to determine the combined effects of statin therapy and very low levels od LDL-C on hemostasis as these results suggest a possible interaction that may affect bleeding propensity.

Table: Platelet activation measures by LDL-C strata and statin use

	COL (% aggregation)			Epi (% aggregation)			ADP (% aggregation)			TxM (ng/mmol creatinine)		
LDL-C strata	Statin	No Statin	p	Statin	No Statin	p	Statin	No Statin	p	Statin	No Statin	p
<70 mg/dL	3.1 (2.0)	8.4 (0.9)	0.016	24 (3)	30 (1)	0.115	67 (3)	69 (1)	0.373	26 (6)	44 (4)	0.051
70–99 mg/dL	7.4 (1.0)	7.6 (0.5)	0.815	29 (2)	28 (1)	0.978	68 (1)	68 (1)	0.969	33 (4)	32 (2)	0.681
100–129 mg/dL	5.4 (1.0)	7.1 (0.4)	0.089	25 (2)	27 (1)	0.227	67 (1)	68 (1)	0.658	32 (4)	31 (1)	0.795
130–159 mg/dL	4.6 (1.3)	5.7 (0.4)	0.388	23 (2)	27 (1)	0.132	65 (2)	67 (1)	0.422	26 (4)	31 (2)	0.304
≥160 mg/dL	4.4 (1.8)	5.6 (0.6)	0.510	26 (3)	26 (1)	0.912	68 (3)	67 (1)	0.745	27 (6)	33 (2)	0.342

Mean (SEM) *standardized to study population composition for sex, race, hypertension, diabetes, and mean age

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The Relation Between Polyunsaturated Fatty Acids and Lipoprotein Subclasses

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Background: N-3 polyunsaturated fatty acids (PUFAs) and lipoprotein subclasses, including small LDL and large HDL particles, may affect coronary heart disease (CHD) risk. Identifying their relation patterns may help delineate how their interplay influences on CHD risk. We aimed to explore associations of PUFAs (eicosapentaenoic acid [EPA], docosahexaenoic acid [DHA], and α-linolenic acid [ALA]) with lipoprotein subclasses. **Methods**: Participants were from a population-based sample of 250 randomly-selected healthy white men aged 40−49. We excluded those taking lipid-lowering medicines. Particle concentration and size were measured by nuclear magnetic resonance spectroscopy (LipoScience Inc., Raleigh, NC). Covariates in multiple regression models were age, BMI, smoking, systolic blood pressure, LDL-C, HDL-C, triglycerides, glucose, insulin, C-reactive protein, fibrinogen, exercise, alcohol drinking, hypertension, and diabetes. **Results**: The participants had a mean age of 44.9±2.9 years and a mean BMI of 27.7±4.1 mg/kg^2. Spearman correlation analyses showed that each of EPA and DHA had significant association with HDL-C and large HDL particles. Each of EPA and DHA had significant association with small LDL particle concentration and size, but not with LDL-C. Each of EPA and DHA had significant association with triglycerides and large VLDL particles. ALA had no significant association with each lipoprotein subclass. After adjusting for the covariates, only DHA had independent associations with small LDL particle concentration and size (Table). Each of DHA and EPA has significant association with large HDL particles. EPA had a significant association with small VLDL particles, but DHA did not. **Conclusions**: Marine-derived DHA and EPA and plant-derived ALA have a different relation pattern with lipoprotein subclasses. DHA appears to have a relation with clinically important lipoprotein subclasses in a more robust than, or a different manner from EPA.

Table. Relation between n-3 PUFAs and lipoprotein subclasses

		DHA (β)	EPA(β)	ALA(β)
VLDL particles	Total	-.004	.002	<.001
	Large	-.064****	-.017*	<-.001
	Small	.004	.007***	.001
LDL particles	Total	<-.001	<.001	<.001
	Large	.001****	.003	.000
	Small	-.0005**	<-.001	<.001
HDL particles	Total	-.002	<.001	-.004
	Large	.080***	.032*	-.004
	Small	-.030	-.013	-.002
Particle Size	VLDL	-.036***	-.015***	.001
	LDL	.396****	.069	-.011
	HDL	.591***	.201*	-.034

****p<.0001, ***p<.005, **p<.01, *p<.05

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Relations of Total Cholesterol and High-Density Lipoprotein Cholesterol to the Incidence of Heart Failure in US Male Physicians

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Introduction: In the United States, heart failure remains the leading cause of hospitalization for individuals aged 65 years and older. Coronary heart disease (CHD) is one cause of heart failure and many risk factors are common to both entities. Although hypercholesterolemia is a well-recognized risk factor for CHD, its association with incident heart failure is not well characterized. **Hypothesis**: We hypothesized that total cholesterol and high density lipoprotein (HDL) cholesterol are not related to incidence of heart failure. **Methods**: We evaluated the relations of total cholesterol and HDL cholesterol to incident heart failure in 10,813 US male physicians (mean age, 68 years) from the Physicians' Health Study who were free of heart failure at baseline. Total and HDL cholesterol were analyzed both as continuous (per increase in one standard deviation [SD]) and as categorical (in quartiles) variables. **Results**: On follow-up (mean 6 years), there were 222 incident heart failure cases. In multivariable Cox models after adjusting for traditional coronary risk factors, one-SD increase in total cholesterol (36.7mg/dL) and HDL cholesterol (15.3mg/dL) were not related to incident heart failure, with a hazard ratio [HR] (95% confidence interval) of 0.91 (0.79–1.05) for total cholesterol and 0.95 (0.82–1.11) for HDL cholesterol . Similarly, the incidence of heart failure for individuals with total and HDL cholesterol in the second to fourth quartiles were similar to those in the first quartile. (Table) **Conclusion**: In initially healthy men, total cholesterol and HDL cholesterol levels were not associated with incident heart failure. Additional research studies are warranted to explore other risk factors which could help to identify individuals at risk for developing heart failure.

Table: Lipids and the Incidence of Heart Failure

Quartiles of serum lipids	Multivariable-adjusted models	
Total cholesterol		
	Number of heart failure cases	Hazard Ratio (95% CI)
Quartile 1	81	Referent
Quartile 2	46	0.72 (0.49–1.05)
Quartile 3	50	0.76 (0.52–1.11)
Quartile 4	45	0.73 (0.50–1.09)
HDL cholesterol		
	Number of heart failure cases	Hazard Ratio (95% CI)
Quartile 1	72	Referent
Quartile 2	50	0.78 (0.53–1.15)
Quartile 3	40	0.66 (0.43–1.00)
Quartile 4	60	1.03 (0.69–1.54)

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Ethnic Differences in Conventional and Novel Lipoprotein-Related Risk Factors in Hypertensive Adults

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Background: Significant differences in lipoprotein profiles are known to be present between African Americans (AA) and non-Hispanic Whites (NHW). Hypertension and dyslipidemia often coexist and aggregate in families (familial dyslipidemic hypertension). We investigated whether 'conventional' and 'novel' lipid risk factors differ between hypertensive AA and NWH subjects. **Methods**: Subjects included 736 AA from Jackson, MS (63.8 years; 75.4% women) and 643 NHW from Rochester, MN (59.3 years; 58.6% women). We assessed whether ethnicity was a significant predictor of 'conventional' (total cholesterol, LDL-C, HDL-C and triglycerides (TG)) and 'novel' (Lp(a), ApoB, LDL size and ox-LDL) lipid risk factors after adjustment for age, BMI, systolic BP, diabetes, statin use, smoking history, physical activity and alcohol consumption. Multiple regression analyses were performed using generalized estimating equations to account for intrafamilial correlations. **Results**: After adjustment for age, plasma lipoprotein markers differed significantly between the two ethnic groups (Table). In men, after additional adjustmen for the covariates listed above, AA ethnicity was associated with lower LDL-C ($P <$ 0.0001), TG ($P < 0.0001$), ApoB ($P = 0.0002$) and LDL size ($P = 0.002$), and higher HDL-C ($P < 0.0001$) and Lp(a) ($P < 0.0001$). No differences were noted in total cholesterol ($P = 0.22$) or ox-LDL levels (0.16). In women, AA ethnicity was associated with lower LDL-C ($P < 0.0001$), TG ($P < 0.0001$), ApoB ($P < 0.0001$), LDL size ($P < 0.0001$), and ox-LDL ($P = 0.003$), and higher HDL-C ($P < 0.0001$) and Lp(a) ($P < 0.0001$) after covariate adjustment. No significant difference was noted in total cholesterol levels ($P = 0.247$). **Conclusions**: Significant ethnic differences in conventional and novel lipoprotein markers exist among hypertensive adults. AA ethnicity was associated with favorable levels of LDL-C, HDL-C, TG, and Apo B but with lower LDL particle size and higher Lp(a).

Age-adjusted levels of novel and conventional lipid markers

	Men			Women		
	NHW	AA	*P*	NHW	AA	*P*
Conventional						
TC (mg/dL)	189.5	192.9	*0.34*	204.5	206.3	*0.32*
LDL-C (mg/dL)	161.6	174.9	*<0.001*	167.6	181.2	*<0.001*
HDL-C (mg/dL)	48.3	43.9	*<0.001*	58.1	54.6	*<0.001*
TG (mg/dL)	104.6	135.1	*<0.001*	108.6	148.0	*<0.001*
Novel						
Lp(a) (mg/dL)	31.8	13.8	*<0.001*	44.4	16.2	*<0.001*
ApoB (mg/dL)	91.5	100.0	*<0.001*	96.5	102.9	*<0.001*
LDL size (nm)	267.9	269.7	*<0.001*	268.6	270.7	*<0.001*
Ox-LDL (mU/mL)	63.7	67.0	*0.037*	62.8	66.1	*0.010*

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Gender- and Age-Specific Differences in the Kinetic Behavior of TRL, IDL, and LDL Apolipoprotein B-100 and HDL Apolipoprotein A-I

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Gender specific differences in lipid and lipoprotein profile, predominantly higher LDL-C, VLDL-C and TG, and lower HDL-C levels have been observed in males compared to females. These differences are influenced by menopausal status and age. To investigate mechanism(s) involved, apolipoprotein (apo) B-100 and apo A-I kinetic behavior was studied in 20 younger men (n=12) and women (n=8, premenopausal) aged <50 years, and 24 older men (n=12) and women (n=12, postmenopausal) aged ≥50 yrs. Subjects were provided with a Western diet for 4−6 weeks, after which a primed-constant infusion of deuterated-leucine was administered in the fed state to determine the kinetic behavior of triglyceride rich lipoprotein (TRL), intermediate density lipoprotein (IDL) and LDL apoB-100, and HDL apoA-I. Data were fit to a multicompartmental model using SAAM II to calculate fractional catabolic rate (FCR) and production rate (PR). Plasma LDL-C, TRL-C and TG levels were lower (-38%, -44% and -45%, respectively, $p<0.05$) in the premenopausal women compared to the younger men. Plasma TRL and LDL apoB-100 pool sizes were correspondingly lower by 47% and 25% ($p<0.05$), respectively, in the younger women than men. These differences were accounted for by lower TRL and LDL apoB-100 FCR ($p<0.05$), with no significant change in PR. No significant differences were observed in the plasma lipoprotein profile and kinetic parameters between the postmenopausal women and older men. Despite higher plasma HDL-C (50%) and HDL apoA-I (13%) levels in women compared to men, apoA-I pool size was similar, as were the kinetic parameters. In both men and women, plasma TRL-C and LDL-C levels were negatively correlated with TRL apoB-100 FCR ($r=-0.34$, $p=0.02$) and LDL apoB-100 FCR ($r=-0.63$, $p<0.0001$), respectively, but not PR. In conclusion, these data suggest that the mechanism for the lower TRL-C and LDL-C levels and apoB-100 pool sizes observed in premenopausal women was determined predominantly by higher TRL and LDL catabolism or clearance rather than lower production. The similar apoB-100 kinetic profiles between postmenopausal women and older men could explain, in part, the higher CVD risk in men and postmenopausal women relative to younger women.

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Prevalence of Musculoskeletal Pain and Statin Use

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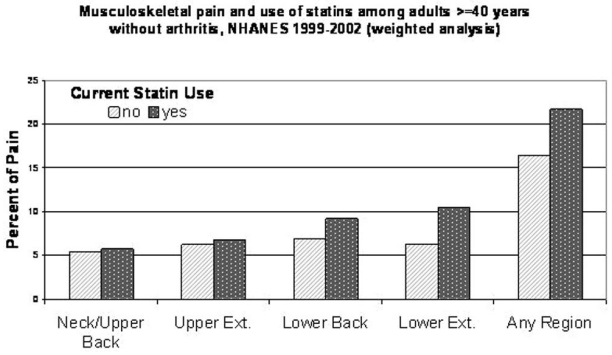
Background: Little is known about the relationship between statin use and the burden of musculoskeletal pain (MSP) in the general population. It remains unclear if use of statins is independently associated with increased MSP. The aim of this study was to evaluate the relationship between statin use and the prevalence of MSP in various anatomical regions in a nationally representative sample. **Methods**: We conducted a cross-sectional analysis of the National Health and Nutrition Examination Survey (NHANES)1999–2002 to estimate prevalence of MSP among adults ≥40y who did not have arthritis. We used multivariable logistic regression to examine the association between statin use and presence of any MSP and MSP at different anatomical regions. **Results**: Among 3606 adults (representing 75 million US adults), 22% (95%CI: 17%, 26%) of those who used a statin reported MSP in at least one anatomical region during the last 30 days, compared with 16% (95% CI: 15%, 18%) who did not use a statin. Particularly strong differences were found in the prevalence of lower back and lower extremity MSP (Figure). Statin use remained significantly associated with any region, lower back, and lower extremity MSP (OR 1.4 (95%CI: 1.1, 2.0); OR 1.6 (95%CI: 1.1, 2.5); OR 1.5 (95%CI: 1.0, 2.5), respectively) after adjusting for age, sex, race, coronary artery disease, hypertension, cholesterol level, diabetes, ankle brachial index, smoking, BMI, physical activity, and health status. **Conclusion**: The prevalence of MSP is high in adults who do not have arthritis. Statin users have a 40 to 60 percent increased likelihood for lower back and lower extremity MSP, after controlling for health and demographic factors.



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Non-High-Density Lipoprotein Cholesterol Is Better than Low-Density Lipoprotein Cholesterol in Explaining the Reduction in First Acute Major Coronary Events with Statin Therapy: A Secondary Analysis of the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS)

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Introduction: Epidemiological studies have suggested that non-high-density lipoprotein cholesterol is better than low-density lipoprotein cholesterol (LDL-C) in predicting cardiovascular risk. However, it is unknown whether non-HDL-C or LDL-C is better at predicting risk reduction in acute major coronary events (MCE's) by statin therapy. **Methods**: Using data from AFCAPS/TexCAPS, we examined the effect of non-HDL-C reduction due to lovastatin, as well as the association of on-treatment non-HDL-C at year 1 with subsequent risk of first MCE's, the primary end point in the trial. We further examined the extent to which the risk reduction of MCE's was explained by on-treatment non-HDL-C, and compared it with that explained by on-treatment LDL-C. **Results**: Among 6605 men and women with an average non-HDL-C of 190 mg/dL at baseline, a decrease of 23% in non-HDL-C at year 1 in the lovastatin arm and a 1% increase in the placebo arm was observed, compared with 25.0% decrease in LDL-C in the lovastatin arm and 1.5% increase in the placebo arm. In placebo patients, baseline non-HDL-C was positively associated with risk of MCE's during follow-up (average 5.2 years); the association was slightly stronger than that of LDL-C with risk of MCE's. In the lovastatin arm, on-treatment non-HDL-C predicted subsequent risk of MCE's better (hazard ratio [HR] 1.80, 95% Confidence Interval [CI] 0.97–3.32 for comparing highest quartile to lowest quartile) than on-treatment LDL-C (HR 1.36, 95% CI 0.73–2.55). Lovastatin reduced the risk of MCE's by 37% after 1 year (HR 0.63, 95% CI 0.48–0.84, $P = .002$). After adjustment for either on-treatment non-HDL-C or LDL-C, this reduction in MCE's by lovastatin was no longer significant. Non-HDL-C explained 41% of the treatment effect of lovastatin compared with 25% explained by LDL-C. Additional analysis confirmed previous findings from this trial that apoB, particularly apoB:apoA-I ratio, better explained the treatment effect of lovastatin than either non-HDL-C or LDL-C, but non-HDL-C was the best among the traditional lipid measures. **Conclusions**: Non-HDL-C is slightly better than LDL-C in explaining the reduction in risk of acute major coronary events by lovastatin in a population of patients with average cholesterol levels.

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Public Health Impact and Cost-Effectiveness of Nationwide Implementation of Different Statin-Prescribing Strategies

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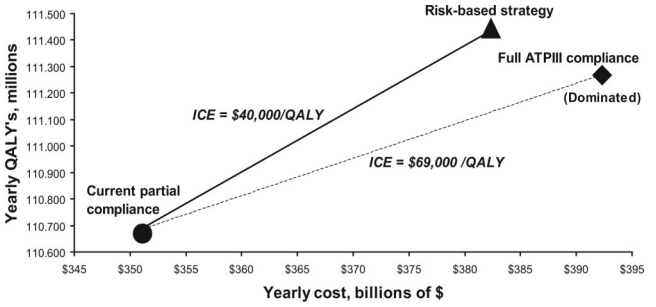
Background: Full compliance with NCEP's Adult Treatment Panel III (ATPIII) guidelines should decrease CHD events, but the full impact and costs of nation-wide implementation have not previously been estimated. **Methods**: We used the CHD Policy Model, a validated state-transition simulation of the coronary heart disease (CHD) epidemic in the US, to model CHD events, costs, quality-adjusted life-years (QALYs), and incremental cost-effectiveness (ICE) of full compliance with NCEP guidelines compared with current partial compliance. Census and national survey data were used to estimate joint distributions of risk factors by age and sex; the CHD risk function was based on Framingham. The cost of statins was set at $806.65/year (generic lovastatin 40mg), or $897.65/year (atorvastatin 80mg, used if already on a statin or requiring secondary prevention), plus $30.90 for lab costs. CHD costs were estimated from a societal perspective. **Results**: The model predicted 866K MI's and 553K CHD deaths each year over the next 30 years. Full APTIII compliance would prevent 162K MI's and 110K CHD deaths/year at an increased cost of $41B/year (ICE=$69,000/QALY). A simple risk-based strategy based on 10-year CHD risk (atorvastatin 80mg if high risk, lovastatin 40mg if 10-year CHD risk between 10–20%) dominated ATPIII, costing $10 billion less and resulting in 50K fewer MI's and 41K fewer CHD deaths each year than full APTIII compliance (Figure). **Conclusions**: Full compliance with ATPIII would result in substantial health benefits for the nation, but at a high price; a simple risk-based strategy would be more effective and less costly.



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Increased Use of Lipid-Lowering Drug Therapy Following Cessation of Hormone Therapy: The Women On the Move through Activity and Nutrition (WOMAN) Study

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Background. The decrease in hormone therapy (HT) usage following the Women's Health Initiative has resulted in an increase in LDLc and, therefore, an increase in the use of lipid lowering therapy. In the current study, we evaluated: 1) effects of diet and exercise on modifying lipoproteins among postmenopausal women in the WOMAN clinical trial initially enrolled while on HT; and 2) subsequent use of lipid lowering treatment and whether this differed by either group assignment or baseline measures of atherosclerotic disease. **Results**. The baseline age was 57 years; 30 month follow-up is reported for 221 in the Lifestyle Change/intervention (LC) and 217 in the Health Education/control (HE). By 30 months, 101 (23%) were still on HT, 160 (36.5%) had stopped within the first few months after randomization, and the remaining 173 (39.5%) had stopped prior to randomization. There were 34 (16%) women in the HE and only 8 (4%) in the LC group on lipid lowering therapy at 30 months. Most women on lipid lowering therapy had stopped HT. At 30 months, LDLc increased approximately 13 mg% for the women in the HE group not on lipid lowering therapy as opposed to a 3 mg% increase in the LC group ($p=0.002$). LDLc at baseline was 137 mg% in the HE group for those who started lipid lowering therapy, increasing to 144 mg% at 6 months, and was 95 mg% at 30 months. For women in the HE group who had never started lipid lowering drug therapy, baseline LDLc was 127 mg%, increased to 134 mg% at 6 months and 140 mg% at 30 months. We measured coronary artery calcium (CAC) at baseline and found no relationship with CAC and use of lipid lowering therapy. In the 34 HE group women who were on lipid lowering drug therapy, 27 had CAC <10 Agatston units and only 2 women had scores >100. Similarly, there was no significant relationship between carotid IMT or carotid plaque at baseline and subsequent use of lipid lowering therapy. **Conclusions**. Large numbers of postmenopausal women are being placed on lipid lowering therapy probably due to elevations of LDLc related to discontinuation of HT. Most have minimal atherosclerotic disease. There is no clinical trial evidence of either benefit or lack of benefit of such drug therapy for these postmenopausal women. Such a trial is probably needed, as diet intervention alone may not lower LDLc enough.

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The Significance of Triglyceride-Rich Atherogenic Lipoproteins in Predicting Future Cardiovascular Events

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Background: Current guidelines for cardiovascular disease prevention recommends serum triglyceride levels and non-HDL cholesterol as secondary targets of management after achieving LDL cholesterol goals. However, it remains unclear how aggressive or successful physicians are with the recommendations. Compliance to the recommendations may be important because despite proven benefits of reducing LDL cholesterol, event rates among treated individuals remain substantial. Our purpose was to evaluate the prognostic significance of triglyceride rich atherogenic lipoproteins in predicting future cardiovascular events in young to middle aged adults undergoing elective coronary angiography. **Methods**: Subjects undergoing elective coronary angiography (n=253) without prior diagnosis of coronary heart disease

or on statins were prospectively enrolled. Men <55 and women <65 were included. Subjects consented to fasting blood drawn for lipoprotein analysis by NMR (Liposcience, Raleigh, NC) and risk stratification prior to the procedure, and were followed over time. Severe coronary artery disease (CAD) was defined as stenosis ≥50%. Major cardiovascular events were defined as death, myocardial infarction (MI), and cerebral vascular accident (CVA). **Results**: Complete data was available on 235 subjects (mean age was 53±8; 55% women [130 of 236]). Mean cholesterol values were: total 207±42 mg/dL; LDL 122±30 mg/dL; HDL 51±14 mg/dL and triglyceride 171±121 mg/dL. Severe CAD was diagnosed in 72. Median follow-up was 32 months. Twelve major events developed in 10 subjects (death=3, MI =5, CVA=4). Mean values for total, LDL and HDL cholesterol were not different in subjects suffering events compared to those who did not. In contrast, Cox proportional hazard analysis revealed increased risk for events with interquartile analysis for triglycerides (HR:4.7,CI:1.3–16.6); VLDL (HR:4.8,CI:1.4–17.0) and LDL particle concentration (HR:4.7,CI:1.3–16.7). **Conclusion**: Atherogenic lipoproteins may play importance role in improving coronary heart disease (CHD) prevention. Physician compliance with guideline recommendations on managing triglyceride and non-HDL cholesterol may be crucial for making further progress in CHD management.

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Low Plasma HDL Cholesterol: Is It Also a Risk Factor for Lung Cancer?

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Objective: The objective of this study was to examine prospectively the association of baseline plasma high density lipoprotein cholesterol (HDL-C) with incident lung cancer in members of the Atherosclerosis Risk in Communities (ARIC) cohort. **Methods**: The sample consisted of 14,793 ARIC participants, aged 45–65, who received a diagnosis of lung cancer from 1987 to 2000. Lung cancer cases were ascertained through medical records review and linkage to state cancer registries. Association of low HDL-C (men: <40 mg/dL, women: <50 mg/dL) and 259 incident lung cancer cases was estimated using Cox proportional hazard models adjusted for age, race, gender, body mass index, smoking status, pack-years of cigarette smoking, triglycerides, physical activity, and alcohol consumption at baseline. **Results**: Low HDL-C was associated with an increased incidence of lung cancer in the total sample ((Hazard Ratio (HR): 1.45, 95% confidence interval (CI) 1.10, 1.92) and among former smokers (HR: 1.77, 95% CI 1.05, 2.97), but not among the current smokers (HR: 1.04, 95% CI 0.74, 1.47). The number of lung cancer cases among never smokers in this study was too small (n=13) for separate determination of associations. Unadjusted lung cancer incidence was inversely associated with HDL-C as a continuous variable, however the trend for this association was not significant after adjustment for covariates (total sample HR: 0.92, 95% CI 0.78, 1.08, former smokers HR: 0.87, 95% CI 0.62 1.22). Elimination of cases occurring within five years of baseline did not appreciably change the point estimates, suggesting lack of reverse causality. **Conclusion**: The strength of smoking as a risk factor for lung cancer among the current smokers may mask an association with HDL-cholesterol. Smoking decreases plasma HDL-C levels, further reducing the likelihood of making a meaningful estimate of the association in that sample group. The modest association of low plasma HDL-C, a traditional cardiovascular disease risk factor, with greater incident lung cancer underscores potential similarities in etiologies of cancer and cardiovascular disease and the importance of antioxidant and other protective properties of HDL-cholesterol.

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Comparison of Paraoxonase Activity Between Groups of Healthy Adults and Individuals Showing Lipid Disorders

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Paraoxonase (PON1) is a high density lipoprotein (HDL)-associated esterase capable to protect low density lipoprotein (LDL) from oxidative modifications, which is known to be associated with the early steps of atherogenesis. PON1 activity may also be modulated by dietary, lifestyle and environmental factors. The aim of our study was to describe PON1 activity in a group of healthy volunteers in comparison to a group of individuals showing lipid disorders and to investigate whether diet and lifestyle might affect this activity. We studied 40 healthy and 27 volunteers with abnormal levels of triglycerides, LDL, HDL or total cholesterol. The variables studied included basal and salt stimulated PON1 activity, arylesterase activity (both tested as described by Eckerson and La Du), serum cholesterol, HDL, LDL, VLDL and triglycerides. Other variables such as energy consumption and nutrients intakes were assessed from a validated food consumption frequency questionnaire. Correlation analysis, T test and ANOVA were used for statistical analysis. We stratified groups setting cut off points from quartile distribution of paraoxonase activity. Using this approach, we have observed significant associations between higher PON1 activity levels and high LDL (p=0,007), and high total cholesterol (p=0,053) levels. We have also stratified groups setting recommended dietary intakes as cut off points. Using this approach, no associations were observed between PON1 activity and nutrient intakes. When groups were dichotomized using the first quartile from PON1 activity distribution as a cut-off, there were significant associations between lower levels of PON1 and higher intakes of carbohydrate, total fat and cholesterol. Our results show that association between high paraoxonase activity and higher levels of LDL and total cholesterol might be a reflection of paraoxonase gene polymorphism since alleles associated with atherosclerosis and coronary heart disease are those associated with paraoxonase high activity using paraoxon as substrate. Our study also shows that diet may affect PON1 activity and points out the need of more studies since little is known about environmental interactions with PON1 gene polymorphism in the multiethnic Brazilian population.

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Plasma Lipid Concentrations in Nondiabetic African-American Adults: Associations with Insulin Resistance and the Metabolic Syndrome

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Background: The metabolic syndrome, a condition of multiple cardiovascular risk factors linked with underlying insulin resistance, markedly increases the risk for cardiovascular disease (CVD). African Americans have higher rates of CVD and diabetes mellitus (DM), despite a lower prevalence of the metabolic syndrome. African Americans tend to have more favorable concentrations of plasma lipids compared to Caucasians. Metabolic syndrome may be under diagnosed in African Americans because they are less likely to meet criterion for elevated triglycerides (TG ≥150 mg/dL). The purpose of this study was to examine the association between plasma lipid concentrations and insulin resistance in African Americans and to determine if insulin resistance is present at a lower TG threshold. **Methods**: Data were examined on 185 non-diabetic African American men (N=61) and women (N=124), having a mean age of 39.8 years, who were enrolled in a previous study on blood pressure and insulin sensitivity. Measurements included blood pressure, anthropometrics, oral glucose tolerance test, and insulin sensitivity (M), quantified by insulin clamp procedure. The relationship between plasma lipid concentrations and insulin sensitivity was analyzed by correlation analysis and by comparing triglyceride levels among tertiles of M. The applicability of different TG thresholds was examined by stratification of the sample by TG concentrations. **Results**: Despite relatively low mean TG (87.8±55.2 mg/dL), there were statistically significant correlations of M with TG (r = -.23, P<0.002), high density lipoprotein cholesterol (HDL-C; r =.19, P < 0.01)), and TG/HDL-C ratio (r = -.23, P<0.002). Subjects with TG in an intermediate range (110–149 mg/dL) had insulin resistance equivalent to the high TG group (≥150 mg/dL). Using the TG threshold of ≥110 mg/dL in place of the current TG criterion (≥150 mg/dl), the rate of metabolic syndrome in the most insulin resistant group increased from 35% to 52%. **Conclusions**: In African Americans, triglyceride levels below the current metabolic syndrome threshold criterion are associated with insulin resistance.

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Apolipoprotein B Predicts Good In-Hospital Outcome in Acute Coronary Syndromes Patients

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Background: Lipid profile influences long term prognosis in acute coronary syndromes (ACS) patients. However, few studies have been performed to evaluate the impact of lipid dismetabolism regarding in-hospital (IH) events. **Aim**: To evaluate the prognostic value of Apolipoproteins (Apo) A1 and B on IH mortality in ACS patients. **Methods**: Retrospective analysis of a database with 501 patients admitted for ACS in a single coronary care unit between May 2004 and September 2005. ApoA1 and B were determined the day after admission, during fasting period. Their values were divided into quartils. We used chi-square test, ROC curve and multivariate analysis for statistical treatment. **Results**: Patients were mainly of male gender (69.9%) with mean age of 67.2±12.5 years. Mean ApoA1 value was 122.3±24.9 mg/dl and ApoB 103.0±29.2 mg/dl. Previous statin therapy was significantly higher in ApoB quartil with the highest mortality rate (p 0.003). There was an inverse relationship between IH mortality and ApoB values (table 1), while with ApoA there was no relationship. The area under the curve was 0.75 for ApoB, revealing a good discriminatory capacity for predicting death (p<0.001). Multivariate analysis showed that ApoB was an independent predictor of good IH prognosis. **Conclusion**: Many studies have already showed that ApoB is associated with an increased long-term cardiovascular (CV) risk while Apo A1 confers CV protection. However, in our series, ApoB was an independent predictor of good IH prognosis in ACS patients (even accounting for statins) and ApoA1 did not show any predictive value.

Table 1 - Results

Apo B (mg/dl)	IH mortality rate (%)	P=0.005
[33–83[	9.6	
[83–100[	3.1	
[100–121[	1.6	
[121–210[	0.8	
Apo A (mg/dl)	**IH mortality rate** (%)	**P=n.s.**
[31–107[	3.4	
[107–121[	3.2	
[121–137[	5.2	
[137–228[	2.9	

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Provider Knowledge Deficit of the Adult Treatment Panel III 2004 Update

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CHD is the leading cause of mortality in the United States. Clinical trials show that lowering cholesterol levels can reduce all-cause mortality. Despite established cholesterol guidelines only 57% percent of persons in the United States at high risk for CHD attained their recommended LDL cholesterol goal according to 2003 data. The same study applied the optional goals identified in the 2004 update to the ATP III, and found that only 18% of those at very high risk for CHD met the LDL-C goal. One factor that may limit guideline adherence is knowledge of the guidelines; however, no recent reports were found that measured knowledge of cholesterol guidelines. The purpose of this study was to assess MDs', ARNPs', and PAs' knowledge of the 2004 ATP III update, and to test the hypothesis that knowledge levels of of the updated ATP III guidelines were the same between provider groups. The study employed a non-experimental descriptive design using a 21 item original questionnaire. A

convenience sample consisted of physicians, ARNPs, and PAs in attendance at continuing nursing and medical education events in Seattle during spring 2006. Data was analyzed using descriptive statistics; one-tailed and two-tailed *t*-tests were used to compare total scores of provider groups. Of the 212 attendees, 96 submitted useable questionnaires. Seventy six of the providers were ARNPs, 16 were MDs, and 4 were PAs. Half of all subjects (57 of 96) and 94% (14 of 16) of the MDs, practiced in primary care fields and 36% (35 of 96) of the subjects provided care to women only. The total scores ranged from 20% (3 out of 15) correct to 93% (14 out of 15) correct, with a mean total score of 54% (8 out of 15). Physicians scored significantly ($p<.001$) higher than ARNPs. Mean total scores varied between providers in primary care (61%) versus non-primary care specialties including women's care (46%), but were not analyzed due to uncontrolled variables. In conclusion, 96 providers scored only 54% on an original questionnaire to assess their knowledge of the 2004 update of the ATP III cholesterol guidelines. ARNPs scored significantly lower than MDs indicating a need for both additional continuing education and a thorough examination of the current curriculum on lipid management and CHD prevention among ARNP training programs.

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The Safety of Grapefruit Juice in Patients Taking Atorvastatin

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Background: Five days of grapefruit juice (GFJ) use can elevate single-dose Atorvastatin (ATOR) levels. The safety of long term GFJ plus ATOR use has not been reported. **Methods**: The study measured (entry, 30, 60, and 90-day) lipid profiles, liver and skeletal muscle toxicity, ATOR drug levels, and quality of life (QOL) for 154 patients on chronic ATOR (10, 20, or 40 mg) plus daily 10 ounce GFJ. Enrollment alternated between Group A (usual ATOR dose) or Group B (½ usual ATOR dose). Lipid profiles included total cholesterol, LDL, HDL, and triglycerides. Potential toxicity was assessed by alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatine phosphokinase (CPK), QOL scores, myalgia score, memory score, and ATOR drug levels. **Results**: ATOR levels increased 37.3% (95% CI, 12.2–67.9%) in Group A and decreased 22.2% (95% CI, 4.0–33.6%) in Group B. The changes in ALT, AST, CPK, myalgia score, memory score, and QOL score were not significant. LDL decreased in all three Group A doses (10 mg: $p=0.09$, 20 mg: $p=0.26$, 40 mg: $p=0.04$) and increased in all three Group B doses (½ 10 mg: $p<0.0001$, ½ 20 mg: $p<0.01$, ½ 40 mg: $p=0.22$). For subgroup "full dose 40 mg ATOR", the LDL decreased from 94.4 to 80.8 mg/dl over 90 days. For subgroup "½ 40 mg ATOR", the LDL increased from 94.9 to 98.9 mg/dl over 90 days. Non-significant reductions in HDL occurred for all subgroups. **Conclusions**: Addition of 90 days of daily GFJ to chronic ≤40 mg ATOR: a) increased bioavailability of ATOR for full dose ATOR; b) produced a trend in LDL reduction for full dose ATOR; c) did not compensate for a 50% reduction in ATOR dose, and d) did not produce skeletal muscle toxicity, hepatic toxicity, or reduce QOL.

P200

Relationships Between Coronary Artery Disease and Serum Lipid Concentrations and Preventive Effects of EPA in Hypercholesterolemic Patients: The Japan EPA Lipid Intervention Study Subanalysis of Total Population

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Introduction: The Japan EPA Lipid Intervention Study (JELIS) was a randomized control trial over five years examining the effect of pure (>98%) eicosapentaenoic acid (EPA) in preventing coronary artery diseases (CAD) in hypercholesterolemic patients (total cholesterol 250mg/dL or higher). The patients received statin only (Control group: n=9,319) or statin plus 1,800 mg/day EPA (EPA group: n=9,326). Major results, presented at the American Heart Association Scientific Sessions 2005, showed EPA significantly reduced the incidence of CAD by 19%. **Methods**: We analyzed relationships between incidence of CAD and serum lipid levels, and preventive effects of EPA. We divided the subjects into quartiles based on serum lipid levels at the first year (TC, LDL-C, HDL-C, TG, Non-HDL-C, and TC/HDL-C ratio), and the correlation with incidence of CAD was analyzed by Cox proportional hazard regression. **Results**: When serum lipid levels at the smallest quartile were taken as the standard, the incidence of CAD in the Control group was significantly elevated at the largest quartile LDL-C, Non-HDL-C, and TC/HDL-C ratio. With the smallest quartile LDL-C (lower than 114 mg/dL) as the standard, the incidence of CAD was significantly elevated at the largest quartile (157 mg/dL or higher) with hazard ratio 1.50 ($P=0.026$, 95%CI: 1.05–2.15). Taking the largest quartile HDL-C (68 mg/dL or higher) as the standard, the incidence of CAD was significantly elevated at the smallest quartile (lower than 47 mg/dl) with hazard ratio 2.19 ($P=0.0002$, 95%CI: 1.44–3.33), and at the second quartile (47–56 mg/dL) with hazard ratio 1.98 ($P=0.001$, 95%CI: 1.31–2.99). For low HDL-C, the incidence of CAD was significantly lower in EPA group, HR was 0.73 ($P=0.034$, 95%CI: 0.54–0.98) at the smallest quartile (lower than 47 mg/dL), and 0.62 ($P=0.004$, 95%CI: 0.45–0.86) at the second quartile (47–56 mg/dL). The incidence of CAD in EPA patients was significantly lower in low HDL-C group. **Conclusions**: The incidence of CAD was significantly higher in high LDL-C, Non-HDL-C and TC/HDL-C ratio groups and in low HDL-C groups. Highly purified EPA demonstrated very strong preventive effects on the incidence of CAD in low HDL-C groups.

P201

Optimal Lipid Value Achievement in Older Women Utilizing Extended-Release Niacin/Lovastatin

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Background: High CHD risk women frequently have complex dyslipidemia, and rarely attain evidence-based optimal values for lipids or receive recommended therapy. Prevention and treatment data specifically in elderly women are sparse. **Methods**: Female patients were selected from a 2.1 M member managed care database based on the following criteria: lipid panel present between 1/1/00 and 12/31/01, no concomitant dyslipidemia therapy, ≥24 months of continuous plan eligibility; and CHD risk (by diagnosis/procedure code). Initial lipid values from each patient were assessed for individual and combined LDL-C, HDL-C and TG and non-HDL-C optimal lipid value (OLV) attainment based upon the 2004 AHA women's cardiovascular disease prevention guideline, and population treatment effects of extended-release niacin/lovastatin 2000/40 mg (ERN/L) were modeled using current product labeling. **Results**: Analysis included 22,006 females: mean (±SD) age 66±13 yrs, secondary prevention 46%, primary prevention 54%, hypertension 70%, diabetes 18%, and metabolic syndrome 56%. Lipids at baseline (BL; mg/dL): TC 219±40; LDL-C 135±36; HDL-C 54±15; TG 155±74; non-HDL-C 166±40. **Conclusions**: As women at-risk for CHD age, there is a trend for increasing HDL-C and decreasing TG at optimal lipid values; however the number of patients requiring therapy targeting LDL-C, HDL-C and TG remains high. The majority of women at all ages are projected to achieve individual and combined optimal lipid values with ERN/L therapy.

	AGE (Years)					
	<65	65 to 69	70 to 74	75 to 79	80 to 84	≥85
	BL→ERN/L	BL→ERN/L	BL→ERN/L	BL→ERN/L	BL→ERN/L	BL→ERN/L
LDL-C (% OLV)	33 → 75	33 → 74	31 → 74	29 → 73	29 → 75	32 → 74
HDL-C (% OLV)	40 → >99	50 → >99	53 → >99	55 → >99	57 → >99	56 → >99
TG (% OLV)	55 → 73	53 → 72	54 → 73	55 → 76	58 → 78	64 → 81
Non-HDL (% OLV)	34 → 87	32 → 85	32 → 87	31 → 84	31 → 86	36 → 86
Combined LDL- C, HDL-C & TG (% OLV)	9 → 55	11 → 54	12 → 55	12 → 56	13 → 60	16 → 62

All modeled ERN/L groups are significantly different from baseline by chi-squared for optimal lipid value ($p<0.0001$)

P202

Prevalence of Clinical and Emerging Lipid Risk Factors in Individuals with a Family History of Premature Coronary Heart Disease but Low Framingham Risk Score

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Introduction: Individuals with a family history of premature coronary heart disease (CHD) are at high risk of developing cardiovascular (CV) disease themselves. However, recent studies suggest that standard risk factors do not accurately predict CV risk in these individuals. The goal of this study was to determine the prevalence of emerging clinical and lipid risk factors in individuals with a family history of premature CHD but a low Framingham risk score. **Methods**: We prospectively evaluated 69 patients; 20 men (mean age 45 years) and 49 women (mean age 48 years) with a family history of premature CHD who were free from cardiovascular disease and had a 10-year Framingham risk score of <10%. We excluded patients with diabetes mellitus. Individuals were screened for levels of high sensitivity C-reactive protein (CRP), coronary calcium using EBCT scanning and the metabolic syndrome as defined by ATP III. Levels of Lp(a) and lipid subclasses were measured by density gradient ultracentrifugation using the Vertical Auto Profile cholesterol test. **Results**: A positive coronary calcium score was present in 33% of the study group, CRP >3 mg/L in 33%, while 12% had the metabolic syndrome. With regards to emerging lipid risk factors, 19% had small dense LDL-C, 30% had high levels of Lp(a), 38% had high levels of remnant lipoproteins (IDL and $VLDL_3$) and 74% of study patients had low levels of HDL_2. Only 29% of patients qualified for LDL lowering drug therapy based on the ATP III guidelines. **Conclusion**: The Framingham risk score poorly predicts CV risk in persons with a family history of premature CHD. In these patients the prevalence of subclinical CHD is high as is the presence of other emerging risk factors. The most prevalent lipid risk factor was low levels of HDL_2. Individuals with a family history of premature CHD may benefit from screening for emerging risk factors to better assess their CV risk.

P203

Renal Dysfunction Is Inversely Correlated to Apolipoprotein A1 Levels in Acute Coronary Syndrome Patients

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Background: Dyslipidaemia is one of the major risk factors for cardiovascular diseases. Renal dysfunction, usually related not only with dyslipidaemia but also with other cardiovascular risk factors, is associated with a worse prognosis in acute coronary syndrome (ACS) patients. **Aim**: To evaluate the relationship between renal dysfunction and lipid profile in ACS patients. **Methods**: Retrospective analysis of a database containing 553 patients admitted for ACS in a single coronary intensive care unit between May 2004 and December 2005. Renal function was determined by the first serum creatinine available since hospital admission and lipid profile was evaluated by apolipoproteins (Apo) A1 and B available the day after admission, during the fasting period. Creatinine values were divided into quartiles. **Results**: Patients were mainly of male gender (70%), with a mean age of 67.4±12.5 years. Previous history of hypertension was present in 70.4% of patients, dyslipidaemia in 68%, diabetes in 30.2%, smoking habits in 18.1% and family history of coronary disease in 11.4%. Spearman correlation test shows a significant decrease in ApoA1 levels as creatinine levels increase (p value < 0.001); the same occurs if we considerer maximum creatinine levels instead of initial ones. **Conclusion**: Our data reveal a strong relationship between

impaired renal function and a worse lipid profile, reinforcing the usefulness of creatinine and Apo A1 as important prognostic markers in ACS patients.

P204

TIMI Risk Score Is Inversely Correlated to Apolipoprotein A1 Levels in Acute Coronary Syndrome Patients

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Background: The influence of TIMI risk score and lipid profile in the prognosis of acute coronary syndromes (ACS) patients is well known. However, the relationship between lipid profile markers and the TIMI risk score in ACS patients is not established. **Aim**: To evaluate the relationship between TIMI risk score and Apolipoprotein A1 in ACS patients. **Methods**: Retrospective analysis of a database containing 613 patients admitted for ACS in a single coronary intensive care unit between May 2004 and December 2005. Lipid profile was evaluated by apolipoproteins (Apo) A1 and B, determined the day after admission during the fasting period. **Results**: Patients were mainly of male gender (70.6%) with mean age of 67.3±12.4 years. Previous history of hypertension was present in 71.1% of patients, dyslipidaemia in 67.9%, diabetes in 29.9%, smoking habits in 17.3% and family history of coronary disease in 11.7%. We observed a significant decrease in ApoA1 levels as the TIMI risk score increases, ranging from 136.8±27.2 mg/dL in TIMI score 0 to 101.4±22.6 mg/dL in TIMI score 7 (p value for Kruskal Wallis test = 0.002). There was also a decrease in ApoB levels, although less pronounced, from 112.1±33.6 to 93.8±39.9 mg/dL (p value for Kruskal Wallis test = 0.04). **Conclusion**: Our data reveal a strong relationship between TIMI risk score and ApoA1 (and B) levels, reinforcing the usefulness of both prognostic markers in ACS patients.

P205

Sleep-Disordered Breathing Is Associated with Elevated Blood Pressure in Children

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Studies in adult populations have consistently demonstrated significant adverse effects of sleep apnea on blood pressure (BP) and hypertension. However, such association has not been reported in children. We examined the cross-sectional association between sleep apnea and BP in a population-based random sample of 556 school-aged children using a two-phase protocol. The first phase surveyed parents for general information of their children in selected elementary schools (response rate 80%.) The second phase evaluated a subsample for a single night with polysomnography (response rate of 70%). Apnea/hypopnea index (AHI, event / hour) was assessed as follows: airflow using both thermistor and pressure; effort using thoracic and abdominal strain gauges; and snoring using a throat microphone. The mean (SD) age of participants was 110.6 (10.6) months, with 50% females and 27% snorers. The average AHI (SD) was 0.52 (0.75) event / hour, and it was higher among snorers 0.71 (0.95) than non-snorers 0.47 (0.63) ($p = 0.001$). We further classified participants into three levels of sleep apnea according to AHI: No-Apnea if AHI=0 (N=164), mild apnea if 0<AHI<1 (N=308), and moderate to sever apnea if AHI ≥1 (N=84). The weighted ANCOVAR models were used to assess the multivariable adjusted mean levels of systolic BP (SBP), diastolic BP (DBP), and their standard errors (SE) according to sleep apnea levels, stratified by snoring status (Table 1). There is dose-response relationship between the degree of sleep apnea and both SBP and DBP among snorers, but not among non-snores. **Conclusions**: Sleep Apnea as measured by AHI is significantly and monotonically associated with elevated BP among snorers, independent of BMI, height, sex and age, even in this healthy population-based sample of young children.

Table 1. Age, Sex, Height, and BMI Adjusted Means (SE) of SBP and DBP According to Sleep Apnea Leve

Apnea Level	Snoring = Yes SBP (SE)	**Snoring = Yes** DBP (SE)	**Snoring = No** SDB (SE)	**Snoring = No** DBP (SE)
No-Apnea	110 (1.84)	64 (1.37)	109 (0.94)	65 (0.73)
Mild Apnea	115 (1.18)	68 (0.88)	112 (0.69)	65 (0.54)
Moderate to Severe Apnea	117 (2.02)	69 (1.51)	111 (1.35)	66 (1.05)
p-value for linear trend	<0.05	<0.05	0.16	0.98

P206

Adult-onset Asthma Is Associated with Incident Stroke and Coronary Heart Disease Among Women in the Atherosclerosis Risk in Communities (ARIC) Study

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Introduction Studies suggest asthma is associated with atherosclerosis and that the association is limited to or stronger among women. However, asthma is a heterogeneous disease with clinically distinct subtypes. Adult onset asthma (AOA) and child onset asthma (COA) differ in regards to systemic inflammation and gender distribution. We used data from the Atherosclerosis Risk in Communities (ARIC) Study to test whether adult onset asthma and child onset asthma are associated with incident coronary heart disease (CHD) and stroke and whether these associations differed by gender. **Methods** Subjects were classified as ever having AOA (onset age ≥21 years) or COA (onset age <21 years) by self report of physician diagnosis and age of onset. Incident ischemic and hemorrhagic strokes, myocardial infarctions, and fatal CHD events were identified through death certificates and hospital records during follow-up. Subjects with CHD at baseline were excluded from analysis of CHD outcomes. We used Cox proportional hazards models to adjust for age, race, smoking status and packyears, lipid profile, diabetes, hypertension and physical activity and tested effect modification by gender. **Results** AOA, but not COA, was a significant risk factor for both incident CHD and stroke in women. After adjustment, women with AOA had 80% higher risk of CHD and > twofold higher risk of stroke (Table). This association was not observed among men. The gender interaction was significant for both CHD ($p<0.10$) and stroke ($p<0.01$). **Conclusion** Adult onset asthma is associated with incident CHD and stroke among women but not men. If our results are verified in another cohort, adult onset asthma would represent a common and moderately strong risk factor for atherosclerosis in women.

Sex-Specific Association of Child and Adult Onset Asthma with Incident CHD and Stroke

Outcome	Analysis Type	Male No History of Asthma	Male *Child Onset Asthma*	Male *Adult Onset Asthma*	Female No History of Asthma	Female *Child Onset Asthma*	Female *Adult Onset Asthma*
Myocardial Infarction or Fatal CHD	Crude Hazard Ratio (95% CI)	*1.0 (Ref)*	1.34 (0.85, 2.10)	0.94 (0.49, 1.82)	*1.0 (Ref)*	1.15 (0.54, 2.44)	2.21 (1.37, 3.57)
Myocardial Infarction or Fatal CHD	Multivariable Adjusted Hazard Ratio (95% CI)	*1.0 (Ref)*	1.44 (0.92, 2.26)	0.80 (0.41, 1.56)	*1.0 (Ref)*	1.01 (0.48, 2.15)	1.82 (1.14, 2.92)
Stroke	Crude Hazard Ratio (95% CI)	*1.0 (Ref)*	0.72 (0.50, 1.04)	0.38 (0.20, 0.70)	*1.0 (Ref)*	1.64 (1.19, 2.25)	2.58 (2.07, 3.23)
Stroke	Multivariable Adjusted Hazard Ratio (95% CI)	*1.0 (Ref)*	0.84 (0.37, 2.04)	0.33 (0.08, 1.13)	*1.0 (Ref)*	1.46 (0.72, 2.96)	2.14 (1.30, 3.53)

P207

Pericoronary Epicardial Adipose Tissue Is Strongly Related to the Metabolic Syndrome: A Population-Based Study

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Background: Epicardial Adipose Tissue (EAT) is a layer of visceral fat between the myocardium and the pericardium. It is a rich source of bioactive molecules directly surrounding the coronary arteries. EAT is associated with common cardiovascular risk factors; however, it is unknown whether an increased prevalence of peri-coronary EAT is associated with the metabolic syndrome. **Methods**: We performed a cross-sectional study among 573 healthy postmenopausal women. Detailed information on vascular risk factors was obtained by questionnaire and during a visit at the research center. Metabolic syndrome was assessed using the National Cholesterol Education Program Adult Treatment Panel III (NCEP) definition. EAT was determined on the CT scans in the areas of right (RCA), left anterior descending (LAD) and circumflex coronary artery (LCX). At each of these sites the area of EAT on transverse sections was measured. A logistic regression model was used to assess the relations. **Results**: Women were between 57 and 81 years of age (average 67±5). Average EAT area was 236.9±170.2 mm^2 (range 90.7, 3207.0) for the RCA area, 182.6±122.7 mm^2 (range 30.7, 908.4) for the LAD area and 192.4±80.5 mm (range 29.7, 519.9) for the LCX. Overall average EAT area was 236.8±94.9 mm^2 (range 66.7, 1152.8). In 26.6 % of women the metabolic syndrome was present. EAT was positively related to age ($p=0.01$). In age-adjusted logistic regression models the risk of the presence of the metabolic syndrome was 4.1 [95% CI 2.3;7.3) times higher in those in the upper quartile of EAT distribution compared to the lowest quartile of the distribution. There was a graded relation between the number of metabolic syndrome factors and peri-coronary EAT. **Conclusion**: Peri-coronary EAT shows a strong relation with the metabolic syndrome. Our findings support the hypothesis that peri-coronary EAT reflects metabolically active fat.

P208

Separate and Combined Impact of Albuminuria and Kidney Function on Risk of Coronary Heart Disease in the Atherosclerosis Risk in Communities (ARIC) Study

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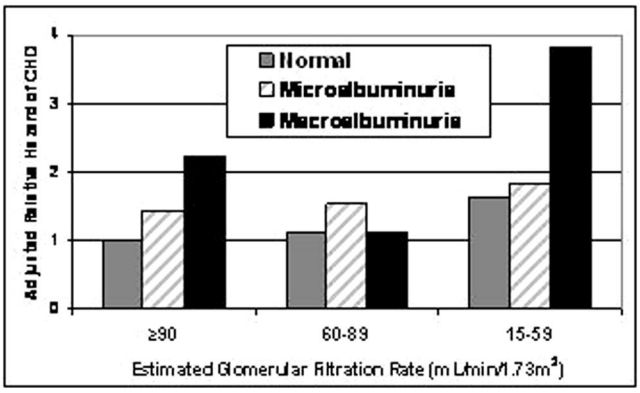
Decreased kidney function and albuminuria are used in combination to define chronic kidney disease (CKD), but their combined effects on coronary heart disease (CHD) have not been studied in the general population. Urinary albumin and creatinine concentrations were measured in 10,212 ARIC Study participants, who were then followed for CHD events (myocardial infarction or fatal CHD). Glomerular filtration rate (eGFR) was estimated from serum creatinine concentration and categorized as 15–59, 60–89 or 90+ ml/min/1.73m2. Urinary albumin-to-creatinine ratio (ACR) was categorized as normal, microalbuminuria (30–300 mg/g), or macroalbuminuria (>300 mg/g). Hazard ratios were adjusted for major coronary heart disease risk factors, including prevalent CHD. Microalbuminuria was present in 608 participants (6.0%) and macroalbuminuria in 141 (1.4%). A total of 352 CHD events occurred over a median of 5.3 years of follow-up. Examined separately, low eGFR (15–59 ml/min/1.73m2) was associated with higher CHD risk (RH=1.7; 95% confidence interval: 1.2–2.5), as was a doubling of ACR (RH=1.1; 1.1–1.2). Low eGFR predicted CHD in the absence of albuminuria (RH=1.6; 1.0–2.5), as did a doubling of ACR among individuals with normal GFR (RH=1.1; 1.1–1.2). Risk increased with decreasing eGFR across all categories of albuminuria, and with increasing ACR across all categories of GFR. Findings were similar after stratification

by diabetes status. Decreased kidney function and albuminuria independently predict CHD events in the general population. These data support recent recommendations defining CKD and stratifying risk based on both decreased kidney function and albuminuria.



P209

Short Sleep Duration and Obesity: Meta-Analyses of Epidemiological Observational Studies

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Background: Recent epidemiological studies have suggested that insufficient night time sleep duration may be an important risk factor for the development of obesity in both adults and children. **Objectives**: Meta-analyses of published studies to assess whether there is evidence of a relationship between short sleep duration and obesity and to obtain a quantitative estimate of the risk, among both adults and children. **Methods**: We performed a systematic search of publications, according to Cochran's standard review methodology up to August 2006. Authors were contacted by email and were asked to provide raw data to allow conclusion. Two meta-analyses were then performed for both adults and children, separately. Results were pooled using a random-effect model. We also carried out sensitivity analyses. Heterogeneity publication bias was also checked. **Results**: Sixteen studies were included in the pooled analysis (7 including adults n=507972 and 9 children, n=28337) and included men and women from around the world. Short sleep duration was defined as equal to or less than five hours of sleep per night and obesity as BMI above 30kg/m^2. The pooled estimate of the odds ratio (OR) was 1.84 (1.44, 2.35) for adults and 1.90 (1.41, 2.55) for children. There was no evidence of publication bias for both adults (p=0.37) and children (p=0.17). Heterogeneity was significant for both adults (p=0.04) and children (p<0.001). Sensitivity analyses in both adults and children did not completely account for heterogeneity. In four studies in adults the regression co-efficient was also pooled between hours of sleep and units of BMI, leading to the pooled effects of -0.40 (-0.58, -0.21). **Conclusions**: Population-based observational studies show a significant association between short sleep duration and obesity both in adults and in children. The pooled estimates are consistent in suggesting an average two-fold increased risk. Causal inference is difficult due to lack of control for confounders. Prospective evidence however, suggests a possible temporal sequence and biological mechanisms would support a possible causal relationship.

P210

Association Between Serum C-peptide Levels and the Risk of Cardiovascular Disease in Nondiabetic Individuals: Data from the National Health and Nutrition Examination Survey, 1999–2004

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Background and Aims: Evidence has been published linking insulin resistance with cardiovascular disease. The aim of this study was to investigate the association between insulin resistance, as measured by fasting C-peptide levels, and the risk of cardiovascular disease (CVD) in a representative sample of the US population with no history of diabetes. **Methods**: Analysis included 14,031 (non-Hispanic Whites, n = 7,169; non-Hispanic Blacks, n = 2,820; and Mexican American and other Hispanic, n = 4,042) adult participants age 18 and over who participated in the National Health and Nutrition Examination Survey between 1999 and 2004. CVD was defined as any participant who reported ever being diagnosed by a doctor with coronary heart disease, angina, stroke, or a heart attack. Other variables included systolic and diastolic blood pressures, anthropometric measurements (BMI, height, weight, waist circumference, skinfolds, lean body mass), serum lipids and lipoproteins (total cholesterol, triglycerides, HDL, LDL), C-peptide, HOMA-IR, physical activity, and substance use (cigarette smoking and alcohol consumption). To account for selection probability, weighted logistic regression models were used to evaluate the association between serum C-peptide levels and CVD. **Results**: The number reporting a history of CVD was 1,729 (mean age 45.1±1.4). Logistic regression analysis revealed a statistically significant two-fold increased risk of CVD for subjects in the highest quartile of C-peptide, which persisted after adjusting for age, race/ethnicity, gender, substance use, physical activity, anthropometrics and CVD risk factors (p for trend 0.04; quartile 4 vs. quartile 1, OR 2.02, 95% CI 1.04–3.93). **Conclusions**: We found a significant association between C-peptide levels and CVD after adjusting for multiple CVD risk factors. These preliminary observations suggest that in non-diabetic individuals, CVD risk is increased with increased fasting C-peptide levels. However, widespread clinical usefulness of this risk factor has not been established.

P211

The Epidemiology, Heritability, and Genetic Linkage of C-Reactive Protein in the Jackson Heart Study Cohort

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Background. Current literature on C-reactive protein (CRP) largely has been from white non-Hispanic cohorts. There is limited information on CRP's reference ranges, heritability and relation to cardiovascular disease (CVD) risk factors and disease in African Americans. **Methods**. The study consists of participants who underwent Exam 1 of JHS (2001–2004). The distribution and correlates of CRP concentrations were analyzed for the entire study cohort. Heritability was estimated for the family cohort nested within the larger JHS (235 families, n=1,364). The relations between log-transformed CRP and traditional CVD risk factors were tested with multivariable step-wise regression analyses. Heritability was estimated using mixed-model regression analysis. QTL linkage analysis was performed using the multipoint variance components approach in SOLAR package. **Results**. The study cohort consisted of 5,202 participants (55±13 years, 64% female). The median CRP was 2.7 mg/L. In step-wise models with age and sex forced in traditional risk factors explained 23% of the variability of CRP, with BMI (partial R^2= 12.9%) explaining 57% of the variability of CRP due to traditional risk factors. The heritability for the age, sex and BMI adjusted CRP residual after winsorizing was 0.37 with a standard error (SE) of 0.06 and the heritability for the log transformed CRP residual was 0.45 with a SE of 0.06. The strongest evidence for linkage to CRP was observed on chromosome 3 (maximum LOD score of 2.92) near marker 295YC9P and chromosome 12 (maximum LOD score of 2.01) near marker D12S297. **Conclusion**. In this large population-based cohort of African Americans, CRP concentrations were heritable and associated with several traditional cardiovascular risk factors, and particularly with elevated BMI. Given the relation between inflammation and CVD further research into the genetic and environmental determinants of CRP are merited.

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Red Blood Cell Omega-3 Fatty Acids in Acute Coronary Syndrome Patients

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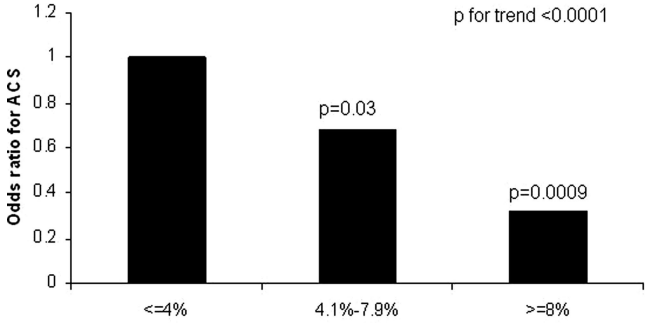
Increased omega-3 fatty acid (n-3 FA) blood levels have been inversely associated with decreased risk for sudden cardiac death, but their relationship with acute coronary syndromes (ACSs) is unclear. We hypothesized that the red blood cell (RBC) content of eicosapentaenoic acid + docosahexaenoic acid (EPA+DHA; the omega-3 index) is reduced in ACS patients. We analyzed the omega-3 index in 768 ACS patients and 768 age-, gender- and race-matched controls. Omega-3 index associations with ACS case status were assessed using multivariable models adjusting for matching variables and educational status, smoking status, alcohol use, diabetes, body mass index, family history of coronary artery disease, personal histories of myocardial infarction, hypertension, and dyslipidemia, and serum lipids. The omega-3 index was 21% lower in cases than controls (3.4±1.6 vs. 4.3±2.0 % of RBC FA, p<0.001). The multivariable-adjusted odds for being an ACS case decreased by 20% (95% CI 11%–26%, p<0.0001) for a 1-unit increase in the omega-3 index. Odds were not altered by exclusion of serum lipids from the model (0.83; 95% CI, 0.77–0.89, p<0.0001). The odds for being an ACS case were greatest in the group with the lowest omega-3 index (≤4% of RBC FA), and decreased by 25% in the intermediate group (4.1%–7.9%) and by 68% in the highest omega-3 index group (≥8% of RBC FA; Figure). These data suggest that a low omega-3 index may be independently associated with increased risk for ACS.



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Association of Inflammatory Marker Levels and Platelet Aggregability in Families with Premature Coronary Disease

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Background: Plasma levels of the inflammatory markers C-reactive protein (CRP) and interleukin-6 (IL6) are associated with increased risk of coronary artery disease (CAD) and stroke. Laboratory studies suggest that cross-talk exists between the inflammatory and thrombotic pathways whereby activation of one leads to enhancement of the other. As an example, IL6 regulates expression of tissue factor, which can participate in generation of thrombin, a potent platelet activator. An interaction between inflammation and platelet function

may contribute to the risk of CAD. **Methods**: To examine this hypothesis further, we measured plasma levels of IL6 and high sensitivity CRP, platelet activation ex-vivo (whole blood aggregometry to different agonists), and platelet activation in vivo (urinary 11-dehydro-thromboxane B2 (uTxM)) in 1706 apparently healthy 21 to 79 year old relatives of a proband with CAD at a young age (<60 years). Mean age of the study population was 44.9±13 years, 43% were male, and 38% Black. **Results**: Mean CRP was 2.73±3.1μg/ml and mean IL6 6.75±13 pg/ml. The Table shows that mean platelet aggregation to each of the different agonists, as well as uTxM, increased significantly with increasing quartiles of hsCRP and IL6 for most assays. **Conclusion**: The results of our adjusted multivariable linear regressions indicate that elevated levels of inflammatory markers are associated with increased platelet activation in multiple pathways, both ex vivo and in vivo. Interaction between inflammatory pathways and platelet function may contribute to premature CAD in high risk families.

Platelet assay	hsCRP***				IL6***				
	Q1: 0.16	Q2: 0.69	Q3: 2.56	Q4: 7.49	Q1: 0.76	Q2: 2.84	Q3: 5.52	Q4: 17.9	p*
Collagen (ohms)	26.5	27.3	27.7	28.3	27.2	27.5	27.4	27.6	CRP 0.01; IL6 0.88
Adenosine Diphosphate (ohms)	12.2	12.6	13.2	14.0	11.9	13.4	13.3	13.4	CRP 0.96; IL6 0.007
Arachidonic Acid (ohms)	15.3	15.9	17.5	18.0	15.3	17.1	16.9	17.3	CRP 0.009; IL6 0.002
uTxM ng/mmol creatinine	204.7	296.2	321.7	318.1	152.8	250.2	339.5	398.5	CRP 0.017**; IL6 <0.0001**

*Adjusted for age, sex, race, smoking, BMI, SBP, glucose, total cholesterol, and nonindependence within families, ** P on log-transformed data, ***Mean values of hsCRP and IL6 given for each quartile (Q1–4)

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Ten-Year Predicted Coronary Heart Disease Risk in HIV-Infected Men and Women

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Background: We examined 10-year predicted coronary heart disease (CHD) risk among HIV-infected and HIV-uninfected participants the Women's Interagency HIV Study (WIHS) and Multicenter AIDS Cohort Study (MACS). **Methods**: We used cross-sectional WIHS and MACS data contributed by 1,455 HIV-infected women and 931 HIV-infected men, as well as 1,099 men and 576 women without HIV infection who were similar to HIV-infected individuals on demographic and socioeconomic factors. The Framingham risk score equation was used to predict 10-year risk of developing total CHD (myocardial infarction, fatal CHD, and angina) or hard CHD events (myocardial infarction or fatal CHD). **Results**: Among men, moderate-to-high predicted CHD risk was more frequent among HIV-infected individuals compared with HIV-uninfected controls (OR [95% CI] for total CHD = 1.44 [1.05, 1.98]; OR for hard CHD events = 1.33 [1.05, 1.71]). Among women, predicted CHD risk was similar or lower among HIV-infected individuals than among HIV-uninfected controls (OR for total CHD = 0.71 [0.41, 1.25] and OR for hard CHD events = 0.64 [0.33, 1.25]). Compared with current PI-based HAART, current non-PI based HAART was associated with significantly lower predicted CHD risk (OR for total CHD = 0.48 [0.28, 0.82] and OR for hard CHD events = 0.67 [0.45, 0.98]). Low income was associated with higher predicted CHD risk among HIV-infected men and women. **Conclusions**: HIV infection was associated with increased predicted CHD risk among men, but not among women. HIV-infected individuals who have low income level or who are treated with PI-based HAART may benefit from targeted screening for vascular risk factors.

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Addition of Nontraditional Risk Markers to Multivariable Risk Scores: Do They Really Add Prognostic Information?

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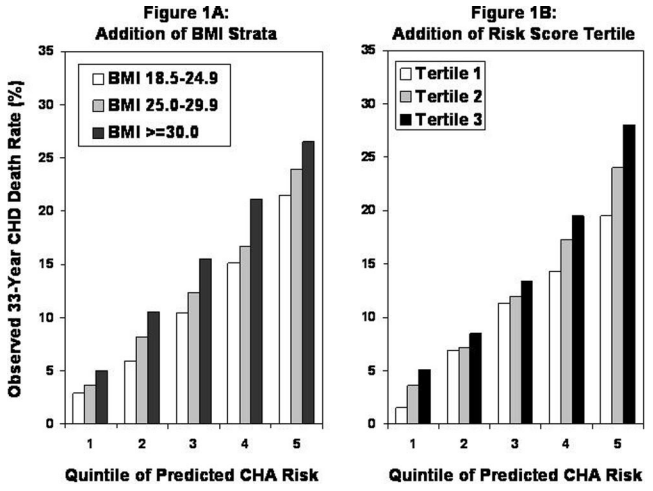
Background: It has become commonplace to assess the "additional prognostic utility" of novel risk markers, e.g. CRP, by examining risk in different strata of the new marker within categories of the Framingham risk score (<10%, 10–20%, >20%). We sought to examine the implications of such analyses. **Methods**: We included men and women free of CHD at age 40–59 years in the Chicago Heart Association Detection Project in Industry (CHA). A multivariable risk score for CHD death over 33 years was developed using baseline age, sex, total cholesterol, systolic BP, diabetes and current smoking. Rates of CHD death were compared across strata of "new" risk markers and within each quintile of CHA risk score. **Results**: Among 16,918 participants (45.7% women), 2166 (12.6%) had CHD death during follow up. CHD death rates were 3.4%, 7.5%, 12.2%, 17.0% and 23.8% for quintiles 1–5, respectively, of the CHA risk score. Within each quintile of the CHA risk score, addition of other significant risk markers, including BMI (Figure 1A), ECG abnormalities, diastolic BP, education level and others further stratified observed rates of CHD death, but they did so in a linear fashion. Similar results were obtained simply by using tertiles of the CHA risk score within each quintile of CHA risk score (effectively creating 15 strata of the CHA risk score; Figure 1B). **Conclusions**: Transformation of continuous risk scores into categorical strata may allow novel risk markers to appear to add prognostic information. However, these findings suggest that some additional risk markers merely restore the continuous risk prediction inherent in the risk score itself, rather than reclassifying risk in clinically meaningful ways.



P216

IL-6 Partially Explained Higher Noncardiovascular Mortality Among Older Adults with Long Sleep Duration

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Background: Both long and short sleep duration have been associated with total mortality; however, the mechanisms are not known. We hypothesized that both long and short sleep would be related to CVD and non-CVD mortality and this would be partially explained by higher markers of inflammation. **Methods**: participants (≥68 years) in the Cardiovascular Health Study (CHS) who self-reported night sleep duration and were free of CVD events at baseline (n=2544) in 1996 were followed for mortality through 2003. Crude rates were assessed and hazard ratios for deaths were calculated using Cox regression models. **Results**: A total of 678 deaths (226 CVD and 449 non-CVD deaths) were adjudicated during 6.4 years of follow up. Compared to those sleeping 7 to 8 hours, those who sleep ≥9 hours had significantly higher CVD (HR=1.5 95%CI 1.1, 2.1; p=0.015) and non-CVD mortality (HR=1.9 95%CI 1.5, 2.4; p<0.001) after adjustment for age, race, and sex (model-1). Adding common CVD risk factors and chronic co-morbidities to model-1 (model-2) attenuated and abolished the significance of CVD (HR=1.3 95%CI 0.8, 2.0; p=0.255) but not non-CVD mortality (HR=1.5 95%CI 1.1, 2.1; p=0.014). Adding IL-6, a marker of inflammation, to model-2 attenuated and abolished the significance of non-CVD mortality (HR=1.4 95%CI 1.0, 1.9; p=0.081). Short sleep duration (<6 hours) was not associated with CVD or non-CVD mortality. **Conclusion**: Older adults who report ≥9 hours of sleep per night have higher risk of CVD and non-CVD mortality. The risk of CVD mortality may be explained by common CVD risk factors while the risk of non-CVD mortality may be explained by higher level of IL-6 combined with common CVD risk factors and chronic co-morbidities.

P217

Automated RF Versus Manual B-Mode Common Carotid Intima-Media Thickness Measurements in Routine Clinical Practice: Direct Comparison of Risk Factor Relations and Relations with Future Events

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Background Carotid intima-media thickness (CIMT) is widely used in observational and intervention studies to study determinants of atherosclerosis and cardiovascular risk. CIMT is measured in various ways. Manual B-mode ultrasound with off-line measurements is the most common method. Automated online CIMT measurement using RF signals offers a less laborious alternative, but the accuracy in higher risk patients is uncertain. **Objective** Objective of our study is a direct comparison between manual and automated method in risk factor relations and future events. **Methods** Data was used from participants of the SMART-study, an ongoing cohort study of patients with manifest arterial disease or cardiovascular risk factors. Far wall common CIMT was measured with manual and automated method. Detailed risk factor information was obtained and all participants were followed for occurrence of vascular events after baseline. CIMT was related to risk factors with univariate and linear regression models and to future events with Cox proportional hazards models. **Results** 2146 participants were assessed. The correlation between the two methods was weak (Spearman r 0.36). The manual method was twice as strong related to the two most important risk factors, notably age and systolic blood pressure, as the automated method. No differences in magnitude of relations were seen for other risk factors. The magnitude of the relation with future stroke per standard deviation increase was lower for the automated method (manual (hazards ratio (HR) 1.03; 95%CI 0.70–1.51) as for the manual method (HR 1.45; 95%CI 1.24–1.69). For future coronary heart disease, no difference between the two methods was found in magnitude of the relations (HR 1.09; 95%CI 0.86–1.37) automated RF (HR 1.24; 95%CI 0.98–1.56)). **Conclusions** The results of our study, performed in routine clinical practice in patients with cardiovascular disease, showed that manually measured common CIMT provides stronger relations with the established risk factors for CIMT, notably age and systolic pressure, as compared to the automated method. In addition, manual B-mode CIMT showed stronger relations with future stroke as compared to the RF signal method.

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Hemoglobin A_{1c} Level Predicts Risk of Incident Coronary Heart Disease Among Healthy Women and Men

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Background: Hemoglobin A_{1c} (HbA_{1c}), a time-integrated marker of glycemic control, may also be an early marker of dyslipidemia and endothelial dysfunction. Few studies have examined HbA_{1c} and risk of coronary heart disease (CHD) among healthy men and women without clinically elevated levels or previously diagnosed diabetes. **Methods**: We conducted nested case-control studies among 2 large prospective cohorts of US female nurses and male health professionals. Among participants who provided a blood sample and were disease free at blood draw, we confirmed 249 (women) and 266 (men) incident CHD deaths and nonfatal myocardial infarctions (MI) over 8 and 6 years of follow-up, respectively. Controls were randomly selected 2:1 matched on age, smoking, month of blood draw, and fasting status (women only), from participants free of CVD at the time the case was diagnosed. Participants with a history of diabetes or HbA_{1c} levels $>6.5\%$ at baseline (67 men; 104 women) were further excluded from these analyses. Unconditional logistic regression was used to estimate the relative risk (RR) and 95% confidence intervals (CI), and multivariable models adjusted for matching factors, CVD risk factors, lipids, and C-reactive protein (CRP). **Results**: Median baseline HbA_{1c} levels were significantly higher among cases than controls (women: 5.66% vs 5.59%, p=0.008; men: 5.68% vs 5.63%, p=0.007). In analyses adjusting only for matching factors, the RR for CHD comparing extreme quintiles (median Q5 vs Q1: 6.05% vs 5.19% in women; 5.95% vs 5.27% in men) of HbA_{1c} was 2.21 (95% CI 1.22, 3.99; p trend=0.01) among women and 1.96 (95% CI 1.18, 3.27; p trend=0.006) among men. After multivariable adjustment, the relative risks remained significantly related to risk of CHD in women (RR=2.84 [95% CI 1.43, 5.67; p trend=0.01]) and in men (RR=1.83 [95% CI 1.07, 3.12; p trend=0.02]). The adjusted RRs were not significantly modified by history of hypertension, parental history of early MI, or obesity (BMI $<$ or $\geq$30 kg/m^2). When we modeled the relative risk as a continuous variable, a 0.2% increase in HbA_{1c} was associated with a RR of CHD of 1.18 (95% CI 1.03, 1.35) in women and 1.14 (95% CI 1.01, 1.29) in men. **Conclusion**: Our findings indicate that HbA_{1c} is an independent predictor of CHD risk among healthy women and men.

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The Association of Soluble ICAM and P-Selectin and Oxidative Stress with Coronary Artery Calcification in a Population of Young Adults: The CARDIA Study

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ICAM and P-selectin are adhesion molecules that act in the uptake of leukocytes and monocytes by the walls of blood vessels, and promote foam cell development. Their chronic overproduction, as indicated by elevated serum levels, may occur in the very early stages of atherosclerosis, as marked by coronary artery calcification (CAC). F_2-isoprostanes (ISOP), a free radical-dependent oxidation product of arachidonic acid, indicates systemic oxidative stress that may induce adhesion molecules. We measured ISOP, ICAM and P-selectin concentrations and all covariates in 2262 subjects (mean age=40) at year 15 of follow-up in the biracial CARDIA cohort. We assessed CAC by cardiac CT at years 15 and 20 of follow-up. At year 20, 194 of 217 participants with CAC at year 15, progressed to a higher Agatston score, while 270 people with a 0 Agatston score at year 15 progressed to a positive value by the year 20 exam, resulting in detected CAC progression in 30% (292/996) of men and 13% (161/1266) of women. In models predicting CAC progression and adjusted for race, center, and age, ISOP, ICAM, and P-selectin were all positively related to CAC in both genders. In models further adjusted for BMI, blood lipids (LDL, HDL, TG, cholesterol-lowering medication), blood pressure (SBP, high blood pressure medication) and smoking, the primary predictors of CAC progression, associations of all 3 analytes with CAC progression were attenuated, but the combined marker, the sum of their z-scores, remained significant (See Table). All findings were similar in men and women analyzed separately, although stronger in men, and support the hypotheses that each of these molecules may signal the processes involved in early atherosclerosis. Longer follow-up of subclinical disease and clinical events are necessary. The Association of CAC with ISOP, ICAM plus P-selectin[1]

	Men	Women	All Subjects
Partially Adjusted[2]	1.16 (1.09, 1.25)	1.21 (1.12, 1.31)	1.18 (1.12, 1.25)
Fully Adjusted	1.08 (1.003, 1.18)	1.09 (0.99, 1.19)	1.08 (1.02, 1.15)

[1] Results of logistic regression analysis: Odds Ratios (Confidence Limits) per unit of sum of z-scores. [2]Adjusted for race, sex, age and center

P220

African-American Ethnicity Is Associated with Higher Levels of Inflammatory Markers in Hypertensive Adults

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Background: Disparity in the prevalence of cardiovascular disease among ethnic groups is well known but poorly understood and not explained by differences in conventional coronary heart disease (CHD) risk factors. We investigated differences in the plasma levels of markers of inflammation (C-reactive protein (CRP) and fibrinogen) between African American (AA) and non-Hispanic White (NHW) hypertensive adults. **Methods**: Subjects (n = 1105 AA from Jackson MS, mean age = 64.3 y; and 892 NHW from Rochester, MN, mean age = 61.0 y) belonged to hypertensive sibships. Plasma CRP was measured by a high-sensitivity immunoassay and fibrinogen by the Claus assay. Multivariable regression analyses, stratified by sex, were performed to assess whether AA ethnicity was associated with CRP and fibrinogen levels after adjustment for age and BMI, and after additional adjustment for CHD risk factors (total cholesterol, HDL-C, triglycerides, systolic BP, diabetes, history of smoking) and medication use (statin and hypertension medications, and estrogen (in women)). Generalized estimating equations were used to correct for intrafamilial correlations. **Results**: Levels of CRP were higher in AA men than in NHW men (4.6±6.0 mg/L vs. 3.1±4.0 mg/L; $P = 0.0008$); and in AA women than in NHW women (6.7±8.0 mg/L vs. 5.5±6.0 mg/L; $P = 0.0028$). Levels of fibrinogen were higher in AA men than in NHW men (349±85 mg/L vs. 320±69 mg/L; $P < .0001$) and in AA women than in NHW women (378±81 mg/L vs. 324±79 mg/L; $P < .0001$). In both sexes, after adjustment for conventional CHD risk factors, AA ethnicity remained associated with higher CRP levels ($P = 0.0011$ in men, $P = 0.0023$ in women) and higher fibrinogen levels ($P < 0.0001$ in men and $P < 0.0001$ in women). **Conclusions**: Among hypertensive adults, AA ethnicity was independently associated with higher plasma levels of CRP and fibrinogen. These results motivate further investigation into whether inflammatory burden contributes to the greater cardiovascular risk of hypertensive African American adults.

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Brain Natriuretic Peptide as a Predictor of Coronary and Cardiovascular Events and All-Cause Deaths in General Population

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Background: Brain natriuretic peptide (BNP) is a sensitive marker of myocardial dysfunction. However, studies on BNP have been mainly performed on patients with various cardiac disorders and studies in the general population are few. **Methods and Results**: A random sample of 8,141 persons aged 25–74 years was examined in the FINRISK 1997 study and followed up until the end of 2004 for cardiovascular disease (CVD) mortality and morbidity and all-cause deaths. We used the case-cohort design to examine the association of BNP with major adverse events during the follow up. Altogether 277 first CVD events (204 in men and 73 in women) occurred during the follow up among participants with no history of CVD event at baseline. The number of all-cause deaths in this group was 230 (154 men and 76 women). Among persons with a history of CVD at baseline, 152 recurrent CVD events occurred (112 in men and 40 in women). In Cox proportional hazards regression analyses taking into account the case cohort design, BNP did not predict coronary events nor major CVD events (coronary + ischemic stroke) among persons free of CVD at baseline. It was, however, a significant predictor of all-cause deaths among men free of CVD at baseline (Hazard Ratio (HR) =2.0, 95% confidence interval (CI) 1.2–3.1, comparing the highest quartile to the lowest, adjusted for traditional CVD risk factors and C-reactive protein (CRP)). Also among women the HR for all-cause deaths was elevated, but did not reach statistical significance. Among men and women with a history of CVD event at baseline, BNP was a strong predictor of a recurrent event during the follow up, independently of traditional risk factors and CRP (HR=3.4, 95% CI 1.8 - 6.4). **Conclusions**: BNP is not a significant predictor of major CVD events in middle-aged clinically healthy individuals. It is, however, a significant marker of all-cause mortality in these individuals, suggesting that it may be a sensitive marker of several subclinical disorders. In persons with a history of CVD event, elevated BNP indicates a high risk of a recurrent event. In this group BNP could be a useful tool for guiding the therapy and secondary prevention.

P222

Bias and Poor Calibration in Self-Reported Sleep Duration Compared to an Objective Measure: The CARDIA Sleep Study

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Epidemiologic studies, based on asking participants how much they usually sleep, have found sleep duration to be associated with obesity, diabetes, and hypertension. However, there has been little validation of subjective reports of habitual sleep. We model the extent to which self-reported habitual (past 30 days) sleep reflects average objectively measured sleep. Eligible participants (n=814) at the Chicago site of Coronary Artery Risk Development in Young Adults were invited to participate in a 2003–2004 ancillary sleep study; 82% (n=669) agreed. Sleep measurements collected in two annual waves included: 3-days of wrist actigraphy, a sleep log, and standard sleep questions, including: "During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spend in bed.) On weekdays? On week-ends?" We use measurement error models to account for the fact that only 3 of the past 30 days were measured. We present three aspects of the subjective-objective relationship: bias, calibration and discrimination, both overall and stratified by demographic, lifestyle and sleep characteristics. Overall, bias was 0.80 hours with subjective reports on average longer than measured sleep. Calibration was substantially less than one: for each additional hour of sleep recorded, average reported sleep increased by 28 minutes. Discrimination was low: measured sleep explained only 17 percent of the variation in reported sleep. Bias varied little by sex, education, income or sleep variability, but bias was less (closer to 0) for the obese, those with high depression scores, high apnea risk, and high sleepiness. Calibration was much better (closer to one) for those with higher sleep efficiency, and also better for those with more income. Our findings suggest that associations found in studies using self-reports of habitual sleep could be misleading. Subjective reports are not simply "noisy" but contain systematic errors in both the mean and calibration. Notably, persons with less refreshing sleep, including the obese, report less sleep given their measured sleep, and an hour's difference in subjective report does not reflect the same difference in objective sleep for different sub-populations.

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A Prospective Study of Osteoprotegerin and the Risk of Future Cardiovascular Events in Initially Healthy Women

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Background: Osteoprotegerin (OPG), a member of the tumor necrosis factor receptor superfamily, is a novel biomarker that appears to play a role in vascular calcification. Previous cross-sectional studies have demonstrated an association between OPG and both atherosclerosis and cardiovascular endpoints; however, prospective analyses on OPG's association with clinical endpoints are sparse. **Methods**: We measured baseline OPG levels in stored plasma samples of 252 women who had a first cardiovascular event (myocardial infarction, ischemic stroke, or cardiovascular death) during 6 years of follow-up, and 252 controls matched for age, smoking status, and time on study, nested within the Women's Health Study, a prospective study of 39,876 initially healthy women. **Results**: Concentrations of OPG in plasma were not significantly different in cases compared to controls (median 4.51 vs. 4.26 pmol/L, respectively, $p = 0.08$). OPG levels correlated positively with age ($r = 0.37$, $p < 0.0001$) and negatively with body-mass index ($r = -0.16$, $p = 0.01$), but were not significantly associated with other traditional cardiac risk factors. In analyses conditioned on age and smoking status, we found minimal association between OPG and cardiovascular events (odds ratios for increasing tertiles of OPG: 1.00, 1.37, and 1.46, p for trend = 0.14). Multivariate models adjusting for other cardiac risk factors did not substantively alter these results. In addition, no threshold effect was apparent at prespecified cutoffs of OPG (odds ratios for OPG levels above the 25th, 50th, 75th, 90th, and 95th percentiles of the control distribution: 1.36, 1.20, 1.22, 1.45, 1.70, respectively, all p-values nonsignificant). Secondary analyses stratified by age and smoking status also yielded similar results, as did models analyzing each of the clinical endpoints individually. **Conclusion**: In contrast to previously published studies, this prospective analysis in initially healthy women demonstrated minimal association between OPG and future cardiovascular events.

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Interleukin-18 and the Risk of Future Cardiovascular Events Among Healthy Women

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Introduction: Elevated levels of interleukin (IL)-18 have been implicated in the development of atherosclerosis in animal models. While epidemiologic studies in humans support this association, data in women are scarce. **Methods**: In a prospective study of 39,876 women without cardiovascular disease, we measured baseline plasma IL-18 levels in 253 cases (109 myocardial infarction, 111 ischemic stroke, 33 cardiovascular death) and 253 controls matched for age (± 1 year) and smoking status. **Results**: Median concentrations of IL-18 were higher among women who subsequently had a cardiovascular event than those who did not (274.1 vs. 233.8 pg/mL, $P < 0.001$) and were most closely correlated with high-density lipoprotein cholesterol (HDL-C) levels (Spearman $r = -0.28$, $P < 0.001$). The unadjusted odds ratio (OR) of a future cardiovascular event increased with increasing quartiles of IL-18 (P-trend < 0.001), such that women in the highest quartile had an OR of 2.53 (95% CI 1.47–4.35) relative to those in the lowest quartile. However, after further adjustment for traditional cardiovascular risk factors (diabetes, family history, blood pressure, cholesterol, and horomone use), the OR for future cardiovascular disease was no longer significant for the highest vs. the lowest quartile (1.59, 95% CI 0.76–3.31, P-trend = 0.17). No interaction was detected between IL-18 levels and any of the significant confounders of its relationship with cardiovascular disease (HDL-C, diabetes, and blood pressure). **Conclusions**: In this population of apparently healthy women, elevated levels of IL-18 were associated with an increased risk of cardiovascular disease, although that risk was attenuated after adjustment for traditional cardiovascular risk factors.

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Association of Serum Amyloid P with Subclinical Atherosclerosis: Results from the Multi-Ethnic Study of Atherosclerosis (MESA)

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Background: Serum amyloid P (SAP), a pentraxin like C-reactive protein (CRP), functions in innate immunity and is localized in atherosclerotic lesions. However, associations of SAP with subclinical cardiovascular disease (CVD) are not well characterized. **Methods**: We examined these associations in 985 White, Black, Chinese and Hispanic men and women from MESA. Mean age was 59 years and all were free of clinical CVD. Subclinical CVD measures were ankle-brachial index (ABI), common and internal carotid intima media thickness (IMT) and coronary calcium (CAC; assessed by cardiac computed tomography). 436 participants had detectable CAC defined as Agatston score >0. **Results**: SAP levels ranged from 20–164 mg/l, mean 57 mg/l, and had a normal distribution. Associations of one standard deviation (SD) increases in continuous variables with SAP were determined using age, sex and ethnicity adjusted linear regression. SAP was associated with CVD risk factors (obesity, blood pressure, lipids, fasting insulin and glucose) and CRP (all $p<0.02$). SAP was also associated with ABI (SD=0.12; regression coefficient R=-1.3, p=0.04) and common carotid IMT (SD=0.18mm; R=1.6, p=0.03), but not internal carotid IMT (SD=0.52mm; R=1.0, p=0.2). In age, sex and ethnicity adjusted relative risk regression models, a standard deviation increase in SAP (19.0 mg/l) was associated with the presence of any detectable CAC; relative risk (95% confidence interval) 1.07 (1.02–1.12). Adjusting for CVD risk factors (obesity, smoking, diabetes, hypertension and dyslipidemia) attenuated the association (1.05; 1.00–1.09). Trends were similar in men and women and across ethnic groups. **Conclusions**: SAP was modestly associated with CVD risk factors, measures of subclinical CVD and the presence of CAC in these MESA participants. However, the precise nature of the relationship between SAP and atherosclerosis remains to be determined.

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Cystatin C Is Associated with Homocysteine and Hemostatic Factors Among Multi-Ethnic Study of Atherosclerosis (MESA) Participants with and Without Chronic Kidney Disease

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Background: As a novel measure of kidney function, cystatin C has been found to have a linear association with cardiovascular disease (CVD) throughout its range of values, whereas estimated GFR (eGFR) only predicts CVD below an eGFR of 60ml/min/1.73m^2. Since many proatherosclerotic markers are cleared renally, they are intriguing potential mediators for the kidney dysfunction-CVD relationship. **Objective**: We investigated the associations of cystatin C with total homocysteine (tHcy), D-dimer, and plasmin-antiplasmin complex (PAP) both in the whole MESA cohort and stratified by CKD status. **Methods**: We used data from the baseline visit of 6,814 adults aged 45–84 enrolled in MESA. Cystatin C was modeled per standard deviation. eGFR was calculated using the MDRD equation, and CKD was defined as eGFR≤60. D-dimer, PAP, and tHcy were log transformed to meet normality assumptions. Multivariate linear regression models were used to determine the adjusted association of cystatin-C with each biomarker. **Results**: Mean (±SD) levels of cystatin C, tHcy, D-dimer and PAP were 0.90±0.24 mg/L, 9.3±3.7 μmol/L, 0.38±0.87 μg/mL, and 4.8±2.2 nM/L, respectively. 651 (9.6%) participants had CKD. In multivariate models adjusted for demographics, comorbidities, medications, lipoprotein levels, fasting glucose, and albumin, a one standard deviation higher cystatin C was associated with a 15% ($p<0.001$) higher tHcy, a 14% ($p<0.001$) higher D-dimer and a 6% ($p<0.001$) higher PAP. Among those with CKD, a one standard deviation higher cystatin C was associated with a 9% ($p<0.001$) higher tHcy, a 12% ($p=0.003$) higher D-dimer, and a 3% ($p=0.04$) higher PAP. In those without CKD, the associations were modestly stronger - a 15% ($p<0.001$) higher tHcy, a 15% ($p<0.001$) higher D-dimer, and a 5% ($p<0.001$) higher PAP. **Conclusions**: Cystatin C is positively associated with tHcy, D-dimer and PAP in participants with and without CKD. These biomarkers may play an important role as mediators for the association of kidney dysfunction with cardiovascular risk.

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Depressive Symptoms Are Associated with Higher Risk of Atherosclerotic Progression Among Patients with Coronary Artery Bypass Grafts

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Background: Depressive symptoms have been associated with increased risk of coronary artery disease (CAD) and poor prognosis in patients with existing CAD, perhaps by promoting the progression of atherosclerosis. We evaluated the hypothesis that depressive symptoms influence atherosclerotic progression in saphenous vein grafts among 1351 patients enrolled in the Post-CABG trial. **Methods**: The Post-CABG Trial used a 2x2 factorial design to randomize patients with a history of CABG surgery (1–11 years prior to enrollment) to either an aggressive or moderate lipid lowering strategy and to either warfarin or warfarin-placebo. Coronary angiography was conducted at study baseline and after a median follow up of 4.2 years. The primary trial endpoint was substantial graft disease progression assessed angiographically. Additional pre-defined trial endpoints included occlusion of grafts that were patent at baseline and a change in minimum lumen diameter. Depressive symptoms were assessed at baseline using the Centers for Epidemiologic Studies Depression (CES-D) scale and subjects were considered to have depressive symptoms if CES-D was ≥16, as in previous studies. We used generalized estimating equations to prospectively evaluate the association between CES-D score and these angiographic endpoints, accounting for the within-subject correlation and controlling for treatment assignment, age, gender, race, and years since CABG surgery. **Results**: CES-D scores were available for 1319 patients with 2496 grafts. A CES-D score ≥16 was associated with a 56% (95% CI: 11, 118%; $p=0.009$) higher risk of substantial graft disease progression and a 0.11 mm (95% CI: -0.23, 0 mm; $p=0.05$) decrease in minimum lumen diameter. CES-D score was not associated with significantly higher risk of graft occlusion ($p=0.27$). Additional adjustment for past medical history, smoking history, and body mass index did not materially alter the results.**Conclusion**: These findings suggest that the presence of depressive symptoms may be associated with higher risk of atherosclerotic progression among patients with saphenous vein grafts. These results may not be generalizable to atherosclerotic progression in other types of grafts or in native coronary arteries.

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Distribution and Metabolic Syndrome Correlates of Serum Alanine Amino Transferase in Children and Adolescents: The Bogalusa Heart Study

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Background: Abnormal levels of serum alanine amino transferase (ALT), a marker of liver dysfunction and non alcoholic fatty liver (NAFL), are considered the metabolic consequence of obesity in adults and children alike. However, population based data on the distribution of ALT and its association with obesity and other components of metabolic syndrome in bi-racial (black-white) children and adolescents is lacking. **Methods**: The study sample consisted of

1,524 children (age: 4–11 years, 62% white, 51% male) and 1,060 adolescents (age: 12–18 years, 58% white, 51% male), examined as part of the Bogalusa Heart Study, with measurements of ALT and other CV risk factor variables. **Results**: ALT levels showed significant race (white>black, $p<0.0001$) in children and gender (male>female, $p=0.0001$) difference in adolescents. Both in children and adolescents, top vs. bottom quartiles of ALT levels had increased prevalence of adverse levels (> than age, race, gender specific 75th percentile) of body mass index (BMI), systolic blood pressure, total-to-HDL cholesterol ratio, insulin resistance index (HOMA-IR), as well as metabolic syndrome. In multivariate analyses, BMI was the major predictor of ALT levels in both children and adolescents. Other significant independent predictors were white race in children and total-to-HDL cholesterol ratio, HOMA-IR, and male gender in adolescents. Clustering of adverse levels of three or four risk factors (BMI, systolic blood pressure, total-to-HDL cholesterol, or HOMA-IR) at top quartile of ALT was displayed by 24.9% children and 29.0% adolescents and was significantly higher than expected by chance alone ($p<0.05$ - <0.01). Moreover, area under the receiver-operating curve values to determine the ability of ALT in classifying individuals with metabolic syndrome were 0.67 and 0.82 in children and adolescents, respectively. **Conclusion**: ALT levels within normal range are strongly associated with metabolic syndrome and its components in children and adolescents, and thus, may be a useful biomarker for this condition.

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Lipoprotein-Associated Phospholipase A2 and Future Coronary Heart Disease Events Among Men with Type 2 Diabetes

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Type 2 diabetics have an increased risk of cardiovascular disease, potentially mediated partially through inflammatory pathways. Lipoprotein-associated phospholipase A_2 (Lp-PLA_2) is an enzyme that hydrolyzes phospholipids of oxidized LDL to form pro-inflammatory mediators, and recent evidence has demonstrated an atherogenic relationship between Lp-PLA_2 and CHD. To date the association between this novel biomarker and risk of CHD has not been examined specifically among diabetics. We measured levels of Lp-PLA_2 activity in a prospective cohort of 745 male diabetic participants in the Health Professionals Follow-up Study. Men were between the ages of 41 and 86 and free of CVD and cancer at the time of blood draw in 1993–1994. During 6837 person-years of follow-up through 2004, 180 cases of CHD occurred. Age-adjusted Cox proportional hazard ratios (HRs) for the second, third, and fourth quartiles compared to the first quartile of Lp-PLA_2 were 1.02 (95% CI 0.64 - 1.62), 1.39 (0.90 - 2.15), and 1.78 (1.17 - 2.71), respectively (p for trend = 0.002). After adjusting for age, HDL, BMI, CRP, family history of MI, hypertension, physical activity, HbA_{1c}, alcohol intake, aspirin use, and smoking the HRs became 1.0 (0.62 - 1.60), 1.31 (0.84 - 2.05), and 1.72 (1.11 - 2.67) (p = 0.005). Adding LDL to the model caused the HRs to become somewhat attenuated (Q4 vs. Q1 HR 1.51 (0.93 - 2.44), p for trend = 0.06). Although there were no statistically significant interactions between Lp-PLA_2 and several traditional risk factors, the association between Lp-PLA_2 and CHD risk was stronger in those with LDL above the median (>= 127 mg/dl). Fully adjusted HRs across quartiles of Lp-PLA_2, relative to the first quartile, were 1.92 (0.78 - 4.73), 2.07 (0.90 - 4.80), and 2.08 (0.88 - 4.88) (p = 0.19) when LDL >= 127, compared to 0.82 (0.44 - 1.51), 0.81 (0.40 - 1.66), and 1.60 (0.83 - 3.12) ($p=0.26$) when LDL <127. This is the first study to look at the relationship between Lp-PLA_2 and CHD among diabetics. Lp-PLA_2 was associated with increased risk of CHD, although this relationship was somewhat attenuated after adjustment for other risk factors, most notably LDL. The relationship between Lp-PLA_2 and CHD appears to be stronger when LDL >= 127 mg/dl, but this needs further confirmation in other diabetic populations.

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Association Between Hemostatic/Inflammatory Markers and Peripheral Artery Disease in US Adults: The 1999–2002 National Health and Nutrition Examination Survey

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Background: Whether hemostatic factors or inflammatory markers relate to peripheral artery disease in a large US population remains incompletely explored. **Objectives**: We investigated the associations of C-reactive protein (CRP), white blood cell count (WBC), and fibrinogen with prevalent peripheral artery disease in 2565 healthy US men and women aged 40 to 85 years from the National Health and Nutrition Examination Survey (1999–2002). **Methods**: Systolic blood pressures were measured twice at the right brachial and posterior tibial arteries in both legs, and right and left ankle-brachial indexes (ABI) were calculated as ankle systolic blood pressure at right and left, respectively, divided by brachial systolic blood pressure. Peripheral artery disease (PAD) was classified as ABI <0.9 in either leg. CRP was assessed using latex-enhanced nephelometry, and fibrinogen was measured using the Clauss clotting method, while WBC count was assessed by Beckman Coulter method. Multivariate logistic regression models were used to investigate the associations of CRP, WBC count, and fibrinogen with PAD after adjustment for age, sex, race, and multiple risk factors. The lowest CRP, WBC count, and fibrinogen quartiles were the reference categories. **Results**: After adjustment for age, sex, and race, there was a direct association between CRP and PAD (p for trend = 0.005), between WBC count and PAD (p for trend = 0.009), and between fibrinogen and PAD (p for trend <0.01), respectively. After additional adjustment for multiple risk factors (education, cigarette smoking, alcohol intake, body mass index, high-density lipoprotein and total cholesterols, systolic blood pressure, diabetes mellitus, and antihypertensive medication use), CRP (p for trend = 0.006) and fibrinogen (p for trend <0.001) were directly associated with PAD, and WBC count was positively but nonsignificantly associated with PAD (p for trend = 0.26). The odds ratios (and 95% CI) of having PAD in those in the highest versus lowest quartile were: CRP, 2.68 (1.26 to 5.70); fibrinogen, 5.05 (2.00, 12.71); and WBC count, 1.62 (0.74, 3.54). **Conclusions**: Increased levels of CRP and fibrinogen are directly associated with prevalence of peripheral artery disease in a large US middle-aged and elderly populations.

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Determinants of Heart Rate Recovery Following Cessation of Maximum-Effort Exercise in Normal Children

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Background: Heart rate (HR) recovery 1-minute after cessation of exercise is predominantly determined by reactivation of vagal tone. Attenuated 1-min HR recovery is considered a cardiovascular risk factor and is associated with increased all-cause mortality and sudden cardiac death in adults. HR recovery after exercise is not well characterized in children. The purpose of this study was to determine the predictors of 1- and 3-min HR recovery following a maximum-effort exercise test in normal children. **Methods**: HR recovery 1- and 3- minute after cessation of a maximal treadmill exercise test (Bruce protocol) was assessed in 102 children (49 female, 53 male, median age 13.4 years, range 6–18 years), who were referred due to a history of chest pain, shortness of breath, palpitations or family history of heart disease, underwent exercise testing as a part of cardiac evaluation and were discharged as having "normal" cardiopulmonary system. The first minute cool down period (1.5 mph, 0% inclination) on the treadmill was standard for all subjects. Multivariable linear regression analyses were performed to determine predictors of 1- and 3-min HR recovery. **Results**: The mean exercise duration was higher in males (15.2±2.8 versus 13.7±2.0 min, P=0.003) and correlated with age (P<0.001). Peak HR was 195±9.5 beats/min for the cohort and was not related to age, gender, exercise duration or 1- minute HR recovery. HR declined by 38±14 beats/min (range 8–73 beats/min) 1-min post-exercise and by 78±12 beats (range 42–121 beats/min) 3-min post-exercise. Both 1-min and 3-min HR recovery correlated inversely with age and BMI. By multivariable linear regression, models that included age, BMI and exercise duration as covariates best predicted 1-min and 3-min HR recovery (Predicted 1-min HR recovery = 57+ (-2.52Age) + (-0.39 BMI) + (1.48 Exercise Duration), P<0.001, Adjusted R^2=0.4). **Conclusions**: HR recovery following a maximum-effort exercise test is attenuated in older children. Children with higher BMI and lower exercise endurance have slower HR recovery. HR recovery after cessation of exercise may be a useful marker of overall cardiovascular health in children.

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Teeth-Flossing Habits Directly Correlate with Serum hs C-Reactive Protein Levels: Plaque in the Mouth=Plaque in the Arteries

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C reactive protein (hs-CRP) has been demonstrated to correlate directly to cardiovascular risk of CAD, PVOD, and Stroke. It is suggeested that oral hygiene and gingivitis impacts CRP in a negative fashion. In the dental community, flossing has long been advocated as the preferred method of mitigating against tooth loss, but to what extent flossing habits impact overall CRP is not known. We hypothesized that flossing frequency directly correlated with CRP, and in infrequent flossers, increasing flossing to qod would normalize CRP. We measured serum hs-CRP at baseline in 300 pts entering a lefstyle modification program while asking them to describe their tooth brushing practices and the number of times per week that they flossed. Hs-CRP was measured at a single lab: all values that were obtained from pts with an active infection or recovering from surgery or accident were excluded from analysis. Once baseline CRP levels were obtained, those pts with CRP>1.5 were asked to double their flossing or to achieve at least q.o.d. flossing. **Results**: There was no correlation between type of tooth brush (manual, electric, ultrasonic) and CRP levels. Once pts began at least q.o.d. flossing, their CRP levels within 6 months fell to the identical levels as that of the same frequency long-term flossers. We conclude that hs-CRP levels directly correlate with pt's flossing habits. A simple behavior modification can have dramatic and rapid effects on downregulating a major cardiovascular risk factor. All pts with elevated CRP should have their flossing history assessed and urged to floss at a minimum of every other day.

Correlation between Flossing Frequency and hs-CRP levels

Reported Frequency of Flossing	No Flossing	Occassional Flossing	Every Other Day Flossing	Daily Flossing	More than Once a Day Flossing
Serum hs-CRP mg/L	6.5+/-4	3.4+/-2	1.0+/-0.4	0.6+/-o.4	0.6+/-0.3

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The Effect of Lifestyle Changes on High-Sensitivity C-Reactive Protein

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Background: Elevation of High Sensitivity C-Reactive Protein (hs-CRP) is associated with cardiovascular disease (CVD). The Dean Ornish Program for the Reversal of Heart Disease (DOP) treats CVD using intensive lifestyle changes including a very low-fat diet, exercise , and stress management techniques. This study was designed to prospectively evaluate the effects of DOP on hs-CRP over a 3 month period. **Methods**: Hs-CRP (mg/L) was measured in 37 participants at baseline and after 3 months of DOP. Hs-CRP levels were analyzed for all participants [Group 1, n=37]. However, since hs-CRP values ≥10 can be spurious secondary to systemic illness or other inflammatory processes, a separate analysis was performed for those with hs-CRP <10 [Group 2, n=28]. Statin therapy and weight loss, both of which can decrease hs-CRP, were evaluated. **Results**: The mean baseline hs-CRP was 6.6±7.3 for Group 1 and 3.8±2.5 for Group 2. At 3 months, the Group 1 hs-CRP was 5.5±6.2 (17% reduction, p=0.04) and the Group 2 hs-CRP was 2.9±2.4 (22% reduction, p<0.001). There was no increase in statin dosage during the study period in 35 of 37 participants. Participants in both groups experienced an average weight loss of 12 pounds, but the correlation coefficients for decrease in hs-CRP and weight loss were -0.02 for Group 1 and 0.08 for Group 2, suggesting no correlation between the amount of hs-CRP reduction and weight loss. **Conclusions**: Participation in DOP was associated with significant reductions in hs-CRP, with the reductions also being

independent of both statin dosage and weight loss. The magnitude of hs-CRP reductions were greater than have been reported previously in patients who practiced only DOP dietary modifications without exercise or stress management, both of which are inherent to complete participation in DOP.

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Levels of Fibrinolytic Markers and Risk of Intermittent Claudication in the Framingham Offspring

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Background: Classic hemostatic factors have been shown to increase risk for peripheral vascular events, but relative risk for intermittent claudication (IC) according to levels of fibrinolytic markers has not been fully evaluated. **Methods**: A prospective community-based cohort of 3128 adults in the Framingham Offspring Study with mean age 55 years and without IC at baseline was followed up to 11 years for the development of IC that was diagnosed with validated Framingham criteria. **Results**: There were 44 new cases of IC during follow up. The age and sex-adjusted relative risk (RR) per standard deviation (SD) unit was 1.37 (95 % confidence interval 1.11–1.69) for plasminogen activator inhibitor antigen (PAI-1) and 1.09 (95% CI 0.88–1.34) for tissue plasminogen activator antigen (tPA). After adjustment for the individual cardiovascular disease risk factors hypertension, smoking and diabetes the association of PAI-1 with PAD remained statistically significant, but full multivariable adjustment for age, sex, LDL cholesterol, hypertension, smoking, diabetes, and baseline CVD weakened the association of PAI-1 with IC (RR 0.99, 0.72–1.35). **Conclusion**: Higher levels of PAI-1, but not tPA antigen, were related to an increased risk for IC, and the association of PAI-1 with IC was largely explained by elevated levels of other CVD risk factors. Although impaired fibrinolysis may be a target for IC prevention, other CVD risk factors also need to be considered.

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Levels of Urinary 8-Iso-Prostaglandin $F_{2\alpha}$ in Overweight Children and Adolescents

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Background. In adult studies, elevated concentrations of oxidative stress markers have been associated with obesity and other risk factors for cardiovascular disease. Urinary 8-iso-prostaglandin $F_{2\varepsilon}$ has been recognized as an accurate method to quantify oxidant stress in humans. **Objective**: To compare concentrations of urinary oxidative stress markers between overweight and normal weight children and adolescents. **Methods and Patients**. This pilot study compare data from 23 children and adolescents with a body mass index (BMI) $\geq 95^{th}$ percentile, in good health conditions except for their obesity, with a group of 17 normal BMI percentile peers. Oxidative stress test, which includes: 8-epi-$PGF_{2\varepsilon}$ and 8-epi-PGF_2£/creatinine ratio, were measured in a spot urine morning sample. Spearman correlation and non-parametric tests were used for statistical analysis. **Results**. Group of overweight kids was composed of 14 boys and 9 females, with mean age of 12.3±2.0 years, and mean BMI Z-score of 2.1±0.4; group of normal weight had 12 boys and 5 girls, mean age: 13.7±2.2 and mean BMI Z-score of -0.5±1.3. There was no significant difference between groups in 8-epi-PG F_2£ (2561.8±1578.2 vs. 2601.5±1337.2 pg/ml, p = 0.7) or 8-epi-$PGF_{2\varepsilon}$/creatinine ratio (17.2±5.2 vs. 17.9±5.9, p = 0.8). 8-epi-PG $F_{2\varepsilon}$ was not correlated with BMI or BMI Z-score (Spearman's coefficients were -0.026, p = 0.8, and -0.03, p = 0.8, respectively). **Conclusions**. This small group of overweight children and adolescents did not show significant elevated levels of oxidative stress markers when compared with their normal weight counterparts. Levels of urinary 8-epi-PG $F_{2\varepsilon}$ did not correlated with BMI or BMI Z-score.

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Impact of Subclinical CVD and Inflammation on the Occurrence of CVD Events and Mortality in Elderly Subjects with Incident Atrial Fibrillation Within the Cardiovascular Health Study

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Background: While it is clear that atrial fibrillation (AF) is associated with clinical cardiovascular disease (CVD), data are sparse regarding the potential role that subclinical CVD (SCVD) measures and inflammation have in mediating this association in the elderly. **Methods**: Accordingly, we examined the association between incident AF (Inc-AF) and CVD outcomes in the elderly, biracial Cardiovascular Health Study (CHS) cohort. Cox regression analysis was used to examine the association between Inc-AF and risks of stroke, congestive heart failure (CHF), and death before and after adjustment for traditional CVD risk factors, SCVD, and inflammatory markers (interleukin-6 (IL-6) and C-reactive protein). **Results**: Of 5,849 participants at baseline, 170 with documented AF were excluded. Among the remaining 5,679 subjects, the mean age was 72.8±5.6 years, 58% were female, and 16% were Black. During 11 years of follow-up, 440 subjects developed Inc-AF. Those with Inc-AF had higher IL-6 levels (1.9 vs. 1.7 pg/ml, $p=0.002$) and greater prevalence of SCVD (78% vs. 66%, $p<0.001$) and clinical CVD (15.7% vs 10.9%, $p=0.003$). In unadjusted Cox models, Inc-AF was significantly associated with increased risk of stroke, CHF, and death (See Table). The association between Inc-AF and all 3 outcomes remained significant after adjustment for multiple covariates and presence of SCVD and clinical CVD. Interestingly, the relation between Inc-AF and stroke was further attenuated by 28% after adjustment for IL-6 levels in the model. **Conclusions**: Our findings suggest that SCVD may not play a significant role in increasing risk for stroke, CHF, and death in the elderly with incident AF. However, inflammation may be involved in modifying the risk of stroke in elderly subjects with new-onset AF.

Risk of Incident Cardiovascular Disease Events in CHS Participants With Incident AF

Models	Stroke	CHF	Death
Unadjusted	1.93 (1.45–2.58)	3.83 (3.16–4.66)	3.56 (3.14–4.04)
Age-adjusted + Sex+ Race	1.78 (1.33–2.38)	3.40 (2.80–4.14)	3.08 (2.71–3.50)
Multivariable-adjusted	1.68 (1.23–2.29)	3.73 (3.05–4.57)	3.14 (2.75–3.58)
Multivariable-adjusted + Subclinical CVD	1.65 (1.21–2.25)	3.71 (3.03–4.54)	3.10 (2.71–3.54)
Multivariable-adjusted + Clinical CVD	1.67 (1.23–2.29)	3.79 (3.10–4.64)	3.12 (2.73–3.56)
Multivariable-adjusted + IL-6	1.47 (1.06–2.10)	3.85 (3.10–4.77)	3.04 (2.64–3.51)

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Estimated Glomerular Filtration Rate and Risk of Incident Heart Failure: Dose Response Before and After Modeling Measurement Error

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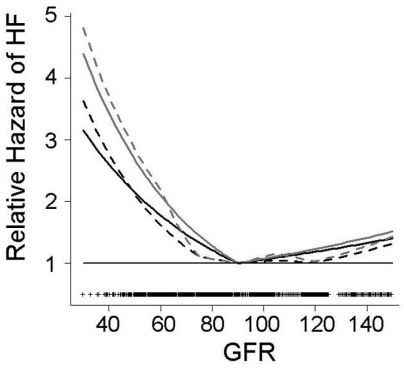
Background: Reduced kidney function is a risk factor for incident heart failure (HF). The estimated glomerular filtration rate (eGFR) as a measure of kidney function is commonly calculated using serum creatinine-based equations and therefore subject to measurement error (ME). Using data from the Atherosclerosis Risk in Communities (ARIC) Study, we investigated the relationship of eGFR to HF incidence evaluating nonlinearity and the impact of modeling ME. **Methods**: Over a mean follow-up of 13 years, 14761 ARIC study participants without HF at baseline were followed for incident HF hospitalization or death. Baseline eGFR was calculated using the abbreviated MDRD Study equation and modelled continuously incorporating linear spline terms. Simulation extrapolation methodology adapted to Cox models was used to account for the impact of ME in eGFR. **Results**: The fully adjusted relative hazard of incident HF showed a non-linear relationship with eGFR (Fig. 1). It was 1.21 (1.14 - 1.29) per 10 ml/min/1.73m2 lower eGFR for eGFR values <90, and 0.94 (0.91 - 0.99) per 10 ml/min/1.73m2 lower eGFR for eGFR values above 90 (p interaction 0.008; Fig. 1: black lines). After accounting for ME in eGFR (SD of eGFR ME 8.8 ml/min/1.73m2, reliability coeff. 0.82), the relative hazard of HF increased to 1.28 (1.19 - 1.37) per 10 ml min/1.73m2 lower eGFR (Fig. 1: grey lines); the relative hazard above 90 remained almost unchanged. **Conclusions**: HF incidence is related to decreased kidney function below the normal range (eGFR <90). In this range, accounting for ME in eGFR led to a 33% increased relative hazard of incident HF per 10 ml min/1.73m2 lower eGFR, but did not change the shape of the dose response relationship.



Linear spline models: one knot (at 90; solid lines), five knots (at 60,75,90,105,120; dashed lines). The Cox model includes age, race, gender, education, prevalent CHD, systolic BP, anti-hypert. meds., DM, smoking, BMI, LDL, HDL, serum albumin, anemia, and carotid atherosclerosis as covariates (n = 13,703).

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Microalbuminuria and Left Ventricular Mass in the HyperGEN Study

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Background: While microalbuminuria has been shown to predict increased left ventricular mass indexed to body surface area (LVM) in hypertensive and diabetic populations, little is known about such an association in normotensive individuals. We hypothesized that microalbuminuria is positively associated with LVM in both normotensive and hypertensive subjects. **Methods and Results**: We analyzed cross-sectionally data from 3,445 participants of the Hypertension Genetic Epidemiology Network (HyperGEN) Study. Left ventricular parameters were obtained by echocardiography. Urinary albumin was assessed using standard methods. Of the total population, 1,468 (42.6%) were men, and the average age was 48.6±13.7 years (range: 18–87 years). From the lowest to highest quartile of microalbuminuria, means of LVM were 72.7, 73.3, 73.0, and 76.8 g/m2, respectively, among normotensive people (p for trend 0.002), controlling for age, sex, ethnicity, field center, body mass index, smoking, systolic blood pressure, history of hypertension treatment, diabetes mellitus, and coronary heart disease. Corresponding means for hypertensive individuals were 87.2, 89.7, 91.4, and 95.5 g/m2, respectively (p for trend <0.0001). Similar associations were observed for LVM indexed to height2.7. In secondary analyses, microalbuminuria was positively

associated with LVM in men and women, with a stronger association observed among hypertensive individuals. Furthermore, microalbuminuria was positively associated with diastolic left ventricular dimension and inversely related to ejection fraction and fractional shortening among hypertensive but not normotensive subjects. **Conclusions**: These results suggest that microalbuminuria is positively associated with LVM in normotensive as well as hypertensive subjects. If confirmed in other studies, microalbuminuria along with other factors could help identify people at risk of left ventricular hypertrophy.

P239

Challenges in Treating Statin-Naive, High-Risk Primary Prevention Patients in a Clinical Setting: Results of the Myalgias with Pravachol and Lipitor Study (MPLS)

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Introduction: The frequency of myalgia and drug discontinuation during statin therapy is perceived to be greater in clinical practice than has been reported in prospective clinical trials. **Objective**: To determine the real world myalgia and other adverse event (AE) rates of two commonly used statins [atorvastatin (A) and pravastatin (P)] in a prospective, placebo-controlled, cross-over design in a statin-naïve, trial-naïve primary prevention population. **Design**: 100 statin naïve patients meeting NCEP ATP III primary prevention drug treatment criteria were evaluated during an 18 week, randomized, double-blind, crossover study. Myalgias were evaluated by use of the "Muscle Pain and Soreness Score" (MPSS) self-report tool; subjects were included if they had no significant muscle pain at baseline (MPSS$<$2). **Intervention**: Subjects were randomized to daily A 20 mg or P 40 mg for sequential six week study periods (SP): Initial statin treatment (SP 1), placebo washout (SP 2), and drug crossover (SP 3). MPSS was recorded weekly **Main Outcome Measures**: MPSS in each study period, AEs, statin compliance, and differences in outcome measures between A and P. **Results**: 81/100 subjects completed the 18 week treatment period. Nineteen subjects discontinued treatment prematurely (8/19 subjects due to statin-associated AE (5/8 secondary to mylagias), 4/19 secondary to other AEs, and 7/19 secondary to "social issues"). In the 81 subjects completing the trial, the average MPSS increased 96% (from 0.53 to 1.04) during exposure to A and P compared to baseline ($p<0.00001$). 15/81 pts (18.5%) had definite statin myalgias (MPSS increased $\geq$1 in SP 1 and 3 compared to baseline and SP 2). 13/81 (16.1%) had probable statin myalgias (MPSS $\geq$1 in SP 1 or 3 compared to baseline and SP2). Overall, only 44% of subjects completed this short treatment period free of any AE. There were no differences between A and P in myalgias or other AEs. **Conclusion**: Early discontinuation of statins and statin myalgias were common regardless of statin used in this study. This very high statin-related AE rate in a statin-naïve primary prevention population affirms the challenges associated with maintaining long-term compliance and clinical efficacy in "real world" asymptomatic patients at high risk for vascular events.

P240

Can a Lifestyle Intervention Attenuate the Effect of Discontinuing Hormone Therapy on Cardiovascular Disease Risk Factors?

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Background: Cardiovascular disease (CVD) continues to be the leading cause of death in postmenopausal (PM) women. Concern and confusion about the potential risks associated with hormone therapy (HT) has left women and their heath care providers searching for safe and effective means for risk factor reduction. **Methods**: The Woman On the Move through Activity and Nutrition (WOMAN) study is a 5 year randomized clinical trial designed to test whether a lifestyle intervention will reduce measures of subclinical CVD. WOMAN participants were randomized at baseline to either a health education (HE) or lifestyle change (LC) group. The impact the lifestyle intervention on CVD risk factors was examined in 240 PM [58.3 (2.9) years] women who were initially on HT at baseline and either continued (n=110) or discontinued HT use (n=130) by 18 months. **Results**: The lifestyle intervention had a beneficial impact on CVD risk factor reduction. When compared to the HE group, women in the LC group had greater reductions in weight, BMI, and average waist circumference (all $p<0.0001$). The LC group also significantly decreased insulin ($p=0.04$), improved saturated fat/cholesterol intake ($p<0.0001$), and increased leisure physical activity ($p=0.005$) levels. Both randomized groups increased total cholesterol and LDL-C levels; however, the increases were significantly less in the LC group ($p=0.02$ and $p=0.01$, respectively). HT discontinuation also resulted in several changes to CVD risk factor levels. CVD risk factor changes were further explored by hormone therapy group, stratified by randomized group assignment. The HT group by randomized group interaction was statistically significant with regards to total cholesterol and LDL-C (both $p=0.02$). Within the HE arm, women who discontinued HT had significantly higher increases in total and LDL-C as compared to HT continuers (both $p<0.01$), whereas no such differences were observed in the LC arm. **Conclusions**: A lifestyle intervention was effective for CVD risk factor reduction in PM women. Negative lipid consequences of discontinuing HT were noted in the HE group and not in the LC group. These findings suggest that a lifestyle behavioral approach can successfully attenuate increases in total and LDL-C that result from HT discontinuation.

P241

Reductions in Angina and Risk Factor Changes in the Multisite Cardiac Lifestyle Intervention Program: Results from the 12-Week Follow-Up

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Objective: To examine angina symptoms and coronary risk factors in female and male CHD patients enrolled in the Multisite Cardiac Lifestyle Intervention Program (MCLIP). **Methods**: We investigated changes in angina symptoms and medical and psychological coronary risk factors in the MCLIP, an ongoing health insurance-covered lifestyle intervention conducted at 22 sites in the US. CHD patients (non-smokers; 700 men, 361 women to date; aged 28 to 89 years) were asked to make changes in diet (10% calories from fat, plant-based), moderate aerobic exercise (180 min/week), and stress management (60 min/day). Data were analyzed with chi square analyses and ANOVAs for repeated measures. **Findings**: At baseline, 28% of women (100 of 361) and 23% of men (162 of 700) experienced angina symptoms at least once a week. By 12 weeks, ¾ of these patients were angina-free. This reduction in angina was significant for both women and men ($p<.001$), with similar effect sizes for both sexes (men: $r=.79$, women: $r=.72$). The observed improvements in angina could not be attributed to changes in standard medical care (e.g., revascularization; medication) over the 12 week period. Angina patients were able to change their diet (from mean $\pm$SEM, 25 ± 0.7 to 10 ± 0.2% dietary fat), to exercise (from 94 ± 7 to 231 ± 7 minutes/week), and to practice stress management (from 21 ± 4 to 380 ± 7 minutes/week); all $p<.001$. By 12 weeks, angina patients also evidenced improved exercise capacity (METs; from 8 ± 0.2 to 10 ± 0.2 ml O_2/min/kg), body weight (from 200 ± 3 to 189 ± 3 lbs), depression (from 13 ± 0.6 to 7 ± 0.5 points on the CES-D), and hostility (from 9 ± 0.3 to 7 ± 0.3 points on the Cook-Medley Hostility Scale; all $p<.01$), with no significant sex-by-time interactions. Significant group-by-time interactions for exercise capacity and weight indicated that patients who were angina-free by 12 weeks showed greater improvements in these variables compared to those with angina at time of follow-up ($p<.05$). **Conclusions**: Multi-component interventions focusing on diet, exercise, and stress management may benefit CHD patients with angina symptoms. This finding takes on added significance considering the economic burden of angina in terms of symptom management, increased risk of cardiovascular events, and lost productivity.

P242

Prevalence of Noncalcified Coronary Plaques Determined by Multislice Computed Tomography: Relationship to Conventional Cardiac Risk Factors

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Background: Coronary plaque contains both calcified and noncalcified components. The relationship between risk factors, nonncalcified plaque (NCP) and coronary stenoses in patients without coronary calcification as assessed by Multislice Computed Tomography (MSCTA) is not well defined. We used MSCTA to examine NCP, significant coronary stenoses ($\geq$50%) and related risk factors (RFs) in a selected population without coronary calcification. **Methods**: Numerous (506) patients underwent 16-slice MSCTA to evaluate chest pain. Of those, 124 patients (30%) had no coronary calcium and comprised the NCP study. We defined NCP as $25\leq HU\leq 130$. **Results**: Fifty five patients (44%) had no NCP, 63 (51%) had NCP without significant stenosis, and 6 (5%) had significant stenosis. These three groups differed markedly in number of risk factors (Table 1). Smoking (current/former) was most prevalent in the stenosis group (83.3%) compared with others (41%, 16%, $p=0.02$). 98 % with 0–3 RFs had no NCP or stenosis. Conversely, 86% with $\geq$4 RFs had NCP or stenosis caused by NCP ($p=0.005$). Pts with $>$3 RFs were more likely to have soft plaque and stenosis. No pt with $<$2 RFs had stenosis. 5/6 pts with stenosis by MSCTA had angiography with 3/5 patients having $\geq$50% stenosis. **Conclusions**: Noncalcified plaque and stenosis are prevalent in patients with chest pain, even without calcification. Smoking may have significant impact on NCP formation. NCP prevalence is highly dependent on aggregate coronary risk. MSCTA is quite useful for detecting both calcified and noncalcified coronary plaque.

	No NCP	NCP, no significant stenosis	NCP, moderate to severe stenosis	P value
	n (%)	n (%)	n (%)	
Number of patients	55 (44.4)	63 (50.8)	6 (4.84)	
Female	36 (65.5)	36 (57.1)	4 (66.7)	ns
Age (avg±SD)	50.2±11.8	50.7 ± 11.6	49.8 ± 8.4	ns
Hyperlipidemia	32 (58.2)	43 (68.3)	5 (83.3)	ns
Family history of CHD	32 (58.2)	47 (74.6)	5 (83.3)	ns
Current or former smoker	9 (16.4)	26 (41.3)	5 (83.3)	0.023*
Diabetes mellitus	1 (1.82)	3 (4.76)	1 (16.7)	ns
Hypertension	15 (27.3)	27 (42.9)	4 (66.7)	ns
Obese (BMI>27)	25 (45.5)	34 (54.0)	6 (100)	ns
Number of risk factors (avg ± SD):	2.20 ± 0.97	3.03 ± 1.16	4.33 ± 1.21	<0.001*
0–3	51 (92.7)	42 (66.7)	2 (33.3)	ns
≥4	4 (7.28)	21 (33.3)	4 (66.7)	0.005*

*(NCP, No S.Stenosis + NCP, S.Stenosis) vs. No NCP

P243

Differences in Risk Factor–Adjusted Subclinical Cardiovascular Disease in Mexican-Americans Versus Non-Hispanic Caucasians: An Echocardiographic/Computed Tomographic Study

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Background: Mexican Americans (MA) are known to exhibit increases in various cardiovascular disease (CVD) risk factors (e.g., diabetes, obesity, etc) compared to non-Hispanic Caucasians (C). MA have also been reported to have lower CVD mortality rates than C. We hypothesized this apparent paradox might relate to lower levels of subclinical disease per level of risk factor in MA. **Methods**: We studied 105 adult MA (42 men, 63 women, age 46 ± 14 yrs) and 100 C (59 men, 41 women, age 50 ± 11 yrs) using blood tests, transthoracic echo, and CT coronary artery calcium (CAC) scan. **Results**: Despite higher BMI, triglycerides and glucose in MA (range of $p=0.04$ to 0.0006), *MA demonstrated lower measures of subclinical disease* (% with CAC score $>$0: mean 13% vs. 26%, $p<0.04$ and LV mass: mean 150 vs 162 gm, $p<0.07$) versus C. (See Table). After age- and gender-adjustment, CAC and LV mass/$Ht^{2.7}$ were associated with ethnicity and BMI. In multivariate analyses, MA ethnicity was significantly

associated with lower LV mass/$Ht^{2.7}$ and lower % with CAC score >0 (P < 0.002). Ethnicity (MA vs C) and BMI, followed by LDLc, were the most important predictors for LV mass/$Ht^{2.7}$. For % with CAC score >0, age, gender and ethnicity, diastolic BP and LDLc were the most important predictor variables. **Conclusion**: Ethnicity is a significant predictor of subclinical disease. Despite higher levels of selected CVD risk factors in Mexican-American adults, they appear to have lower levels of subclinical disease than do Caucasians. This may explain their apparently lower CVD mortality rates than Caucasians. Longitudinal and genetic studies should provide additional insights.

	MA (N=105)	C (N=100)	
Risk Factors	Mean±SD	Mean±SD	P Value
Age (yrs)	46±13	49±11	<0.03
BMI (kg/m^2)	30±7	28±4	<0.003
Diastolic BP (mm Hg)	72±10	75±9	0.1
Total Cholesterol (mg/dl)	199±36	204±37	0.3
LDLc (mg/dl)	111±29	124±30	0.002
Triglycerides (mg/dl)	173±116	125±66	0.0006
Glucose (mg/dl)	91±13	89±21	0.04
Current or previous smoker(%)	40%	61%	0.08
Subclinical Disease			
CAC (% with score >0)	13%	26%	0.04
LV Mass (g)	150±43	162±50	0.07

P244

Impact of a Women's Cardiovascular Disease Screening and Educational Outreach Program on Preventive Action at 6 Months

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Background: The impact of public health education and screening programs to activate participants to reduce cardiovascular disease (CVD) risk is unknown. The purpose of this study was to evaluate predictors of preventive action 6 months following a national standardized CVD screening program for women. **Methods**: Participants included women who underwent systematic screening of CVD risk factors (waist circumference [WC], body mass index [BMI], blood pressure [BP], total cholesterol, high density lipoprotein [HDL] cholesterol and glucose), received education/counseling on risk reduction based on the AHA evidence-based CVD prevention guidelines for women and completed a follow-up phone interview at 6 months (n=151, mean age 53 years, 32% white). Adherence to follow-up recommendations, medication use, and lifestyle changes were assessed by interviewer-assisted questionnaires. **Results**: At baseline, almost half of participants (49%) had >3 risk factors. At 6 months, 82% of women contacted reported initiating lifestyle change (diet, physical activity, or weight loss), 62% reported following up with a physician if they were recommended to do so, and 10% reported initiating blood pressure or cholesterol medication. Women who were overweight at baseline (BMI≥25kg/m^2 and WC>35 in) were more likely to report that they initiated dietary changes (OR=3.21, p<0.01), increased physical activity (OR=3.26, p<0.01), lost weight (OR=7.41, p<0.01), and followed-up with a physician (OR=3.56, p<0.01) compared to non-overweight women. Those with BP≥140/90 were also more likely to report dietary change (OR=1.96, p=0.05), increased physical activity (OR=2.01, p=0.04), weight loss (OR=2.12, p=0.02), follow-up with a physician (OR=2.77, p<0.01), and initiation of medication (OR=3.71, p=0.02) versus normotensives. **Conclusions**: Women who attended an outreach program to increase CVD awareness reported positive lifestyle changes at 6 months and those given immediate feedback of abnormal risk factors were more likely to engage in preventive behaviors. These results are consistent with a recent AHA survey linking personal awareness of risk to preventive action in women and underscores the importance of communication and education in reducing the burden of CVD.

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Change of Cardiovascular Mortality After Cessation of Smoking: Korea Medical Insurance Corporation Study

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Background: To examine the effect of smoking cessation on cardiovascular disease mortality in general population, we analyzed association between change of smoking status and change in cardiovascular mortality in the Korea Medical Insurance Corporation (KMIC) study. **Methods**: The KMIC study is a prospective cohort study, which started in 1990 with 115,200 men and 67932 women. We restricted this analysis to 71,285 men who informed of their smoking habits in 1992, 1994, and 1996. Baseline cardiovascular risk factors such as body mass index, blood pressure, total cholesterol, and fasting glucose level were measured in 1990 and 1992. Outcomes were deaths from cardiovascular disease from 1997 and 2002. **Results**: According to the repeated questionnaire, study participants were classified to 14,680 never smokers, 13,672 ex-smokers who quit smoking before 1992, 3,535 ex-smokers who quit between 1992 and 1994, 3,285 ex-smokers who quit between 1994 and 1996, and 36,113 sustained smokers who continuously consumed tobacco until 1996. Compared with never smokers, relative risks of total mortality for sustained smokers was 1.48 (95% CI: 1.48–2.11). However the relative risks decreased according to the time after smoking cessation: 1.67 (1.23–2.28), 1.41 (1.03–1.94) and 1.20 (0.97–1.49) for ex-smokers who quit smoking between 1994–1996, between 1992–1994, and before 1992, respectively. Relative risk of cardiovascular mortality showed a similar trend: 2.14 (1.06–1.10) for sustained smokers, 2.04 (1.04–4.03) for ex-smokers who quit between 1994–1996, 1.40 (.67–2.97) for ex-smokers who quit between 1992–1994, and 1.33 (0.80–2.19) for ex-smokers who quit before 1992. **Conclusions**: These findings support that cigarette smoking is a modifiable risk factor of cardiovascular mortality. We can recommend people either never start or stop smoking as soon as possible to prevent cardiovascular diseases.

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Effect of Fish Oil on Ventricular Tachyarrhythmia in Patients with Implantable Defibrillators: A Pooled Analysis

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Background: Evidence from trials investigating effects of fish oil on life-threatening cardiac arrhythmia in patients with implantable cardioverter defibrillators (ICDs) is not consistent. **Objective**: To determine the effect of omega-3 PUFAs on the incidence of recurrent ventricular arrhythmia in patients with an ICD from a combined analysis of two trials. **Design and Setting**: We pooled data of two randomized, double-blind, placebo-controlled trials performed in the US and Europe. **Patients**: Patients at risk of arrhythmia with an ICD and prior malignant ventricular tachycardia (VT) or ventricular fibrillation (VF). **Intervention**: Patients from the Portland study (n=200) randomly received either 1.8 g/d of marine omega-3 PUFAs or placebo; patients from the SOFA study (n=546) randomly received either 0.9 g/d of marine omega-3 PUFAs or placebo. We used all data up to 379 days of intervention (1 year and 14 days). **Main outcome measurement**: Appropriate ICD treatment for a spontaneous VF or VT, as confirmed by judgment by cardiologists. Effect of treatment was analyzed on an intention-to-treat basis of all patients as randomized. **Results**: The survival free from appropriate ICD intervention was similar in treatment and placebo group (log-rank p=0.79).The primary endpoint occurred in 126 (34%) patients taking fish oil versus 121 (32%) patients taking placebo (crude hazard ratio (HR) 1.04, 95% confidence interval (CI) 0.81–1.33; n=722). The best fit model which included 576 patients with 197 events resulted in an HR of 1.07 (95% CI 0.81–1.41). For 444 patients who had experienced a VT but no VF before entrance in the study, the crude HR was 1.06 (95%CI 0.79–1.43; best fit model HR=1.12; 0.80–1.58, n=341, 134 events). For 275 patients who entered the study with a VT and no VF and who used no anti-arrhythmic medication, the crude HR was 1.28; 0.89–1.83 (best fit model HR=1.48; 95% CI 0.97–2.24; n=220, 91 events). **Discussion**: These findings do not suggest that omega-3 PUFAs from fish oil prevent cardiac arrhythmia in patients with ICDs. In addition, our data cannot exclude that fish oil may have a modest adverse effect in ICD patients with previous VT who do not use anti-arrhythmic medication.

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Differences in Cardiovascular Risk Factor Profiles Between Patients with and Without Rheumatoid Arthritis

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Introduction: People with rheumatoid arthritis (RA) have an increased risk of cardiovascular disease (CVD) compared with the general population. This study sought to clarify the relative contribution of traditional cardiovascular risk factors to this elevated risk. **Methods**: Forty nine RA subjects and 147 age and sex-matched controls attended an outpatient-based cardiovascular risk assessment clinic at the Baker Heart Research Institute between March and July 2006. Comparisons were made between the groups in terms of traditional cardiovascular risk factors and absolute risk of CVD, using the Framingham risk equation published by Anderson et al (1991). Chi-squared tests and t-tests were applied to categorical and continuous variables, respectively. **Results**: Significant differences between the groups were noted for smoking and physical inactivity. No significant differences were found in BMI, waist-hip ratio, lipid or glucose levels, or in the proportions with diabetes, hypertension and pre-existing CVD. Overall, mean absolute risk of CVD was higher in the RA group (Table 2), with differences remaining significant even after excluding smokers (p<0.04). **Conclusion**: Smoking and physical inactivity are important risk factors to address in the management of RA. RA subjects without pre-existing CVD have higher absolute risks of CVD compared with controls, which highlights the importance of treating *all* modifiable risk factors in those with RA despite that individually, very few may be conspicuous. Further research is required to identify a method of cardiovascular risk characterisation (ideally incorporating inflammatory markers) that is better suited to those with RA.

Table 1: Cardiovascular risk factors between RA subjects and controls

Risk factor	RA group (n=49)	Controls (n=147)	p value
Current Smoker	25%	4%	<0.0001
Physical Inactivity	35%	15%	<0.009

Table 2: Mean absolute risk of cardiovascular disease between RA subjects and controls*

Absolute risk of CVD	RA group (n=39)	Controls (n=66)	p value
Mean 5-year risk of CVD	9.6%	6.8%	<0.02
Mean 10-year risk of CVD	19.8%	14.9%	<0.02

* Excluding those with pre-existing CVD

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The Effect of an Intensive 1-Year Lifestyle Intervention Program on Carotid Intima-Medial Thickness

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Background: Improvement of lifestyle behaviors can reduce cardiovascular (CV) risk factors; however, the impact of lifestyle intervention on the progression of atherosclerosis is less well

established. The purpose of this study was to assess the response of CIMT to an intensive, case-managed, lifestyle intervention program. **Methods**: Participants, at-risk for or with coronary artery disease (CAD), enrolled in a 1-year prospective, cohort intervention study (vegan diet, exercise, yoga, group support) underwent serial carotid ultrasound images. CIMT was calculated as the mean value on a 10 mm length in the far wall of both common carotid arteries using commercial software (ProSolv Echo Analyzer). We determined the overall change in CIMT and the relationship between CIMT change and number of measures achieved (range 0 - 5) in a 5-component Heart Health Index (HHI): BMI <25 kg/m^2, exercise $\geq$150 min/wk, BP$<$140/90 mmHg, LDL Cholesterol (LDL-C) $<$100 mg/dL, fiber intake $>$25 g/day. **Results**: Serial images of 60 participants (mean age$=$58.5$\pm$9.5) were compared. The change (-0.011$\pm$0.118 mm) between CIMT at baseline (0.731$\pm$0.151 mm) and 1-yr (0.720$\pm$0.129 mm) was not statistically significant (p$=$0.48, paired t-test). From comparable baseline values, CIMT progression differed significantly between subjects with a 1-year HHI Score $\geq$3 (n$=$43) and those with a HHI Score $<$3 (n$=$17): CIMT change -0.030$\pm$0.114mm vs. $+$0.038$\pm$0.118 mm; p$=$0.04 by one-way ANOVA. In HHI $\geq$3 compared to HHI $<$3 subjects, there was significant improvement from baseline in Systolic BP (-6% vs. $+$1.5%, p$=$0.01) and LDL-C (-11% vs. $+$1.5%, p$=$0.02) with a trend for lower weight (-8% vs. -3.5%, p$=$0.06) and C-Reactive Protein (-16% vs. $+$9%, p$=$0.08). **Conclusion**: Participation in an intensive lifestyle intervention program with achievement of CV health measures appears to promote carotid atherosclerosis regression while less successful participation results in atherosclerosis progression. Our novel finding of CIMT regression may be attributable to the intensive nature of our program's case-managed lifestyle intervention.

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Physician Advice for Diet and Exercise for Populations at Risk for Cardiovascular Disease: Opportunities for Telemedicine

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Background: Obesity has reached epidemic proportions with nearly two-thirds of the US population overweight or obese. Lifestyle modifications including exercise and diet are essential for treating patients at risk for cardiovascular disease (CVD). The purpose of this study was to examine PCPs' diet and exercise advice to patients at risk for CVD. **Methods**: Inner city and rural patients with 10% or greater CVD risk (Framingham 10-year risk score) were enrolled in an ongoing telemedicine study to reduce CVD risk. During follow-up, patients were asked about the frequency of PCP diet and exercise advice. Respondents were classified as receiving either diet or exercise advice "always/frequently," "sometimes," or "rarely/never" and differential CVD risk characteristics were considered across advice groups. **Results**: A total of 357 patients had office visits with their PCP. Physicians for 159 patients frequently suggested diet and weight loss advice (FREQ), and physicians for 110 patients did not make such recommendations (RARELY). Baseline blood pressure, cholesterol, and overall CVD risk were similar between FREQ and RARELY groups. FREQ group was heavier (BMI 32.9$\pm$6.4 vs 29.8$\pm$6.8, p$<$0.01), had higher blood glucose levels (138.5$\pm$64.3 vs 112.6$\pm$34.2 mg/dl), and lower HDL levels (45.5$\pm$13.0 vs 49.9$\pm$13.3 mg/dl). Similar trends were observed with exercise advice. **Conclusion**: Physicians are missing key opportunities to provide guidance to obese and overweight patients, an intervention which could prevent further health complications. Given insurance reimbursement limitations and time constraints during office visits, implementing new systems to compliment physicians' visits, such as telemedicine, may be necessary tools of the future.

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Improving Cardiovascular Health in Primary Prevention: Preliminary Results of the Educoeur Interdisciplinary Randomized Controlled Trial

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Objective : Determine if an interdisciplinary intervention combining medical, pharmacological, nutritional, physical activity and psychosocial approaches can lead to greater cardiovascular risk reduction than usual care or specialized clinics in patients at high risk of cardiovascular disease. **Methods** :124 patients with at least two cardiovascular risk were randomized to usual care (UC : N$=$ 41), specialized clinics (SC : N$=$ 41) or to the interdisciplinary Educoeur program (IEP : N$=$ 42). The IEP includes : 1) an individualized treatment program established according to the patients' risk factors and 2) a weekly cardiovascular preventive group treatment program of 12 weeks along with periodical follow-ups for two years. The primary end point of this randomized trial is the cardiovascular risk reduction as measured by PROCAM at 6 and 24 months. In the IEP, 27 patients have completed 6 months of the Educoeur program. **Results** : At 6 months, pre and post treatment program changes demonstrate significant improvements on the following variables: **Conclusion** : The Educoeur interdisciplinary program is effective in reducing cardiovascular risk in patients. Patients demonstrate improved cardiovascular health, dietary habits, physical fitness and psychological symptoms.

	Comparisons after 6 months of interdisciplinary interventions	
VARIABLES	INTAKE	6 MONTHS
Procam***	7.78$\pm$5.92	5.13$\pm$4.93
Weight***	89.76$\pm$19.88	86.37$\pm$18.35
BMI***	30.78$\pm$6.7	29.60$\pm$6.10
Waist circumf**	100.81$\pm$16.10	97.45$\pm$14.20
SBP**	136.63$\pm$15.2	122.61$\pm$14.1
DBP***	88$\pm$9.7	79.59$\pm$9.03
Cholesterol***	5.53$\pm$1.19	4.85$\pm$1.2
LDL**	3.33$\pm$0.96	2.87$\pm$0.90
Triglycerides**	2$\pm$1.32	1.45$\pm$0.62
VO2Max***	30$\pm$7.1	31.9$\pm$7.2
METS-hr/wk**	19.6$\pm$20.1	31.3$\pm$23
Kcal***	2779.74$\pm$971.48	2209.04$\pm$1058.09
Lipids***	108$\pm$50.53	73.37$\pm$40.15
Carbohydrates*	316.45$\pm$116.43	269.95$\pm$128.25
Sugars*	104.11$\pm$45.54	93.17$\pm$47.35
Depression***	8.37	4.96
Hostility*	17.81	15.67

* $\leq$.05 **$\leq$ .01 ***$\leq$ .001

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Hospitalization Outcomes in Individuals Undergoing Coronary Computed Tomographic Angiography, Myocardial Perfusion Imaging, or Cardiac Angiogram Catheterization for the Diagnosis of Coronary Artery Disease

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Background: Cardiac computed tomographic angiography (CTA), myocardial perfusion imaging (MPI), and cardiac angiogram catheterization (CAC) are three diagnostic modalities capable of diagnosis of coronary artery disease (CAD). We determined 1-year CAD-related hospitalizations (hosp) and CAD-related hosp costs in patients (pts) referred to CTA, MPI, or CAC as an initial screen for diagnosis of CAD, and stratified results by cardiac risk factors, including diabetes and hypertension. **Methods**: Private payer administrative claims with complete facility, physician and pharmacy data from 2 large health plans for 2002–2005 were employed. Pts who received CTA, MPI, or CAC as an initial diagnostic screen for CAD, with no screen within six months, were studied. Endpoints included 1-yr CAD-related hosp and CAD-related hosp costs. Cox proportional hazards and log transform regression were used to model endpoints, controlling for pt demographics, health status, screen year and baseline cardiac risk level. All results were stratified by baseline risk factors including diabetes mellitus (DM), hypertension (HTN), hyperlipidemia, myocardial infarction (MI) and known CAD. **Results**: CTA pts (N$=$1,832), compared to MPI (N$=$37,862) or CAC (N$=$4,564) pts, respectively, had higher cardiac risk scores (cardiac risk score: 0.19 vs 0.32 and 1.79, p$<$.0001) but were younger (51 vs 54 vs. 56 yrs, p$<$.0001) and had fewer comorbidities (comorbid score: 0.6 vs 1.0 and 1.7, p$<$.0001). CAC pts had higher rates of risk factors compared to MPI or CAC pts. After multivariate adjustment, the risk of being hospitalized for CAD was higher for MPI (Hazard Ratio [HR] 1.49 DM, 1.54 HTN, p$<$0.0001 for both) and CAC (HR 2.75 DM, 2.83 HTN, p$<$0.0001) compared to CTA. In pts with pre-screen MI, there was no difference in post-screen CAD hosp risk between CAC and CTA. Downstream CAD-related hosp costs were nearly 300% higher for CAC and 95% higher for MPI compared to CTA pts (p$<$.0001). **Conclusion**: Pts who undergo CTA as an initial diagnostic screen for CAD have a lower risk of being hospitalized for CAD and incur lower CAD-related hosp costs compared to MPI and CAC pts in 1 year of followup. These results suggest that CTA may be a cost-effective alternative to MPI and CAC for the evaluation of CAD.

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Effects of Lifestyle Interventions on Quality of Life: Results from the PREMIER Trial

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Health behavior interventions are expected to improve quality of life (QOL) by empowering participants to change their behaviors and improve health. However, health behavior change is difficult, with pressure to maintain status quo. PREMIER was a multi-center, randomized trial that demonstrated multi-faceted lifestyle interventions can effectively reduce blood pressure. This report examines the effects of 2 lifestyle interventions and an advice only condition on QOL. Participants were 295 men and 467 women (34% African American) mean age 50 years with prehypertension or stage 1 hypertension (BP 120–159/80–95 mmHg). QOL was assessed by the SF-36; its 8 subscales and 2 aggregate scores were computed. Participants were assigned randomly to (1) advice only (ADVICE); (2) established guidelines (weight loss $\geq$6.8 kg, $<$100 mmol/day of dietary sodium, 180 min/week of physical activity) (EST); or (3) established guidelines plus the DASH dietary pattern (established guidelines plus 9–12 servings fruits and vegetables, 2–3 servings low-fat dairy products, and dietary intake of total fat $\leq$25% and saturated fat $\leq$7% of total energy) (EST$+$DASH). The intensive intervention lasted 6 months; the maintenance intervention continued another 12 months. Results indicated both intervention groups had greater increases in the QOL subcomponent Vitality at 6 months (EST$+$DASH: parameter estimate [β]$\pm$SE: $\beta$$=2.59\pm$0.71, p$=$0.0003; EST: $\beta$$=1.37\pm$0.71, p$=$0.05) and 18 months (EST$+$DASH: $\beta$$=1.51\pm$0.71, p$=$0.03; EST: $\beta$$=1.33\pm$0.71, p$=$0.06) compared with ADVICE. EST$+$DASH had increases in General Health (6 mo: $\beta$$=1.25\pm$0.54, p$=$0.02; 18 mo: $\beta$$=1.62\pm$0.54, p$=$0.003) compared with ADVICE. At 6 months, EST had greater increase in the Physical Composite score ($\beta$$=1.28\pm$0.62, p$=$0.04) and decrease in Emotional Limitations ($\beta$$=-2.51\pm$1.09, p$=$0.02) compared with ADVICE. EST$+$DASH had greater change in Emotional Limitations ($\beta$$=2.16\pm$1.09, p$=$0.05) and Mental Health Composite scores ($\beta$$=1.74\pm$0.81, p$=$0.03) compared with EST at 6 months. Not only can multiple lifestyle interventions reduce BP, they may result in improve QOL, particularly for Vitality and General Health subscales. The possible negative role of the EST intervention on emotional QOL needs further investigation.

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Perceived Stress and Depression: The Impact of Race and Residence in the "Black Belt" Region of the Southeastern United States

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Introduction*:* The "Black Belt" is contained within the "Stroke Belt" and is an economically depressed region with at least 40% African American population. Here we examine geographic differences in levels of stress and depression, both of which are linked to risk factors associated with stroke including cardiovascular disease and hypertension. **Methods***:* Using data from the REasons for Geographical And Racial Differences in Stroke [REGARDS] study, an ongoing national longitudinal study of 30,000 African American and Caucasian adults at least 45 years of age, we assessed depression (based on the Center for Epidemiologic Studies

Depression Scale (CESD-4)) and stress (based on Cohen's Perceived Stress Scale (PSS-4) measured stress) levels across three regions: 1) the "black belt," 2) the rest of the South, and 3) the rest of the nation. **Results**: For black men and women, and for white women, age and marital status adjusted mean CESD depression scores or Cohen Stress Scores were generally significantly higher (approximately 0.2 and 0.4 points) in the black belt or the rest of the South relative to the rest of the nation (see table). With additional adjustment for income and education (as SES indices), differences were substantially attenuated and became nonsignificant. For white men, age and marital status differences were not evident, and became borderline significantly below the rest of the nation with SES adjustment. No differences were evident in either depression or stress scores between the "Black Belt" and the rest of the South for any race-gender strata ($p > 0.05$). **Conclusions***:* For African Americans and white women, higher stress and depression may be contributors to the higher stroke mortality rates observed in the South; however, hypothesized differences within the South were not confirmed, and differences were not observed for white men. Observed differences appear to be largely attenuated by adjustment for SES, offering the opportunity for interventions.

Difference in mean CESD and stress scores (est / 95% CI) relative to rest of nation

	Depression: Demographic	Depression: + SES	Stress: Demographic	Stress: + SES
BF: Black Belt	0.32 (0.16:0.49)	0.15 (-0.02:0.33)	0.32 (0.09:0.55)	0.12 (-0.12:0.36)
BF: Rest of South	0.38 (0.21:0.54)	0.17 (0.00:0.35)	0.20 (-0.03:0.42)	-0.08 (-0.32:0.16)
BM: Black Belt	0.09 (-0.07:0.26)	-0.02 (-0.19:0.15)	0.16 (-0.09:0.41)	-0.04 (-0.03:0.21)
BM: Rest of South	0.19 (0.03:0.35)	0.05 (-0.12:0.21)	0.05 (-0.19:0.30)	-0.21 (-0.46:0.04)
WF: Black Belt	0.14 (-0.03:0.30)	0.00 (-0.18:0.18)	0.27 (0.04:0.51)	0.20 (-0.05:0.45)
WF: Rest of South	0.23 (0.10:0.36)	0.06 (-0.08:0.20)	0.26 (0.07:0.44)	0.06 (-0.14:0.26)
WM: Black Belt	0.01 (-0.10:0.12)	-0.08 (-0.19:0.04)	-0.06 (-0.24:0.13)	-0.15 (-0.34:0.04)
WM: Rest of South	0.01 (-0.08:0.09)	-0.03 (-0.12:0.05)	-0.08 (-0.21:0.06)	-0.11 (-0.26:0.03)

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Physiological and Psychological Factors Mediate Disparities in Insulin Resistance in Adolescence

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Background: Lower socioeconomic status (SES) is associated with greater insulin resistance (IR), adiposity, and hostility. These findings suggest that adiposity, a physiological factor, and hostility, a psychological factor, may be mechanisms through which lower SES increases IR. This hypothesis was tested in a 1 year prospective study of black and white youth from a Midwestern public school district. **Methods**: The cohort consisted of 1222 healthy, non-Hispanic black and white teens (mean age 16.0, SD 2.0 yr; 55.2% white: 48.3% male; 73.1% postpubertal). At baseline, a parent reported parent education (PE) as a measure of SES and adolescents completed the youth-specific version of the Cook-Medley hostility scale and had waist circumference (WC), height, weight, and fasting plasma insulin and glucose measured. CDC BMI% and IR were calculated using weight (kg)/height-sq(M) and HOMA model, respectively. IR was reassessed 1 year later. Regression analyses utilizing bootstrapping ($N=2000$), a nonparametric resampling procedure recommended for testing mediational hypotheses when assumptions of normality may not be met, were used to derive estimates of the direct and indirect effects of PE on IR and assess the role of hostility and adiposity while adjusting for covariates (baseline age, IR, pubertal status; time to follow up; gender; race). The models using WC and BMI% were nearly identical, but the WC model is reported because it explained more variance in IR (r-sq=.29 vs r-sq=.20). **Results**: Lower PE was associated with increased hostility ($B= 1.08$, $p<.001$), WC ($B=.82$, $p=.03$), and IR ($B=.40$, $p=.001$). Hostility ($B=.04$, $p<.01$) and WC ($B=.10$, $p<.001$) were also associated with IR. The effect of PE on IR was mediated by both hostility and adiposity. The direct effect estimate of PE on IR was -.272 ($p=.02$). The total indirect effect estimate was -.125 (95%CI -.222, -.056, $p<.05$). Hostility accounted for 32.8% of the mediational effect (hostility mediation effect = -.041, 95%CI -.081, -.017; WC mediation effect = -.084, 95% CI -.173, -.019; $p<.05$ for both). **Conclusions**: Lower PE influences IR through adiposity and hostility. Thus, interventions to reduce cardiovascular health disparities associated with IR may require both physiological and psychological approaches.

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Depression and Inflammation in Patients with Coronary Heart Disease: Findings from the Heart and Soul Study

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Background: Depression and inflammation are independently associated with adverse cardiovascular outcomes in patients with coronary heart disease (CHD). Depression has been associated with inflammation in otherwise healthy patients without known CHD. However, studies investigating the link between depression and inflammation in patients with established CHD have produced inconclusive results. **Methods**: We sought to examine the association of depression with inflammation in 984 outpatients with established CHD from the Heart and Soul Study. We assessed current depression using the Computerized Diagnostic Interview Schedule (CDIS) and collected venous blood samples for measurement of eight inflammatory biomarkers [fibrinogen, white blood cell count, albumin, C-reactive protein (CRP), hemoglobin, platelet count, interleukin-6 (IL-6), and CD40 ligand]. We used multivariate analysis of variance to examine the association of current depression with inflammatory markers, adjusted for potential confounding variables **Results**: Of the 984 participants, 22% had depression. Depression was not associated with increased concentrations of any inflammatory marker. Contrary to our hypothesis, depression was associated with lower concentrations of CRP, fibrinogen, and IL-6 (Table). Moreover, the inverse association of depression with CRP, fibrinogen and IL-6 appeared to differ by gender, use of statins, and obesity (p values for interaction <0.10). Specifically, depression was associated with lower inflammation in men, statin users, and non-obese participants, but not in their respective counterparts. **Conclusion**: We found no evidence that current depression is associated with greater inflammation. Inflammation is unlikely to explain the adverse outcomes associated with depression in patients with CHD.

Table: Adjusted mean (± standard error) concentrations of inflammatory markers by current depression status.

	Depressed n=217	*Not depressed n=767*	*p value*
WBC (K/cmm)	7.2±.23	7.1±.21	.62
Hemoglobin (g/dl)	13.3±.16	13.3±.14	.91
Platelets (K/cmm)	246±8	244±7.2	.71
CD40 Lig (pg/ml)	5766±392	5922±352	.61
Albumin (g/dl)	3.8±.04	3.8±.04	.84
Log CRP (mg/L)	1.4±.15	1.6±.13	.09
Fibrinogen (mg/dl)	400±10.5	423±9.5	.006
Log IL-6 (pg/ml)	1.05±.08	1.2±.07	.007

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The Relationship Between Depressive Symptoms, Cardiovascular Disease Risk Factors, and Inflammation in Rural Communities

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The obesity epidemic in the United States is now well documented, with the prevalence of overweight and obesity continuing to rise in nearly all segments of the population. The long-term physical and psychological health consequences for the overweight are of particular public health concern. Numerous studies have established an epidemiologic link between traditional cardiovascular disease risk factors (CVDRF) and a chronic, sub-acute inflammatory state on one hand, and cardiovascular disease on the other. Further, some studies have established a direct link between depression and inflammation.To better evaluate the relationship between depression and inflammation, plasma samples from 245 human participants in a community-based study were analysed using multi-plexed assay technology.In additional to anthropometric measurements obtained during a screening (incl. height, weight, blood pressure, estimate of % body adiposity (%BA) using body impedance analysis), multiple markers of inflammation were obtained from blood plasma. Participants also completed the Centers for Epidemiologic Studies Depression screener (CES-D). In univariate analysis, total depression score (TDS, higher indicating more depressive symptoms) was higher in females ($p<0.05$) and was moderately correlated to age ($p=0.06$) and triglycerides ($p=0.9$). In univariate correlation with inflammatory markers, TDS was related to IL-1b, IL-1ra, and CRP (p,0.05), and moderately related to sE-Selectin ($p<0.1$). To better understand interactions between CVDRF and inflammation, a multiple linear regression model was developed. In a model predicting 28% of the variance in TDS, TDS was predicted by IL-10, IL-13, CRP, and fibrinogen after conrolling for gender, age, IL-1b, %BA, and IL-1ra. TDS increased with increasing IL-10 and CRP, but decreasing IL-13 and fibrinogen. The results of this study report the relationship between depressive symptoms, inflammation, and CVDRF; further study is needed to better understand the relationships between vascular function, depressive symptoms, inflammation and CVDRF. Additionally, further study is needed to better understand the mechanisms underlying the relationships reported here.

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Association of Depressive Symptoms in Young Adults with Health-Related Quality of Life (HRQoL) 10 Years Later: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

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Background: A large proportion (28%) of the U.S. population will experience depressive symptoms in their lifetime. Individuals with depressive symptoms are more likely to experience cardiac events compared to those without symptoms. However, little is known about the association between depressive symptoms at a young age and HRQoL years later. **Methods**: The sample includes 3234 black and white men and women from the CARDIA Study, ages 23–35 in 1990–91. Depressive symptoms were assessed by the Center for Epidemiologic Studies Depression Scale (CES-D) in 1990–91. Participants were classified as having depression if their CES-D score was ≥16. HRQoL (physical, mental, social well-being) was measured by the Medical Outcomes Study Short Form-12 (SF-12) in 2000–01. The SF-12 provides two summary scales: Physical Component Summary (PCS) and Mental Component Summary (MCS). Linear regression analyses were used to examine the association between depression and HRQoL. **Results**: Mean age was 40.1 in 2000–01. About 23% of the cohort had depressive symptoms [mean (SD) CES-D score = 22.5 (6.5); range 16–52]. Black women had the highest percent depressive symptoms (32%) and white men the lowest (14%). Multivariate-adjusted mean scores for the physical and mental component summary scales (PCS and MCS) were significantly lower (worse) in participants with depressive symptoms than in those without (see Table). **Conclusion**: Depressive symptoms in young adults are associated with lower HRQoL ten years later.

Table. Adjusted^ Mean PCS and MCS Scores After 10 Years of Follow-Up According to Depressive Symptoms (Dep) ‡

	Black				White			
	Men		Women		Men		Women	
SF-12 Scale	Dep (n=161)	Not dep (n=451)	Dep (n=280)	Not dep (n=586)	Dep (n=119)	Not dep (n=723)	Dep (n=185)	Not dep (n=729)
PCS$^{\Delta}$	318.4**	337.4	301.9***	325.3	327.7***	353.7	322.2***	343.7
MCS$^{\Delta}$	284.3***	320.7	247.4***	300.6	261.9***	317.1	264.1***	303.9

^Adjusted for age, education, marital status, alcohol use, smoking, physical activity, diabetes, hypertension, antidepressant use, and BMI in 1990–91. ‡Using the Rand SF-12 percentage scoring method $^{\Delta}$Scores ranged from 0–400. * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$

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Differential Effects of Psychosocial Factors on Cardiovascular Reactivity to Psychological and Physiological Stressors in African Americans

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Cardiovascular reactivity to psychological or physiological stressors has been used to identify individuals who are likely to develop hypertension. The contribution of psychosocial factors to the cardiovascular reactivity response is not well understood. Therefore, the following study was designed to determine whether 1) psychosocial factors are associated with the cardiovascular reactivity response to psychological (anger recall) and physiological (cold pressor test) stressors in a population of African Americans, and 2) psychosocial factors' influence on cardiovascular reactivity differed between psychological and physiological stressors. We measured systolic pressure (SP), diastolic pressure (DP), and heart rate (HR) response to anger recall (AR) and cold pressor test (CP) in 180 normotensive African Americans (116 females and 64 males; 18–45 years old). Average SP and DP were measured at baseline and during AR and CP testing. The AR stressor consisted of recalling and verbally describing an angry event and the CP test consisted of immersion of the hand in ice-cold water for 3 minutes. The change in SP/DP/HR was calculated as average SP during the stressor minus the average baseline SP/DP/HR. The psychosocial factors measured included emotional and behavioral responses to perceived racism, hostility, anxiety, and self-esteem. Hostility was negatively correlated with SP ($p<0.04$) and DP ($p<0.002$) responses to AR while emotional response to racism was positively associated with the SP ($p<0.01$) and DP ($p<0.02$) changes. Self-esteem was negatively correlated with HR ($p<0.02$) change to AR. In contrast, perceived racism ($p<0.02$) and anxiety ($p<0.01$) were positively associated with SP changes during CP. These data suggest that psychosocial factors are more predictive of cardiovascular responses to psychological than to physiological stressors. Interestingly, a centrally initiated process such as occurs during perceived racism assessment can influence a peripherally mediated reflex event that occurs during severe cold. These findings suggest that psychosocial factors contribute to the development of cardiovascular disease via influences on biological responses to both psychological and physical stressors encountered in everyday life.

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Psychosocial Factors Contribute to Resting Blood Pressures in African Americans

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Some of the well established risk factors in cardiovascular disease include cholesterol, body mass index, insulin resistance, and elevated resting blood pressure (BP). Recent findings indicate that psychosocial factors may contribute to these biological risk factors. However, what is not clear is the role of psychosocial factors on normal resting BP in healthy individuals, particularly African Americans. Using participants from a larger study that assesses gene-environment interaction and stress on hypertension development in African Americans, psychosocial factor measurements were analyzed to determine if they contributed to resting BP in healthy African Americans. This study presents data from 180 normotensive African Americans (116 females and 64 males) ranging in age from 18–45 years old. The study protocol consisted of anxiety assessment, resting BP measurement, second resting BP measurement, cold pressor test, self-esteem and perceived racism assessments, third resting BP measurement, anger recall stressor, anger expression, depression, hostility, active coping and body mass index measurements. Once the protocol was completed blood samples were collected for serum measurements of glucose, insulin, triglycerides, and cholesterol. Blood pressures were taken each minute over five minutes using an automated monitoring system. Resting systolic (SP) and diastolic (DP) BPs as well as heart rate (HR) were calculated as the mean of the five readings during each session. Resting SP was positively associated with age ($p<0.0001$) and gender ($p<0.001$) but not with any of the measured psychosocial factors. However, DP negatively correlated with anger-in expression ($p=0.02$) and positively associated with age ($p<0.001$). Both HOMA (index of insulin resistance;high values indicate increased insulin resistance) and insulin were positively correlated with resting HR ($p<0.001$). Unlike anger-in and DP, anger control ($p<0.003$) was positively correlated with HR. These data show that psychosocial factors such as anger expression can significantly contribute to normal resting cardiovascular function, and, thus, may be involved in modulating behavioral and/or traditional biological risk factors that determine resting cardiovascular physiology.

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Transdermal Estradiol and Progesterone Improve Mood Indicators, Quality of Life, and Biomarkers of Cardiovascular Disease in Perimenopausal and Postmenopausal Women

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40 million US women suffer from perimenopausal/ menopausal symptoms and there is cause for concern in using conventional HRT due to adverse risks determined by the WHI. In sharp contrast to experimental data, which reveals favorable effects of estradiol and progesterone on vascular biology and physiology,oral conjugated equine estrogens and medroxyprogesterone acetate failed to demonstrate a cardioprotective effect of HRT in the WHI and HERS.Our study investigates the effects of transdermal estradiol and progesterone on mood indicators of anxiety and depression,quality of life (QOL), and biomarkers of cardiovascular disease(CVD).150 women of Caucasian,Black,Native American and Hispanic ethnic descent(mean age 51.8 yrs)who met strict inclusion/exclusion criteria were enrolled in our prospective,case-controlled study(75 controls,75 interventional). The 8 week effects of low dose daily transdermal progesterone and estradiol therapy on mood, QOL, and gender-specific biomarkers of CVD were identified.Baseline analyses of the control group did not show a significant difference from the interventional group for cardiovascular measures.QOL measures demonstrated significant improvement in Greene Climacteric Scale scores($p<0.002$) Hamilton Anxiety scores($p<0.005$)and Hamilton Depression scores ($p<0.004$) with application of transdermal hormone.Subjective report of hormone related symptoms was significantly decreased from baseline($p<0.0005$).Transdermal progesterone and estradiol significantly decreased Systolic Blood Pressure ($p<0.05$) and Pulse Pressure decreased ($p<0.02$).Fasting Blood Glucose was significantly decreased ($p<0.001$) in the interventional group after 8 weeks of hormone therapy. In women with TG levels $>/=130$ mg/dL, levels were decreased ($p<0.02$) by 20% from baseline levels.Homeostasis Metabolic Assessment of Insulin Resistance was significantly reduced ($p<0.04$) in subjects with baseline levels of $>/=2.0$.Plasma fibrinogen,nitric oxide,myeloperoxidase and plasminogen activator inhibitor were unchanged.Transdermal progesterone and estradiol demonstrate statistically significant favorable effects on mood, QOL and biomarkers for CVD in perimenopausal and postmenopausal women.

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Cardiovascular Disease Risk Factor Education in Mississippi Adolescents

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Introduction: Among young people, chronic diseases such as hypertension, diabetes, obesity, and dyslipidemia are increasing at alarming rates, especially in minorities. Increasing cardiovascular disease (CVD) awareness is imperative because of very early onset of risk factors. In many Mississippi homes, these young people are the highest functioning member of the family and an appropriate target for improving overall family health. Training adolescents as health promoters is an effective strategy for increasing health awareness in the family and community. The Science, Language Arts and Mathematics (SLAM) program, is a summer-long collaboration of Jackson Heart Study and Tougaloo College for adolescents. Participants have CVD risk assessment and education regarding risk factors, as part of an ongoing "Know Your Numbers" initiative. This project assessed the effectiveness of this part of SLAM. **Methods**: Seventy students participated in SLAM 2006, 33 returning (RS) and 37 new students (NS).They were 66% (46/70) female, age 14–17 years, and 96% (67/70) black. A validated "Do You Know Your Numbers?" questionnaire consisting of 5 questions was administered after the risk assessment but prior to the education series. For this assessment, responses were divided into two groups, RS and NS. **Results**: The majority, 94% (31/33) of RS and 89% (33/37) of NS, identified optimal blood pressure. Only 55% (18/33) of RS and 22% (8/37) of NS identified an optimal BMI. Of RS 73% (24/33) knew optimal glucose compared to only 38% (14/37) of NS. Also, 67% of RS identifed optimal cholesterol levels compared with 43% of NS. The correct definition for BMI was identified by 88% (29/33) of RS and 65% (24/37) of NS. **Conclusion**: This assessment shows that most could not identify normal blood pressure, glucose, cholesterol, and BMI parameters prior to SLAM participation. This assessment also demonstrates one area of effectiveness of the summer outreach program. RS outscored NS in every category and also had self-reported changes in health behaviors. Educating adolescents is the first step in decreasing the prevalence of CVD risk factors in this population and also has the potential to influence overall family health awareness and change the cardiovascular health and future of Mississippi.

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Assessment of Health Literacy Using Nutrition Labels

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Purpose: People with low health literacy make more medication and treatment errors, are less able to follow treatment procedures, and lack skills needed to negotiate the health care system. In general, adults over age 65 have lower health literacy. Rates also vary among racial groups with white and Asian adults having higher health literacy rates than blacks, Hispanics, and American Indians. To improve health literacy and health outcomes, it is critical that patients be provided with both verbal and written information they can understand. As part of a health focus conference, this project assessed the baseline health literacy of a population of state employees with the use of a validated survey instrument, the New Vital Signs (NVS) test. **Methods**: Participants included state employees in Jackson, MS, attending a work-site health conference. The participants were asked to complete the NVS test, which was identified as the "Ice Cream Label" survey. The NVS test contains six questions answered by reviewing a nutrition label from an ice cream container. Participants were asked to read the survey and provide written answers. Demographic information was also provided by participants. **Results**: The survey was completed by 129 participants; total and individual question scores were calculated. Test scores correlate with health literacy, above 4 indicating adequate health literacy and below 4 possible limited health literacy. In our population, 35% (45/129) had scores that implied adequate health literacy, 14% (18/129) had a borderline score of 4, and 51% (66/129) fell below the score of 4, indicating limited health literacy. No significant associations were found between total score and gender, age, or BMI. Race did show a significant correlation with overall score. Black participants generally had lower scores than white participants ($p=0.000$). The majority of questions on the survey were answered correctly by 60% (77/129) or more of the population. **Conclusions**: People of any age, income, race, or background can find it challenging to understand health information. The findings of this project

reinforce that minority groups may be at higher risk for inadequate understanding of health information and highlight the need for appropriate health literacy interventions.

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Pattern of Change in Chronic Angina Symptoms Predicts Decreased Physical Function in Outpatients with Coronary Artery Disease

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Purpose: Using slope analysis, we prospectively documented patients' patterns of change over a 6 month period in chronic angina symptoms along 5 dimensions: angina frequency, duration, severity, emotional upset because of angina, and perceptions of angina as a serious health problem. We then examined if patterns of change predicted decline in physical function (PF). **Method** The sample included 71 outpatients with chronic angina (43.2% women, mean age 64.1(SD 12.1). Subjects completed an angina symptom diary weekly for 6 months. Self-reported PF was measured with the Seattle Angina Questionnaire PF subscale (SAQ). Slope analysis was used to characterize subjects' symptom pattern for each dimension. Subjects' symptom patterns were classified as "decreasing" if they had significant,negative slopes for their angina ratings over time. Subjects with non-significant slopes were classified as "stable" and subjects with positive, significant slopes were classified as having an "increasing" symptom pattern. Change in PF was calculated by subtracting the baseline SAQ score from the 6 month SAQ score. Negative change scores indicated PF had worsened over time. **Results**: See Table. The majority of subjects had a stable symptom pattern in each of the 5 dimensions. Controlling for age, subjects with "increasing" symptom patterns for angina symptom duration, severity, emotional upset because of angina, and perception of angina as a serious health problem demonstrated a significant decline in PF over 6 months compared to patients with stable or decreasing symptom patterns. **Conclusion**: Findings suggest that change in pattern of angina frequency over time may not be as important in predicting PF as other aspects of the angina experience, such as whether it is perceived as becoming a more serious health problem. Clinicians' understanding of patients' perceptions of angina and managing these perceptions may be important to promoting physical function.

% of Sample Reporting Angina Pattern and Mean (SE) Change in Physical Function By Symptom Pattern

	Decreasing % Mean (SE)	Stable % Mean (SE)	Increasing % Mean (SE)	ANCOVA p value
Angina frequency	26.8% 4.00_a (4.4)	59.2% 2.90_a (2.7)	14.1% 1.16_a (7.3)	NS
Angina episode duration	14.1% 9.4_a (5.9)	79.7% 2.5_a (2.5)	06.3% -16.4_b (8.3)	.046
Angina severity	10.9% 3.3_a (5.8)	67.2% 6.2_a (2.4)	21.9% -15.9_b (5.2)	.001
Angina is emotionally upsetting	15.6% 1.8_a (6.2)	67.2% 6.5_a (2.5)	17.2% -15.2_b (5.5)	.006
Angina is a serious health problem	14.1% -0.18_a (8.2)	62.5% 7.4_a (2.6)	23.4% -13.8_b (5.2)	.002

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Reasons for Poor Adherence in a Prospective Cohort of New Statin Users

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Background Statins are a highly effective intervention for reducing cardiovascular outcomes but their benefits have been limited by low rates of adherence. This prospective cohort study was designed to assess adherence among new statin users and identify patient factors related to poor adherence. **Methods** 71 VA patients without CVD or diabetes and newly started on a statin were interviewed at baseline, 3 month and 6 month regarding demographics, co-morbidities, depression, physical activity, diet, and patient beliefs potentially related to medication adherence. Poor adherence was defined as a Morisky adherence score of <10 corroborated with pharmacy data. **Results** 10% of patients never filled their first statin prescription while 61% and 58% were non-adherent at 3 at 6 months (mean length of statin use, 39 days). 79% of patients preferred diet before a statin but only 52% reported being given a trial of diet alone. Significant predictors of poor adherence in univariate models ($p<.05$) included: Demographics (age$<$50, Hispanic ethnicity, higher education, less comorbidity), Low Perceived MI risk, Medication/Treatment beliefs (statins are curative, short expected treatment duration, Medication Concerns (statin may be harmful, pill not easier than diet), and Diet Treatment beliefs (diet is curative, plans to further modify diet, belief in the efficacy of diet). In multivariate logistic models poor adherence at 3 months was associated with age$<$50, short expected treatment duration, a belief that statins are curative, disbelief in statin's cholesterol reducing power, and recent emphasis on dietary change by their MD ($p<.05$). At 6 months correlates included age$<$50, low perceived MI risk, short expected treatment duration, and a recent emphasis on diet change by patient or MD. **Conclusions** Most patients who were started on statins had poor adherence at 3 and 6 months with 1 in 10 patients never filling their prescription. Patient beliefs related to poor adherence were perceived low risk, a recent emphasis on dietary change and short statin treatment duration expectations. Future studies must incorporate these beliefs into statin adherence interventions.

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Over-the-Counter Use of Orlistat 60 mg Results in Positive Changes in Lifestyle

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Background and Design: Orlistat is pending final FDA approval as an over-the-counter (OTC) medication at a new lower dose of 60 mg. Few data are available on behavioral changes associated with pharmacological treatment, particularly within an OTC environment. A 3-month open-label, naturalistic study was conducted in 18 pharmacies to examine the impact of orlistat 60 mg plus self-instructional educational materials (orlistat program) on changes in diet and physical activity in the absence of supervision from any healthcare professional. **Methods**: A total of 237 subjects purchased and used one or more orlistat 60 mg packages, which included a bottle of orlistat 60 mg capsules along with educational lifestyle tools (User Guide, Food Diary, Calorie & Fat Gram Counter, Diet Success Planner). The label instructed subjects to take orlistat 60 mg 3 times daily with meals along with a reduced calorie, low fat diet. Dietary and exercise variables were collected at the time of enrollment and at 14, 30, 60, and 90 days post-enrollment. **Results**: At the time of enrollment, 26% of subjects (61 of 237) were following a diet (self-imposed, commercial or medically supervised). Within 2 weeks of starting the orlistat program, 80% of subjects (173 of 217) reported following a diet, with 62% (135 of 217) specifically citing a reduced fat or fat-free diet. Three-quarters (177 of 237) of subjects reported some physical activity at the time of enrollment and within 2 weeks of starting the orlistat program 85% of subjects (184 of 217) reported exercising. Importantly, 57% of these subjects (104 of 184) increased their activity from enrollment, with a median increase of 30 minutes per week. At the day 90 interview, over 80 percent of subjects who made changes in diet or exercise reported satisfaction with the study medicine. The median self-reported weight loss for subjects who increased their physical activity was 11.5 lb (6% weight loss) and 10 lbs (5% weight loss) for subjects who adopted or continued on a diet since enrollment. **Conclusions**: Subjects taking orlistat 60 mg do not rely on the medication alone but also make appropriate changes in diet and activity. These changes were accompanied by weight loss and consumer satisfaction.

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Marital Status and Heart Disease Mortality Among Elderly African-American, Hispanic, and White Women

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Background: Heart disease is the leading cause of death in women nationwide. Previous studies have found an association between marital status and heart disease mortality; married women have a lower risk of mortality then women who are unmarried. However, previous studies have not assessed effect modification by race/ethnicity and age. In this study, we investigated whether the increased risk of heart disease mortality for unmarried women by varied race/ethnicity and age. **Methods**: Our study population consisted of women aged 65 years and older who resided in the Tampa Metropolitan Statistical Area during the years 1998–2000. Population estimates for the Tampa MSA were obtained from the 2000 U.S. Census Public Use Microdata Sample (PUMS). Total person-years analyzed were 1,317,070. Death data were obtained from the Florida State Office of Vital Statistics. Deaths for which the underlying cause was coded to "diseases of the heart" or "symptoms, signs, and ill-defined conditions" were included in our analyses. A total of 22,713 deaths were included in this study. Heart disease death rates were calculated for 24 demographic groups, defined by marital status (unmarried vs. married), age (65–69, 70–74, 75–79, 80+ years), and race/ethnicity (Blacks, Hispanics, Whites). Detailed socioeconomic indicators were calculated using the 2000 PUMS dataset. **Results**: Overall, unmarried women had higher heart disease mortality rates than married women, with relative risks (RR) ranging from 1.8 for ages 65–69 to 3.0 for ages 80+. Results for white women were similar to results for all women combined. For Black women, the RRs by age were 1.5 (65–69 years), 1.4 (70–74 years), 1.9 (75–79 years) and 4.3 (80+ years). For Hispanic women, the RRs by age were 1.5, 1.9, 1.7, and 2.7, respectively. For all groups, unmarried women had lower incomes, were much more likely to live alone, and had higher rates of disability than married women. **Conclusions**: Unmarried elderly women are at higher risk for heart disease mortality than their married counterparts. The majority of these women live alone, outside of nursing homes or other institutions. Future research should focus on psychosocial, socioeconomic, biomedical, and behavioral risk factors for heart disease among elderly unmarried women.

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Psychometric Evaluation of a Short Form of the Coping Strategies Inventory in the Jackson Heart Study Cohort

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Objective: We studied data on coping skills from 5302 participants in the Jackson Heart Study (JHS) cohort to establish the psychometric properties, including the factor structure of a shortened form of the Coping Skills Instrument (*CSI*) that was used. This was a necessary precursor to utilizing this instrument in future efforts to understand the role of coping in moderating health outcomes in a large sample of African Americans. **Hypothesis**: We assessed the hypothesis that the *CSI-SF* would be an adequate measure of coping behaviors in the Jackson Heart Study cohort. **Methods**: We used exploratory and confirmatory factor analysis to examine the responses of the JHS participants ages 21 to 95. Participants were administered the 16-item *CSI -SF*, a modified form of the original Coping Strategies Inventory (*CSI*). In addition, reliability and validity procedures were computed, utilizing Pearson r correlation coefficients and Cronbach Alpha coefficients. **Results**: Each of the four hypothesized scales was confirmed. Items were retained on the basis of item-factor loadings and overall model fit. One item was dropped from the 16-item *CSI-SF*, making it a 15-item instrument. Additional analysis was completed examining the effects of gender and age. No significant effects were found in any of these dimensions, strengthening the generalizability of the *CSI-SF*. The internal consistency reliability analysis revealed levels of reliability between alpha $= 0.58-0.72$ for all of the scales. **Conclusion**: This study served to establish the psychometric properties of the *CSI-SF* and support its use as an instrument to adequately measure coping behaviors of African Americans in the Jackson Heart Study. We concluded that the responses to the *CSI-SF* can be evaluated through the use of the same four levels of factors that were used in the original CSI. In conclusion, the analyses conducted confirm that the recommended 15-items for the shortened CSI-SF are adequately representative of the scales under investigation, and that this 15-item *CSI-SF* is reliable for measuring the coping behaviors of the Jackson Heart Study African American cohort.

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Self-Efficacy, Health Locus of Control, and Perceived Risk Among Individuals at Elevated Risk for Cardiovascular Disease

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Background: Self-efficacy, risk perception and health locus of control have all been implicated as predictors of health information seeking and the adoption of healthy life-style behaviors. The aim of this study was to explore the relationship between these psychosocial constructs and health status among subjects at increased risk for cardiovascular disease. **Methods**: Subjects were enrolled in a one-year internet-based telemedicine randomized controlled trial to reduce cardiovascular disease (CVD) risk. To be eligible for the trial, individuals were required to have ≥10% Framingham risk score. At baseline, risk perception, self-efficacy (exercise, medication adherence, and nutrition action) and multidimensional health locus of control were assessed via questionnaire. **Results**: Data were available for 465 subjects (age= 60.4±10.1 years; mean Framingham risk score = 16.9±9.6 %; 45% female/55% male; 45% diabetes and 27% smokers). Health locus of control was not consistently correlated with either health status or self-efficacy. Individuals with a higher belief in powerful others had significantly higher Framingham risk scores (18.5±7.5 % vs. 15.2±11.1%; p <0.001), lower HDL levels (45.5±12.8 vs. 48.6±12.9 mg/dl; p <0.01) and decreased feelings of exercise self-efficacy (2.6±0.8 vs. 2.8±0.9; p<0.01) as compared to individuals with low belief. Individuals with a high internal locus of control had significantly increased levels of nutrition action self-efficacy (2.6±0.8 vs. 2.4±0.7; p<0.0) but these did not correlate with health status. Higher levels of both exercise (-0.2; p<0.001) and nutrition self-efficacy (r=-0.1; p <0.001) were associated with lower fasting blood glucose levels. Perceived risk did not correlate with either actual risk or health locus of control. **Conclusions**: Increased self-efficacy had a positive affect on health status while a higher belief in powerful others as a determinant of health has a negative impact among individuals at increased risk for cardiovascular disease. Risk perception was not an important determinant of either self-efficacy or health status.

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Neighborhood Socioeconomic Characteristics and Risk of Myocardial Infarction

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Neighborhood socioeconomic characteristics are associated with cardiovascular disease risk, but measurement of neighborhood socioeconomic context varies across studies. **Hypothesis**: We hypothesized that high neighborhood income, wealth, or educational attainment would be associated with lower risk of incident myocardial infarction (MI). Further, we hypothesized that these associations would be strongest for neighborhood definitions that capture a smaller, more local area that may more directly affect health behavior, stress, social support, and exposure to hazards such as air pollution. **Methods**: We used data on incident MI cases and frequency matched controls from a population-based case-control study in the Puget Sound region of Washington State. Individual characteristics were collected by telephone interview and medical record review. Five neighborhood socioeconomic characteristics were assigned or estimated using census data: (1) median household income, and percentages (2) below poverty level, (3) home ownership, (4) with a high school degree, and (5) with a college degree. We considered 4 neighborhood definitions: 1-km airline buffer around the home, census block group, census tract, ZIP and code. Logistic models were used to examine risk of MI across quartiles of neighborhood characteristics, adjusted for individual socioeconomic characteristics and matching variables. **Results**: Our analysis included 487 MI cases and 1,873 controls. Each of the 5 neighborhood socioeconomic characteristics had an association with MI for at least one of the 4 neighborhood definitions. Only percent with a college degree was significant across all neighborhood definitions; odds ratios for low versus high quartile of this measure ranged from 1.6 at the census tract level (95% confidence interval: 1.1 to 2.1) to 1.7 for a one-km buffer (95% confidence interval: 1.2 to 2.3). No neighborhood definition had consistently stronger associations with MI. **Conclusion**: The association between neighborhood socioeconomic characteristics and risk of MI was not consistently stronger for any of the neighborhood spatial definitions considered, but did appear stronger for education-based neighborhood characteristics compared with measures of income and wealth.

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Agreement Between Stage of Change and Measured Behavioral End Points: Implications for Intervention Design

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Background: The Transtheoretical Model-Stage of Change is commonly used both as a theoretical framework and a surrogate endpoint for cardiovascular disease (CVD) risk reduction interventions. We examined the relationship between stage of change for three different behaviors, corresponding behavioral self-reports, and objectively measured behavior among 230 (80% of 289 randomized) persons who completed an 18-month trial to encourage smoking cessation, dietary sodium reduction to <2300 mg, and increased physical activity. **Methods**: African-American smokers, aged 45–65, with hypertension, dietary sodium intake >2300 mg/day (100 mmol/L/day), and low levels of leisure time physical activity were randomized to one of three arms: 1) stage-of-change based telephone counseling targeting all three behaviors at once for 18 months, 2) the same counseling protocol targeting one behavior for six months, then proceeding to the next; or 3) referral to group education classes (usual care). Objective measures (urine cotinine, 24-hour urine sodium, and pedometer steps) and behavioral self-reports (7-day smoking abstinence, the Willett food frequency questionnaire, and the Stanford 7-day physical activity recall) were obtained every six months. **Results**: Simultaneous counseling resulted in significant shifts in stage of change for smoking cessation and physical activity compared to sequential counseling or referral only. Agreement between baseline urine cotinine level and stage of change for smoking cessation was 98% (219/223). However, at 18 months, urine cotinine was detected in 181 of 197 (92%) of those not yet in action or maintenance, 9 of 17 (53%) of those in action, and 5 of 19 (26%) of those reporting to be in maintenance. Stage of change for low dietary sodium was not related to urine sodium or sodium intake estimated from the Willett FFQ, either at baseline or 18 months. Similarly, physical activity stage of change was not associated with pedometer steps or physical activity recall scores at baseline or 18 months. **Conclusion**: Stage of change is poorly correlated with both behavioral questionnaires and objectively measured behavioral endpoints, and should not be used as a surrogate endpoint for CVD risk reduction behavioral interventions.

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Longitudinal Association of Educational Attainment and Health-Related Quality of Life in Adults 65 Years and Older: The Chicago Heart Association Detection Project in Industry

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Background and Objective: Existing data on the association of education to health-related quality of life (HRQOL) are mostly cross-sectional and findings are inconsistent. We examine the longitudinal association of educational attainment with HRQOL and changes in HRQOL among older adults using repeated measures of HRQOL at 3 time points over 7 years of follow-up. **Methods**: We included men (n=2572) and women (n=1836) from the CHA Study ages ≥65 in 1996 with HRQOL assessments by Health Status Questionnaire-12 (HSQ-12) on health perception, and physical and mental well-being in 1996, and at least once again in 2001 and/or 2003. The higher the HSQ-12 score, the better the outcome. Educational attainment in 1996 was categorized into 3 groups: high school or less, some college, college graduate or more. **Results**: On average, women were older and less educated than men (age in 1996, 73.3 vs. 71.8; college graduate or more, 18.7 % vs. 46.3%, respectively). With adjustment for socio-demographic factors, higher education level was associated with higher (better) HSQ-12 scores in 1996. The relation was similar in both men and women (p-values: <0.05-<0.001). Higher education level was also associated with lower annual declines in HSQ-12 scores for sum of all, mental, and physical components in men (p-values:<0.1- <0.05 - see Table) but not in women. With additional adjustment for smoking, alcohol use, exercise, body mass index (BMI), and comorbidities, differences in 1996 HRQOL score by education were attenuated but remained significant while differences in annual HRQOL score changes were no longer significant. **Conclusions**: Higher education level in older adults is associated with higher quality of life in both men and women as well as lower decline of quality of life in men. These findings are explained in part by lifestyle factors, BMI, and comorbidities.

Multivariate Adjusted 7-Year Association of Education and HRQOL – Men

	Regression coefficients (β)		
Education Level	Total Scores (0–800)	Physical Component Scores (0–400)	Mental Component Scores (0–400)
	Average 1996 HSQ-12 Scores		
High school or less	570.6	276.6	293.4
Some college	594.0‖	292.1	301.3§
College or more	616.8¶	308.7¶	307.6¶
	Average Annual Changes in HSQ-12 Scores		
High school or less	-11.5	-6.8	-4.6
Some college	-10.1	-6.5	-3.5*
College or more	-8.9§	-5.5*	-3.2§

Adjusted for time as a continuous variable; fixed covariates: race, baseline age; time-dependent covariates: dummy variables for marital status, living arrangement; and interaction terms of time with dummy variables for education. *p<0.1; §p<0.05; ‖p<0.01; ¶p<0.001 for comparison with the lowest education group based on GEE models.

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Alcohol Consumption and Mortality Among Men and Women in China

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Epidemiologic studies indicate that moderate alcohol consumption may lower all-cause mortality while heavy consumption may increase mortality. We examined the relationship between alcohol consumption and mortality in a prospective cohort study of 169,871 Chinese adults aged 40 years or older. Data on alcohol intake and covariables were obtained at a baseline examination in 1991 using a standard protocol. Follow-up was conducted in 1999–2000, with a response rate over 93% (n=158,666). Multivariate-adjusted Cox proportional hazards models were used to calculate the relative risk of all-cause mortality at various levels of alcohol consumption using non-drinkers as the reference. After excluding participants missing data on alcohol consumption, 142,235 adults (69,364 men and 72,871 women) were included in this analysis. During a mean follow-up of 8.3 years (1,100,610 person-years), 17,757 deaths were documented (10,037 among men and 7,720 among women). After adjustment for age, education, cigarette smoking, body mass index, physical inactivity, systolic blood pressure, geographic region (north vs. south) and urbanization (urban vs. rural), a non-linear association between alcohol intake and mortality was observed among men (p<0.001) while a linear association was observed among women (p=0.008). Compared to non-drinkers, the relative risks (95% confidence interval [CI]) of all-cause mortality were 0.87 (0.79–0.94) for men who drank ≤6 drinks/week, 0.85 (0.78–0.93) for 7–13 drinks/week, 0.87 (0.80–0.95) for 14–20 drinks/week, 0.88 (0.80–0.96) for 21–34 drinks/week, and 0.96 (0.89–1.03) for ≥35 drinks/week. Compared to non-drinkers, the relative risks (95% CI) of all-cause mortality among women were 0.98 (0.80–1.21) for women who drank ≤6 drinks/week, 1.29 (1.03–1.63) for 7–13 drinks/week and 1.17 (0.96–1.42) for ≥14

drinks/week. Similar associations were found after excluding participants who had a chronic illness at the baseline examination or who died during the first 3 years of follow-up. These data indicate that a J-shaped association between alcohol consumption and mortality exists among men but not women in China.

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Association Between Education and Peripheral Artery Disease in US Adults: The 1999–2002 National Health and Nutrition Examination Survey

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Background: Little is known about whether education is associated with peripheral artery disease in US adults. **Objectives**: We investigated the association between education and PAD in 4015 healthy US men and women aged 40 to 85 years from the National Health and Nutrition Examination Survey (1999–2002). **Methods**: Education level was classified by number of years of education: less than high school (<HS), completion of high school (HS), or college graduation or more. Systolic blood pressures were measured twice at the right brachial and posterior tibial arteries in both legs, and the average of two measurements was used for analysis. Right and left ankle-brachial indexes (ABI) were calculated as ankle systolic blood pressure at right and left, respectively, divided by brachial systolic blood pressure. Peripheral artery disease (PAD) was classified as ABI <0.9 in either leg. Multivariate logistic regression models were used to investigate the association between education and PAD after adjustment for age, sex, race, and multiple risk factors. The lowest education (<HS) was the reference category. **Results**: After adjustment for age, sex, and race, there was a direct inverse association between education and PAD (p for trend <0.001). These associations persisted after additional adjustment for multiple risk factors (cigarette smoking, alcohol intake, body mass index, physical activity, high-density lipoprotein and total cholesterols, hypertension, and diabetes mellitus). The odds ratios (and 95 % CI) of having PAD across educational levels were: 1.00 (<HS), 0.70 (0.43, 1.12), and 0.42 (0.25, 0.68) (p for trend <0.001). Individuals with high school graduates and college graduates or more had a 30% and a 58%, respectively, lower odds of having PAD as compared with individuals with less than high school education. **Conclusions**: Education is inversely associated with prevalence of peripheral artery disease in a large US middle-aged and elderly populations.

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Cardiovascular Disease Risk Factors in Former Smokers

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Smoking is a strong independent risk factor for cardiovascular disease (CVD), and smoking cessation has beneficial effects on health. This cross-sectional study compared cardiovascular risk factors in former smokers (n=20242) and lifelong non-smokers (n=26907). The study aimed to determine whether those who cease smoking differ from lifelong non-smokers in their physical activity and dietary behaviors and CVD risk profile. Male (n=12935) and female (n=7307) former smokers had significantly higher BMI than male (n=9384) and female (n=17523) non-smokers (0.4 kg/m2 and 0.6 kg/m2 greater for males and females respectively, p<0.001). In both men and women, a greater prevalence of existing coronary heart disease (CHD) and peripheral vascular disease (PVD) was seen in former smokers compared to lifelong non-smokers (28.6% vs. 18.3% and 17.2% vs. 14.1% for males and females respectively, p<0.001). In women, former smoking was associated with a lower diabetes prevalence compared to non-smokers (28.8% vs 31.0%, p=0.001) while male former smokers had a greater prevalence of diabetes than non-smokers (40.2% vs 34.8%, p<0.001). Estimated Framingham 10-year risk of coronary heart disease was significantly higher in male former smokers compared to lifelong non-smokers, but significantly lower in female former smokers (24.5% vs 21.4% in males and 14.6% vs 15.6% in females for former and lifelong non-smokers respectively, p<0.001). Former smokers and lifelong non-smokers did not differ in rates of adherence to a low-fat diet, but former smokers were significantly less likely to adhere to a low-salt diet than non-smokers (53.2% vs 58.1%, p<0.001). Former smokers were more likely to undertake at least 30 min exercise 5 or more times per week, but also more likely to be inactive, while lifelong non-smokers were more likely to be exercising 1–2 times per week. Former smoking is not accounted for in many commonly used risk calculators, including the Framingham risk score. The higher rates of CVD in the former smoking cohort contrast with the lower calculated CVD risk scores in female former smokers. In conclusion, former smokers and lifelong non-smokers differ significantly in their estimated CVD risk and in the lifestyle behaviors which influence CVD risk.

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The National Prevalence of Healthy Lifestyles Is Low and Varies by Race and Geographic Region

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Introduction: Some preventable chronic diseases cluster by race and geographic region. Higher prevalence of preventable chronic diseases in some subgroups may be due to low levels of healthy lifestyle characteristics (HLC).We hypothesized the prevalence of HLC would vary by race, socio-economic status (SES), regions of the country, and existence of chronic disease risk factors. **Methods**: This cross-sectional analysis was based on data from the REasons for Geographic And Racial Differences in Stroke (REGARDS) study, a national longitudinal cohort study of black and white individuals over age 45 years, with data obtained from January 2003 to June 2006. Fifty percent of the sample was selected from the Stroke Belt (NC, SC, GA, AL, MS, TN, AR, and LA). HLC were defined for diet (≥5 fruit and vegetable servings/day), physical activity (≥4 times/week), weight (body mass index [BMI] <25 kg/m^2) and smoking (current non-smoker). Outcomes include estimates for prevalence of each HLC by region, demographics, health status, and chronic disease status subgroups and proportional odds from univariate and multivariate logistic regression models predicting HLC, adjusted for subgroup characteristics. **Results**: Of the 17,326 study participants, 10.4% had ≥5 fruit and vegetable servings/day, 30.6% exercised ≥4 times/week, 24.9% had a BMI <25 kg/m2, and 86.5% were non-smokers. Only 1.5% had all 4 HLC and fewer than 35% had at least 2 HLC. In univariate analyses, whites were more likely than African Americans to have HLC (OR 1.86; 95% CI 1.75–1.97) and, residents in the stroke belt were more likely to have HLC than residents of other states (OR 1.10; 95% CI 1.04–1.18). These relationships remained after multivariate adjustment for income, education, and health status. Significant linear trends for increased HLC were seen for incrementally higher levels of income, education, and self-reported general health status in univariate models; however, in the multivariate models the trend was attenuated for income and education. **Conclusions**: Few study participants reported multiple HLC. Although the prevalence of multiple HLC in the REGARDS sample was very low, there were still significant variations by demographic, regional, SES, and health status subgroups.

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Mortality and Smoking in China: A Prospective Study of 169,871 Men and Women

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We studied the cause-specific mortality attributable to cigarette smoking in a nationally representative cohort of 169,871 men and women aged 40 years and older in China. Data on cigarette smoking, demographic information, and medical history were obtained at a baseline examination in 1991 by trained observers using a standard protocol. Follow-up was conducted in 1999–2000 with a response rate of 93.4%. Cox proportional hazard analysis was used to adjust for age, education, physical activity, alcohol consumption, hypertension, obesity, diabetes, geographic region (north vs. south) and urbanization (urban vs. rural). The multivariate-adjusted relative risk (RR), population attributable risk (PAR %), and absolute number of deaths in China attributable to cigarette smoking are shown in the table. Overall, cigarette smoking caused about 458,225 deaths per year in Chinese men and women aged 40 years and old, chiefly from cancer, vascular, and respiratory diseases. Our study indicates that cigarette smoking is a major preventable cause of death in the Chinese general adult population. Furthermore, these data underscore the importance of developing a national policy for smoking cessation in China.

	Men			Women		
	RR	PAR %	Deaths	RR	PAR %	Deaths
Total	1.21 (1.16, 1.26)	13.0	390,481	1.31 (1.23, 1.39)	2.9	67,744
Cancer	1.56 (1.42, 1.71)	28.5	211,463	1.62 (1.42, 1.85)	5.8	23,938
Respiratory	1.16 (1.04, 1.29)	10.2	48,469	1.48 (1.29, 1.71)	4.5	17,302
Vascular	1.16 (1.08, 1.25)	10.4	106,743	1.22 (1.11, 1.35)	2.1	17,258

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Evaluation of Prenatal Diagnosis of Significant Structural Heart Disease by Echocardiography in Clark County, Nevada, from 2004 to 2006

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Background: Congenital heart disease (CHD) is a significant cause of perinatal mortality and morbidity worldwide. Its prenatal detection rate remains low in most part of the world; an important proportion of infants with serious CHD are diagnosed only postnatally. **Objectives**: To evaluate the proportion of significant CHD prenatally diagnosed. **Methods**: This report includes data from 1546 patients seen from January 2004 to July 2006 by our group which is the only referral group for pediatric cardiac evaluation in Clark County, Nevada. Study population is composed of all prenatal cardiac evaluations and all patients with significant CHD diagnosed in the first year of life, born in Las Vegas and without prenatal echocardiography. **Results**: From 775 fetal evaluations, 60 patients were diagnosed with serious CHD (8%), in all sixty patients the prenatal diagnosis was confirmed at postnatal examination (100% accuracy). Of 771 patients with a CHD seen postnatally without prenatal evaluation, 130 patients were diagnosed with serious CHD (17%). The most frequent diagnoses were: aortic coarctation/hypoplasia (17%), tetralogy of Fallot (16%), abnormal atrio-ventricular connections (13%), ventricular septal defects (10%), and hypoplastic left heart (6%). **Conclusions**: This study shows that only one-third of patients with serious CHD were diagnosed prenatally, therefore, further efforts should be made to encourage referring pregnant women who are suspected of carrying a fetus with CHD for prenatal cardiac evaluation.

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Tobacco Smoke Exposure of Pregnant Mothers and Blood Pressure in Their Healthy Newborn Infants: Results from the Whistler Birth Cohort

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Background: there is evidence to suggest that antenatal exposure of pregnant women to tobacco smoke is related to higher childhood blood pressure in their offspring. It is not well known whether this association is set in utero or by shared postnatal environments. **Objective**: to assess the association between exposure to tobacco smoke of pregnant mothers and blood pressure and heart rate of their young infant offspring. **Methods**: in an unselected birth cohort, blood pressure and heart rate were measured in 346 infants at about 2 months of age. Smoking

exposure of mothers in pregnancy was obtained by questionnaire. **Results**: Of 346 mothers whose infants had blood pressure measured, 264 (76.3%) were not exposed to tobacco smoke in pregnancy, in the table below stated as 'mothers no, others no', 59 (17.1%) did not smoke in pregnancy but were exposed by others ('mothers no, others yes'), and 23 (6.6%) smoked, in the table defined as 'mothers yes'. Infant offspring of mothers who had smoked during pregnancy had 5.4 mmHg (95% Confidence interval: 0.9, 9.9, p-value 0.02) higher systolic blood pressure levels than offspring of mothers who were not exposed to tobacco smoke in pregnancy, taking account of birth weight, infant age, gender, nutrition (breast and/ or bottle feeding), and age of mother in the adjusted analysis. There were no associations found between maternal exposure to tobacco smoke in pregnancy and diastolic blood pressure. A positive association between maternal exposure to tobacco smoke and heart rate was largely explained by confounding. **Table 1.** Tobacco smoke exposure of pregnant mothers and blood pressure and heart rate of their infant offspring. **Conclusion**: maternal exposure to tobacco smoke in pregnancy has a substantial increasing effect on systolic blood pressure in early infancy.

	Unadjusted analysis			Adjusted analysis		
Smoking categories		Difference (95% CI)	p-value		Difference (95% CI)	p-value
	SBP (mmHg)			SBP (mmHg)		
Mothers no, others no	82.4	-	-	82.5	-	-
Mothers no, others yes	84.3	1.9 (-1.0, 4.9)	0.20	84.2	1.7 (-1.2, 4.6)	0.25
Mothers yes	87.4	5.0 (0.5, 9.5)	0.03	87.9	5.4 (0.9, 9.9)	0.02
	DBP (mmHg)			DBP (mmHg)		
Mothers no, others no	38.0	-	-	38.1	-	-
Mothers no, others yes	37.1	-0.9 (-3.6, 1.7)	0.49	37.1	-0.9 (-3.6, 1.8)	0.50
Mothers yes	37.9	-0.4 (-4.4, 3.7)	0.85	38.0	-0.1 (-4.3, 4.1)	0.96
	HR (beats/min)			HR (beats/min)		
Mothers no, others no	136.8	-	-	136.7	-	-
Mothers no, others yes	137.2	0.5 (-3.0, 3.9)	0.79	137.1	0.4 (-2.9, 3.7)	0.83
Mothers yes	141.6	4.9 (-0.4, 10.1)	0.07	139.4	2.7 (-2.4, 7.8)	0.29

SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate. 95% CI: 95% confidence interval.

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Blood Pressure Trends in US Children and Adolescents from 1988 Through 2004

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A previous report documented a marked increase in systolic and diastolic blood pressure between 1988–1994 and 1999–2000 among children and adolescents, 8 through 17 years of age, in the United States. Using more recent data from serial National Health and Nutrition Examination Surveys, previously reported changes in blood pressure were examined from 1988–1994 (n=3496) through 1999–2004 (n=5725). Additionally, trends in systolic and diastolic blood pressure from 1999–2000 (n=2082), 2001–2002 (n=2110), and 2003–2004 (n=1533) were determined. Between 1988–1994 and 1999–2004, mean systolic and diastolic blood pressure increased 1.5 mmHg and 1.8 mmHg, respectively (each $p<0.001$). The increase in systolic and diastolic blood pressure was larger for children 8–12 years of age (2.4 and 3.0 mmHg, respectively; each $p<0.001$) compared to their counterparts 13–17 years of age (0.7 and 0.3 mmHg, respectively; each $p>0.10$). Time trends from 1999–2000 through 2003–2004 indicated mean systolic blood pressure increased 2.0 mmHg (95% CI: 0.3, 3.7) among children 8 to 12 years of age and decreased by -0.4 mmHg (95% CI: -1.6, 0.8) among children and adolescents 13 to 17 years of age. Diastolic blood pressure decreased -3.1 mmHg (95% confidence interval: -4.4, -1.7) and -4.2 mmHg (95% confidence interval: -5.8, -2.6) between 1999–2000 and 2003–2004. Although diastolic blood pressure increased from 1988–1994 through 1999–2000, a decrease has occurred through 2004. Despite a recent trend toward stabilization in children 13–17 years, average systolic blood pressure has increased significantly over the past decade. Measures to lower blood pressure among children and adolescents should be a high national priority.

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Early Growth and Blood Pressure in British White European and South Asian Origin Babies: The Manchester UK Children's Heart and Growth Study

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Specific indices of early postnatal growth may be markers for the development of adult cardiovascular disorders, whose risk differs between ethnic groups. **Objective**: To examine size at birth, catch up growth (≥0.67SD) and their associations with blood pressure (BP), in British born South Asian (SA) and White European (WE) infants in the first 3 years of life. **Subjects/Methods**: Women were recruited in pregnancy and their healthy infants born at term were followed up with similarly standardized measures of weight (W), length (L), head circumference (HC) and BP analyzed using multilevel modeling correlation and regression. 567 babies (324 WE, 178 SA, 61 other) were measured. The study was mixed longitudinal in design. **Results**: Over the 36 months, SA weighed less than WE babies by 0.32 SDS (95% CI 0.43, 0.22) and had a lower BMI SDS by 0.34 (0.2, 0.46). They were shorter by 0.18 SDS (0.33, 0.03) for L-SDS and had 0.36-SDS (0.57, 0.15) smaller HCSDS. No Differences in mean (SD) systolic or diastolic BP between the 2 ethnic groups were found only at 24 months. Catch-up growth for W-SDS and BMI-SDS was greater over the first 3 months in SA than WE (Δ W-SDS 0.1(1.0) vs. -0.28 (0.9), p=0.005). SBP at 24 months correlated positively with change in W, L and HC at 24 months (r=0.5, p=0.000, r= 0.3, p=0.006, r=0.3, p=0.018), relations which had weakened by 36 months. In multiple regression, when change in weight from 0–24 months was included, the ethnic effect on BP was no longer significant. **Conclusions**: Ethnic differences in growth and catch-up are evident in this cohort in early life and are likely to be responsible for transient differences between groups in blood pressures at these early ages. However, differential growth patterns may still affect later cardiovascular and metabolic risk.

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Angiotensinogen Gene Polymorphism M235t Is Related to Hypertension in Pregnancy: Prospect-epic Study

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Introduction: A missense mutation of the human Angiotensinogen gene replacing methionine (M) with threonine (T) at residue 235 of the mature protein has been related to an increased risk of hypertension. This finding may suggest also an increased risk of pregnancy hypertension. Yet, results from previous studies were inconsistent. **Hypothesis**: We assessed the hypothesis that there is an association between this polymorphism and the risk of elevated blood pressure during pregnancy. **Methods**: We performed a cross-sectional study in a randomly selected sample of prospective cohort (Prospect-EPIC cohort) of 15,236 initially healthy Dutch women (N=1522), which, after excluding non-related subjects, were 429 cases with and 921 subjects without a history of elevated BP during pregnancy. We applied a series of multivariate analyses. **Results**: Individuals with T235T genotype had higher odds ratio for having a history of elevated BP during pregnancy than the M235M genotype, adjusted for BMI and current hypertension (odds ratio=1.55; 95% CI, 1.09 to 2.20; *P=0.014*), but for heterozygote individuals it did not reach statistically significant level. **Conclusions**: In conclusion our study provides support for a relation between replacing methionine with threonine at position 235 of the human AGT gene and having a history of elevated BP during pregnancy.

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Angiotensinogen Polymorphism M235T Is Associated with Risk of Hypertension in Pregnancy: A Meta-Analysis

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Introduction: A missense mutation of the human Angiotensinogen gene replacing methionine (M) with threonine (T) at residue 235 of the mature protein has been related to an increased risk of hypertension. This finding may suggest also an increased risk of pregnancy hypertension. **Hypothesis**: We assessed the hypothesis that replacing methionine with threonine at position 235 of the angiotensinogen gene is associated with the risk of hypertension in pregnancy, including preeclampsia/eclampsia, and transient hypertension in pregnancy. **Methods**: Pubmed/Medline was searched and a hand search of bibliographies was conducted. 16 studies (1839 cases and 2931 controls) published in English between 1993 and August 2006 examining the association of angiotensinogen gene M235T polymorphism with the above-mentioned endpoints were selected. Pooled effect sizes and Mantel-Haenszel odds ratios were calculated using review Manager. **Results**: In white subjects, TT genotype compared to MM genotype was associated with increased risk of all types hypertension in pregnancy (odds ratio=1.58; 95% CI, 1.14 to 2.18; *P=0.006*), and preeclampsia/eclampsia (OR=1.83; 95% CI, 1.07 to 3.12; *P=0.03*) but not with risk of transient hypertension of pregnancy. In Asian subjects the genotype was associated with increased risk of all types of pregnancy hypertension (OR=1.93; 95% CI, 1.05 to 3.55; *P=0.04*) but not with preeclampsia/eclampsia (OR=1.74; 95% CI, 0.92 to 3.28; *P=0.09*) and transient hypertension of pregnancy. **Conclusions**: In conclusion TT genotype of angiotensinogen gene M235T polymorphism was associated with an increased risk of preeclampsia/eclampsia in white subjects but not in Asian subjects and with all types of hypertension in pregnancy in both ethnic groups.

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Histopathology of the Placenta and Childhood Growth

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Although low birth weight is a well known predictor of abnormal growth in children and CVD in adults, there are few epidemiologic studies of the placenta. Data from the National Collborative Perinatal Project (CPP, n=23,962) show that gross placental measures predict childhood body mass index at age 7. We hypothesized that placental histopathology would predict abnormal infant growth and subsequent childhood growth. We analyzed longitudinal data on 43 infant-mother pairs who participated in the Johns Hopkins CPP. Standard anthropometric measures were collected periodically. An expert pathologist re-read existing placental slides and applied a standardized tool to score histopathology in 3 domains: 1) fetal vascular pathology, 2) pathology of the villi and intervillous space, and 3) uteroplacental pathology. Mean birth weight was 3198 g (range 1021 - 4819 g). Mean placental weight was 452 g (140 - 1036 g). At age 7, mean (SD) BMI was 15.3 kg/m^2 (1.6). Table 1 summarizes multiple linear regression analyses including maternal age and annual household income as covariates. Infant with placentas that were scored ≥1 were on average 2.66cm longer at birth than those placentas that were scored <1. There were no significant relationships between placental histopathology and z-score BMI at age 7. However, the general trend suggests that for each unit increase in histopathology score in all domains with the exception of uteroplacental pathology, there is a decrease in BMI at age 7. If confirmed in a larger sample, these data suggest that placental histopathology may be predictive of childhood growth. The placenta deserves greater attention in epidemiologic and studies of fetal programming. Table

1. Adjusted Associations Placental Histopathology and Birth Weight, Birth Length and BMI at Age 7.

	Birth Weight		Birth Length		z-score BMI at Age 7	
	β	95% CI	β	95% CI	β	95% CI
Histopathology Global Score	-6.28	-18.24, 5.67	0.01	-0.05, 0.07	-0.01	-0.03, 0.01
Fetal Vascular Pathology	146.39	-264.96, 557.74	0.21	-1.80, 2.21	-0.34	-1.46, 0.78
Villi & Intervillous Space Pathology Score	-13.91	-32.49, 4.67	-0.03	-0.12, 0.06	-0.01	-0.05, 0.02
Uteroplacental Pathology Score	35.47	-488.21, 559.15	2.66*	0.27, 5.04	0.07	-1.22, 1.36

Adjusted for, maternal age, annual household income, *$p<0.05$

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Prospective Study of Activated Partial Thromboplastin Time and the Risk of Future Venous Thrombosis: The Atherosclerosis Risk in Communities Study

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Introduction: The activated partial thromboplastin time (aPTT) is a common screening test for bleeding disorders, with longer values suggesting procoagulant factor deficiencies. A shorter aPTT is associated with venous thrombosis (VT) though prior studies were retrospective or in hospitalized patients. **Methods**: Subjects were from a nested case-control study in the ARIC cohort with added measurements of VT risk factors. With 12 years of follow-up, 283 cases of new VT were age-, sex-, and race-matched with 609 controls. The odds ratio for VT was determined for quartiles of aPTT in logistic regression models adjusting for demographics, coagulation factors reflected in the aPTT, and other VT risk factors. **Results**: A lower aPTT was seen in females, with higher body mass index (BMI), higher factors VIII, IX, XI, protein C, von Willebrand factor, and with non-O blood type, but was not associated with fibrinogen, D-dimer, factor V Leiden or the prothombin 20210A mutation. In demographic and BMI-adjusted models, subjects below the median aPTT had a higher risk of future VT (Table). Adjustment for the coagulation factors and other VT risk factors listed in the table only partly attenuated the risk estimate (Table). Associations were stronger for idiopathic than secondary VT (Table). An aPTT below the median was synergistic with obesity and the factor V Leiden mutation (37% and 63% relative excess risk respectively than expected under an additive model; both additive interactions $p<0.05$). **Discussion**: In this prospective study, aPTT below the median was associated with increased risk of future VT, even after adjusting for coagulation factors contributing to both the aPTT and VT risk. Synergy with other common risk factors suggests possible clinical utility. This widely used coagulation test may assess complex interactions between inherited and acquired VT risk factors, though more study is needed to define its precise role in medical practice.

Odds Ratio of Incident Venous Thromboembolism by aPTT Quartile

	Quartile (OR, 95% CI)			
aPTT Quartile	1	2	3	4
aPTT range (s)	21.1–27.0	27.1–28.7	28.8–30.6	30.7–35.8
Cases (n)	115	89	40	39
Controls (n)	146	150	159	154
Unadjusted	3.1 (2.0, 4.8)	2.3 (1.5, 3.6)	1.0 (0.6, 1.6)	1.0 (ref)
Model 1	3.0 (1.9, 4.6)	2.3 (1.5, 3.6)	1.0 (0.6, 1.6)	1.0 (ref)
Model 2	2.1 (1.2, 3.5)	2.0 (1.2, 3.3)	1.0 (0.6, 1.7)	1.0 (ref)
Model 2 Idiopathic VT n = 125	3.2 (1.3, 7.7)	3.3 (1.4, 7.5)	1.5 (0.6, 3.7)	1.0 (ref)
Model 2 Secondary VT n = 158	1.7 (0.9, 2.9)	1.6 (0.9, 2.9)	0.8 (0.4, 1.5)	1.0 (ref)
Model 3	2.1 (1.2, 3.8)	2.3 (1.3, 3.8)	1.0 (0.6, 1.8)	1.0 (ref)

Model 1 adjusted for age, gender, race, field center, and body mass index **Model 2** adjusted for Model 1, fibrinogen, factor VIII, factor IX, factor XI, and von Willebrand factor **Model 3** adjusted for Model 2, factor V Leiden, ABO blood group, prothombin G20210a polymorphism, D-dimer, and protein C

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Association of Progestin Use with Hemostatic Factor Levels in Postmenopausal Women: The PEPI Trial

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Background: Evidence is accumulating that estrogen type and formulation are differentially associated with clotting risk. It is not known whether type of progestin is also associated with different clotting potentials in post-menopausal women using hormone therapy. **Methods**: Using data from the Postmenopausal Estrogen/Progestin Intervention (PEPI) study, a randomized, placebo-controlled trial of the effects of four types of hormone regimens on cardiovascular risk factors in postmenopausal women, we investigated changes from baseline in hemostatic measures among women assigned to cyclic micronized progesterone (MP) compared with women assigned to cyclic medroxyprogesterone (MPA). A sub-group of women (383 of 875) provided baseline, 12- and 36-month blood samples that were assayed for hemostatic factors, including factor VII and VIII, prothrombin fragments 1 and 2, fibrinopeptide, antithrombin, protein C, free and total protein S, tPA antigen, PAI-1 antigen, PAP complex, and D-Dimer. We measured changes in hemostatic profile for the two progestin types and tested for differences at 12-and 36-months using repeated measures of analysis covariance models. **Results**: Factor VII levels increased more in the MP arm than the MPA arm at both 12- and 36-months (see Table). PAI-1 levels decreased less in the MP arm than the MPA arm at both 12- and 36-months. At 36-months, Protein C levels were increased more in the MP arm than the MPA arm. No other 12- or 36-month changes were significantly different at the $p<0.05$ level (data not shown). **Conclusions**: These data suggest that type of progestin has a minimal differential effect on some hemostatic measures and no strong pattern of clotting potential differences between cyclic MP and cyclic MPA.

Table. Mean (SD) values for Baseline, 12- and 36-month hemostatic measures.

	CEE and Progestin		
Hemostatic Measure	**Cyclic MP** Mean (SD)	**Cyclic MPA** Mean (SD)	p-value*
Factor VII (%)			
Baseline	119 (23.2)	131 (22.7)	
Change from baseline (12 months)	20.8 (2.4)	13.6 (2.4)	0.04
Change from baseline (36 months)	8.8 (2.4)	-4.0 (3.6)	0.01
Ln(PAI-1) antigen (ng/mL)			
Baseline	1.0 (0.4)	1.0 (0.4)	
Change from baseline (12 months)	-0.1 (0.0)	-0.3 (0.0)	0.03
Change from baseline (36 months)	-0.1 (0.0)	-0.3 (0.0)	0.01
Protein C (%)			
Baseline	3.6 (18.2)	-0.2 (18.4)	
Change from baseline (12 months)	3.4 (2.1)	-0.9 (2.1)	0.15
Change from baseline (36 months)	13.8 (2.3)	6.6 (2.3)	0.03

CEE = conjugated equine estrogen; *P-value for 12- or 36-month change in hemostatic factors for MP versus MPA

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Sports Activities Are Associated with an Increased Risk of Venous Thrombosis in the Elderly

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Background: While stasis of the blood and immobilization are known to increase the risk of venous thrombosis, little is known about the association of exercise with the risk of venous thrombosis. Results from observational studies of exercise and the risk venous thrombosis are inconsistent. **Methods**: We investigated whether sport activities influenced the risk of venous thrombosis within the Cardiovascular Health Study, an observational follow-up study of 5888 individuals aged 65 years and older. Individuals without a prior venous thrombosis were included in the present analysis. Self-reported exercise was measured at baseline and 1 or 2 times during follow-up (at years 3 or 4 and 7) and was defined as expending more than 500 kilocalories per week on sports activities such as walking for exercise and cycling. **Results**: During a median of 11.6 years follow-up, 171 of 5543 participants developed a first venous thrombosis. Exercise at baseline was not related to the risk of venous thrombosis after adjustment for sex, age and race (hazard ratio (HR) 1.0 95% confidence interval (CI) 0.8–1.4). Further adjustment for self-reported health and body mass index at baseline resulted in a HRadj of 1.2 (95% CI 0.8–1.6). Exercise modeled as a time-varying exposure was associated with a small increase in the risk of venous thrombosis (HRadj 1.4, 95% CI 1.0–1.9). Considering person-time in the year after an exercise assessment, with 43 venous thrombotic events, the adjusted hazard ratio for exercise compared with no exercise was 1.5 (95%CI 0.8–2.8). Results were similar for the risk of idiopathic venous thrombosis and when the analysis was restricted to healthy individuals. In the 2081 subjects who participated in sports activities, strenuous sports activities were associated with a higher venous thrombosis risk than mild intensity sports activities (HRadj 2.3 95% CI 1.4–3.9), as was expending more kilocalories compared with expending fewer kilocalories (HRadj 1.7 95% CI 0.93–3.24). **Conclusion**: In the elderly, strenuous sport activities were associated with increased risk of venous thrombosis. Although the reason for this association is unclear, we speculate that it may relate to an increased risk of injuries.

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Parental Smoking and Vascular Damage in Young Adult Offspring: Is Early Life Exposure Critical? The Atherosclerosis Risk in Young Adults Study

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Background: there is little knowledge of the consequences of tobacco smoke exposure in pregnancy for cardiovascular disease risk in offspring. **Hypothesis**: there is an association between foetal tobacco smoke exposure and vascular damage in young adulthood. **Methods**: a birth cohort of 732 Dutch young adults born between 1970–1973 with registered pregnancy and birth data, anthropometric and blood pressure data at adolescence, and cardiovascular risk profiles in young adulthood, including ultrasound measurement of common carotid artery intima-media thickness (CIMT) in 1999 and 2000. Data on pregnancy and current smoking habits of parents were obtained by standardized questionnaires. **Findings**: 215 out of 732 mothers (29%) reported to have smoked in their pregnancy of the participant. Adult offspring of mothers who smoked in pregnancy had 13.4 μm thicker CIMT (95% CI: 5.5, 21.3; $p=0.001$) than offspring of mothers who did not smoke in pregnancy. Adjustment for known CIMT risk factors (participant's age, gender, BMI, pulse pressure, and LDL-cholesterol) did attenuate, but not abolish this estimate (9,4 μm, 95% CI: 1.9, 16.3, $p=0.01$). Similarly, adjustment for current smoking of mothers (yes/no) and fathers (yes/no) did not change the association (10.6 μm, 95% CI: 0.4 - 20.8, $p=0.04$) nor did adjustment for participants' current smoking (yes/no) and pack-years (11.5 μm, 95% CI: 3.5 - 19.4, $p=0.004$). Offspring of parents who both smoked in pregnancy had thicker CIMT than offspring with one smoking parent or no smoking parents ($p_{\text{linear trend}}<0.0001$), and offspring of particularly mothers who smoked an above median number of cigarettes in pregnancy had thicker CIMT than those smoking less than median or no cigarettes ($p_{\text{linear trend}}<0.0001$). **Conclusion**: permanent vascular damage due to tobacco smoke exposure is initiated in gestation.

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Earlier Menopause Is Associated with Coronary Calcium: The Multi-Ethnic Study of Atherosclerosis (MESA)

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Early menopause is associated with increased cardiovascular mortality. We hypothesized that among postmenopausal women the time from menopause adjusted for current age is associated with subclinical atherosclerosis as measured by coronary artery calcium (CAC). **Methods**: Analysis included 1164 postmenopausal women (ages 55–84, 388 white, 200 Chinese, 282 African-American, 294 Hispanic) from the sex hormone ancillary study of MESA who were not on HRT, had intact uteri/ovaries and had CAC measurement by spiral CT or EBCT during baseline examination. Serum sex hormones (SH: total testosterone, estradiol, dehydroepiandrostenedione, SH binding globulin) were measured. We used multiple logistic regression to estimate the association of CAC presence (non-zero vs. zero Agatston score) with time since menopause. In women with detectable CAC, we used multiple linear regression to estimate the association of extent of CAC (log(CAC)) with time since menopause. Current age and race were included in model 1. Current smoking, hypertension (JNC VI criteria), diabetes (ADA 2003 criteria), total and HDL cholesterol, and BMI were added in model 2. SH were added in model 3. **Results**: The means±SD of the age at MESA examination and age at menopause in women without detectable CAC were 65.1±6.9 and 50.1±4.9 years, and in women with detectable CAC, 70.0±7.5 ($p<0.001$) and 49.3±5.5 years ($p=0.015$), respectively. For any given age and race (Model 1, table), every 5 years of earlier menopausal age were associated with an odds ratio of 1.142 (14.2% higher odds) for detectable CAC. This association persisted after adjustment for cardiovascular risk factors (Model 2) and endogenous SH levels (Model 3). Among women with detectable CAC, the extent of CAC was not significantly associated with time since menopause in any model. **Conclusion**: Earlier age at menopause is associated with detectable CAC, independent of cardiovascular risk factors and postmenopausal levels of endogenous SH.

Association of detectable CAC with age-adjusted postmenopausal time (MESA baseline)

	Model 1 (95% CI)	Model 2 (95% CI)	Model 3 (95% CI)
Relative Odds of detectable CAC per 5 years of earlier menopause	1.142 (1.014, 1.286)	1.143 (1.011, 1.293)	1.134 (1.005, 1.287)

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A Threonine to Alanine Substitution in the Matrix Gla Protein Gene Is Associated with Faster Coronary Artery Calcification Progression

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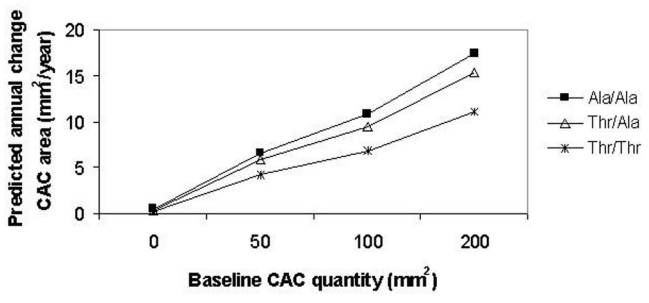
Matrix gla protein (MGP) inhibits arterial and cartilaginous calcification. A Threonine to Alanine (Thr/Ala) polymorphism (codon 83) in *MGP* is associated with myocardial infarction (MI) and femoral artery calcification. Coronary artery calcification (CAC), a measure of subclinical coronary atherosclerosis, is associated with serum MGP levels in some studies. Variation in CAC progression is heritable, yet specific genes are largely unknown. We examined the association of *MGP* Thr/Ala with CAC progression in a community-based sample. 414 (46% male) participants ≥age 45 at follow-up had *MGP* genotyping and baseline and follow-up electron beam CT measures of CAC ~10 years apart. CAC progression was defined as log[((follow-up - baseline CAC area) + 1) χ years between scans]. Linear regression models were fit to examine the *MGP* Thr/Ala and CAC progression association, adjusted for baseline CAC area, 10-year CHD risk and waist circumference. Median CAC area increased from 18 mm^2 to 56 mm^2 between baseline and follow-up. *MGP* Thr/Ala was not associated with baseline CAC presence, quantity, or traditional CHD risk factors. Baseline CAC area, 10-year CHD risk and waist circumference were ($P<0.02$) positively associated with CAC progression. Compared to those with *MGP* Thr/Thr genotype (n=128), the relative increase (95% CI) in CAC progression for those with Thr/Ala genotype (n=229) was 1.39 (1.06, 1.83; P=0.02) and for those with Ala/Ala genotype (n=57) was 1.58 (1.06, 2.36; P=0.03). Increased risk of MI in individuals with the *MGP* Ala allele observed in other studies may be related to faster progression of subclinical coronary atherosclerosis relative to those with the Thr/Thr genotype.

Predicted CAC progression, by *MGP* genotype, based on linear regression model, for hypothetical participant with mean waist circumference and 10-year CHD risk



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History of Oophorectomy Is Associated with Higher Risk of Subclinical Coronary Artery Disease in Women with Hysterectomy

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Introduction: We tested the hypothesis that oophorectomy is significantly related to the coronary artery calcified (CAC) plaque; a component of atherosclerosis that is independently predictive of future CHD events. **Methods**: In a sub-study to the Women's Health Initiative (WHI) trial of conjugated equine estrogen (0.625 mg per day) or placebo among women with a history of hysterectomy, CAC was measured by cardiac computed tomography in 1,064 women aged 50 to 59 years at the time of randomization. The mean treatment period was 7.1 years. Imaging was performed at a mean of 1.3 years after the trial was stopped. Agatston calcium scores were measured by a central reading center. **Results**: The mean age at randomization was 55.1 years. Unilateral, bilateral or partial oophorectomy was reported by 523 women (53.6%), with 337 having both ovaries removed. The mean duration since bilateral oophorectomy was 14 years. Forty-nine percent reported pre-randomization use of hormone therapy (HT). The median calcium scores among those who reported any HT use was lower than those who reported no use (65 vs. 76, p = NS). Compared to those with no history of oophorectomy and in a multivariable logistic regression model, there were no significant associations between type of oophorectomy and the presence of any CAC. However, there was a significant interaction between oophorectomy status and HT use after oophorectomy ($p = 0.005$). Specifically, when the analyses were restricted to women who reported not using any HT after oophorectomy and with adjustment for CHD risk factors, education and randomization status, women who had undergone bilateral oophorectomy had an odds ratio of 2.2 (95% CI: 1.3–4.0) for any CAC compared to those who had no history of oophorectomy. The odds of having any CAC for those who had a unilateral or partial oophorectomy was 1.5 (95% CI: 0.8–2.7). Conversely, there were no significant associations between oophorectomy status and CAC among those who reported using HT after oophorectomy. **Conclusions**: Women with hysterectomy and bilateral oophorectomy who report not using HT after oophorectomy have over a 2-fold higher odds for the presence of subclinical coronary artery disease independent of traditional CHD risk factors, education and randomization assignment.

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A High Ankle Brachial Index Is Associated with Increased Cardiovascular Disease Morbidity and Worse Quality of Life

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Background: ABI values >= 1.30 have been associated with cardiovascular disease (CVD) risk factors and with increased coronary artery calcium scores, but the relationship to quality of life (QoL) has not been previously evaluated. This study tested the hypothesis that an ABI >= 1.30 would be associated with worse quality of life compared with ABI values in the normal range (1.00–1.29). **Methods**: The PAD Awareness, Risk and Treatment: New Resources for Survival (PARTNERS) program was a national cross-sectional study of 7000 patients over the age of 50 years recruited from 350 primary care sites. All sites performed the ABI using a Doppler probe and a standardized technique. Subjects completed a study questionnaire providing information on medical history, lower extremity symptoms, CVD events and quality of life using the SF-36 and walking impairment questionnaire (WIQ). **Results**: The mean age was 70.8, 53% were female, over 83% were hypertensive, 37% were diagnosed with diabetes mellitus and 48% were either current or former cigarette smokers. The mean ABI was 1.00±0.21 and 323 (4.5%) had an ABI >= 1.30 in either leg. In a multivariable logistic regression model containing all CVD and socioeconomic risk factors, diabetes (Odds Ratio: 1.5, 95% CI: 1.1 - 2.0), current smoking (0.5, 0.3 - 0.9) and male sex (2.4, 1.6 - 3.2) were significantly associated with an ABI >= 1.30. Compared to those with an ABI from 1.0 to 1.29, the odds for coronary artery bypass graft (CABG) and deep venous thrombosis (DVT) were significantly higher (1.6, 1.0 - 2.7 and 2.3, 1.2 - 4.6; respectively) in the high ABI group while the odds for peripheral neuropathy and CHF were of borderline significance (1.5, 1.0 - 2.5 and 1.5, 0.9 - 2.7). With adjustment for CVD risk factors and leg pain, those in the ABI >= 1.30 group had impaired quality of life as defined by their significantly higher odds for the lowest quartile of SF-36 vitality (OR: 1.4), SF-36 role emotional (1.3), WIQ walking distance (1.4), WIQ walking speed (1.4) and WIQ stair climbing (1.3). **Conclusion**: Individuals with a high ABI have higher rates of CVD co-morbidities, as well as major decrements in quality of life across many major functional domains.

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Sex-Hormone Binding Globulin Level Is Inversely Associated with Presence and Severity of Abdominal Aortic Calcification in Women but Not Men in the Multi-Ethnic Study of Atherosclerosis (MESA)

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Background: Endogenous sex hormones (SH) may influence the development of atherosclerosis. Conflicting findings exist regarding the associations of total testosterone (T), estradiol

(E2), and dehydroepiandrostenedione (DHEA) with subclinical atherosclerosis, while most studies show a protective effect of SH binding globulin (SHBG) in both postmenopausal women and men. SH are also associated with lipoprotein levels. Because cardiovascular disease (CVD) risk differs by sex, we examined if the relation of SH with abdominal aortic calcium (AAC) differs between men and women. **Methods**: We analyzed cross-sectional data of 881 postmenopausal women and 978 men from the baseline visit of MESA, a multicenter NHLBI study of participants free of clinical CVD, who had both AAC quantified by computed tomography and SH levels assessed (T, E2, DHEA, and SHBG). We examined the association of log(SH levels) with presence of AAC by logistic regression, and in subjects with AAC, determined the association with log(AAC) extent using linear regression. For each SH, we adjusted for covariates of age, race, hypertension, smoking, diabetes, BMI, hormone replacement therapy [women only], and the other SH (Model 1) and then additionally adjusted for total cholesterol /HDL ratio and use of cholesterol medications (Model 2). **Results**: AAC was present in 73% of men (mean age 62±10 years) and 74% of women (mean age 64±9 years). For women, Model 1 showed an inverse association of SHBG with both AAC presence (OR 0.61, 95% CI 0.42 to 0.90) and extent (0.30% lower AAC score for every 1% higher SHBG level, β=-0.30 [95% CI -0.58 to -0.015]). After further adjustment for cholesterol (Model 2), SHBG was no longer independently associated with either presence or extent of AAC. In men, we found no association of SHBG with either presence or severity of AAC in Models 1 or 2. There was no independent association of T, E2, or DHEA with presence or extent of AAC in either men or women in Models 1 or 2. **Conclusion**: SHBG levels are inversely associated with both the presence and severity of AAC in women but not in men after adjustment for non-lipid CVD risk factors. The association of SHBG with AAC in women may be accounted for by lipoprotein levels.

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Serum 25-Hydroxyvitamin D Levels Are Modestly Associated with Increased Carotid Intimal-Medial Thickness but Not C-Reactive Protein or Coronary Calcium in the Amish

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Background: There are conflicting observations regarding the potential association between elevated serum 25-hydroxyvitamin D (25-OH D) levels and vascular calcification, with studies showing both protective and harmful effects. Activated vitamin D (1,25 dihydroxyvitamin D) has been shown to have anti-inflammatory properties. We hypothesized that higher serum 25-OH D levels would be associated with less inflammation as measured by C-reactive protein (CRP) and with less subclinical atherosclerosis as measured by carotid intimal medial thickness (cIMT) and coronary artery calcification (CAC). **Methods**: We assessed subclinical atherosclerosis and serum 25-OH D levels in subjects from large Amish families. CAC was measured by electron beam computed tomography, and cIMT by ultrasound. Correlations of serum 25-OH D levels with cIMT (n=167), categories of CAC severity (n=628), log transformed CAC for those with CAC scores >0 (n=310), and log transformed CRP levels (n=468) were estimated following adjustment for age, sex, body mass index (BMI), and season. **Results**: Higher serum 25-OH D levels were modestly associated with increasing cIMT (R^2=0.013), which was borderline significant after adjusting for age, sex, BMI, and season (0.003 mm increased cIMT for every 1 ng/ml higher adjusted 25-OH D levels, p=0.057). Mean cIMT across increasing quartiles of adjusted serum 25-OH D levels were 0.62, 0.65, 0.70, and 0.64 mm respectively (p=0.09). 25-OH D levels were not correlated with either the degree of log(CAC) (p=0.67), categories of CAC severity (p=0.56), or log(CRP) (p=0.67). **Conclusion**: Contrary to our hypothesis, this study failed to detect an association between serum 25-OH D levels and either CAC or CRP levels. However, a modest correlation was observed between 25-OH D and cIMT, but the clinical significance of this finding is unclear.

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Dyslipidemia Differentially Mediates the Association Between Hepatic Steatosis and Calcified Atherosclerosis in Different Vascular Beds

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Background: Hepatic steatosis (HS) is closely associated with dyslipidemia, metabolic syndrome and diabetes. These conditions have also been associated with calcified atherosclerosis in the coronary arteries and aorta. We tested the hypothesis that HS would be significantly associated with vascular calcium, independent of cardiovascular disease (CVD) risk factors. **Methods**: Whole body electron beam computed tomography (EBCT) was conducted on 1,224 consecutive patients to ascertain the extent of coronary calcium (CAC), aortic calcium (AC) and carotid calcium (CAR). At the time of the scan, demographic, social, medication and CVD risk factor data was collected by blood assay and questionnaires. Calcium scoring was conducted using the Agatston method. Using archived EBCT scans, we retrospectively determined the densities of the liver and spleen, expressed in Hounsfield units. A liver to spleen density ratio <1.0 was considered evidence of HS. **Results**: The mean age was 62 years and 44% were female. The prevalence of any CAC, AC and CAR was 61.2%, 58.5% and 32.0%, respectively. For each higher level of these calcium groups, there was a significant trend for increasing prevalence of HS (6.6 to 17.5% for CAC, p < 0.01; 8.7 to 14.8% for AC, p = 0.06; 10.2 to 15.5% for CAR, p = 0.03). In separate multivariable logistic regression models adjusted for age and sex, those with HS had significantly higher odds for CAC (Odds Ratio: 2.14, p-value: <0.01), AC (1.60, 0.03) and CAR (1.74, <0.01). However, with further adjustment for hypertension, diabetes, body mass index, smoking and dyslipidemia, the odds were attenuated to non-significance for all three vascular beds (CAC: 1.16, p = 0.57; AC: 1.48, p = 0.12; CAR: 1.55, p = 0.06). Notably, when dyslipidemia was removed from this model, the odds remained non-significant for CAC (1.19, 0.51) but became borderline significant for AC (1.56, 0.07) and significant for CAR (1.59, 0.04). **Conclusion**: The association between hepatic steatosis and extra-coronary calcified atherosclerosis appears to be mediated, to various degrees, by dyslipidemia while the association between HS and CAC is not mediated by dyslipidemia. These results suggest that other risk factors account for this association.

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Parental Coronary Heart Disease Increases Vulnerability of the Arterial Wall to Metabolic Syndrome and Aging: The Bogalusa Heart Study

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Introduction: Genetic susceptibility is considered as an important mediator of the impact of cardiovascular risk factors on coronary heart disease (CHD). This study assessed the hypothesis that parental CHD, a surrogate measure of genetic susceptibility, increases the vulnerability of arterial structure-function dynamics to the adverse effects of metabolic syndrome and the aging process even in asymptomatic young adults with parental CHD. **Methods**: The study cohort consisted of 1073 black and white subjects (31% black, 43.4% male) aged 25–44 years enrolled in the Bogalusa Heart Study. Arterial structure-function dynamics was assessed in terms of carotid artery intima-media thickness (IMT) measured by B-mode ultrasound and aorta-femoral pulse wave velocity (af-PWV) by echo-Doppler. Metabolic syndrome was defined by the NCEP guidelines. **Results**: Subjects with positive parental history of CHD had greater carotid IMT (0.839 vs 0.802 mm, p=0.017), higher af-PWV (5.4 vs 5.2 m/sec, p=0.097) and higher prevalence of metabolic syndrome (12.1% vs 7.6 %, p=0.019), compared with those without such history. Carotid IMT and af-PWV were significantly increased with increasing number of components of metabolic syndrome and age (both p<0.001). Further, the number of metabolic syndrome components associated more strongly with carotid IMT in subjects with parental history of CHD (β=0.05, p<0.001) than those without such history (β=0.03, p<0.001), with p=0.008 for comparison of slopes. Likewise, after adjusting for metabolic syndrome components, carotid IMT increased relatively more with age in subjects with parental history of CHD (β=0.012, p<0.001) than those without such history (β=0.007, p<0.001), with p=0.023 for comparison of slopes. af-PWV showed similar but nonsignificant differences in slopes with increasing number of metabolic syndrome components and age. **Conclusions**: Parental CHD increases the susceptibility of arterial structure-function dynamics, especially carotid artery IMT, to metabolic syndrome and aging process even in asymptomatic young adults.

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T-Wave Axis Is Associated with Coronary Artery Calcium Score in an Asymptomatic Elderly Population

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Introduction: Deviation of the T wave axis from normal on electrocardiography (ECG) is associated with increased risk of non-fatal cardiac events and cardiovascular death in the elderly. We hypothesized that T axis deviation would be associated with coronary artery calcification (CAC) score, a marker of subclinical atherosclerosis, in older persons without clinically identified coronary heart disease (CHD). **Methods**: We used data from the Age-Gene/Environment Susceptibility-Reykjavik Study, a population-based study of adults between the ages of 66 and 95. From an eligible population of 2300, we excluded persons with known CHD, bundle branch block, or those with incomplete data, giving n=1564 (563 men, 1001 women). CAC was measured by multi-detector computed tomography, quantified by the Agatston method, and transformed by natural logarithm. T axis on 12-lead ECG was categorized as normal (15° to 75°, n=1202), borderline (-15° to 15°, or 75° to 105°, n=280), or abnormal (105° to 180° or -180° to -15°, n=82). In a gender-specific logistic regression, we calculated odds for the highest versus the lowest quartile of gender-specific CAC score for the three categories of T axis. We first adjusted only for age, then added cardiovascular risk factors to the model. **Results**: The mean log-transformed CAC score was higher in men than women and increased with age and deviation of T axis. In both regression models, high CAC score was associated with a greater deviation from normal T axis, particularly in men (Table 1). **Conclusion**: In older persons with no known CHD, T wave axis is associated with CAC score, a measurement of subclinical CHD. This association is stronger in men than women. Further study is warranted to assess the use of T axis in screening for subclinical atherosclerosis.

Table 1: Association of T axis deviation with CAC score, OR (95% CI)

T Wave Axis	Men Model 1†	Men Model 2+	Women Model 1†	Women Model 2+
Normal‡	1.00	1.00	1.00	1.00
Borderline	1.03 (0.59–1.79)	1.03 (0.58–1.85)	1.23 (0.71–2.15)	1.21 (0.68–2.16)
Abnormal	4.58* (0.97–21.70)	10.44** (1.27–85.57)	2.07*** (0.83–5.16)	1.76 (0.69–4.48)

† adjusted for age + Model 1, plus BMI, smoking, DM, dyslipidemia, and HTN status. ‡Reference category *p=0.055 **p=0.029 ***p=0.121

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Association Between Health-Related Quality of Life and Coronary Artery Calcium in Young/Middle-Aged Adults: The CARDIA Study

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Background: Previous studies have shown significant associations between health-related quality of life (HRQOL) and mortality and morbidity. However, the question of whether quality of life measured subjectively is related to prevalence of coronary artery calcium (CAC) in young/middle adulthood has not been previously examined. **Methods**: We conducted analyses among 2,936 men and women from the Coronary Artery Risk Development in Young Adults (CARDIA) Study who had CAC and quality of life measured at Year 15 (2000–01). Participants were apparently healthy young adults, aged 18 to 30 years old at baseline in 1985–86. HRQOL (physical and mental well-being) was assessed by the Medical Outcomes Study Short Form-12

(SF12) questionnaire. Physical and mental health summary scores (PCS and MCS) were calculated. CAC was measured by ultrafast CT of the chest. A total calcium score was calculated for all calcified lesions by the Agatston method. **Results**: At Year 15 examination, 279 (9.5%) participants had positive CAC (score >0), including 136 (17.6%) white men, 62 (11.1%) black men, 45 (5.4%) white women and 36 (4.7%) black women. A significantly inverse association was observed between physical quality of life and prevalence of CAC with adjustment for age, gender, race, education, smoking status, alcohol consumption, total serum cholesterol, BMI, blood pressure, total physical intensity, BP medication use, and use of cholesterol lowering medications. The higher the PCS score, the lower the odds of having CAC (odds ratio for 1SD difference in PCS is 0.86, 95%CI=0.76–0.98). Similar trends were found in analyses conducted separately by gender or race. No association between mental quality of life and CAC was observed (OR for 1SD difference in MCS is 1.11, 95%CI=0.96–1.28). **Conclusion** Our results suggest that young/middle age adults who reported having lower physical quality of life are more likely to have positive CAC score.

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Influence of Serum Bilirubin on Pulsatile Arterial Function in Asymptomatic Young Adults: The Bogalusa Heart Study

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Background: The inverse association between serum bilirubin, a potent antioxidant, and oxidative stress-mediated diseases like cardiovascular (CV) disease is known. However, information is scant regarding the influence of bilirubin in relation to traditional CV risk factors on pulsatile arterial function in asymptomatic younger adults. **Methods**: The pulsatile arterial function, serum bilirubin and CV risk factor variables were measured in 777 black and white subjects (71% white, 42% male) aged 18–44 years. Pulsatile arterial function was assessed in terms of large artery (capacitive) and small artery (oscillatory) compliances by radial artery pressure pulse contour analysis. **Results**: In bivariate analysis adjusted for race and gender, bilirubin related significantly and positively to large and small artery compliances and HDL cholesterol; inversely to age, body mass index, blood pressure variables, non-HDL cholesterol, triglycerides and insulin resistance index. In multivariate analysis including race, gender, body surface area and risk factor variables mentioned above, bilirubin did not relate to large artery compliance, without or with smoking status in the model. Whereas, bilirubin associated beneficially with small artery compliance ($p=0.01$) in a model that excluded smoking status; When smoking status was included in the model, this association became less stronger ($p=0.04$), and smoking entered the model as an adverse predictor ($p=0.003$). Further, after adjusting for age, race and gender, smokers vs nonsmokers displayed lower bilirubin levels ($p=0.02$). **Conclusions**: The observed beneficial effect of serum bilirubin on pulsatile arterial function, albeit the attenuating effect of smoking on this relationship, in asymptomatic younger adults supports the antioxidant function of bilirubin in providing protection against oxidative stress-mediated vascular dysfunction.

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Aortic Wall Thickness and Distensibility: Relationship with Subclinical Measures of Cardiovascular Disease

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Background: While increased carotid intima-media thickness (IMT) is considered an independent risk factor for cardiovascular disease (CVD), little is known about the relationship of aortic thickness (AWT) and aortic distensibility (AD) with cardiovascular risk factors. We studied the association of these aortic parameters with other measures of subclinical CVD. **Methods**: The Multi-Ethnic Study of Atherosclerosis (MESA) includes 6,814 men and women, aged 45–85 years; white, African-American, Hispanic, and Chinese. AD and AWT were measured by MRI. Average and maximum AWT of the proximal descending thoracic aorta were used as two measures of AWT. AD was calculated as the difference in aortic cross-sectional area indexed by diastolic cross-sectional area and average pulse pressure. IMT of the common and internal carotid arteries were determined by high-resolution B-mode ultrasonography and LV mass was determined by MRI. Phantom-adjusted Agatston calcium score from CT images was used to define coronary artery calcification (CAC). **Results**: In univariable analyses, higher carotid IMT, CAC score, LV mass, and presence of coronary calcium were associated with lower AD and higher AWT (table). However, in multivariable analyses, the only measures of subclinical CVD that had significant associations with both AD and AWT were LV mass and carotid IMT. After adding age to the models, CAC score was no longer associated with either AD or AWT. The relationship between CAC score and AD varied by ethnicity; higher CAC score was associated with higher AD only in African Americans. None of the other associations were modified by ethnicity. **Conclusions**: AD and AWT are related to carotid IMT and LV mass, even after controlling for traditional risk factors. The associations of AD and AWT with CAC appears to be mainly due to their relationship with conventional risk factors, particularly age. Overall, AWT and AD may have closer relationship with LV mass than with subclinical atherosclerosis.

	Linear Regression Coefficients (95% Confidence Intervals)*					
	Aortic Distensibility (percent/ 100 mmHg)		Average AWT (mm)		Maximal AWT(mm)	
	Unadjusted	Adjusted**	Unadjusted	Adjusted**	Unadjusted	Adjusted**
Carotid maximal IMT						
Common carotid maximal IMT [per 0.22 log mm]	**-3.2 (-3.6, -2.7)‡**	-0.5 (-1.0, -0.1) †	0.17 (0.14, 0.20) ‡	0.08 (0.05, 0.12) ‡	0.22 (0.16, 0.27) ‡	0.12 (0.06, 0.19) ‡
Internal carotid maximal IMT [per 0.47 log mm]	**-2.0 (-2.4, -1.6) ‡**	0.2 (-0.2, 0.6)	**0.11 (0.08, 0.14) ‡**	0.03 (0.001, 0.06) †	0.17 **(0.12, 0.23) ‡**	0.08 **(0.02, 0.14) ‡**
Coronary artery calcification (CAC) score						
Presence of coronary calcification [CAC>0]	**-4.0 (-4.9, -3.3) ‡**	0.4 (-0.4, 0.1)	**0.18 (0.12, 0.24) ‡**	0.001 (-0.06, 0.06)	**0.24 (0.12, 0.36) ‡**	0.02 (-0.11, 0.15)
phantom-adjusted Agatston calcium score [per 2.5 log unit]***	**-2.0 (-2.8, -1.1) ‡**	Overall: 0.6 (-0.2, 1.5)	**0.08 (0.02, 0.14) ‡**	-0.004 (-0.06, 0.05)	0.07 (-0.04, 0.19)	0.006 (-0.107, 0.12)
LV Mass						
LV mass indexed by BSA [per 16.2 gr/mm^2]	**-1.7 (-2.1, -1.3) ‡**	-1.6 **(-2.1, -1.1) ‡**	0.05 (0.02, 0.08) ‡	0.04 **(0.003, 0.07) †**	0.08 **(0.02, 0.14) ‡**	0.04 **(0.03, 0.07) ‡**

Abbreviations: AWT: aortic wall thickness, BSA: body surface area, IMT: intima-media thickness, LV: left ventricle. * All regression coefficients are calculated for 1 standard deviation increase in continuous variables or transfer from one level to another of categorical variables. ** Adjusted for age, gender, ethnicity, body mass index, hypertension and use of hypertension medications, diabetes mellitus, family history of cardiovascular disease, history of familial hypercholesterolemia, serum cholesterol (LDL and HDL cholesterol), and cigarette smoking. *** Log(CAC score+1) was used as the primary independent variable in this model. A dummy variable indicating whether calcium score was zero or not were included in the models for phantom-adjusted Agatston calcium score. † p-value ≤0.05, ‡ p-value ≤ 0.01

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QRS Interval Duration Correlates with Coronary Artery Calcium Scores in the Diabetes Heart Study

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Objective: QT interval duration predicts cardiovascular events, but the mechanism of this association remains unclear. Data linking subclinical atherosclerosis and QT interval duration may indicate that coronary artery disease (CAD) affects the electrophysiologic properties of cardiac myocytes as measured by ECG. In a predominantly diabetic population, we evaluated the associations between QRS, JT, and QT interval duration with the extent of coronary artery calcium (CAC). **Methods**: The Diabetes Heart Study is an ongoing study of diabetic sibling pairs and their families. The present study sample included 1123 subjects (85% diabetic). The correlations between ECG interval durations and ln-transformed CAC were assessed in univariate models and after adjustment for heart rate, age, race, gender, diabetes status, BMI, smoking, blood pressure, LDL, medications, serum electrolytes, and familial correlations. **Results**: The QRS and QT intervals correlated with CAC scores in the univariate model (QRS: $r=0.23$, $p=<0.0001$; QT: $r=0.091$, $p=0.014$) with correlations remaining after adjustment. In contrast, the JT interval was not associated with CAC scores in the full cohort ($r=-0.034$, $p=0.21$) or after subgroup analysis. Stronger correlations existed between the QRS and QT intervals with CAC scores in men (QRS: $r=0.24$, $p=<0.0001$; QT: $r=0.21$, $p=<0.0001$) but not in women (QRS: $r=0.080$, $p=0.089$; QT: $r=0.0048$, $p=0.91$). After excluding non-diabetics, the associations between QRS and QT intervals with CAC scores were strengthened (QRS: $r=0.25$, $p=<0.0001$; QT: $r=0.15$, $p=<0.0001$). These statistical relationships were not modified by a history of clinical CVD events, race, or after exclusion of QRS intervals greater than 120ms. **Conclusion**: QRS interval duration correlates with CAC scores in a predominantly diabetic population. This relationship in the overall study sample was driven by stronger correlations in the male and diabetic subgroups. The association between heart rate adjusted QT interval duration and CAC scores was a result of QRS and not JT interval length, raising the possibility that prolonged QT intervals in the setting of CAD may be due to prolonged ventricular depolarization and not ventricular repolarization as has been previously assumed.

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Carotid Intima-Media Thickness (cIMT) Cosegregates with Blood Pressure and Renal Function in Hypertensive Hispanic Families

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Introduction We have previously shown that cIMT is heritable in Hispanic American (HA) families. Atherosclerosis is correlated with metabolic abnormalities, including insulin resistance, hypertension, and hyperlipidemia. We now present evidence that there is a genetic basis for the observed relationship between cIMT, BP and renal function. **Methods** The study included 603 nondiabetic individuals from 149 HA families ascertained via a hypertensive parent. All participants were at least 16 years of age. Subjects were assessed for subclinical atherosclerosis by ultrasound assessment of cIMT, and underwent an exam that included BMI, BP, and fasting blood and urine collection. Renal function was assessed by urine microalbumin (ALB), blood urea nitrogen (BUN), creatinine (Cr), and Cr clearance (Ccr) calculated using the Cockcroft-Gault equation. A bivariate variance components approach was used in evaluating heritabilities of the traits and their correlations. **Results** After adjusting for age, sex, and BMI, significant heritability ($p<0.0001$ for each) was found for cIMT (37%), SBP (35%), DBP (39%), ALB (57%), BUN (37%), Cr (60%), and Ccr (57%). When partitioned into genetic and environmental factors, the genetic correlations were significant between cIMT and SBP ($r_g = 0.40$), DBP ($r_g = 0.36$), ALB ($r_g = 0.36$), BUN ($r_g = 0.46$), Cr ($r_g = 0.36$), and Ccr ($r_g = 0.36$) ($p<0.05$ for each). There was no environmental correlation between cIMT and the other traits,

except Ccr (r_e = -0.28, $p<0.05$). **Conclusions** Familial aggregation and cosegregation were exhibited between cIMT and SBP, DBP, ALB, and renal function in hypertensive HA families. This suggests that subclinical atherosclerosis measured by cIMT shares common genetic determinants with blood pressure and renal function, with environment having little effect on these interrelationships.

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Early Determinants of Preclinical Atherosclerosis: A Life Course Analysis—The Amsterdam Growth and Health Longitudinal Study

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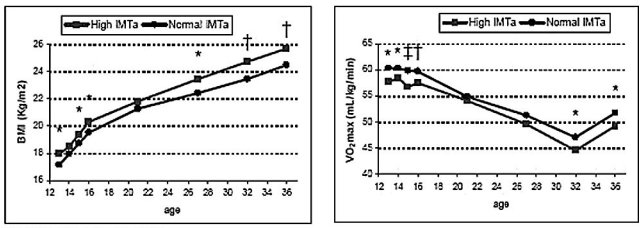
Background & Aims: Childhood body fatness, elevated cholesterol and blood pressure, have been associated with greater carotid IMT in adulthood. However, these adverse associations may have been due to concomitant associations with and increased carotid diameter, and therefore investigation of the determinants of carotid IMT area (IMTa) may be more appropriate. In addition, how the 'natural' development over time of cardiovascular risk factors (RFs), impact on adult carotid IMTa is not known; this needs to be investigated not only for a better understanding of the the aetiology of atherosclerosis, but also to allow the identification of critical periods [e.g. adolescence (12–16 yrs)] in which such RFs can be more deleterious and preventive measures most opportune. **Methods**: Data on RFs were derived from the AGAHLS (n=372, 8 follow-up measurements between the ages of 12 and 36 yrs). We used generalized estimating equations, to analyze the extent to which the longitudinal development of body fatness, blood pressure, cholesterol levels and cardiorespiratory fitness, differed between those subjects characterized by a 'high' (highest sex-specific quartile) vs. 'normal' IMTa at the age of 36 yrs. **Results**: When compared to subjects with 'normal' IMTa, those with 'high' IMTa were characterized by a more marked increase in systolic pressure (women), total-to-HDL cholesterol ratio and BMI (men - fig) and a steeper decrease in VO_2max (men - fig.); these differences emerged as early as in adolescence with exception of cholesterol levels. **Conclusions**: Prevention of atherosclerosis should start early in life, but interventions may need to target different RFs in boys and girls separately.



* P≤0.05; †P≤0.01, ‡P≤0.001

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Cross-sectional Association of Fasting Glucose Levels with Coronary Artery Calcium: The Coronary Artery Risk Development in Youth Adults (CARDIA) Study

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Background: Epidemiological studies have shown that impaired fasting glucose (IFG) is associated with increased risk of diabetes and cardiovascular disease (CVD). However, the association of IFG and subclinical atherosclerosis has not been extensively evaluated. **Objective and Methods**: To assess the cross-sectional association of fasting glucose levels with coronary artery calcium (CAC >0) in a sample of 2810 adults (45% African-Americans, 57% women) from the CARDIA Study, aged 38–50 years in 2005–06. CAC was measured by computed tomography and scored using the Agatston method. **Results**: In the overall cohort, 70% had normal fasting glucose (NFG), 21% IFG, and 9% diabetes (based on the 2003 ADA criteria). A significantly higher proportion of diabetics and those with IFG had less than high school education, were taking medications for high cholesterol and hypertension and had higher levels of BMI, systolic (SBP) and diastolic blood pressures, triglycerides and lower HDL compared to those with NFG ($p<0.05$). After adjusting for age, gender, race, education, smoking, SBP, BMI, LDL, HDL and triglycerides, diabetics and those with IFG had higher prevalence of CAC >0 compared to NFG (i.e. 27% and 22% vs. 18%, respectively). Similar patterns were observed in African-Americans (20%, 18%, 16%), Caucasians (37%, 23%, 20%), women (18%, 15%, 10%), but not in men (44%, 30%, 30%). In a logistic regression analysis adjusting for age, gender, race, education and center, diabetics (OR=2.40; 95%CI, 1.63–3.54) and those with IFG (OR=1.42; 95%CI, 1.08–1.86) are more likely to have coronary calcification compared to NFG. With further adjustment for SBP, BMI, HDL, LDL and triglycerides, the association continued to be significant among diabetics (OR=1.82; 95%CI, 1.19–2.78), but it was no longer significant in the IFG group (OR=1.10; 95%CI, 0.82–1.48). **Conclusion**: Individuals with IFG and diabetes have higher prevalence of CVD risk factors and higher odds for subclinical atherosclerosis compared to those with NFG. The relation between fasting glucose and CAC in the IFG group was essentially accounted by the effect of traditional CVD risk factors. These findings suggest that more attention should be paid to the atherogenic profile shown by individuals with IFG.

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Association of Endothelial Function and Cardiovascular Disease Status in an Elderly Cohort: The Cardiovascular Health Study

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Introduction: Endothelial function measured by brachial flow-mediated dilation (FMD) has been associated with cardiovascular (CVD) risk and CVD events. Subclinical CVD is prevalent in older adults and have been associated with high CHD event rate (Kuller et al). However the association between FMD and subclinical CVD has been less well characterized. We assessed the association of brachial FMD and the presence or absence of subclinical and clinical CVD in a population based cohort of older adults. **Methods and Design**: Brachial FMD was measured at year ten in 2792 adults aged 72–98 years in the cardiovascular health study(CHS), a population based cohort of adults >65years at baseline recruited from four clinic sites in the USA. ANCOVA was used to examine the association between brachial FMD and CVD status adjusting for age, race, gender, cholesterol, diabetes, hypertension, ACE inhibitor use, HMG CoA reductase use and smoking. Clinical CVD in CHS is defined as h/o afib/pacemaker, peripheral vascular surgery, CHF, stroke, TIA, MI or CABG/ PCI. Subclinical CVD in CHS is defined as low ankle brachial index (<0.9), carotid stenosis >25%, wall thickness of the internal or common carotid artery >80th percentile, major ECG abnormality, echocardiographic abnormality (abnormal ejection fraction or wall motion abnormality), or positive response to the Rose questionnaire for angina pectoris or claudication. **Results**: 82.7% were Caucasians and 60% females.Out of 2791 with complete data, 743 had h/o clinical CVD, 607 had subclinical CVD and 1441 had neither clinical CVD nor subclinical CVD (CVD free). Data presented in table CONCUSION: Older adults free of clinical or subclinical CVD have higher brachial FMD compared with either adults with clinical CVD or subclinical CVD.Brachial FMD of older adults with subclinical CVD is similar to adults with clinical CVD. This observation is consistent with similar CV risk and CVD event rates in older adults with h/o clinical CVD and subclinical CVD.

COMPARISON OF BRACHIAL FMD OF SUBJECTS WITH CLINICAL, SUBCLINICAL AND CVD FREE(N=2791)

Variable	[a]Clinical (mean±se)	[b]Subclinical (mean±se)	[c]CVD FREE (mean±se)	Pvalue (a&b)	Pvalue (a&c)	Pvalue (b&c)
FMD(%)						
Unadjusted	2.80±0.07	2.92±0.08	3.22±0.05	0.215	<0.0001	0.001
Adjusted	2.93±0.07	2.93±0.07	3.13±0.05	0.969	0.025	0.030

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Intima-Media Thickness of the Carotid Artery and Associated Risk Factors in Japanese Men in Japan and Hawaii

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Background: Among developed countries, Japan has one of the lowest rates of mortality from coronary heart disease. Rates are markedly lower than in the United States in spite of an increasing trend by Japanese to adopt lifestyles that are associated with a high risk of coronary heart disease. Whether findings include progression to clinical disease through differences in susceptibility to subclinical atherosclerosis remains to be determined. The purpose of this report is to explore differences in subclincal disease between Japanese men in Japan and Hawaii by comparing levels of carotid intima media thickness (IMT) and its associated risk factors. **Methods**: Risk factor and IMT measurements were made in a population-based random sample of 313 Japanese men in Japan and 303 Japanese men in Hawaii. Men were aged 40 to 49 years and free of cardiovascular disease. **Results**: The mean IMT in Japan (0.614±0.070) was significantly lower than in Hawaii (0.712±0.123, $p<0.001$). Men in Japan were also leaner ($p<0.001$), less likely to have diabetes ($p=0.003$) and hypercholesterolemia ($p<0.001$), had lower levels of C-reactive protein ($p=0.001$), and had higher levels of high-density lipoprotein cholesterol ($p=0.003$). In contrast, men in Japan smoked cigarettes an average of 15 pack-years more than men in Hawaii ($p<0.001$). After risk factor adjustment, elevated body mass index was significantly related to higher IMT levels in both Japan ($p<0.001$) and Hawaii ($p=0.023$). In Japan, IMT levels also rose with increasing systolic blood pressure ($p=0.015$) and CRP concentrations ($p=0.016$). None of the risk factors, however, explained the low levels of IMT in Japan versus Hawaii. **Conclusion**: In spite of genetic similarities, levels of IMT are lower in the Japanese men in Japan versus the Japanese men in Hawaii. Observed differences are also unexplained by risk factor difference that are often considerable. Further studies are needed to identify factors that protect Japanese men in Japan from subclinical atherosclerosis.

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Endothelial Dysfunction in Asymptomatic Mexican-Americans versus Non-Hispanic Whites

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Background: Mexican-Americans (MA) are known to exhibit increases in various cardiovascular disease (CVD) risk factors compared to non-Hispanic Caucasians (C), yet have been

reported to have lower CVD mortality rates than C. Although endothelial dysfunction (ED) is known to be an early marker of vascular disease- e.g., atherosclerosis- there is a lack of data examining ethnic differences in ED between *asymptomatic* MA and C. Consequently, we examined in MA vs C adults the distribution, and demographic and CVD risk factor correlates, of a non-invasive measure of ED: brachial artery flow-mediated dilatation (FMD). **Methods**: Two hundred-five adult participants–105 MA, 42 men and 63 women, age 46±14 years (mean±SD) and 100 C, 59 men and 41 women, age 50±11 years– were studied by FMD, blood and urine tests. **Results**: Despite significantly higher BMI, triglycerides and fasting glucose in MA compared to C (range of p: $<$ 0.0006 to $<$0.04), MA demonstrated higher FMD compared to C (9.1±7.3 % vs 7.1±6.3 %, respectively, p $<$0.04). In contrast, urine microalbumin values were not significantly different in the overall MA versus the C cohort. Urine microalbumin in MA participants with ≥7 %FMD (normal) was consistently lower than in MA participants with $<$7% FMD (p$<$0.006). In contrast, there was no such relation in C. In multivariate analyses, in the overall cohort, BMI and height (r= 0.297, p$<$0.02; r=0.432, p$<$ 0.0001) were the most important predictors of FMD. After inclusion of these body size measures in the model, ethnicity (MA vs C) was no longer a predictor of FMD. Furthermore, in multivariate analyses, microalbuminuria was the only predictor of $<$7% FMD in MA (r=0.537, p$<$0.01), but not in C. **Conclusion**: To our knowledge, this is the first study to analyze in *asymptomatic* adults, the relation of MA and C ethnicity to FMD and microalbuminuria. Apparent MA vs C differences in FMD were importantly related to BMI and height. Of interest, microalbuminuria was the only independent predictor of ED ($<$7% FMD) in the MA cohort, but not in C.

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Serum Docosahexaenoic Acid Is Associated with Aortic Calcification Independent of Cardiovascular Risk Factors in a Population-Based Sample of Middle-Aged White Men

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Background and Purpose: We have previously reported that in white men aged 40–49 the ratio of polyunsaturated to saturated fatty acids in the serum (PS ratio) is a strong determinant of the presence of coronary calcification. We explored the association of serum fatty acids with calcification of the aorta. **Methods**: We examined a population-based sample of 273 randomly-selected white men aged 40–49 in Allegheny County, PA, without clinical cardiovascular disease. Calcification of the aorta was evaluated using electron beam tomography by acquiring 6mm images from the aortic arch to the iliac bifurcation. Scans were read by a trained reader and aortic calcium score (ACS) was calculated using Agatston method. We used cutoff points of 0 and 100 for ACS and performed ordinal logistic regressions to examine the association of each fatty acid with aortic calcification. **Results**: Table shows the basic characteristics of the participants including the distribution of serum fatty acids. Prevalence of ACS $>$0 was 69% and ACS ≥100 was 18.6%. In age-adjusted analyses, aortic calcification was significantly and inversely associated with each of total n3 fatty acids, eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and PS ratio; it was positively and significantly associated with monounsaturated fatty acids. After adjusting for age, body-mass index, systolic blood pressure, lipids, glucose, insulin, fibrinogen, and current smoking, the association of aortic calcification with DHA remained significant but other associations did not. **Conclusion**: Serum DHA is a determinant of aortic calcification independent of cardiovascular risk factors.

Table. Basic characteristics of the participants (n=273)

	Mean (SD) , median (interquartile rage), or %
Age (years)	45.0±2.8
Body-mass index (kg/m^2)	27.9±4.3
Systolic blood pressure (mmHg)	123.0±11.3
Diastolic blood pressure (mmHg)	73.4±8.7
Total cholesterol (mg/dL)	211.4±38.1
Low-density-lipoproiten cholesterol (mg/dL)	134.5±34.0
High-density-lipoprotein choleseterol (mg/dL)	47.5±12.8
Triglycerides (mg/dL)	128.0 (92.5. 186.0)
Fasting glucose (mg/dL)	101.2±14.1
Fasting insulin (μU/mL)	15.2±8.4
Fibrinogen (mg/dL)	292.6±70.6
C-reactive protein (mg/L)	0.92 (0.50, 1.82)
Current smoker (%)	7.3
Hypertension (%)	15.4
Diabetes (%)	3.5
Medication for lipid (%)	12.6
Serum fatty acids	
Total n3 fatty acids (%)	4.1±1.7
Alpha-linolenic acid (ALA) (%)	0.2±0.2
Eicosapentaenoic acid (EPA) (%)	0.8±0.6
Docosahexaenoic acid (DHA) (%)	2.3±1.2
Total n6 fatty acids (%)	41.1±4.0
Linoleic acid (%)	29.6±4.0
Arachidonic acid (%)	8.9±1.9
Total saturated fatty acids (%)	30.1±2.2
Total monounsaturated fatty acids (%)	19.1±3.0
Ratio of polyunsaturated to saturated fatty acids	1.5±0.2

Hypertension was defined as systolic BP ≥140 mmHg, diastolic BP ≥90 mmHg, or use of anti-hypertensive medications. Diabetes mellitus was defined as fasting serum glucose level ≥124 mg/dL or use of anti-diabetic medications.

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Supine Bicycle Stress Echocardiography for Chest Pain and Shortness of Breath in Women: The Importance of More Comprehensive Studies

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Background: Chest pain (CP) and/or shortness of breath (SOB) may be caused by coronary and noncoronary etiologies. Prevalence of macro/microvascular and noncoronary causes of CP and SOB is unknown and may be especially important in women. Supine bicycle stress echocardiography permits comprehensive evaluation of cardiopulmonary function and is ideal for study of this issue. Accurate identification of the etiology may optimize management and minimize morbidity. **Objective**: Evaluate the prevalence of macro/microvascular and noncoronary causes of CP and SOB in women. **Method**: 638 consecutive women presenting with CP and/or SOB underwent multistage supine bicycle stress echo/Doppler imaging for left ventricular wall motion abnormalities (WMA) and ejection fraction (LVEF) analysis, right ventricular (RV) size and function, quantitative analysis of mitral regurgitation (MR), tricuspid regurgitation (TR), right heart pressures and valve function. **Results**: Complete data was available on 606 women. Mean age 63±13 years, mean BMI 30±15, 17% diabetic, and 80% post-menopausal. Mean LVEF was 62±12%. Supine bicycle stress echo/Doppler at peak exercise revealed moderate/severe RV enlargement 26%, RV hypokinesis 26%, LV enlargement 4%, moderate/severe MR 21%, moderate/severe TR 40%, and induced pulmonary hypertension in 37% of women. Only 36% of studies were totally normal. Coronary angiography was performed within one year of the supine bike echocardiography in 201 women (33%) including 75 women (37%) with epicardial coronary disease ≥70%. In this group, WMA or EF $<$55% with concomitant coronary artery disease (CAD) was present in 68% of women (51/75) versus 67% (85/126) of women without CAD. Majority of women with CAD without WMA were identified by other means. **Conclusion**: COP and SOB are more often due to etiologies other than epicardial CAD. It is essential that women presenting with symptoms be evaluated comprehensively, rather than only screened for epicardial CAD.

Abnormalities on Supine Bicycle Stress Echocardiography

	Any Abnormality	≥ Moderate TR	Pulmonary Hypertension	RV Enlargement	RV Hypokinesis	≥ Moderate MR	LV Dilation
Percent of Subjects	64%	40%	37%	26%	26%	21%	4%

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Ankle Brachial Index Is Lower in Asymptomatic African Americans Independent of Risk Factors and Body Mass Index in Families at High Risk for Premature Coronary Disease

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Background: Low ankle-brachial index (ABI) has been associated with an increased risk of incident clinical peripheral vascular disease (PVD) and has also been strongly associated with the presence of cardiovascular risk factors in large population-based studies. African Americans have both a higher prevalence of clinically manifest PVD and of risk factors. The extent to which CVD risk factors explain any racial differences in resting ABI in individuals without clinical PVD remains unknown. We sought to determine whether differences in ABI in an apparently healthy biracial population of 30–59 year old siblings of individuals with a history of premature coronary artery disease (CAD) at less than 60 years of age, persisted when accounting for known risk factors, body mass index (BMI), and fitness level. **Methods**: We screened for cardiovascular risk factors, calculated BMI, and conducted maximal graded treadmill testing to obtain fitness levels (MET) in 614 African-American and 441 White siblings. We used Doppler-assisted methods to determine resting ABI. A sex-specific Framingham Risk Score (FRS) was calculated for each individual as an aggregate measure of CVD risk factors. Multivariable regression analyses predicting ABI included race, FRS, MET, and BMI. **Results**: Participants had a mean age of 46.8±7 years, a mean BMI of 30.2±6.4; 62% were female, 10% diabetic, 53% hypertensive, 28% current smokers. The unadjusted mean level of resting ABI in AA was lower (1.10±0.13) than in whites (1.12 ±0.12) p=0.003. The lower ABI level in African Americans was found in each quartile of FRS. In the multivariable analysis, AA race remained a significant independent predictor of ABI, p=0.02 even accounting for aggregate risk factors, fitness, and body mass. **Conclusions**: In young individuals with a high prevalence of all major CVD risk factors and a high risk of subsequent PVD, African Americans still have a lower ABI compared to Whites even when adjusting for CVD risk factors, fitness level, and BMI. This suggests that genetic and other causes may play a role in observed racial differences in resting ABI in high risk families.

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Aortic and Carotid Intimal-Medial Thickness in Adolescents and Young Adults: The Muscatine Offspring Study

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Introduction: The atherosclerotic process begins in childhood and the earliest lesions are found in the distal aorta. We performed ultrasonography to measure the aortic and carotid intimal-medial thickness (aIMT and cIMT) in 87 normal subjects (46 males and 41 females) between the ages of 10 and 25 (mean age 14.7 years), in order to a) examine the feasibility and reliability of measuring aIMT and cIMT, b) measure the correlation between the aIMT and cIMT, and c) determine the cardiovascular risk factors associated with aIMT and cIMT. **Methods**: Each subject had a single frame fasting recording of the aorta 15 mm proximal to the iliac bifurcation, and the mean far wall IMT was determined using an automated reading program. Similarly, maximum cIMT values were measured at up to 12 locations for each subject with the mean of these measurements used for analysis. Cardiovascular risk factors

included LDL cholesterol, HDL cholesterol, triglycerides, systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate, BMI, and waist/hip ratio. **Results**: Ninety-three subjects were enrolled and 87 (94%) had ultrasound images adequate to measure aIMT. Carotid IMT was measured in all subjects, with an average of 11.7 walls per subject. Means (SDs) for aIMT were 0.56 (0.13) mm and 0.53 (0.10) mm for males and females, respectively. For cIMT, the means (SDs) were 0.67 (0.04) mm for males and 0.64 (0.04) mm for females. Twelve subjects returned for a second examination and the median absolute differences were 0.050 mm for aIMT and 0.035 mm for cIMT. In males, aIMT and cIMT were slightly correlated with each other ($r=0.29$, $p=0.048$), but not in females ($p=0.902$). After adjusting for age, sex, and height, aIMT was associated with HDL cholesterol, triglycerides, DBP, BMI, and waist/hip ratio in both genders combined, and with SBP in males only. By contrast, cIMT was associated with no risk factor when combining genders, and with SBP and waist/hip ratio in males only. **Conclusion**: Both aIMT and cIMT can be reproducibly measured in adolescents and young adults; however, cardiovascular risk factors appear to have stronger associations with aIMT than with cIMT. Measurement of aIMT may allow detection of the atherosclerotic process at an earlier age than cIMT.

P311

Lack of Improvement in Outcomes of Black Patients After Myocardial Infarction: 17-Year Trends in New Jersey

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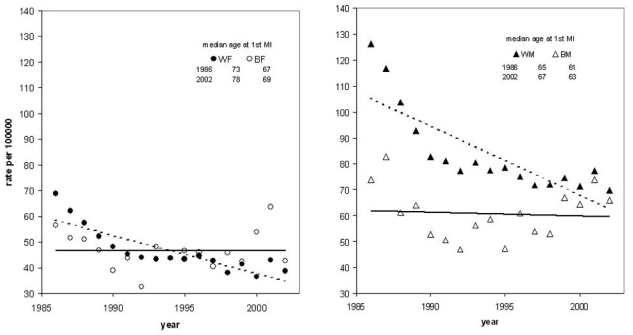
Background. Racial disparities in outcomes after acute myocardial infarction (MI) have been documented. However, it is unknown whether these differences have narrowed over time. **Methods**. We used the Myocardial Infarction Data Acquisition System (MIDAS), a database including all patients discharged with the diagnosis of MI from non-federal hospitals in New Jersey to examine the clinical characteristics, use of invasive intervention and 1 year mortality among 207,925 white (W) and 17,884 black (B) patients from 1986 to 2002. **Results**. Marked decline in age adjusted 1 year mortality rates were shown in W (female (F): 69 to 39, male (M): 126 to 70 per 100,000, 1986 to 2002) (figure). However, not much improvement was found in B (F: 57 to 43, M: 74 to 66 per 100,000, 1986 to 2002). Poisson regression models indicated that the time trends in age adjusted MI mortality differed according to race ($p<0.0001$ in both sexes). Over the past 17 years, the disparities in clinical characteristics between B and W increased. Higher prevalence of diabetes (B 31.2–38.5%, W 21.8–26.7%), hypertension (B 50.3–70.5%, W 33.1–54.7%), and anemia (B 11.0–16.5%, W 6.6–12.8%), and higher occurrence of left ventricular dysfunction (B 19.3–23.7%, W 18.6–17.6%) were all found in B. The use of invasive intervention within 30 days was lower in B (PCI: B 2.2–29.0%, W 3.1–33.9%; CABG: B 3.2 to 9.3%, W 4.0–13.3%) (All comparisons reach $p<0.0001$). **Conclusion**. Higher comorbidity and complication rates and lower invasive intervention use may explain the lack of improvement of MI mortality in blacks in the past 17 years.

Trends in AMI population mortality in New Jersey from 1986 to 2002 by race and gender, adjusted by the direct method to the age distribution of the 2000 US population



P312

Medication Adherence Does Not Explain Disparities in Blood Pressure Control: The REasons for Geographic And Racial Differences in Stroke (REGARDS) Study

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Introduction: Blood pressure (BP) disparities between hypertensive African Americans (AA) and European Americans (EA) are widely reported, even among treated individuals. Prior reports suggest racial differences in medication adherence may play a role. **Hypothesis**: In REGARDS, medication adherence will be worse for AA, which will explain some of the AA-EA BP difference. **Methods**: REGARDS is recruiting 30,000 community-dwelling adults nationwide aged ≥45, half AA, half female and over sampled from the stroke belt. Telephone interviews were followed by in-home assessments including height, weight, BP, blood sampling and documentation of current medications. Medication adherence was self-reported using an adapted Morisky scale. Logistic regression examined the effect of medication adherence on BP control for each race/ethnicity group, adjusting for age, gender, body mass index, creatinine and specific BP medications. We repeated this analysis stratified by the 19 most commonly prescribed BP regimens. **Results**: The 10,831 treated hypertensive individuals had mean age 68±8.6 years; 64% of AA (3324) and 74% of EA (4171) achieved BP<140/90 mmHg. Adherence was similar for AA and EA: 44% of AA (2206) and 45% (2593) of EA reported perfect adherence. Both AA and EA with better adherence had lower BPs. Including adherence in the logistic regression model did not change the odds of uncontrolled BP for AA vs. EA (adjusted OR=1.6, 95% CI 1.44, 1.73). In stratified analyses of individuals on the 19 most commonly prescribed regimens, adjusted BP differences were not changed by including adherence in the models. The 3 regimens associated with the smallest (≤1.5 mmHg) AA-EA difference in adjusted systolic BP were all diuretic-containing multidrug regimens, while 4 of 5 regimens associated with the greatest difference (6.7–8.7 mmHg) all contained ACEI. **Conclusions**: Medication adherence was an important predictor of BP levels and control, did not differ by race/ethnicity, and did not explain AA-EA BP differences. Similar to other studies, selected BP regimens were associated with greater and lesser disparity in BP control cross-sectionally, a finding that, if confirmed longitudinally, may open the door to decreasing racial disparities in BP control.

P313

Coronary Calcification Is More Predictive of Carotid Intimal-Medial Thickness in Black Compared to White Middle-Aged Men

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Background: Both coronary artery calcification (CAC) and carotid intimal medial thickness (IMT) are measures of subclinical atherosclerosis and are predictive of future coronary heart disease. Race-specific data for association between CAC and carotid IMT are limited. We sought to examine black-white specific associations of these two measures. **Methods**: We conducted a population-based study of 379 randomly-selected men aged 40–49 years (84 black and 295 white) from Allegheny County, US (2004–2006). Agatston coronary calcium score (CCS) was evaluated by electron-beam tomography and carotid IMT was evaluated by ultra-sonography. **Results**: The prevalence of any CAC was not significantly different between black and white men (54.8% vs 51.2% respectively, $p=0.56$). Total carotid IMT (mm) was significantly higher in black (Mean±SE = 0.73±0.01) than white men (Mean±SE = 0.68±0.01) after adjustment for traditional coronary risk factors ($p<0.001$). In both populations, CCS had moderate but significant positive correlation with total carotid IMT ($r=0.47$ for black men and 0.24 for white men, $p<0.001$ for both) as well as IMT for common carotid artery (CCA), internal carotid artery (ICA) and carotid bulb. The association of CAC with total and CCA IMT were significantly stronger in black than white men after adjustment of common coronary risk factors ($p=0.046$ and $p=0.036$ respectively). **Conclusions**: In black and white middle aged men, CAC had moderate but significant positive correlations with total and segmental carotid IMT. CAC was more predictive of total and CCA IMT in black than white men independent of coronary risk factors.

P314

Does Left Ventricular Mass Differ Between Apparently Normal Adults of Different Ethnicities? The Family Blood Pressure Program

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Background: Left ventricular hypertrophy (LVH) strongly predicts cardiovascular events, but little is known about whether normal LV mass (LVM) differs among normal individuals of different ethnicities. **Methods**: A total of 1,210 normotensive participants in the Family Blood Pressure Program, with body mass index (BMI) <30 kg/m^2 underwent echocardiography: 233 non-Hispanic white, 311 Hispanic, 266 black and 400 Japanese-American, 54% women (NS). LVM and LVM/body surface area (BSA) and height$^{2.7}$ were compared between women and men of different ethnicities by analysis of covariance, adjusting for age, systolic blood pressure (BP), diabetes and, for absolute LVM, height and body mass index (BMI). **Results**: Upper limits of 95% confidence intervals for LVM, LVM/BSA and LVM/height$^{2.7}$ were 209 g, 108 g/m^2 and 48 g/m$^{2.7}$ in men and 160 g, 94 g/m^2 and 45 g/m$^{2.7}$ in women, similar to recent large MRI or echocardiographic surveys. LVM was highest in Hispanic women and men without other consistent differences among ethnic groups (Table). Adjustment for fat-free mass did not eliminate that in LVM between Hispanic and Japanese-American women and men. **Conclusions**: LVM differs modestly between normotensive, non-obese adults of different ethnicities. Indexed LVM is higher in Hispanic than Japanese-Americans, independent of age, BP and body size, suggesting that other factors may contribute to this ethnic difference.

Variable	Non-Hispanic White	Hispanic	Black	Japanese-American
Men	(n=119)	(n=139)	(n=135)	(n=172)
LVM (g)	145±28	152±42	154±37	129±28‡†
LVM/BSA(g/m^2)	72±13	83±22*	78±17	71±15‡†
LVM/Height$^{2.7}$	30±6	38±11*	33±8‡	32±7‡
Women	(n=115)	(n=183	(n=128)	(n=229)
LVM (g)	107±26	113±24	116±24	96±22*‡†
LVM/BSA (g/m^2)	61±13	68±14*	67±13	62±14‡
LVM/Height$^{2.7}$	27±6	33±7	31±7	29±7‡†

Statistical significance by ANCOVA: *=p<0.05 vs. whites, ‡=p<0.05 vs. Hispanics; †=p<0.05 vs. blacks

P315

The Association Between Mortality Following Initial Hospitalization for Heart Failure and SES in Whites and Blacks: The ARIC Study

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Associations of socio-economic status (SES) with short-term survival following a heart failure (HF) episode have been reported; however the influence of SES on long-term mortality following a hospitalization for HF is unknown. We examined the role of individual-level adulthood SES indicators on all-cause mortality among 1,162 ARIC participants aged 45–64 years at baseline who experienced an incident hospitalized HF event over a 12-year follow-up period. SES indicators included participants' total household income (<$16,000 vs. >=$16,000) and education (<HS vs. >= HS) at baseline. Cases were ascertained via annual contacts, review of medical records, and death certificates. Initial hospitalized HF was defined as the first occurrence of either ICD-9-CM 428 or underlying cause of death of 428 or ICD-10-CM 150 for hospitalization without a previous record of 428. Participants with prevalent HF were identified via self-report and the Gothenburg criteria, and were excluded. The cumulative all-cause mortality for 2, 5, and 12-years was 25% (287/1162), 38% (443/1162), and 48% (558/1162), respectively. The short-term all-cause mortality for Blacks and Whites was similar, 26% (93/359) and 24% (194/803), respectively. The 5 and 12-year case-fatalities were significantly greater for Blacks than Whites: 43% (155/359) vs. 36% (288/803) and 55% (196/359) vs. 45% (362/803). Cox Proportional Hazards regression was used to estimate hazard rate ratios (HR) and 95% confidence intervals (CI) by ethnicity adjusted for age and gender. SES was not associated with short or long-term mortality after an initial hospitalization for HF in Whites. Both lower income and education were consistently, but not statistically significantly associated with higher mortality in Blacks. Adjustment for age, gender, study center and also BMI, diabetes, hypertension control, prevalent CHD, smoking, health insurance, and marital status at time of HF attenuated the associations.

Age and gender-adjusted HR [95% CI] for all-cause mortality following hospitalization due to HF

	2 years	5 years	12 years
Whites:			
Income	1.06 (0.82, 1.37)	0.96 (0.69, 1.32)	0.81 (0.40, 1.64)
Education	0.99 (0.78, 1.24)	0.94 (0.71, 1.25)	0.88 (0.48, 1.61)
Blacks:			
Income	1.15 (0.81, 1.63)	1.51 (0.98, 2.33)	2.37 (0.92, 6.14)
Education	1.23 (0.90, 1.68)	1.22 (0.85, 1.76)	1.22 (0.55, 2.71)

P316

The Association Between Albuminuria and Uric Acid Is Stronger in Hypertensive Non-Hispanic Blacks than Whites

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Background: Hyperuricemia may contribute to the development of arteriosclerotic target organ damage through endothelial dysfunction, of which albuminuria is a renal manifestation. An association between uric acid and albuminuria has been described, particularly among hypertensive patients. We sought to determine whether this association differs between hypertensive non-Hispanic blacks and hypertensive non-Hispanic whites, since blacks are more susceptible to kidney disease than whites. **Methods**: The Genetic Epidemiology Network of Arteriopathy study provided a sample of community hypertensives from Minnesota (whites) and Mississippi (blacks). Participants underwent a physical exam, an administered questionnaire, and provided serum and urine samples during a clinic visit. Uric acid and urine albumin-to-creatinine ratio (ACR) were measured. For multivariable analyses, the following covariates were also measured: sex, age, co-morbidities (body mass index, history of diabetes, serum creatinine, cholesterol, C-reactive protein), and medications (anti-gout, diuretics, losartan, fenofibrate, warfarin, and aspirin). Albuminuria was defined using sex-specific thresholds for ACR (>25 mg/g for women, >17 mg/g for men). **Results**: The prevalence of albuminuria was 25.8% (303 of 1175) among non-Hispanic blacks and 7.2% (61 of 852) among whites. Among blacks, uric acid (per 1-mg/dL) predicted albuminuria with an unadjusted OR=1.26 (p<.0001), age-sex-adjusted OR=1.23 (p<.0001), and multivariable-adjusted OR=1.14 (p=.008). For whites, uric acid predicted albuminuria with an unadjusted OR=1.17 (p=.03), age-sex-adjusted OR=1.08 (p=.35), and multivariable-adjusted OR=1.00 (p=.99). **Conclusion**: Serum uric acid had a strong independent association with albuminuria in black but not white hypertensives from the community. Uric acid may contribute to higher rates of albuminuria and subsequently higher rates of kidney failure among hypertensive blacks than whites.

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Racial Differences in the Prevalence of Cardiovascular Risk Factors and Coronary Calcium in Siblings of Individuals with Premature Coronary Disease

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Background: Few studies have examined coronary disease risk factors in relation to the presence of coronary calcium (CAC). We sought to describe the racial differences in traditional cardiovascular risk factors and CAC in an apparently healthy biracial population of 30–59 year old siblings of individuals with coronary artery disease (CAD) at less than 60 years of age. **Methods**: We studied 310 (54.5%) white and 258 (45.5%) black apparently healthy 30–59 year old siblings of probands with a coronary disease event at <60 years of age. We measured total cholesterol, HDL cholesterol, triglycerides, blood pressure, fasting plasma glucose, height, weight, and obtained a complete medical history and history of smoking. We also calculated body mass index and conducted maximal graded treadmill testing to obtain fitness level in the 568 siblings of probands with premature CAD. CAC was measured by MDCT, and the presence of CAC was defined as any measure >0. **Results**: After adjustment for all other risk factors, education, age and sex, blacks had significantly more diabetes (OR=2.4, 95%CI 1.34–4.28), hypertension (OR=1.5, 95%CI 1.08–2.21), obesity (OR=2.47, 95%CI 1.73–3.52), a higher rate of smoking (OR=1.27, 95% CI 0.84–1.94), and a non-significant trend toward less hyperlipidemia (LDL≥160) (OR=0.78, 95%CI 0.47–1.28. Blacks were found to have a significantly lower prevalence of CAC (38% vs. 47.7%, p=0.03). Using generalized estimating equations to adjust for age, sex, diabetes, hypertension, smoking, obesity, hyperlipidemia, fitness level, level of education, and clustering within families, we found that black race is an independent negative predictor of CAC, OR= 0.40 (95%CI 0.26–0.62). OR for male sex was 2.95 (95%CI 1.94, 4.49), for smoking it was 2.02 (95%CI 1.26, 3.25), for hypertension 1.39 (95%CI 0.95, 2.03), and for obesity 1.35 (95%CI 0.88, 2.07) for the presence of CAC. **Conclusions**: In this randomly selected population of siblings we found that while blacks had significantly higher prevalence of traditional cardiovascular risk factors, they had significantly less CAC than whites. This suggests that traditional risk factors are only partially responsible for CAC burden, and genetics may play an important role.

P318

Differences in the Association of ECG Abnormalities with 32-Year CHD Mortality in Black and White Women and Men

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Background: The association between electrocardiographic (ECG) abnormalities and coronary heart disease (CHD) mortality may vary by sex and race. We investigated whether ECG abnormalities were similarly associated with long-term CHD mortality in black and white women and men free from CHD. **Methods**: Age-matched samples of 2243 black women (BW), 6393 white women (WW), 1441 black men (BM) and 4323 white men (WM) were selected from the Chicago Heart Association Detection Project in Industry cohort. Major and minor ECG abnormalities at baseline (1967 - 73) screening were defined according to the Pooling Project criteria. Participants were followed through 2002 for CHD mortality (ICD-8/9: 410.0 - 414.9). Sex-specific multivariable Cox proportional hazards models were used to calculate hazard ratios (HR) and test for interactions (race*ECG abnormality). **Results**: In women (mean age = 31 years) the prevalence of major ECG abnormalities was lower (p<0.01) among BW (4 %) compared with WW (7 %), whereas the prevalence of minor abnormalities was higher among BW (5 % vs. 3 % WW). The prevalence of major abnormalities did not differ between BM and WM (6% in both; mean age = 37 years), but minor abnormalities were more common (p<0.01) in BM (10%) compared with WM (5%). Over 32 years, 55 BW (3%) and 132 WW (2%) experienced CHD mortality; rates for BM and WM were 107 (7%) and 343 (8%), respectively. Following adjustment for other baseline risk factors, major ECG abnormalities were not associated with CHD mortality in BW (HR = 1.0; 95% CI: 0.4, 2.9) or WW (HR = 1.5; 95% CI: 0.9, 2.5), interaction $P = 0.41$. Minor ECG abnormalities were associated with a non-significant risk elevation in WW (HR = 1.8; 95% CI: 0.9, 3.6) but not BW (HR = 0.4; 95% CI: 0.1, 1.7), interaction $P = 0.06$. Major ECG abnormalities were not associated with CHD mortality in BM (HR = 1.1, 95% CI: 0.5, 2.2), whereas they were among WM (HR = 2.5, 95% CI: 1.8, 3.3), interaction $P = 0.03$. There was no association between minor ECG abnormalities and CHD mortality in men of either race. **Conclusions**: The prevalence and association of ECG abnormalities with CHD mortality differs by race and sex. Major and minor ECG abnormalities do not appear to be associated with long-term CHD mortality in young black men and women.

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Withdrawn

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Do Awareness, Preventive Action, and Barriers to Cardiovascular Disease Prevention Vary by Race/Ethnicity in Women?

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Background: Racial and ethnic disparities in cardiovascular disease (CVD) outcomes and risk factors are well documented but few data have evaluated population differences in CVD awareness, preventive action, and barriers to prevention. **Methods**: A nationally representative sample of 1008 women (17% Hispanic, 22% black, 61% white/other) selected through random digit dialing in July 2005 were given a standardized questionnaire about knowledge of healthy risk factor levels, recent preventive actions, and barriers to prevention. Main outcomes measured were 1) Correlates of knowledge of optimal risk factor goals defined by AHA Evidence-Based Guidelines for Women, 2) Predictors of taking preventive action (add physical activity, avoid unhealthy food, lose weight) in the past year, and 3) Proportion reporting barriers to CVD prevention. Logistic regression models were used to determine if race/ethnicity was independently associated with awareness and preventive action, adjusted for age, marital status, education, income and having children. **Results**: No significant racial and ethnic differences in knowledge of risk factor goals were identified except Hispanic women were 44% less likely than whites to know the optimal level for HDL-Cholesterol (OR=0.56; 95% CI=0.35–0.91). Knowledge of blood pressure goal was lower among those without a college degree (OR=0.59; CI=0.44–0.79). Hispanic women were twice as likely as whites to help *someone else* lose weight (OR=1.78; CI=1.17–2.71) or add physical activity (OR=2.0; CI=1.18–3.22) in the past year. Blacks were more likely than whites to decrease unhealthy food consumption (OR=1.77; CI=1.08–2.93) and try to lose weight (OR=1.62; CI=1.06–2.47). Fear of change was reported by significantly more Hispanics than whites as a barrier to preventive action (24% vs 17%; p=.03). Blacks were more likely than whites to take action because they experienced CVD symptoms (30% vs 23%; p=.03). Physician encouragement was cited as the reason for taking action to lower CVD risk more often by black (59%; p=.002) and Hispanic (54%; p=.03) women than whites (43%). **Conclusion**: Initiatives to translate

awareness into preventive action are needed, especially among less educated and Hispanic women who may activate others to reduce risk.

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Prevalence of Overweight and Characteristics Associated with Higher Body Mass Index Among Haitian Immigrant Children

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Introduction The relation of weight and risk factors for premature cardiovascular disease are not known in pediatric Haitian immigrants. **Hypotheses** We assessed the hypotheses that:1.Haitian born children have lower BMI% than Haitian children born in the US,and other pediatric populations and 2.Their BMI% increases with longer US residence. **Methods** Demographic/anthropometric characteristics were abstracted from medical records of 250 Haitian children seen at Center for Haitian Studies, Miami, FL from 1/04–7/06. Covariates included: gender, age, birthplace (Haiti vs US), and length of US residence. Primary outcome measures included: 1) "at risk" for being overweight ($\geq 85^{th}$ % BMI - $<95^{th}$ % BMI) and 2) overweight ($\geq 95^{th}$ % BMI). The comparison group was 3958 children from the 2003–2004 National Health and Nutrition Survey (NHANES). **Results** The mean age was 10.8 ± 4.5y. 48.5% were male. 56% were born in Haiti, and of those, 38% lived in the US <1 yr and 22% >5 yrs. 19.4% of the population was "at risk" for being overweight and 22% was overweight. No significant differences in BMI% were seen by gender or age. US born children had significantly higher BMI% than Haitian born children ($p=.022$). Increased US resident time among Haitian born children resulted in higher BMI% ($p=.047$). BMI% was 22% higher among Haitian born children living in the US >5 yrs than among Haitian born children living in the US <1 yr ($p=.02$). Compared to NHANES estimates, Haitian born children were significantly less likely to be "at risk" for overweight than all race/ethnic groups (14.9% vs 33.6%) but were as likely to be overweight (15.0% vs17.7%). Haitian children born in the US were as likely to be "at risk" for overweight (24.7% vs 33.6%) and overweight (26% vs 17.3%) as other pediatric populations. **Conclusions** Haitian born children have a lower BMI% than US born Haitian children but their BMI% increases with length of US residence. Although Haitian born children are less likely to be "at risk" for overweight than other pediatric minority populations, they are as likely to be overweight, making them potentially at greater risk for premature CVD. With acculturation, these children become more "at risk" for overweight and may benefit from primary prevention strategies to reduce modifiable CVD risk factors.

P322

Prevalence of Cardiovascular Risk Factors in Rural Mexico: Results of the Puentes de Salud Project

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Background: Latinos are the largest and fastest growing minority in the US. According to census data, most Latino immigrants are from rural Mexican communities. However, there is a paucity of data on the prevalence of CV risk factors in rural Mexico. We sought to assess the prevalence of cardiovascular risk factors in 6 rural communities in the state of Guanajuato. **Methods**: The "Puentes de Salud" project was designed to raise awareness of CV diseases and assess the prevalence of factors and behaviors associated with increased CV risk in 6 rural Mexican communities. Participants were asked to attend educational and screening sessions held at each one of these communities in June and July of 2006. Investigators interviewed each participant in Spanish utilizing a standardized questionnaire. Glycemia and Serum lipid levels were assessed with a point-of-care device. **Results**: A total of 428 participants, mostly females were recruited. Prevalence of hypertension was 35.8% and glycemia greater than 200 mg/dL was 5.1%. Total cholesterol greater than 200 mg/dL was present in 20.3%, and HDL-cholesterol lower than 40 mg/dl in 63.7%. Most participants with abnormal blood pressure, glycemia, and/or lipid values were unaware of any pre-existing CV risk factors. **Conclusions**: In this study we detected a high prevalence of abnormal serum lipids in rural Mexicans. Awareness of chronic diseases appears to be a problem that warrants further investigation.

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Knowledge of Pulse-Checking, Irregular Heart Beats, and Risk for Stroke: HealthStyles, 2005

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Background: Monthly pulse checking for 60 seconds has been suggested to detect irregular heart beats (IRRHB), an indicator of atrial fibrillation (AF), which is a risk factor for stroke. Little is known about public knowledge regarding pulse-checking, risk of stroke from IRRHB or AF, or racial/ethnic disparities in this knowledge. We examined disparities in knowledge regarding pulse-checking, follow-up actions, and risk for stroke. **Methods**: In a stratified, random sample of 4,819 adults aged ≥ 18 years who completed a mailed survey (HealthStyles, 2005), respondents were asked if they knew how to check their pulse and if so, for how long, and whether they agreed that monthly pulse checks gave a better chance to discover IRRHB and prevent stroke, if a person with an IRRHB should see a doctor for diagnosis, and if people with AF or IRRHB are at increased risk of stroke. Differences were assessed using the chi-square of weighted proportions. **Results**: Overall, 63.2% reported knowing how to check their pulse; of these, only 32.8% reported that they should check pulses for 60 seconds. More whites (W) reported knowing how to check their pulse (65.8%) than blacks (B) (50.9%) or Hispanics (H)(57.3%) ($p<0.05$). Regardless of race/ethnicity, 30.0% agreed that monthly pulse checks gave a better chance to discover IRRHB. Few (34.3%) agreed that those with AF or IRRHB are at increased risk of stroke (35.4% of W, 28.4% of B, 32.8% of H; $p<0.05$). The majority (87.5%) agreed that those with IRRHB should see a doctor (88.6% of W, 83.0% of B, 84.3% of H; $p<0.05$). **Conclusions**: Knowledge of IRRHB/AF and risk of stroke were suboptimal for all groups; however, racial/ethnic disparities were evident in knowledge of pulse-checking and the association of IRRHB or AF with risk for stroke. Few reported counting their pulse for the 60 seconds necessary to detect IRRHB. Gaps in knowledge of pulse-checking and risk for stroke suggest areas for public education.

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Thrombo-Metabolic Profile of Hispanic Postinfarction Patients

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The thrombo-metabolic profile of Hispanics with cardiovascular disease is unknown. This study aimed to determine the racial-related diffrences in the thrombogenic and lipid factors in Hispanics and NHW post-MI patients. **Methods**: Blood levels of the following were measured at 2 mo. after MI 777 NHW and 75 Hispanics: total cholesterol,LDL cholesterol, HDL cholesterol, triglycerides, apolipoprotein B, aplipopritein A, factor VII, factor Vlla,von Willebrand factor, D-Dimer, and plasminogen activator inhibitor. Patients were followed for a mean 26 mo. with primary cardiac events (PCE) defined as nonfatal MI or cardiac death and secondary cardiac events (SCE)defined as unstable angina or nonfatal MI or cardiac death. **Results**: In comparison to NHW, Hispanic were more obese (BMI 29.0+-5.5 vs. 27.6+-4.5 kg/m2; $p=0.022$) had more diabetes (36% vs. 15% $p<0.001$) and more frequent prior angina (50% vs 31%; $p<0.001$). After adjustment for clinical covariates, levels of apoB, total cholesterol, LDL, and PAI-1 were significantly higher in Hispanics than NHW post-MI pts (see table). There were 61 (8%) PCE in NHW and 6 (8%) in Hlspanics ($p=$ns). SCE were observed more frequently in Hispanics (28%) than in NHW (19%)pts ($p=0.051$), due to higher occurrence of unstable angina. In multivariate Cox model, there was a non-significant trend indicating a 10% increase in the risk of SCE in post-MI Hispanics (HR=1.10; $p=0.113$)when compared to NHW. **Conclusion**: There is significant difference in thrombo-metabolic profile between Hispanics and NHW post-MI patients manifested by higher levels of Apo B, total choelsterol, LDL and PAI-1 in Hispanics. This thrombo-metabolic profile combined with increased frequency of obesity and diabetes might predispose Hispanic post-MI patients to more frequent secondary cardiac events.

Variable	Odds Ratio	P Value
Apo B	1.95	0.012
Cholesterol	2.27	0.002
LDL	2.18	0.004
PAI-1	1.72	0.041

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Comprehensive Therapeutic Lifestyle Changes in the Underserved Population: A Longitudinal Study

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Therapeutic lifestyle changes centered around diet, education, or exercise have been shown to be effective methods of lowering ones risk for Coronary Artery Disease (CAD). Unfortunately, these programs results are typically based on based middle classed Caucasian males. This study intends to demonstrate the superiority of a uniquely comprehensive and individualized approach to risk reduction through a longitudinal measurement system that will evaluate the long-range effectiveness of a focused, patient-specific cardiovascular disease risk reduction program in accordance with the guidelines set by the American Heart Association (AHA). **Methods**: One hundred-fourteen (*Men n=30 Women n=84)* ethnically diverse *(African American n=81 Caucasian n=29 Hispanic n=4)*, indigent persons considered high risk for cardiovascular disease were identified through physician and client referrals, community screenings, or door-to-door solicitation, and placed into our comprehensive preventive cardiology system. Each participant underwent risk assessments, were counseled by various health care professionals, given a risk reduction plan, and assigned to an array of programs that suited their personal needs. Individual risks were monitored and tracked to ensure the acquisition of goals set by the AHA. **Results**: Although data is still being collected, thus far, cardiovascular risk factors have decreased significantly within the sample group. Participants have experienced an 86% quit rate from smoking, a 7.8% decrease in SBP, a 9.5% decrease in DBP, 24.3% decrease in TC, 10.2% increase in male HDL-C, 8.3% increase in female HDL-C, 35% decrease in LDL-C, and a 25.9% decrease in Triglycerides. **Conclusion**: Our multi-disciplined approach to lifestyle modifications yields significant reductions in the risk factors for heart disease. Our goal is to track the risk reductions to determine their effect on the mortality and morbidity rates of this underserved sector of our population. Additionally, this study demonstrates the success for such a program with a demographic known to experience health care disparities and to have higher coronary artery disease mortality rates.

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Racial Differences in PAI-1 Levels Among Healthy African-American and Caucasian Women

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Plasminogen Activator Inhibitor-1 (PAI-1) is an emerging risk factor for cardiovascular disease. Levels may differ by race/ethnicity and are influenced by interplay among metabolic factors. Minimal data exist, regarding the cardiometabolic correlates and predictors of PAI-1 in Caucasian (Caus.) or African-American women (AAW). This cross-sectional study of healthy, women (N=129; 51% AAW), participants of a weight loss study, was designed to address this issue. We hypothesized that PAI-1 levels would differ by race. **Methods**: Fasting insulin, triglycerides(TGs) and baseline PAI-1 concentrations were measured using standardized protocols; insulin sensitivity(Si) was determined by minimal modeling after an intravenous

glucose tolerance test; fat distribution was determined by CT scanning. Data analyses included t-tests to examine Caus./AAW differences in cardiometabolic risk and regression analyses to determine predictors of PAI-1 levels by race controlling for age and BMI. **Results**: PAI-1 levels, TGs, amount of visceral adipose tissue (VAT) and levels of Si were higher in Caus. than AAW. In contrast, AAW had higher acute responses to insulin by glucose (AIRg). Regression analysis controling for age and BMI indicated that TGs {($p=0.009$) $R^2=0.213$} was the only predictor of PAI-1 levels in Caus. **Conclusion**: Although Cauc.women appear to have more adverse cardiometabolic risk profile, the higher AIRg among AAW - relative to the degree of insulin sensitivity - suggests a specific need for a greater degree of post-prandial hyperinsulinemia in order to maintain glucose homeostasis in the post-challenge state. In these AAW, this may in turn contribute to earlier beta cell dysfunction. Viewed in the context of other recent research, these findings suggest the need to consider racial differences in the assessment of cardiometabolic risk and warrant additional research (with larger diverse samples) focused on determinants of PAI-1 in women.

Physiological Variables by Race

VARIABLES	Cauca.Women (n=62) MEAN	SD	RANGE	AAW (n=65) MEAN	SD	RANGE	P‡
AGE	38.40	11.10	23.20–66.20	35.66	9.61	18.90–63.90	0.17
BMI (kg/m^2)	27.01	2.49	20.01–30.93	26.96	2.48	22.67–36.43	0.93
TGs†(mg/dL)	105.90	54.79	34–335	62.69	22.79	23.113	**<0.001**
Fasting Insulin† u/U/ml	12.40	3.84	7.20–20.80	11.69	3.76	6.3–19.2	0.49
AIRg	573.29	355.47	221.50–1677.20	1058.17	493.40	264.3–1729.7	**<0.001**
S_I†	3.59	2.51	1.07–12.08	2.83	2.02	1.0–8.3	0.18
PAI-1† (ng/ml)	28.62	32.34	1.39–186.0	20.10	29.80	1.57–176.81	**0.033**
IAAT	94.06	38.79	30.12–163.10	56.86	29.87	12.16–154.10	**0.002**

†Log-transformed ‡P<0.05 indicates statistical significance.

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Disproving the Hispanic Paradox: Cardiovascular Risk Is Higher in Hispanic Women than Commonly Believed

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Background: The "Hispanic Paradox" is the common belief in medical practice that Hispanics have lower cardiac morbidity and mortality than non-Hispanic whites (NHW) despite a higher prevalence of risk factors. Our hypothesis was that Hispanic women have earlier onset of disease, more risk factors, and an equal, if not higher risk of cardiac disease. **Methods**: Women participants, 18 and older, attended a series of free community health screens specifically targeted to reach Hispanic women at a variety of locales including churches, community centers, and outpatient cardiology. At the centers we collected vital statistics on each patient, and self-reported medical history. Using standardized, validated and commonly used cardiometabolic risk screenings tools, we obtained blood pressure, body mass index, waist circumference, lipid profiles, and blood sugar. Statistical analysis utilized two-sample t-testing and chi square analysis for data assessment. **Results**: In our population of 170 women (79 Hispanic and 91 non-Hispanic), we showed that there was a statistically significant difference between Hispanic and non-Hispanic women, respectively, for the following variables: age (53 *+/-14.75* vs. 63 *+/- 11.79* years old, $p<0.0001$); post-menopausal status (61% vs. 85%, *p=0.004*); pre-hypertension (32% vs. 19%, *p=0.05*); and Duke Activity Status Index score (34.68 *+/-12.5* vs. 44.08 *+/-15.3*, *p=0.04*). There was no significant difference in hypertension (29% vs. 29%, *p=0.95*), diabetes (13% vs. 15%, *p=0.79*), hyperlipidemia (38% vs. 53%, *p=0.29*), BMI (29.2 vs. 28.5, *p=0.41*), waist circumference (37.9 vs. 36.9 inches, *p=0.27*), presence of metabolic syndrome (50% vs. 45%, *p=0.52*), ATP-III (3.7% vs. 4.6%, *p=0.33*), or Framingham risk scores (8.07% vs. 8.88%, *p=0.47*). **Conclusion**: Hispanic women reached the same level of cardiac risk as NHW, as defined by the Framingham risk score, despite being a decade younger and less into menopause. A higher number of pre-hypertensives and less active women in the Hispanic group probably contributes to this observation stressing the importance of early intervention in these women. This study suggests that Hispanic ethnicity may be an independent risk factor for premature cardiac disease and argues against the "Hispanic Paradox".

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Variation in Rates of Incident Myocardial Infarction by Neighborhood Socioeconomic Characteristics: The Atherosclerosis Risk in Communities Surveillance

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Although variations in rates of CHD mortality by socioeconomic status (SES) are well documented, SES is not recorded on medical records in the U.S. Thus, associations between SES and the community burden of myocardial infarction (MI) have rarely been studied systematically. We examined the association of neighborhood socioeconomic status (nSES) with incident MI (weighted N=8193) among persons ages 35 to 74 years in four U.S. communities under surveillance by the Atherosclerosis Risk in Communities study (1993–2002). Events included the first validated, definite or probable hospitalized MI occurring between 1993 and 2002 among persons without a prior history of MI. Tertiles of census tract median household income [low (L-), medium (M-), high (H-)] were used to quantify nSES. Weighted MI counts in eight age strata and U.S. census population estimates were used to calculate (indirect) age-standardized expected MI rates within census tracts. Poisson generalized linear mixed models were used to generate race-specific standardized rate ratios (RR) and to account for the clustering of cases within census tracts. In models that included gender, year of MI, study center, and nSES - covariate interaction terms, there was significant effect modification of the nSES - incident MI association by gender [$p < .0001$ for whites; $p < 0.05$ for African Americans]. Race-gender-specific results are presented below: Age-standardized rates of incident MI events were higher among those living in less affluent neighborhoods in the ARIC surveillance communities during the period 1993–2002. These associations were stronger in women and in African Americans.

Adjusted Age Standardized Rate Ratios of Incident MI by nSES, ARIC Surveillance (1993–2002)

	African American		White	
	Women	Men	Women	Men
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
L-nSES vs. H-nSES	2.11 (1.60, 2.61)	1.69 (1.31, 2.07)	1.80 (1.59, 2.01)	1.25 (1.08, 1.42)
M-nSES vs. H-nSES	1.37 (0.82, 1.91)	1.47 (1.06, 1.88)	1.35 (1.19, 1.52)	1.19 (1.06, 1.33)

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Use of Evidence-Based Medications in Patients Undergoing Coronary Revascularization in Finland During 1995–2003

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Background: Coronary artery bypass graft surgery (CABG) and percutaneous transluminal coronary angioplasty (PTCA) are commonly performed both in acute and chronic coronary heart disease (CHD). We analyzed how well secondary prevention with evidence-based medications is put into practice before and after the procedure. **Methods and Results**: We used the National Hospital Discharge Register to identify all survivors of first revascularization among patients aged 35–74 years during 1995–2003 in Finland (32,653 CABG and 16,857 PTCAs). These data were linked to the drug reimbursement database, which includes the purchases of all drugs prescribed by a doctor. We analyzed the use of beta-blockers, hypolipidemic medications, angiotensin converting enzyme inhibitors and hypoglycaemic medications at three points in time: (1) the three month period before the procedure; (2) the three month period after the procedure; and (3) the period 10 to 12 months after the procedure. In this abstract data on the use of hypolipidemic medication are presented as an example. In 2000–2003, about 56% of patients having CABG and 44% of those having PTCA were on hypolipidemic medication before the procedure. After the procedure, these proportions increased to 69% and 75%, respectively. Of those patients who were not on hypolipidemic medication before the CABG, 57% started using the medication after the procedure. After PTCA the corresponding figure was 68%. Nine to twelve months after the procedure 56% and 61% of the CABG and PTCA patients continued to use hypolipidemic medication. Female sex and later study years were significantly associated with a smaller probability of discontinuing. Proportional hazards regression analyses showed that the use of hypolipidemic medication at least for 6 months after the procedure was associated with a smaller risk of dying during the subsequent year (months 6–18): Adjusted hazard ratio 0.60 (95% CI 0.45–0.78) after CABG and 0.54 (95% CI 0.38 - 0.75) after PTCA. **Conclusions**: The use of evidence based medications for secondary prevention after revascularization has increased over time in Finland, but is still suboptimal. Regular use of hypolipidemic medication was associated with a better survival after the procedure.

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Comparison of Observed Community CHD Rates and Trends with Cohort-Based Expected Rates and Trends: ARIC, 1987–1999

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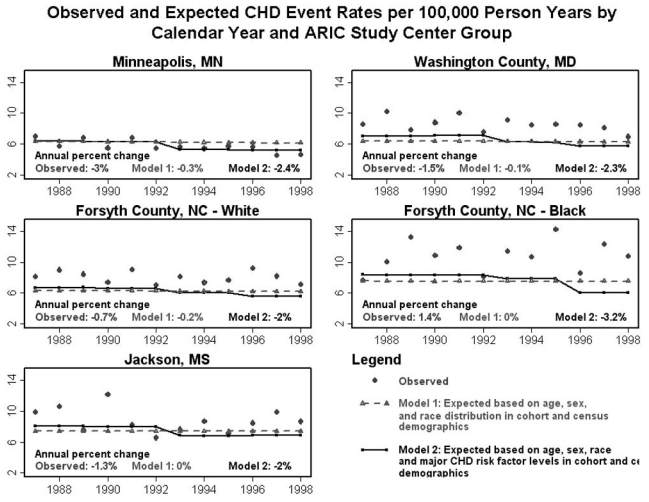
Background: The relationship of coronary heart disease (CHD) risk to major CHD risk factors is well established. However, estimating the extent to which individuals' risk factor levels and trends explain community CHD rates has been difficult. **Methods**: The Atherosclerosis Risk in Communities (ARIC) Study provided two sources of data from each of four US communities: 1) a sampled cohort; and 2) surveillance of hospitalized myocardial infarctions and CHD deaths in each community. Cohort members' information from each visit and follow-up was combined to generate two overall models for predicted probability of a CHD event: 1) with only demographics; and 2) adding risk factors. The probability was then summarized across the individual risk factor distributions for each geographic, chronologic and demographic group and compared to the observed rate obtained from the surveillance and census data. The analysis was limited to ages 53 to 64 to ensure availability of risk information from the cohort throughout the time period. **Results**: The figure shows the observed and expected CHD event probabilities from 1987 to 1999. Expected risk was closest to observed risk in Minneapolis and underestimated by an average of 19% to 44% in the other communities. Both observed and expected CHD rates showed a decline over time in all groups except the Forsyth Blacks. The annual percent decline was steeper after incorporation of risk factor levels in all groups and

closer to the observed percent decline in all groups except Forsyth. **Conclusions**: The relationship between observed and cohort-predicted CHD risk varies across communities but risk factor trends translate to a 2–3% expected decline in CHD.



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Neighborhood Socioeconomic Status, Health Insurance, and Prehospital Delay Time for Acute Myocardial Infarction: Atherosclerosis Risk in Communities (ARIC) Surveillance

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Outcomes following an acute myocardial infarction (MI) are generally more favorable if medical treatment is received in a timely manner. Thus, much attention has been focused on reducing the time elapsed between onset of MI symptoms and hospital arrival (prehospital delay time). We examined the association of neighborhood socioeconomic (nSES) and health insurance status with prehospital delay among a weighted sample of 11745 men and women with a validated, definite or probable MI in the ARIC community surveillance study (1993–2002). nSES was based on U.S. Census tract median household income and grouped into tertiles (low, medium and high). Health insurance was categorized as: Medicaid, Medicaid and Medicare, Medicare, prepaid (e.g., Blue Cross/Blue Shield, HMO), prepaid and Medicare, and other (e.g., government insurance and workers' compensation). Delay time was classified into three clinically meaningful categories: short ($<$2 hr), medium (2–12 hr), and long ($>$ 12 hr). Weighted multinomial regression using generalized estimation equations was used to estimate odds ratios (OR) and 95% confidence intervals (CI) and to account for the clustering of residents within census tracts. In models with income, insurance, age, gender, race, diabetes status, emergency medical service use, chest pain, study center, year of MI event and distance from residence to hospital, low nSES was associated with a higher odds of long versus short delay (OR=1.38, 95% CI = 1.11, 1.72) and long versus medium delay (OR=1.33, 95% CI = 1.10, 1.60) compared to high nSES. Compared to participants with prepaid insurance, participants with Medicaid were more likely to have a long versus short delay (OR=1.51, 95% CI = 1.01, 2.28), as were participants with both Medicaid and Medicare (OR=1.66, 95% CI = 1.04, 2.66), and Medicare alone (OR=1.52, 95% CI = 1.05, 2.20). The odds of having long versus medium delay did not vary by insurance status with the exception of the "Medicaid and Medicare" category (OR=1.78, 95% CI = 1.16, 2.72). In summary, this analysis found that both low nSES and some types of health insurance are associated with longer prehospital delay. Reducing socioeconomic and insurance disparities in prehospital delay is critical, as excess delay time may hinder effective care for MI.

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Coronary Heart Disease Mortality Among Young Adults in the United States from 1980 Through 2002: Unfavorable Developments in Recent Years

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Trends of risk factors for coronary heart disease among U.S. adults present a complex picture. Particularly ominous trends for obesity, diabetes, blood pressure, and metabolic syndrome among young adults raise concerns about the mortality rates from coronary heart disease in this group. The objective of our study was to examine age-specific mortality rates from coronary heart disease, particularly those among younger adults. We used mortality data from 1980–2002 to calculate age-specific mortality rates for U.S. adults aged $\geq$35 years. Overall, the age-adjusted mortality rate decreased by 52% in men and 49% in women. The smallest decrease (27%) occurred among women aged 35–44 years, whereas among other sex- and age-specific groups, the decreases ranged from 43% to 58%. Among women aged 35–44 years, the nadir occurred during 1991, and the rate was 15% higher by 2002. Among men aged 35–44 years, the rate of mortality from coronary heart disease in 2002 increased for the first time in more than two decades. Among men and women aged 45–54 years, mortality rates continued to decrease albeit at slower rates in more recent years. Among adults aged $\geq$55 years, mortality rates continued to decrease steadily. In conclusion, the mortality rates for coronary heart disease among younger adults may serve as a sentinel event. Unfavorable trends in several risk factors for coronary heart disease provide the most likely explanation for the observed mortality rates.

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Explaining the Decline in Coronary Heart Disease Mortality in Italy Between 1980 and 2000

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Introduction Coronary heart disease (CHD) mortality rates in Italy are far lower than in Northern Europe. Furthermore, Italian CHD mortality rates have been falling since the 1970s. **Hypothesis** To examine how much of the fall in CHD mortality between 1980 and 2000 could be attributed to trends in risk factors, and medical and surgical treatments. **Methods** A previously validated model was used to combine and analyse data on uptake and effectiveness of specific cardiological treatments and risk factor trends in the Italian population of 57 million, stratified by age and sex. Published trials, meta-analyses, official statistics, longitudinal studies, and surveys were the main data sources. **Results** Between 1980 and 2000, CHD mortality rates in Italy fell by 41% in men and 43% in women aged 25–84; with 42,927 fewer deaths in 2000 (24,954 in men, 17,973 in women) than expected. Approximately half the mortality fall was attributed to treatments: substantial contributions came from specific treatments for secondary prevention, heart failure and angina; CABG surgery and angioplasty were estimated to explain approximately 3% of the total mortality fall. The remaining half the mortality fall was due to population changes in major risk factors: in men, greater improvements in cholesterol (38%) and smoking (19%) rather than physical activity (7%) and blood pressure (5%); adverse trends were seen in BMI (-2%) and diabetes (-4%). In Women about 40% of the mortality fall was attributable to improvements in cholesterol (28%), blood pressure (4%) and physical activity (3%); worrying adverse trends were seen in smoking (-4%), representing approximately 642 additional deaths. The adverse contributions from diabetes (-0.5%) and BMI (-2%) were small. **Conclusions** Approximately one half of the CHD mortality fall in Italy between 1980 and 2000 was attributable to reductions in major risk factors, principally cholesterol in men and women and smoking in men. The rise in smoking rates in women generated substantial additional deaths. These findings emphasise the importance of a comprehensive strategy which actively promotes primary prevention, particularly tobacco control and a healthy diet, and which maximises population coverage of effective treatments.

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Temporal Trends in the Utilization of Coronary Revascularization in the Community

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Background: Previous reports on revascularization utilization have focused on inpatient settings and did not distinguish between incident and recurrent procedures. Further, little is known on age and gender specific trends. Finally, longitudinal data on the utilization and results of coronary angiography as explanatory factors for the changing revascularization practice are lacking. **Methods**: Data integrating diagnostic and therapeutic coronary procedures performed in Olmsted County, MN, between 1990 and 2004 were analyzed. Standardized rates were calculated applying the direct method and temporal trends compared using Poisson regression models. **Results**: Revascularization utilization increased by 24% during the study (95% confidence interval [CI]: 5% to 46%), but the trends diverged by procedure type, with a sustained increase (69%, 95% CI: 43% to 101%) for percutaneous coronary interventions (PCI) contrasting with a stabilization, then decline (-33%, 95% CI: -16% to -47%) for coronary artery bypass grafting (CABG). For PCI, while the use increased in all categories, greater increases were noted in the elderly, in women, and for recurrent procedures (Table). No such patterns were detected for CABG. Angiography use remained stable and the rate of three-vessel and/or left main coronary artery disease (CAD) declined by 22% (95% CI: -8% to -33%). Using the Coronary Artery Surgery Study scores, decreases in both the extent and severity of angiographic CAD were observed (all $P<0.001$ after adjustment for age and gender). **Conclusions**: Over the 15 year period, revascularization increased in the community with a large increase in PCI partially offset by a decrease in CABG. More PCI are performed in women and the elderly and for recurrent disease. These changes occurred within the context of a decline in multivessel disease and thus likely reflect the natural history of CAD.

Table. Trends in PCI utilization in Olmsted County across 5-year tertiles

	Crude Rates per 100,000 / Age and Gender Adj. Rate Ratios (95% CI)				
	1990–1994	1995–1999	2000–2004	P Linear trend	P Interaction
Overall	203.5	270.7	335.4		-
	1 (ref.)	1.25 (1.09–1.44)	1.50 (1.31–1.72)	<0.0001	
Age Group					
25–74 yrs	184.7	221.0	259.7		<0.0001
	1 (ref.)	1.19 (0.82–1.77)	1.40 (0.98–2.01)	0.0817	
75+ yrs	430.5	836.1	1171.8		
	1 (ref.)	1.92 (1.42–2.59)	2.67 (2.01–3.55)	<0.0001	
Gender					
Men	298.3	390.7	469.5		0.0654
	1 (ref.)	1.23 (1.03–1.46)	1.43 (1.21–1.69)	0.0001	
Women	117.2	160.1	211.1		
	1 (ref.)	1.32 (1.05–1.66)	1.71 (1.38–2.11)	<0.0001	
Incident Status					
Incident	140.1	177.0	201.3		0.0013
	1 (ref.)	1.19 (1.03–1.37)	1.31 (1.15–1.50)	<0.0001	
Recurrent	63.1	93.6	134.0		
	1 (ref.)	1.39 (1.13–1.71)	1.93 (1.59–2.34)	<0.0001	

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Validation of Health Insurance Claim Data on Acute Myocardial Infarction for the National Cardiovascular Disease Surveillance System

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Background: We're developing the Korean National Cardiovascular Disease Surveillance System, which is based on health insurance claim data. The purpose of this study was to validate the discharge diagnosis on the National Health Insurance (NHI) claim database. **Methods**: From the NHI claim database of year 2004, we randomly sampled 2,008 hospital admissions, which were suspected due to acute myocardial infarctions (ICD-10 code: I-21, I-22, I-23, I-250, and I-251). Each medical records were trained medical record technicians with a standardized from. The admission events were considered newly developed acute myocardial infarction, when the events met any one of the two diagnostic criteria: 1) A Consensus Document of the Joint European Society of Cardiology/American College of Cardiology Committee for the Redefinition of Myocardial Infarction (ESC/ACC definition); 2) A Statement From the AHA Council on Epidemiology and Prevention; AHA Statistics Committee; WHF Council on Epidemiology and Prevention; the ESC Working Group on Epidemiology and Prevention; CDC and the NHLBI (AHA-EPI definition). The inter-observer reliability was tested by kappa coefficient between two independent reviewers in a pilot study on 222 randomly selected medical records. **Results**: Agreement (kappa) between two reviewers was 0.87 (95% CI: 0.80–0.95) for ESC/ACC definition and 0.64 (95% CI: 0.54–0.75) for AHA-EPI definition. Among the 2,008 hospital admissions, 71.4% (95% CI: 82.1%–93.3%) were validated to acute myocardial infarction: 51.6% in primary, 77.2% in secondary, and 88.9% in tertiary hospitals. The validity was 93.9% when the analysis was confined to the admission with primary diagnosis code of I-21. When these estimates were applied to the NHI claim database, 85.1% (95% CI: 78.5%–89.9%) of 51,591 tentative events were estimated due to acute myocardial infarction, and incidence of acute myocardial infarction was estimated to 81 (95% CI: 75–87) per 100,000 population in 2004. **Conclusions**: The NHI claim database can be used as a cost-effective method to monitor change in incidence of acute myocardial infarction, because the NHI covers all Korean residents. However insurance claim data should not be used without careful adjustment based-on the validity of diagnosis.

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Surveillance, Identification, and Notification of Teenagers at Risk of Cardiovascular Disease

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Background The epidemic of obesity, diabetes, and cardiovascular disease is a national concern. While obesity is often an early self assessment, the diagnosis of diabetes and cardiovascular disease is frequently delayed until adulthood, with the onset of symptoms. Since the management and prevention of both diseases would benefit from early diagnosis, we looked for opportunities to screen young adults. This group of individuals are the least likely to have been screened before and would benefit most from early awareness and intervention. Teenage volunteer blood donors are routinely tested for serological markers of transfusion transmitted infectious disease. We decided that supplementation of this testing with non-fasting total cholesterol could give insight into the prevalence of the potential risk for cardiovascular disease in teenagers. **Methods** All volunteer donors at a large community blood program, drawing about 300,000 volunteers a year, were routinely screened for total non-fasting cholesterol (Abbott Aeroset C800). Donors were invited to retrieve their results from the blood program's web site by a process which ensured that the donor could retrieve only his or her results. Data were analyzed by age group, gender, and whether individuals retrieved their test results. **Results** Total non-fasting serum cholesterol values for 23,718 donors in the 17 to 19 year old age range are shown in the table. Neither male nor female teenagers were diligent in retrieving results. Most retrievals were made by the 17 year olds, for both females (19%, i.e., 1,160 of 6,101) and males (14%, i.e., 812 of 5,904). **Conclusions** The blood donor setting can also provide community health screening for evidence of cardiovascular risk. Although teenagers will be identified who deserve counseling about their elevated total non-fasting cholesterol levels, most will ignore the opportunity to retrieve their results. More effective notification is important if health benefit is to be realized.

	11,765 Females		11,953 Males	
Cholesterol (mg/dL)	n	%	n	%
<170	7,363	62.6	8,500	71.1
170 - 200	3,033	25.8	2,463	20.6
>200	1,369	11.6	990	8.3

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Increased Hospitalizations for Any-Listed Cardiomyopathy in 2003–2004 vs 1989–1990 Despite Decline in First-Listed Rates

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Background: Cardiomyopathy, a heterogeneous disease affecting heart muscle through multiple mechanisms, is a major cause of heart failure and an underlying or contributing cause of 54,700 annual deaths. **Methods**: We compared hospitalization rates (per 100,000, year 2000 US standard population), in-hospital death, and subtypes in 1989–90 and 2003–04 for both first-listed and any-listed (1^{st}-7^{th}) diagnoses of cardiomyopathy (ICD9-CM codes 425.0–425.9) using the National Hospital Discharge Survey. **Results**: There were an estimated 630,000 hospitalizations with cardiomyopathy as any-listed diagnosis in 1989–90 and 1,200,000 in 2003–04. The age-standardized rate of hospitalization for any-listed diagnosis increased 1.6 fold, from 136.3 in 1989–90 to 215.3 in 2003–04; however, rates for a first-listed diagnosis declined from 21.7 in 1989–90 to 12.2 in 2003–04. Age-specific rates of any-listed increased between the two time periods among all age groups with the largest change in those aged 18–44 (5.3 to 9.2, 2.2 fold) and ≥75 (691.7 to 1346.7, 1.9 fold) while there was a modest increase in rates of first-listed cardiomyopathy at ages <45, there was a decline for ages 45–64 (37.9 to 16.9), 65–74 (86.2 to 29.0), and ≥75 years (78.1 to 51.5) for 1989–90 and 2003–04, respectively. In-hospital death declined from 10.1% to 1.9% (first-listed) and from 8.7% to 4.7% (any-listed) between time periods. Among any-listed diagnoses, the major subtype was "other primary cardiomyopathy" (ICD9-CM 425.4), occurring in 89.5% in 1989–90 and 89.8% in 2003–04. Among any-listed cardiomyopathy hospitalizations in 1989–90 and 2003–04, respectively, a first-listed diagnosis of cardiomyopathy occurred in 22.3% and 9.4%; Heart failure (ICD9-CM 428) was the first-listed diagnosis in 39.4% and 44.5%; and cardiac dysrhythmias (ICD9-CM 427) was the first-listed diagnosis in 10.5% and 10.9%. **Conclusions**: Although first-listed diagnoses of cardiomyopathy are now relatively infrequent among any-listed diagnoses, hospitalizations for cardiomyopathy have nearly doubled and have implications for health care expenditures. Further study is needed to examine the influence of evaluation and detection, disease severity, co-morbidities, and multiple readmissions on these changes.

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The Difficult Transition from Epidemiology Research to Clinical Practice: The CUORE Project Experience

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Introduction and Objectives. The project CUORE was launched in 1998, supported by the Ministry of Health and coordinated by the National Institute of Health with the following aims: implementing a national population-based register; describing risk factors distribution through a health examination survey; estimating cardiovascular risk function of the Italian population; implementing risk score in clinical practice for the evaluation of cardiovascular risk in men and women ages 35–64 years. **Methods**. The first and the second objectives were achieved through the National Register of Coronary and Cerebrovascular Events and the Osservatorio Epidemiologico Cardiovascolare. Methods and results are already published and available on the Progetto CUORE website (www.cuore.iss.it). The third objective was reached through the identification of the risk function and the construction of the risk score in 10 years. A free downloadable software (cuore.exe) that allows to calculate individual risk score is available on the CUORE project website. In connection with the CUORE Project, the RIACE Project was launched by the National Drug Government Agency, with the following aims: disseminate the risk score, train general practitioners (GPs) to use global absolute risk, promote rational and continuous prescription of drugs, train GPs to recommend patients to adopt a healthy lifestyle. Cardiovascular prevention has been included among the main objectives of the National Prevention Plan for 2005–2007 as agreement of Ministry of Health and regions, which are designed to implement risk assessment through a national training programme for GPs. **Results**. Presently, about 4.000 professionals (GPs, cardiologists, centres for blood transfusion and for preventive medicine) from all over Italy have downloaded the software cuore.exe, about 300 participated to the training programme. **Conclusions**. This close cooperation among the Ministry of Health, the National Drug Governance Agency, the National Institute of Health, the Federation of Cardiologists and College of General Practitioners is the greatest step forward a sustainable disease prevention strategy.

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Evidence for Association Between CHEK2 Variants and Type 2 Diabetes: The HyperGEN Study

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Type 2 diabetes' increasing prevalence is a major public health burden. Improved characterization of the genetic variants underlying type 2 diabetes susceptibility can provide important insight on disease etiology. We previously identified strong evidence of linkage for type 2 diabetes on chromosome 22 among 3383 Hypertension Genetic Epidemiology Network (HyperGEN) participants from 1124 families. The Checkpoint 2 (CHEK2) gene, an important mediator of diverse cellular responses to DNA damage, is located 0.22 Mb from this peak linkage. In this study, we tested the hypothesis that the CHEK2 gene contains one or more polymorphic variants that are associated with type 2 diabetes. Hypertensive siblings and their offspring and/or parents were recruited from five field centers. Individuals who received insulin treatment, an oral hypoglycemic agent, or had a fasting plasma glucose ≥126 mg/dl were classified as diabetics. We genotyped 1584 African American and 1531 Caucasian HyperGEN participants for five SNPs in the CHEK2 gene. Using a cross-sectional design, we evaluated the additive effect of CHEK2 SNPs on prevalent type 2 diabetes using mixed effects logistic

regression models (PROC GLIMMIX procedure in SAS 9.1), that allow for random effects of families and fixed effects of age, age2, sex, sex-by-age interaction and study center. Haplotype analyses stratified by race were performed using FBAT. Four of the five CHEK2 variants were associated with type 2 diabetes in Caucasian participants ($P < 0.05$), with the variant rs2078555 associated with 42% and 97% higher prevalence in individuals heterozygous and homozygous for the risk allele, respectively. Although SNP variants were not associated with diabetes risk among African American participants, we identified two haplotypes associated with type 2 diabetes in this population. One haplotype was tagged by the risk allele for rs2078555 and rs9608698 and the protective allele for rs2346397 ($P=0.02$) and another haplotype tagged by the risk alleles for rs4035540 and rs9608698 ($P=0.01$). All single SNP results were replicated using FBAT and a measured genotype approach in SOLAR. These results suggest a new pathway in the pathogenesis of type 2 diabetes that involves pancreatic beta cell damage and apoptosis.

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Common Variation in Fibrinogen Genes Is Associated with Plasma Fibrinogen Levels but Not Future Cardiovascular Events: The Cardiovascular Health Study

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Background: While elevated plasma fibrinogen is an independent risk factor for cardiovascular disease (CVD), associations between fibrinogen single nucleotide polymorphisms (SNPs) and disease risk have been less consistent. We investigated whether common variation in the three fibrinogen genes (*FGA, FGB, FGG*) is associated with fibrinogen concentration, carotid intima-medial thickness (IMT) and risk of incident MI and ischemic stroke in older (65+ years at baseline) Caucasian- (CA) and African-descent (AA) adults from the Cardiovascular Health Study. **Methods**: Baseline fibrinogen was measured using a functional assay. Common (frequency ≥5%) tagSNPs (n=16) in *FGA, FGB* and *FGG* were genotyped in CA (n=3969) and AA (n=719) free of MI or stroke at baseline. Haplotypes were estimated across the entire 3-gene locus using *Phase* 2.0. Race-specific linear regression and Cox proportional hazards models included haplotype probability-weighting, adjustment for sex, age and clinic and correction for multiple testing of SNPs. **Results**: Fibrinogen tagSNPs and haplotypes were significantly associated with levels in CA. *FGA*3807, *FGB*1437 and *FGG*902 were associated with higher levels; *FGA*251, *FGA*2224, *FGA*6534 and *FGG*10034 were associated with lower levels, $p<0.004$ for each. Results for AA followed similar trends (not significant). Haplotypes were not associated with CVD events in CA (Table). Adjusted for traditional risk factors, fibrinogen level (upper vs. lower tertiles) was significantly associated with carotid IMT and risk of MI (HR=1.3, 95%CI: 1.1–1.6), but not ischemic stroke (HR=1.2, 95%CI: 1.0–1.4) in CA. **Conclusion**: Although associated with fibrinogen level, variation in fibrinogen genes was not associated with carotid IMT or risk of CVD events in older adults. If fibrinogen is in the CVD causal pathway, it is possible that the modest differences in fibrinogen level associated with haplotypes were not large enough to influence risk of CVD in our study population.

Table: Associations between Fibrinogen Haplotype and Level and Risk* of CVD Events

		% Frequency		Fibrinogen in mg/dL beta (95% CI)		MI HR (95% CI)	Ischemic Stroke HR (95% CI)
Haplotype	tagSNPs	CA	AA	CA	AA	CA	CA
A	*FGB*9952 *FGG*902	20.6	5.9	7.5 (3.0,12.0)	4.5 (-11.7, 20.7)	0.9 (0.8,1.2)	0.9 (0.7,1.2)
B	*FGA*6534 *FGA*2224 *FGA*251 *FGG*10034	15.5	6.4	referent	referent	referent	referent
C	*FGB*1038 *FGA*9205 *FGG*9340	13.5	8.5	8.4 (3.4,13.4)	12.0 (-4.1, 28.4)	1.1 (0.9,1.4)	1.1(0.9,1.5)
D	*FGB*1437 *FGA*3807 *FGG*902	12.4	<5	20.3 (15.2,25.4)	not tested	1.1 (0.9,1.4)	1.0(0.8,1.3)
E	*FGA*5498 *FGA*2224 *FGA*251 *FGG*9340	9.4	<5	10.0 (4.6,15.5)	not tested	1.0 (0.7,1.2)	1.0(0.8.1.3)
global test p-value				<0.0001	0.5574	0.6378	0.5925

Association between haplotypes and incident events tested only in CA

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Association of SNPs in Adiponectin Receptor 2 (ADIPOR2) with Cardiovascular Risk Factors in Mexican-Americans from the San Antonio Family Heart Study

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Adiponectin mediates its effects through its receptors ADIPOR1 and ADIPOR2, both of which are abundantly expressed in human liver and skeletal muscle. The purpose of the study was to explore the association between genetic variants in ADIPOR2 and changes in cardiovascular disease (CVD) risk factors across three visits spanning a period of 15 years (1991–2006) in Mexican Americans from the San Antonio Family Heart Study (SAFHS). We genotyped 1280 individuals (females 59.5%) for single nucleotide polymorphisms (SNPs) in ADIPOR2 and performed association analyses for changes in CVD risk factors (MANOVA for repeated measurements). All variables were normalized by Z transformation to maintain equivalences in measured units. Mean age, BMI, waist circumference and % body fat were 39.1 ±17 years, 29.2±6.4 kg/m2, 89±9 cm and 29.9±11.9 %, respectively. Of the 19 SNPs examined, we found two SNPs rs2286382 and rs767870, to be consistently associated with systolic blood pressure, fasting glucose, waist-hip ratio, and percent body fat across the visits. According to Hardy-Weinberg Equilibrium (HWE) test the two SNPs did not show population stratification. Of these SNPs rs2286382 was associated with lowered systolic blood pressure ($p = 9.6x10-6$; $p = 0.00003$; $p = 0.006$), fasting glucose ($p = 0.001$; $p = 0.04$; $p = 0.007$), waist hip ratio ($p = 0.0004$; $p = 0.002$; $p = 0.05$), and waist circumference ($p = 0.0007$; $p = 0.01$, $p = 0.05$) across visits 1, 2 and 3. Percent body fat ($p = 0.02$; $p = 0.007$) was associated with rs2286382 in visits 1 and 2. SNP rs767870 was significantly associated with an increase in systolic blood pressure ($p = 0.00006$; $p = 0.002$) and waist-hip ratio ($p = 0.007$; $p = 0.0001$) in visits 1 and 2 only. In addition, SNP rs2286382 was associated with lowered triglyceride ($p = 0.0009$), diastolic blood pressure ($p = 0.03$), BMI ($p = 0.03$), and 2 hour glucose ($p = 0.0008$) in visit 1 but not in subsequent visits. These results provide strong evidence of association between genetic variants in ADIPOR2 and CVD risk factors in Mexican Americans.

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Deciphering Genetic Determinants for Subclinical Atherosclerosis in Multiple Arterial Beds: Genome-Wide Association Study in the NHLBI Framingham Heart Study

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Introduction: Heritable subclinical atherosclerosis indices in multiple arterial beds are associated with increased incidence of cardiovascular disease. We conducted a genome-wide association study (GWAS) for subclinical atherosclerosis measurements in the community-based Framingham Heart Study. **Methods and Results**: Over 100,000 single nucleotide polymorphisms (SNPs) were genotyped (Human 100K GeneChip, Affymetrix) in 1345 subjects from 330 families. We calculated age- and sex-adjusted and multivariable-adjusted residuals for quantitative atherosclerosis phenotypes, after transformation for skewness, using measures of peripheral arterial disease from ankle-brachial blood pressure, coronary artery and abdominal aortic calcification using multi-detector computed tomography (MDCT), and carotid intimal medial thickness using carotid ultrasonography. Generalized estimating equations (GEE) and family-based association testing (FBAT) were used to examine associations between SNPs and phenotypes. We focused on autosomal SNPs in or near known protein-encoding genes or conserved non-coding regions, after excluding SNPs with minor allele frequency≤0.10, genotype call rate≤0.9, or a Hardy-Weinberg equilibrium p≤0.001. GEE results were rank-ordered for each imaging modality to identify SNPs most strongly associated with each subclinical disease modality. We then further ranked by presence of significant ($p<0.01$) associations using FBAT. The strongest associated SNP residing in or near a gene was noted for the following genes: for ankle-brachial index, *ATP8A2* (chromosome 13, GEE p=0.00003); for MDCT, *CSMD3* (chromosome 8, p=0.0004); and for carotid ultrasonography, *TBC1D1* (chromosome 4, p=0.005). These results do not survive bonferroni correction, an adjustment that may be overly conservative. Complete genotype-phenotype associations will be posted on the internet. **Conclusions**: We provide genotype-phenotype hypotheses from this GWAS for SNPs associated with subclinical atherosclerosis traits in multiple arterial beds. Subsequent replication will be essential in independent subjects. A dense GWAS that will be a resource for the scientific community is now underway in ~10,000 Framingham Heart Study subjects.

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UGT2B15 Variants, Tobacco Exposure, and CHD: The Atherosclerosis Risk in Communities (ARIC) Study

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Cigarette smoking is a well established risk factor for coronary heart disease (CHD) but the mechanisms by which smoking causes CHD are not well understood. The UDP-glucuronosyltransferases (UGTs) are important in the glucuronidation and detoxification of tobacco smoke constituents, and therefore may contribute to atherosclerosis. Here we address how genetic variation in *UGT2B15* interacts with smoking exposure to influence CHD in the ARIC cohort. We conducted a case-cohort study including genotyped data from all incident CHD cases 1987–1998 (n=1086) and a stratified random sample (n=1065) for three *UGT2B15* single nucleotide polymorphisms (SNP). Haplotypes were reconstructed using PHASE. Logistic regression stratified by race and adjusted for sampling strategy and center, with controls weighted proportional to person-time at risk, was employed to estimate incidence rate ratios (IRR). SNPs and haplotypes were measured with a general model and a dominant model, respectively. Additivity departures measured by interaction contrast ratios (ICR) evaluated the influence of smoking history (ever/never smoker) on associations between genotype/haplotype and CHD. In Caucasians, the CC genotype in rs1902023 synergistically [ICR: 0.44(-0.32, 1.20)] increased the causative effect of smoking exposure on the rate of CHD with IRR estimates for both exposures, smoking alone, and the SNP alone of 1.86(1.17, 2.94), 1.49(0.95, 2.34) and 0.93(0.55, 1.56), respectively. Similarly the TT genotype in rs2331424 synergistically [ICR: 0.74(-1.05, 2.53)] increased the causative effect of smoking exposure on the rate of CHD with IRR estimates for both exposures, smoking alone, and the SNP alone of 2.64(1.39, 5.02), 1.66(1.21, 2.27) and 1.24(0.60, 2.55), respectively. In Caucasians, the halpotype **CCC** (tagged by the rs1902023 and rs7661667 variants alleles) synergistically [ICR: 0.58(-0.22, 1.38)] increased the causative effect of ever-smoking exposure on the rate of CHD [IRR: 1.90(1.27, 2.84)], which supports the SNP analysis. No association between CHD and *UGT2B15* variants

was noted in African-Americans. Our results suggest that the *UGT2B15* gene is of interest to further study susceptibility to tobacco products.

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Single Nucleotide Polymorphisms in the Kallikrein Genes Are Associated with Intracranial Aneurysms in the Finns

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Background: The kallikrein (KLK) gene family includes at least 15 genes and is a promising candidate gene cluster for association analysis with intracranial aneurysms (IAs). KLK genes function in the regulation of vascular tone, are expressed in the central nervous system, and are proximal to a previously implicated linkage region for IAs on chromosome 19q13. **Methods**: We analyzed common sequence variations using 19 single nucleotide polymorphisms (SNPs) from 13 of the 15 KLK genes, including 11 intronic, 6 intergenic and 2 mis-sense SNPs. The 19 SNPs span a 244 kb region with an average distance of 14 kb between SNPs. The available sample of 944 individuals included 760 individuals from a case/control study, and 184 relatives of cases. The case/control study included 266 Finnish IA cases and 290 Finnish controls, and in a second stage we genotyped 2 SNPs (rs1722561 and rs1701946) in an additional set of 102 Finnish IA cases and 102 Finnish controls. The chi-square test of association was used to evaluate single locus association, and the distribution of haplotypes in cases versus controls was compared using the EM algorithm. Finally, we evaluated evidence of linkage with two model-free linkage tests, the means test and the proportions test. **Results**: Single locus tests of association identified three SNPs with nominally significant p-values (*rs1722561, rs1701946* and rs2659096, p-value=0.0395, 0.0253 and 0.0437, respectively), none of which are statistically significant after correcting for multiple testing. Haplotype analysis revealed nominally significant association for the C-C haplotype of SNPs rs1722561 and rs1701946 (empirical p-value=0.0195). In addition, we observed excess sharing among affected sib-pairs (p-value=0.0008). **Conclusion**: Our results provide modest evidence of linkage and association between genetic variants (rs1722561 and rs1701946) in the KLK8 gene and IAs. Further work is needed to determine whether variants in the KLK gene family account for the linkage signal for IA on chromosome 19.

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Genetic Influences on Inflammatory Responses to a Single High-Fat Meal in Old-Order Amish Population

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Inflammation has been recognized to play a role in atherosclerosis. Although dietary fat may influence circulating levels of cytokines, little is known about the role of genetic factors in determining an individual's inflammatory response to dietary fat intake. The aim of the study is to quantify the change in inflammatory markers in response to a single high-fat meal and evaluate the genetic influence on both the baseline and post-consumption change in inflammatory markers. The present study included up to 732 Amish individuals (singletons and relatives from multi-generation families) enrolled in the Amish Heredity And Phenotype Intervention (HAPI) Heart study. Inflammatory markers [C-reactive protein (CRP), interleukin 1B (IL1B), matrix metalloproteinase 1 and 9 (MMP1 and MMP9), and white blood cell (WBC) count] were measured at 0 and 4 hours (T_0 and T_4) after a high-fat meal (700 calories per m^2 of body surface area). Heritability (h^2) was estimated using variance components (Table). H^2 of baseline levels ranged from negligible (0.03±0.13 for MMP9) to high and significant (0.89±0.14; $p < 0.001$ for MMP1). After consumption of a single high-fat meal, MMP1, MMP9, and WBC levels increased significantly; however, h^2 estimates of the post-consumption changes were lower than those for baseline and not significant. These results indicate that levels of at least some circulating inflammatory markers rise in response to a short-term dietary intake of fat. Our data further support a genetic contribution to baseline levels of some circulating inflammatory markers, although evidence for a genetic contribution to inflammatory response to fat intake is less clear and will require additional data to fully evaluate.

	Baseline			Post-consumption			
Marker	n	Median of T_0 (Inter-quartile range)	h^2 of $\log_e$ (T_0) (S.E.) £	n	Median of T_4 (Inter-quartile range)	Mean of (T_4-T_0) (S.E.)	h^2 of (T_4-T_0) (S.E.) §
CRP (mg/l)	695	0.9 (0.4–2.1)	0.30 (0.10)*	127	0.8 (0.4–2.1)	-0.13 (0.10)	—
IL1B (pg/ml)	292	0.78 (0.78–1.08)	0.20 (0.19)	195	0.78 (0.78–1.53)	0.14 (0.08)	—
MMP1 (ng/ml)	293	2.83 (1.72–4.61)	0.89 (0.14)*	196	3.43 (2.36- 5.31)	0.66 (0.06)†	0.40 (0.39)
MMP9 (ng/ml)	293	396.84 (286.86- 598.24)	0.03 (0.13)	196	507.96 (355.96- 735.98)	76.19 (18.53)†	0 (—)
WBC (thous/mcl)	732	5.1 (4.5–5.85)	0.34 (0.12)*	698	6.0 (5.2–6.9)	0.82 (0.03)†	0.16 (0.10)

£: Heritability estimated using log transformed data; results adjusted for age, age^2 and sex. §: Results adjusted for age, age^2, sex and T_0 level. * $p<0.01$ † Significant ($p<0.001$) change from baseline

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Association of Apolipoprotein E e4 Polymorphism with Age: The Third National Health and Nutrition Examination Survey Genetic Study

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The e4 allele of *Apolipoprotein E (APOE)* is associated with markedly increased risk of Alzheimer's disease and weakly increased risk of cardiovascular disease. Previous studies have shown lower e4 frequency in the elderly but none have examined this across a wide age range in a nationally representative sample. The objective of this study is to investigate *APOE* allele frequency by age groups (20–39, 40–59, 60–69, and >70 years) in a subset of 5,583 participants of the Third National Health and Nutrition Examination Survey (NHANES III) who were included in the genetic study. Allele frequencies were estimated with NHANES III sampling weights and stratified by race/ethnicity [non-Hispanic whites (NHW), non-Hispanic blacks (NHB), and Mexican Americans (MA)]. Weighted linear regression was used to determine the association between *APOE* e4 and age. The overall frequency of the e4 allele in NHW, NHB, and MA was 15.2%, 22.0% and 10.7%, respectively, consistent with previous reports. In NHW, the frequency of e4 decreased with increasing age ($p = 0.001$). Similarly, frequency of the e4 allele was the lowest in the >70 group in both NHB and MA, but neither association was statistically significant (Table). There was no significant association of the *APOE* e4 allele with prevalent CVD, diabetes, hypertension or dyslipidemia. A significantly lower *APOE* e4 allele frequency in older age was found in this nationally representative sample of non-Hispanic whites. This suggests differential selection for mortality or non-participation of *APOE* e4 carriers at older age which can bias cross-sectional studies of *APOE* variation.

APOE allele frequency by race-ethnicity and age

	Non-Hispanic White N=2,328		Non-Hispanic Black N=1,599		Mexican American N=1,656	
	e4	e2	e4	e2	e4	e2
Overall	15.2	8.2	22.0	10.2	10.7	3.4
Age category						
20–39	16.4*	7.7	22.0	9.3	10.5	3.5
40–59	15.8*	7.8	21.6	11.7	11.4	3.2
60–69	13.3*	8.6	25.2	9.1	10.4	3.7
70+	11.9*	10.9	19.2	9.3	10.1	2.6

* p=0.001 for trend from linear regression

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CETP, IL8, PPARα, and *TLR4* Genetic Variations and Risk of Incident Myocardial Infarction and Ischemic Stroke

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Background: Studies of associations of genetic variation in candidate genes involved in oxidative stress and inflammation with cardiovascular diseases (CVD) have reported inconsistent findings, often for a limited number of genotypes. We investigated associations of gene-wide variation in the cholesterol ester transfer protein (*CETP*), interleukin 8 (*IL8*), peroxisome proliferator activator receptor, alpha (*PPARA*) and toll-like receptor 4 (*TLR4*) genes with incident non-fatal MI and ischemic stroke. **Methods**: A population-based case-control study was conducted among 1228 cases (850 MI and 370 stroke) and 2683 controls. Participants, aged 30–79, were selected from hypertensive men/women and nonhypertensive women enrolled in Group Health Cooperative in Washington state. Gene-specific sets of tag single nucleotide polymorphisms (SNPs) were selected based on pairwise linkage disequilibrium. Haplotypes were inferred using *Phase (v2.0).* Multivariate logistic regression evaluated individual haplotype and SNP-disease associations in log-additive models. Global haplotype tests assessed overall gene-level associations, with either MI or stroke. **Results**: A total of 34 tag SNPs (13 *CETP*, 3 *IL8*, 6 *PPARA* and 12 *TLR4*) and 19 haplotypes (5 *CETP*, 3 *IL8*, 5 *PPARA* and 6 *TLR4*) were evaluated. In whole-gene analysis, variation in *PPARA* and *TLR4* genes was associated with MI. $CETP_{8914}$ and $CETP_{8764}$ SNPs were associated with increased risk of stroke, although overall, the global test of *CETP* gene haplotype and stroke association was not significant. Variation in the *IL8* gene was not associated with MI or stroke. **Conclusion**: Modest associations of *PPARA* and *TLR4* genetic variation with MI were demonstrated, in agreement with some previous reports. However, all specific SNP-disease associations identified in the current study are novel and further studies are needed to confirm these findings.

	Myocardial Infarction		Ischemic Stroke	
	Global test (p-value)*	OR **(95%CI)****	Global test **(p-value)***	OR **(95%CI)****
CETP	0.068		0.641	
***CETP* 6914**		1.10 (0.96–1.27)		**1.24 (1.02–1.50)**
***CETP* 8764**		1.07 (0.94–1.23)		**1.25 (1.04–1.50)**
IL8	0.718		0.889	
PPARA	0.035		0.450	
***PPARA* 3343**		**1.24 (1.06–1.44)**		1.13 (0.91–1.41)
TLR4	0.015		0.804	
***TLR4* 7764**		**0.87 (0.77–0.99)**		1.05 (0.89–1.25)

* Global association test p-value. **Odds ratios (95%CI) per copy of minor allele for SNPs with significant associations (p-values <0.05) with MI or ischemic stroke.

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Association of Alox15 Gene Polymorphisms with Prevalence and Progression of Coronary Artery Calcification: The CARDIA Study

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Reticulocyte-type 15-lipoxygenase (ALOX15), a lipid-peroxidizing enzyme, has been implicated in atherogenesis in animal models. Functional inactivation of ALOX15 in murine atherosclerosis models consistently reduced atherosclerotic lesion formation. We investigated the association of 11 polymorphisms of the ALOX15 gene with prevalence and progression of coronary artery calcification (CAC) in 3,443 self-identified blacks and whites CARDIA participants. Polymorphisms were selected from the SeattleSNPs database based on linkage disequilibrium

relationships and/or functionality. Presence of coronary calcification was determined at the year 15 and year 20 examinations by computed tomography. CAC progression was defined as a >0 (vs. 0) difference in CAC scores between year 20 and year 15 (N=2,920). Logistic regression models adjusting for age, sex, field center, and established cardiovascular risk factors were constructed to investigate the association of ALOX15 polymorphisms with CAC prevalence and progression. Single-SNP and haplotype-based analyses were performed. Correction for multiple testing was carried out using the direct simulation approach, a fast approximation to permutation. In whites, there was no statistically significant association of ALOX15 genotypes and haplotypes with prevalence or progression of subclinical atherosclerosis. However, a rare variant, D90H, (freq 1%) showed a trend toward an association with year 20 CAC prevalence and progression (P=0.05 and 0.06, respectively). This variant was not observed in blacks. In blacks, there was a significant association between a common haplotype (freq 8%) with higher CAC prevalence at both examinations (P=0.002 and 0.003, respectively), but association of this haplotype with CAC progression was not significant (P=0.08). This haplotype was uniquely tagged by a promoter SNP, which itself was significantly associated with greater Y15 and Y20 CAC prevalence and progression (P=0.04, 0.001, and 0.002, respectively). This is the first study to implicate sequence variation in the ALOX15 gene in the development and progression of subclinical atherosclerosis. Promoter assays are being developed to investigate the functional relevance of the identified polymorphism.

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Association of C-Reactive Protein Haplotypes with 20-Year Incidence of Hypertension: The CARDIA Study

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Plasma CRP levels have been associated with development of hypertension. We investigated the association of common haplotypes of the CRP gene with 20-years incidence of hypertension in self-identified Black and White CARDIA participants. Seven CRP polymorphisms, selected based on linkage disequilibrium relationships, were genotyped in 3,874 individuals. Incident hypertension was defined as a blood pressure (BP)>=140/90 mm Hg or use of BP medication in any examination among individuals without hypertension at baseline. Association of common CRP haplotypes (freq >= 3%) with incident hypertension was investigated using a regression method for unphased haplotypes based on score statistics, adjusting for center, age, sex, and BMI at baseline (Model 1), and further for logCRP levels at year 7 (Model 2). In Whites, there was a significant association of CRP haplotypes with incident hypertension and this association was not modified by further adjustment for CRP levels (Table). In particular, haplotype AAAGCGA was independently associated with a significantly lower risk of developing hypertension (RR=0.49; P=0.009). This haplotype was uniquely tagged by the A allele of SNP1440, which itself was associated with a 50% lower risk of incident hypertension per copy (P=0.01). In Blacks, there was no association of CRP haplotypes with incident hypertension. Racial differences in effects of haplotype AAAGCGA may be explained by differences in frequency (freq 0.06 (W); 0.03 (B)). Haplotype AAAGCGA and A1440 have been previously associated with greater CRP levels. Thus, their independent association with lower risk of hypertension is surprising. These data do not support evidence that sequence variation in the CRP gene underlies the association between higher incidence of hypertension and greater CRP levels observed in this and other studies. However, we cannot exclude that CRP gene polymorphisms influence development of hypertension through other mechanisms.

Haplotypes are designated by alleles at pos. 790, 1440, 1919, 2667, 3006, 3872, and 5237

		Model 1		Model 2	
Global P (permutation)		0.011			0.017
Haplotype	Frequency	Relative Risk (95% CI)per haplotype copy	P (Permutation)	Relative Risk (95% CI)per haplotype copy	P (Permutation)
AAAGCGA	0.06	0.52 (0.30; 0.88)	0.01	0.49 (0.28; 0.85)	0.009
ACACCAA	0.05	0.60 (0.35; 1.01)	0.05	0.65 (0.37; 1.12)	0.10
ACAGCAA	0.28	1.19 (0.95; 1.51)	0.70	1.27 (0.99; 1.62)	0.64
ATTGCGA	0.29	1.08 (0.86; 1.37)	0.61	1.03 (0.81; 1.31)	0.92
ACAGCGG	0.28	0.95 (0.75; 1.22)	0.11	0.95 (0.73;1.12)	0.05

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Effect of Endothelin 1 Genotype on Blood Pressure Is Dependent on Physical Activity or Fitness Level

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The contributions of the DNA sequence variation at the endothelin 1 (EDN1) locus to the risk of hypertension and on endurance training-induced changes in blood pressure were investigated in the Aerobics Center Longitudinal Study (ACLS) and the HERITAGE Family Study cohorts. We prospectively identified 586 normotensive controls and 615 incident hypertensive cases from the ACLS cohort (all Caucasians). Both cases and controls were normotensive at their first clinic visit. The cases were diagnosed with hypertension during a follow-up 9.5 years later (on average), whereas the controls remained normotensive during the same time period. The allele and genotype frequencies of five EDN1 tagSNPs did not differ significantly between the cases and controls. However, we observed a significant (p=0.003) interaction between the EDN1 Lys198Asn genotype and cardiorespiratory fitness level on the risk of hypertension: among low-fit subjects (362 cases, 229 controls), the 198Asn allele was associated with increased risk of hypertension (odds ratio 1.95 [95% CI 1.36 to 2.81]; p=0.0003), whereas the risk did not differ among genotypes in high-fit subjects (253 cases, 357 controls). In the Caucasian HERITAGE Family Study subjects (N=480; all sedentary at baseline), the EDN1 198Asn allele was associated with a blunted systolic blood pressure (SBP) response to a 20-week endurance training program (100% compliance): Lys198 homozygotes showed a 2-fold greater reduction in SBP (adjusted for age, sex and BMI) during submaximal exercise than 198Asn homozygotes with heterozygotes exhibiting an intermediate response (p=0.0016). In conclusion, the EDN1 198Asn allele is associated with adverse blood pressure phenotypes in Caucasians. However, the expression of the genotype effect seems to depend on physical activity or cardiorespiratory fitness level.

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Common Genes Contribute to the Correlation Between Heart Rate Variability and Inflammation: The Twins Heart Study

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Introduction: Heart rate variability (HRV), a measure of autonomic dysfunction, is associated with inflammation markers, both of which are strong predictors of coronary heart disease (CHD). However, little is known to what extend the association between these two factors can be explained by common genes and/or common environments. **Methods**: We assessed HRV on 24-hour electrocardiographic Holter recordings, and measured interleukin-6 (IL-6) plasma levels, in 95 (58 monozygotic and 37 dizygotic) middle-age male twin pairs and 34 singletons free of symptomatic CHD. Five frequency domain variables were used, including ultra low frequency (ULF), very low frequency (VLF), low frequency (LF), high frequency (HF) and total power (TPow). Traditional CHD risk factors were also measured. Structural equation modeling was used to construct the genetic models. **Results**: The mean age of the twins was 54 years (age range: 47–59 years). Univariate analyses indicated that all measurements of HRV were highly heritable (heritability estimation ranging from 0.48 to 0.67), as well as IL-6 (0.46). A significant inverse correlation was found between IL-6 and all HRV parameters except HF, with the highest coefficient shown with VLF (r=-0.35; p<0.001). After adjusting for covariates, including age, BMI, diastolic blood pressure, physical activity, smoking status, history of major depression and HDL-cholesterol, the associations remained significant ($P<0.02$). Bivariate genetic modeling revealed significant genetic correlations ($P=0.0001-0.02$) between IL-6 and ULF, VLF, LF and TPow ($r_g=0.54$, 0.48, 0.42, and 0.37, respectively). Corresponding unique environmental correlations were $r_e=0.16$ ($P=0.21$), 0.25 ($P=0.04$), 0.14 ($P=0.26$) and 0.21 ($P=0.13$). Genetic contributions explained 70–76% of the correlation between IL-6 and HRV parameters. After adjustment for covariates, the heritability estimates were slightly decreased but the overall results remained similar. **Conclusion**: All HRV parameters and inflammatory markers are highly heritable and their covariation is due, in large part, to common genes. Identification of these genetic variations should may provide important clues on the genetic basis of CHD.

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C-Reactive Protein and Interleukin-6 Polymorphisms in Relation to Subclinical Atherosclerotic Disease

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Background: Plasma levels of C-reactive protein (CRP) and interleukin-6 (IL-6) have been associated with the development and progression of atherosclerotic disease. However, the reported associations may be due to cause, coincidence or consequence. **Methods**: In the Edinburgh Artery Study (1,592 men and women, 55–74 years old) we used Mendelian randomization to test whether the associations between CRP and IL-6 levels and the extent of atherosclerotic disease are likely to be causal. Subjects were genotyped for 3 CRP single nucleotide polymorphisms (SNPs) (C1444T, G2302A, T4899G) and for one IL-6 promoter polymorphism (174G/C). The ankle brachial index (ABI) was used as a measure of asymptomatic atherosclerotic disease. **Results**: All three CRP genotypes (p=0.001, 0.001 and 0.02, respectively) and the haplotypes (p=0.002) derived from them were significantly associated with CRP plasma levels. However, none showed association with peripheral atherosclerosis measured by the ABI. On the other hand, the C allele of the 174G/C IL-6 polymorphism was significantly associated with lower ABI values and thus increased peripheral atheroma (mean ABI: 1.03, 1.05, 1.06 in subjects CC, CG and GG genotype, respectively, p for trend 0.007) without showing any relationship to IL-6 or CRP plasma levels. **Conclusions**: In agreement with previous studies on coronary atherosclerosis, several CRP gene polymorphisms which influenced CRP plasma levels showed no associations with asymptomatic atherosclerosis. Therefore, the associations between CRP plasma levels and atherosclerotic disease are more likely to be due to their mutual associations with cardiovascular risk factors or due to pre-existing arterial disease which may further induce their production. On the other hand, the association between the C allele of the 174G/C IL-6 genotype with lower ABI levels supports a causal link between IL-6 and atherosclerosis which merits further investigation in larger studies.

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DNA Base Excision Repair Gene Variants, Tobacco Exposure, and Incident CHD: The Atherosclerosis Risk in Communities (ARIC) Study

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Cigarette smoke contains over 4,800 compounds, 69 of which have been identified as carcinogenic. Variation in the multi-step metabolic response to cigarette smoke constituents can be informative in the study of heritable differences in DNA repair capacity, including base excision repair (BER). As *XRCC1* is an integral BER gene, we conducted a series of case-cohort analyses to examine how *XRCC1* variants modify the relationship between smoking and CHD in the ARIC cohort. All CHD cases 1987–98 (n=1086) and a random sample (n=1065) were selected from the entire cohort of 15,792 participants. Analyses were stratified by race and adjusted for sampling strategy and study center. Incidence rate ratios (IRR) were estimated with controls weighted proportionally to person-time at risk. Departures from additivity for the interaction between *XRCC1* tagSNPs and smoking (ever/never) were measured with interaction contrast ratios (ICR). Hierarchical modeling was used to improve estimation by incorporating second stages (priors) into models including all tagSNPs and models extended to examine modification by ever-smoking. *XRCC1* variation in Caucasians and African Americans was captured by five and seven tagSNPs respectively. Addition of a prior implying dependence between tagSNPs markedly increased the precision of the first stage model. Among Caucasians, IRR estimates for rs1475933, rs3213245 and rs1799782 were 1.6(0.9, 2.6), 0.6(0.4, 1.0) and 0.7(0.5, 1.0). When ever-smoking and two priors for genetic and environmental effects were added to the first stage model, rs3213245 was associated with a reduction in the estimated effect of ever-smoking [ICR = -0.7(-1.5, 0.1)], with IRR estimates for joint exposure, ever-smoking alone and SNP alone of 1.1(0.7, 2.0), 2.1(1.3, 3.2) and 0.8(0.4, 1.4). A similar relationship was seen for rs1799782 [ICR = -0.5(-1.2, 0.2)], although negligible departure from additivity was observed for rs1475933 [ICR = 0.1(-0.7, 1.0)]. Comparable but less precise results were seen for African Americans. While the estimates are imprecise, ours is the first study to examine the relationship of *XRCC1* variants to CHD and explore whether it is modified by cigarette smoking, a potent mutagenic agent.

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Variation in Inflammation-Related Genes and Risk of Incident Nonfatal Myocardial Infarction or Ischemic Stroke

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Background: From initiation to plaque rupture, immune system components contribute to the atherosclerotic process. We investigated variation in inflammation-related genes - Interleukin(IL)-1β, IL-6, C-reactive protein (CRP), IL-10, IL-18, and the Tumor Necrosis Factor (TNF) superfamily [Lymphotoxin(LT)-α, TNF-α, LT-β] - with respect to nonfatal incident myocardial infarction (MI) or ischemic stroke risk. **Methods**: We conducted a population-based case-control study among postmenopausal and/or hypertensive Group Health Cooperative members aged 30 to 79 years. We chose a subset of single nucleotide polymorphisms (SNPs) identified by genomic resequencing to describe common gene-wide variation on the basis of linkage disequilibrium. 38 SNPs, describing 41 common (>2.5%) haplotypes for 5 genes and a 3-gene cluster, were genotyped among 856 MI cases, 368 stroke cases, and 2688 controls. Associations of SNPs or PHASE-inferred haplotypes and risk were estimated using logistic regression; significance was assessed with global tests of gene-level associations. **Results**: In global association tests, only IL-18 variation was associated with MI risk; no genes were associated with stroke risk. In individual SNP analyses, we observed associations of several IL-1β polymorphisms with risk of MI or stroke. IL-6, CRP, IL-10, and TNF superfamily gene variation was not associated with MI or stroke risk. **Discussion**: Results from our study of inflammation gene variation and incident MI and stroke risk support prior reports associating an IL-18 variant and MI risk, contribute additional evidence to conflicting reports of IL-1β and cardiovascular risk, and fail to confirm risk differences previously observed for CRP, IL-6, and TNF-α promoter variants. Because our findings of modest risk associations are limited to survivors of incident events and were not significant after multiple comparison correction, it will be important to confirm these results in other settings.

Table: Association of inflammation-related genes with MI or stroke risk

	global tests (p-value)		Ref. Sequence #	Odds Ratios (95% CI) [per copy of minor allele]	
gene	MI	Stroke		**MI**	Stroke
IL-18	0.009	0.308	rs2043055	**0.81 (0.72 to 0.91)**	1.03 (0.88 to 1.21)
IL-1β	0.334	0.071	rs1143629	**1.13 (1.01 to 1.27)**	1.13 (0.96 to 1.33)
			rs3917356	0.93 (0.83 to 1.04)	**0.84 (0.72 to 0.98)**
			rs3136558	**0.86 (0.75 to 0.98)**	1.03 (0.86 to 1.24)
			rs1143633	0.98 (0.88 to 1.10)	**0.83 (0.70 to 0.99)**

SNPs with significant associations with either outcome are shown above; IL-10, IL-6, CRP, TNF superfamily omitted (p-values all >0.05)

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Interleukin Genes, Tag-SNP Haplotypes, and Risk of Myocardial Infarction: A Population-Based Case–Control Study

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Introduction. Inflammation and the genes regulating this complex process have been hypothesized to play an important role in the aetiology of cardiovascular disease. **Methods**. We investigated whether IL-1β and IL6 genetic variations (using a Tag-SNP approach) were associated with MI risk using a population based case-control study. MI cases and healthy controls (without cardiovascular disease or cancer) were all residents of the Erie and Niagara counties in NY. State 637 white MI male patients (35–69 yr) were individually matched with 637 controls and 225 white MI females with 450 controls by age (+/-5 years), smoking habits, menopausal status and years since menopause (+/- 2 years). Diabetic cases and controls were excluded. SNPs were identified at http://pga.mbt.washington.edu/. Linkage disequilibrium was used to select SNPs that tagged common genetic variation. SNPs within a BIN were selected on the basis of allele frequency (<=10%), position in the gene, type of sequence and already known associations with quantitative or disease phenotypes. The following SNPs were finally selected: rs1143634, rs16944, rs3917354, rs3917356 for IL 1-beta and rs1818879, rs1548216, rs1800795, rs2069825 for IL 6. Conditional logistic regression analysis was performed. Haplotype based association analyses were also conducted. For haplotype construction, SNPHAP by D. Clayton was used. **Results**. In males, SNP rs3917356 of IL 1β gene was significantly associated with a reduction in MI risk, in and additive inheritance model (OR:0.82; 95%CI: 0.69−0.98, p<0.03), while SNP rs1800795 and rs2069825 of IL 6 gene were associated with an increased MI risk in dominant inheritance models (OR:1.30; 95%CI: 1.02–1.66, p<0.03 and OR: 1.30; 95%CI: 1.01–1.6, p<0.04, respectively). No significant associations were found in females for these selected SNPs. Haplotypes analysis was consistent with SNP results for IL1b gene (OR: 0.82; 95% CI: 0.69−0.97, p<0.02 for the common haplotype), but did not showed significant associations for IL-6 gene. **Conclusions**. Inflammatory genes are associated with the risk of MI. Tag-haplotyping adds new insight into the association between inflammatory genes and cardiovascular disease

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Interleukin-18 Gene Polymorphisms, Interleukin-18 Serum Concentrations, and Risk for Type 2 Diabetes: Results from the MONICA/KORA Augsburg Case-cohort Study, 1984–2002

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Interleukin-18 (IL-18), an important mediator of innate immunity, has recently been shown to be associated with risk of type 2 diabetes. Therefore, it was the aim of the present study to examine whether DNA variants in the corresponding gene modulate the IL-18 serum concentration and whether these polymorphisms are associated with the risk to develop type 2 diabetes. A case-cohort study was conducted in initially healthy, middle-aged men and women based on data from the MONICA/KORA Augsburg studies collected between 1984 and 2002 (mean follow-up time 10.1 years). The case-cohort study comprised 498 cases with type 2 diabetes and 1,569 non-cases. All cross-sectional analyses were performed in the subcohort which was drawn as part of the case-cohort study and comprised 1,687 subjects which were representative for the whole study sample. We genotyped the following five single nucleotide polymorphisms (SNPs) in the IL-18 gene with the Sequenom MALDI-TOF MS System: a) rs5744222, -2163 C/A, promoter region; b) rs1946518 -607 C/A, promoter region; c) rs2043055 3228 T/C, 3'UTR, intron-1; d) rs5744263 15311 C/T, intron-3; e) rs3882891 20091 A/C, intron-4. Two of the five examined SNPs were significantly associated with IL-18 serum concentrations. For the rs2043055 SNP (3'UTR, Intron-1), carriers of the T/T genotype had geometric mean IL-18 serum concentrations of 153 pg/ml, whereas the corresponding values were 156 pg/ml and 188 pg/ml in T/C and C/C carriers, respectively (p-value for trend: <0.001). For the rs5744222 SNP (promoter region) mean IL-18 serum concentrations were 166 pg/ml for the common C/C genotype, 149 pg/ml for the C/A genotype, and 136 pg/ml for the relatively rare A/A genotype (p-value for trend: <0,001). We found no significant association between any of the genotypes and the risk to develop type 2 diabetes. These data support the hypothesis that SNPs within the IL-18 gene modulate IL-18 serum concentrations but they do not support the hypothesis that these SNPs play a causal role in the aetiology of type 2 diabetes.

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Adiponectin Receptor 1 Gene, Plasma Adiponectin, and Coronary Heart Disease in Women with Type 2 Diabetes

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Objective: Adiponectin is an antiatherogenic hormonal cytokine. The protective effects of adiponectin are mediated by its receptors. We assessed the associations of variants in adiponectin receptor 1 gene (*ADIPOR1*) with circulating adiponectin levels and the risk of coronary heart disease among women with type 2 diabetes. **Research Design and Methods**: We genotyped seven LD-tagging SNPs in 989 women with and without coronary heart disease (CHD). **Results**: Two polymorphisms rs12733285 (intron 1) and rs1342387 (intron 6) was significantly associated with higher plasma adiponectin levels (adjusted P=0.005 and 0.003). Haplotypes possessing these two polymorphisms were also associated with plasma adiponectin levels (P=0.01). There were not main associations between *ADIPOR1* variations, individually or in haplotypes, and the risk of CHD. We found significant interactions between variations in *ADIPOR1* gene and adiponectin gene (*ADIPOQ*) using the Multifactor dimensionality reduction (MDR) method. The best interaction model included the combination of *ADIPOR1* rs1342387, *ADIPOQ* -4034A>C and +276G>T, and plasma levels of tumor necrosis factor-alpha receptor 2 (TNF-R2), with the maximum cross-validation consistency of 10 out of 10 and a prediction accuracy of 67% (P<0.001 on the basis of 1000-fold permutation testing). **Conclusions**: Variations in *ADIPOR1* gene were associated with circulating adiponectin levels and might interact with *ADIPOQ* variations and TNF-R2 in relation to CHD risk in diabetic women.

Table. Interactions in relation to the risk of coronary heart disease using the MDR method

Interaction factors	CV Consistency	Prediction accuracy	Significance test, P*
ADIPOR1 rs1342387, *ADIPOQ* -4034A>C, +276G>T, TNF-R2	10	0.67	<0.001
ADIPOR1 rs12733285, rs4950894, TNF-R2	7	0.63	0.002
ADIPOR1 rs4950894, TNF-R2	3	0.61	0.01

CV: cross-validation
*: on the basis of 1000 permutation.

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Variation in 24 Clotting Genes and Risk of Incident Nonfatal Myocardial Infarction or Ischemic Stroke

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Background: Arterial thrombosis involves platelet aggregation and clot formation, yet little is known about the contribution of genetic variation in hemostatic factors to arterial clotting risk. We hypothesized that common variation in 24 clotting genes would contribute to risk of incident MI or IS. **Methods**: Data were from a population-based case-control study of hypertensive adults and post-menopausal women 30–79 years of age who were members of a large health maintenance organization in Washington State. Subjects included 856 cases with non-fatal incident MI and 368 cases with non-fatal incident IS events that occurred between 1995 and 2002, and 2689 controls matched to cases on age, sex, hypertension status, and year of identification. A blood sample was obtained from all subjects and DNA was extracted. A set of tagging single nucleotide polymorphisms (SNPs) was used to describe variation across the 24 candidate genes: factors II, III, V, VII, VIII, IX, X, XI, XII XIIIa1 and b; fibrinogen α, β, and γ; antithrombin; proteins C and S; endothelial protein C receptor; thrombomodulin; tissue-factor pathway inhibitor; plasminogen; tPA; PAI-1; and thrombin-activatable fibrinolysis inhibitor. Logistic regression was used to test the association of global gene-level variation, individual haplotypes, and SNPs with the risk of MI and IS separately. **Results**: In global analyses, only gene-level variation in FVIII was associated with IS risk ($p=0.008$). No genes were globally associated with MI risk. For MI analyses, 8 (4.3%) of the 185 haplotypes and 8 (4.4%) of the 181 SNPs were significantly associated with risk. For IS analyses, 9 (4.9%) of the 184 haplotypes and 10 (5.6%) of the 180 SNPs were significantly associated with risk. Few associations were associated with more than a doubling or halving of MI or IS risk. None of the significant associations was found for both arterial thrombotic outcomes. Discussion: The number of associations did not exceed what would have been expected by chance alone. Replication of null and significant findings in other populations is necessary but our data suggest that common variation in these 24 clotting genes has little impact on risk of arterial thrombosis.

P360

The Effect of LDL Receptor Diplotypes and Their Interaction with Apolipoprotein E Polymorphisms on Carotid Artery Wall Thickness: The Atherosclerosis Risk in Communities Study

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Carotid artery intima media thickness (IMT) is a measure of subclinical atherosclerosis and a predictor of cardiovascular events. In previous work among African American and Caucasian participants of the Atherosclerosis Risk in Communities (ARIC) Study, associations between apolipoprotein E (APOE) E2 and E4 genotypes with LDL cholesterol and IMT measures were observed. In addition, our previous work has shown that LDL receptor (LDLR) variants also affect circulating lipid values in Caucasians. In the present study, we evaluated the association of 3' UTR LDLR genetic variants with prevalent IMT and potential interactions among the LDLR and APOE variants on IMT measures. Two single nucleotide polymorphisms (SNPs) in exon 3 of APOE and two SNPs in the 3' regulatory region of LDLR (rs1433099 and rs2738466) were genotyped in 10,602 Caucasian and 3,497 African American ARIC participants. LDLR diplotypes were estimated using the phase reconstruction method (PHASE 2.1). In each race strata, the association between LDLR haplotypes and IMT was estimated using multivariable linear regression models adjusting for age and sex using SAS 9.1. Interactions between APOE genotypes E2 (E2/E2, E2/E3, E2/E4) and E4 (E4/E3, E4/E4) and the four inferred LDLR diplotypes on IMT were assessed using interaction terms and an alpha of 0.05. LDLR diplotypes frequencies were 22% for h1 (CA/CA), 25% h2 (CA/TA), 8% h3 (TA/TA) and 25% h4 (CA/CG) in Caucasians, and 9% h1, 31% h2, 28% h3 and 10% h4 in African Americans. LDLR h1 was associated with significantly lower IMT (mean 0.719 mm [standard deviation 0.184] versus 0.733 mm [0.191] for others, $P=0.005$) while LDLR h2 was associated with significantly higher IMT (0.724 mm [0.186] versus 0.716 [0.187], $P=0.02$) among Caucasian but not African American subjects. A significant interaction was observed among 2 LDLR diplotypes and APOE genotypes ($P=0.01$) in Caucasians only. APOE E4 was associated with higher IMT measures among individuals with the LDLR h3, and E2 was associated with higher IMT among individuals with LDLR h4. These findings suggest that genetic variants of the LDLR and APOE interact to influence subclinical atherosclerosis among Caucasians.

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Monocyte Chemoattractant Protein-1 (MCP-1) Gene Polymorphisms, MCP-1 Plasma Levels, and Incident Coronary Heart Disease in Middle-Aged Men and Women: Results from the MONICA/KORA Augsburg Case–Cohort Study, 1984–2002

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Background: MCP-1, a novel chemokine plays a pivotal role in the recruitment of monocytes into atherosclerotic plaque. It has been suggested that genetic variations within the MCP-1 gene (CCL2) might modify circulating MCP-1 levels. We prospectively investigated whether various SNPs, covering the whole region of the CCL2 gene, affect MCP-1 concentrations and whether these genetic variants account for an increased risk of future CHD events. **Methods**: A case-cohort study was conducted in initially healthy, middle-aged men and women based on data from the MONICA/KORA Augsburg studies collected between 1984 and 2002 (mean follow-up 10.9 yrs). Concentrations of MCP-1 were measured in 324 case subjects (252 men, 72 women) with incident CHD (fatal/non-fatal MI and coronary death) and 1736 non-case subjects (903 men, 833 women). Taking into account possible gender differences, all analyses were carried out for men and women separately. Genotyping of 6 SNPs (rs1024610 (-2136A/T) and rs2857656 (-362C/G) in the promoter region; rs2857657 (+763C/G) in intron 1; rs4586 (+900C/T) in exon 2; rs13900 (+1542C/T) in exon 3, and one SNP in 3' flanking region (+3726T/C, rs2530797)) was performed on the Sequenom MALDI-TOF MS system. **Results**: No consistent association was found between various SNPs within the CCL2 gene and incident CHD neither in men, nor in women in crude and in multivariate adjusted analyses. However, MCP-1 baseline concentrations in female participants from the randomly drawn subcohort (n=1,834, 983 men, 851 women) were significantly modulated by two of the 6 analysed DNA variants (rs1024610 and rs2857657). In particular, for rs1024610, age- and survey adjusted MCP-1 plasma levels were 160.3 vs 187.5 vs 199.4 pg/mL for TT (n=549) vs TA (n=269) vs AA (n=33) genotype carriers, respectively (p for trend=0.003); whereas no accociations between these 6 SNPs and MCP-1 baseline concentrations were found in male participants. **Conclusions**: Despite the fact that polymorphic alleles of rs1024610 and rs2857657 strongly contributed to increased MCP-1 concentrations in women, no association was found between these 6 SNPs within the CCL2 gene and incident CHD, thereby questioning a causal role of systemic MCP-1 levels in the pathophysiology of CHD.

P362

Weighted-Logistic Method for Correcting Confounding Effect of Population Stratification and Testing Ancestral Population Specific Effect Sizes in Genetic Association Studies in Admixed Populations

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Analytical methods have been proposed for detecting the presence of population stratification and also for addressing the confounding effects that this often causes in genetic association studies of complex human diseases. However, not much attention has been given to estimating the ancestral population specific effect sizes in association studies in admixed populations. Using admixture probabilities, we describe a weighted-logistic method that both corrects for the confounding effect of population structure and also enables estimation of ancestral population specific effects in both genome-wide and candidate gene association studies in admixed populations. Our method uses estimates of individual admixture proportions both to correct for population stratification or admixture, and also to estimate and test the ancestral population specific effect sizes. We present results from the application of this method to simulated data on candidate gene association study in admixed population, and also on population based genetic association study on hypertension in African American population as an example of real admixed population.

P363

Ala379Val Variant of the Lipoprotein Associated Phospholipase A_2 Gene and Acute Myocardial Infarction in a Multiethnic Case–Control Study

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Lipoprotein associated phospholipase A_2 (Lp-PLA_2) exerts pro-inflammatory effects through generation of lyso-phosphatydilcholine (lyso-PC) and has been associated with increased cardiovascular disease (CVD) risk. A prior large European case-control study among men (HIFMECH study) with 527 post-MI cases and 566 age-matched controls showed that rare homozygotes for Ala379Val (i.e., VV genotype) had significant lower odds of myocardial infarction (MI) independent of known risk factors. This genotype has been shown to result in impaired Lp-PLA_2 catalytic activity. We sought to replicate (among whites) and extend (to other race/ethnic groups) this finding in a multiethnic case-control study including 1,046 MI cases and 1,593 healthy controls. MI cases and the controls were recruited from a large healthcare system; a subset of white and African-American controls were recruited from the CARDIA study. Mean age±SD was 58±11 years for MI cases and 56±12 years for controls. Analysis by logistic regression was stratified by race and adjusted for age, sex, body mass index, waist circumference, smoking, alcohol intake, diabetes mellitus and hypertension. We did not control

for hypercholesterolemia because 86% of MI cases (vs. 17% of controls) were on lipid-lowering medication. VV homozygosity varied from 0% in east Asian cases to 7% in African-American controls. As shown in the Table below, our data failed to replicate the inverse association between the rare homozygote of the Ala379Val variant and MI among whites. Non-significant trends toward an inverse association were observed in African-Americans and Hispanics, but (given the low frequency of the VV genotype), even larger studies are needed to clarify its potential clinical utility for improving risk stratification for MI.

Association between Ala379Val Genotypes and MI

(No cases, No controls)	AA (Cases, Controls)	AV (Cases, Controls)	VV (Cases, Controls)
Whites (776,1031)	66%, 63%	30%, 33%	4%, 4%
AV vs. AA		0.89 (0.71–1.11)	.28
VV vs. AA		0.92 (0.55–1.54)	.75
Afr-Am (74,324)	66%, 52%	31%, 41%	3%, 7%
AV vs. AA		0.62 (0.32–1.22)	.17
VV vs. AA		0.33 (0.06–1.79)	.20
Hispanics (121,136)	63%, 61%	35%, 33%	2%, 6%
AV vs. AA		1.23 (0.69, 2.19)	.48
VV vs. AA		0.44 (0.10–1.96)	.28
East Asians (75,102)	81%, 76%	19%, 23%	0%, 1%
Av vs. AA		0.65 (0.28–1.51)	.32

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The R229Q Polymorphism in the NPHS2 Gene Is Associated with Reduced Estimated Glomerular Filtration Rate (eGFR) in the Atherosclerosis Risk in Communities (ARIC) Study

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Background: NPHS2 encodes podocin, a critical component of the renal filtration barrier. Mutations in NPHS2 can cause severe autosomal-recessive kidney disease; the R229Q variant alters functional properties of podocin in vitro. Although previous studies inconsistently implicated an association between R229Q and microalbuminuria in the general population, association with reduced eGFR, another marker of kidney dysfunction, has not been described to date. **Methods**: The present analysis is a random subset of a previous diabetes case-control study in ARIC. It includes 2,690 Caucasian ARIC participants with both genotype and phenotype data at visit 4. The abbreviated MDRD Study equation was used to calculate eGFR (ml/min/1.73m2). Reduced kidney function was defined as eGFR <60 (n = 242). Multiple logistic and linear regression models were used to control for demographic and cardiovascular risk factors. **Results**: The frequency of the Q allele in this Caucasian population was 0.04, similar to previous estimates (n=251 R/Q and n=2 Q/Q). R229Q was not associated with either continuous albuminuria or macroalbuminuria; however, it was associated with eGFR. Assuming a dominant mode of inheritance, individuals with at least one copy of the Q allele had significantly lower eGFR compared to those with R/R genotype (fully adjusted mean eGFR 80.9 (SE 0.34) for R/R vs. 78.3 (SE 1.24) for all others; p 0.037). Similarly, these individuals were more likely to have reduced kidney function compared to those with R/R (OR 1.83, 95% CI 1.13 - 2.96; table 1) after adjustment for other covariates. OR estimates were similar stratified by hypertension and diabetes mellitus status. **Conclusions**: Carriers of the Q allele of NPHS2 R229Q have significantly reduced kidney function as measured by eGFR in a group of Caucasian community-based adults. These results indicate that further investigation of the effect of R229Q of NPHS2 on traits related to kidney function and in other populations is warranted.

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Heritability, Linkage, and Genetic Associations of Exercise Treadmill Test Performance Measures

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Background The blood pressure (BP) and heart rate responses to exercise treadmill testing (ETT) predict incidence of cardiovascular disease; however, the contributions of genetic factors to inter-individual variation in the hemodynamic and chronotropic responses to ETT have not been investigated comprehensively. **Methods** We assessed systolic blood pressure (BP), diastolic BP, and heart rate during the second stage of the Bruce protocol and at the third minute of recovery in 2982 Framingham Offspring participants (mean age, 43 years; 53 % women). Using residuals from multivariable models adjusting for the clinical determinants of ETT responses, we estimated the heritability (variance-components methods), genetic linkage (multipoint quantitative trait analyses), and association with 334 single nucleotide polymorphisms in 18 candidate genes selected *a priori* from neurohormonal, inflammatory and hemostatic pathways. **Results** Heritability estimates for heart rate at exercise and during recovery were 0.32 and 0.34, respectively. Heritability estimates for BP variables at exercise were 0.25 and 0.26 (systolic and diastolic BP) and during recovery, 0.16 and 0.13 (systolic and diastolic BP). Suggestive linkage was found for systolic BP during recovery from exercise (locus 1q43–44, log-of-the-odds [LOD] score 2.59) and diastolic BP during recovery from exercise (locus 4p15.3, LOD score 2.37). Among 334 SNPs tested for association with ETT responses, the minimum nominal P value was 0.0031; after accounting for multiple testing, none of the associations remained significant. **Conclusion** Hemodynamic and chronotropic responses to exercise are heritable, and demonstrate suggestive linkage to select loci. Genetic mapping using newer approaches such as genome-wide association may yield novel insights into the physiological response to exercise.

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Suggestive Linkage for QTL Influencing Visceral Adiposity on Chromosomes 13 and 17: The Southwest Ohio Family Study

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Introduction: High visceral adiposity poses increased risk for cardiovascular disease, independent of and in addition to the risks associated with generalized obesity. Although many studies examine the genetic determinants of visceral adipose tissue (VAT) deposition using a variety of imaging techniques, few studies use multiple-slice magnetic resonance imaging to adequately capture individual variation in the spatial distribution of both VAT and subcutaneous adipose tissue (SAT) throughout the abdomen. **Objective**: The purpose of this study is to conduct a preliminary whole genome scan to search for quantitative trait loci influencing VAT and SAT. **Methods**: Abdominal magnetic resonance imaging was performed on subset of 359 individuals (166 males and 193 females from the Southwest Ohio Family Study. Participants ranged in age from 8 and 85 years and were distributed across 5 large extended families. Contiguous 1 cm thick axial images were acquired across the abdominal region to measure total SAT and VAT volumes. Using SOLAR, a variance components based linkage analysis program, an initial 10 cM whole-genome scan was performed to identify quantitative trait loci (QTL) influencing VAT and SAT volumes. Age and sex effects were simultaneously estimated in the models. **Results**: Significant ($p < 0.05$) heritabilities were found for VAT ($h^2 = 0.352 \pm 0.094$) and SAT ($h^2 = 0.640 \pm 0.093$). Covariate effects explained 57.5% and 31.3% of the variance in VAT and SAT, respectively. Suggestive linkages were found for VAT on chromosome 13q at 105 cM (LOD=2.41) and on chromosome 17q at 65 cM (LOD=2.27). The highest LOD score for SAT was on chromosome 17q at 67 cM (LOD=1.75). These regions on chromosomes 13 and 17 have been linked to other adiposity measures such as body mass index and SAT, but only one group to date has reported a QTL specifically for abdominal VAT on 17q. To our knowledge, the QTL on chromosome 13q has not previously been reported specifically for VAT. **Conclusions**: Our preliminary linkage analysis identified two QTL, one on chromosome 13q and one on chromosome 17q, that influence measured visceral adipose tissue volume. Further analysis will include fine mapping to identify functional polymorphisms underlying this important cardiovascular disease risk factor.

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No Association Between C-Reactive Protein Gene Polymorphisms, CRP Haplotypes, and Incident Type 2 Diabetes Mellitus (T2DM) in Middle-Aged Men and Women: Results from the MONICA/KORA Augsburg Case-cohort Study, 1984–2002

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Background: It has been suggested that circulating levels of CRP could be modulated by genetic variations within the gene coding for this protein, thereby accounting for the independent association between CRP concentration and risk of incident coronary heart disease (CHD) as well as incident T2DM. We have previously shown that various single nucleotide polymorphisms (SNPs) contributed to CRP levels in the general population. However, no consistent association was found between these SNPs and incident CHD. Here we prospectively investigate whether various SNPs within the CRP gene might be associated with incident T2DM. **Methods**: A case-cohort study was conducted in initially healthy, middle-aged men and women based on data from the MONICA/KORA Augsburg studies collected between 1984 and 2002 (mean follow-up 11.0 yrs). Concentrations of CRP were measured in 435 case subjects with incident T2DM and 1,408 non-case subjects. Genotyping was performed on the Sequenom MALDI-TOF MS system. **Results**: We analysed four SNPs: two in the CRP promoter region (-390C/T/A rs3091244; -717C/T rs2794521), one intronic (T/A rs1417938) and one exonic (+1059G/C rs1800947). Haplotype estimation yielded 5 haplotypes with frequencies $>=5\%$ (GATT 30.5%, GTCC 28.0%, GTCT 27.3%, CTCT 7.3%, GTAT 6.5%). All other haplotypes were pooled in a group of rare haplotypes. Neither the 4 different SNPs, nor the 5 more common haplotypes were found to be consistently associated with incident T2DM in crude and in multivariable adjusted analyses in all study participants. In particular, with respect to the intronic SNP rs1417938, subjects, bearing the TA genotype (n=805) or subjects homozygous for the A allele (n=163) compared to TT genotype carriers (n=875) showed no significant increase in the risk for incident T2DM (HR 0.91, 95% 0.70–1.18; and HR 1.24, 95% CI 0.80–1.91, respectively). **Conclusions**: These data therefore suggest that these SNPs within the CRP gene do not play a major role in the susceptibility to T2DM in initially healthy subjects, despite the fact that individuals, carrying several of these polymorphic alleles (e.g. A allele of rs1417938) were exposed to moderately elevated CRP concentrations long-term.

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A Genome-Wide Linkage Scan for Aortic Root Diameter: The Southwest Ohio Family Study

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Introduction: Aortic root dilatation is pathogenically related to aortic regurgitation, and further linked to various cardiovascular diseases including aortic dissection and aneurysm. However,

little is known about specific sources of variation in aortic root diameter. Recently, some studies have suggested that there are genetic influences on aortic root diameter. Study aim: The goal of this study was to conduct an initial genome-wide linkage scan to identify quantitative trait loci influencing inter-individual variation in aortic root diameter. **Methods**: Data were collected from 450 individuals (202 males, 248 females) aged 8 to 85 years from 5 kindreds participating in the Southwest Ohio Family Study. These individuals have been genotyped for ~400 autosomal markers spaced approximately every 10 cM. Aortic root diameter was assessed using M-Mode echocardiography. A variance components-based linkage analysis method, implemented in SOLAR, was used to analyze the data and obtain multipoint LOD scores across the genome. Covariates included age, age^2, sex, age-by-sex interaction, and age^2-by-sex interaction. **Results**: The heritability estimate ($h^2 \pm$SE, 0.42$\pm$0.11) for aortic root diameter was highly significant (p-value $<$ 0.00001). The preliminary genome-wide linkage analysis showed suggestive evidence for linkage to markers on chromosome 3q22–23 with a LOD score of 2.05. LOD scores greater than 1 were found linked to markers on chromosome 1q, 2p, 9q, 16p, and 20p. **Conclusions**: This preliminary whole-genome scan identified one chromosomal location (3q22–23) that may harbor a gene(s) influencing the aortic root diameter. This finding represents a possible novel region linked to inter-individual variation in aortic root diameter that has not been identified previously.

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Heritability of Flow-Mediated Dilation: A Twin Study

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Introduction: Atherosclerotic vascular disease is the leading cause of death and disability worldwide. Impaired endothelial function plays an important role in atherosclerotic vascular disorders. Flow-mediated vasodilation (FMD) is a reliable tool for assessing endothelial function. The contribution of genetics to the variation in FMD is poorly understood. **Methods**: We estimated the heritability of FMD using 98 middle-aged male twin pairs (55 monozygotic [MZ] twin pairs and 43 dizygotic [DZ] twin pairs) from the Vietnam Era Twin Registry. All twins were free of an overt cardiovascular disease. FMD for each twin was measured by ultrasound. Regression analyses were used to determine the clinical correlates for FMD. The intraclass correlations of FMD were compared between MZ and DZ twin pairs. Structural equation modeling was used to determine the relative contributions of genetic and environmental factors to the variation in FMD. **Results**: The intraclass correlation for FMD was significantly larger in MZ twins (0.36, 95% CI, 0.30–0.42) than in DZ twins (0.20, 95% CI, 0.12- 0.27), suggesting genetic additive influences in FMD variation. Structural equation modeling showed that both genetic and unique environmental factors contributed to the variation in FMD. After adjusting for traditional CHD risk factors, the heritability of FMD was 0.35 (95% CI 0.12–0.54). **Conclusion**: This is the first study using twins to estimate the relative contributions of genetics and the environment to the variation in FMD in a U.S. population. Our results demonstrate that both genetic and environmental factors contribute to the variation of brachial arterial FMD.

P370

β1-Adrenergic Receptor Gene Modulates the Effect of Heart Rate on Arterial Stiffness in Young Adults: The Bogalusa Heart Study

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Introduction: Heart rate and sympathetic nervous activity are important determinants of arterial stiffness. However, whether the relationship between heart rate and arterial stiffness is modulated by β_1-adrenergic receptor (β_1-AR) gene variation is not known. This study examines the genetic modulation by β_1-AR gene polymorphism (Arg389Gly) on the effect of heart rate on arterial stiffness in young adults. **Methods**: The study cohort included 183 blacks and 502 whites aged 19–44 years enrolled in the Bogalusa Heart Study. Aorta-femoral pulse wave velocity (af-PWV) was measured by echo-Doppler. **Results**: Heart rate was significantly associated with af-PWV in blacks, whites and the total sample. However, there was no difference in heart rate between carriers and noncarriers of Gly389 allele in both blacks and whites. Carriers vs noncarriers of the Gly389 allele showed higher values of af-PWV (5.29 m/sec vs 5.19 m/sec, p$<$0.01) in whites, but not in blacks (5.40 m/sec vs 5.37 m/sec, p$=$0.524). In multivariate regression analysis for the total sample, both heart rate and Gly389 allele were significantly and positively associated with af-PWV, adjusting for race, sex, age, body mass index and pulse pressure. Furthermore, the adverse positive relationship between heart rate and af-PWV was noted only among carriers of Gly389 allele (comparison of slopes p$=$0.018). **Conclusions**: These results indicate that the allelic variation (Arg389Gly) of the β_1-AR gene modulates arterial stiffness and its association with heart rate in young adults.

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Effect of Variants in the APM1 Gene on Risk for Coronary Heart Disease, Type 2 Diabetes, and Parameters of the Metabolic Syndrome: MONICA/KORA Augsburg Cohort Study, 1984–2002

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Adiponectin is an adipocyte-secreted hormone encoded by the APM1 gene. Decreased levels of adiponectin are reported in obesity, coronary heart disease (CHD) and type 2 diabetes and variants in the APM1 gene have been shown to be associated with type 2 diabetes and parameters of the metabolic syndrome even though results are not consistent. Type 2 diabetes and CHD share several established causal risk factors and have been postulated to arise from common genetic and environmental roots (common soil hypothesis). A case-cohort study was conducted in initially healthy, middle-aged men and women based on data from the MONICA/KORA Augsburg studies collected between 1984 and 2002 (mean follow-up time 11.0 years) to investigate the influence of the APM1 gene on 339 individuals with incident CHD (vs 1816 non-cases) and 498 individuals with incident type 2 diabetes (vs 1569 non-cases). We systematically genotyped 14 common polymorphisms in the APM1 gene, most of them have been previously shown to influence adiponectin plasma levels. We found the minor allele of a polymorphism in the 5 ′region of the APM1 gene (rs860291) associated with incident CHD (HR [95% CI] 0.63 [0.44–0.90]; p-value$=$0.011). A polymorphism in exon 2 of the gene (rs22241766) was associated with type 2 diabetes in univariate but not in multivariate analysis. Additionally, several variants in the APM1 gene were associated with parameters of the metabolic syndrome or inflammatory markers. However, after correction for multiple testing, most of the associations disappeared.

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Heritability of Lipid Phenotypes Among African Americans: Jackson Heart Study

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Background: Determinants of serum lipid levels include both genetic and non-genetic components. More research is needed to determine the role each plays in serum lipid levels of African-Americans. The Jackson Heart Study Family Sub-Study (JHS, FSS) represents a cohort of African-American adults for which both plasma lipid and lifestyle data are available. We tested the hypothesis that a significant genetic component to serum lipid levels in the Jackson Heart Study does exist when adjusting for non-genetic covariates. **Methods and Results**: Using Solar 2.1.4 genetics software heritability estimates were calculated for adjusted and non-adjusted lipid phenotypes in 1546 African-American adults participating in the JHS,FSS (310 pedigrees), age 21–95 years. Phenotypes included high density lipoprotein-C (HDL), low density lipoprotein-C (LDL), triglycerides (TG), total cholesterol (TC) and TC:HDL C ratio. Adjustments were made for age, sex, body mass index (BMI) and waist circumference (WC), as well as dietary cholesterol, saturated fatty-acids, poly-unsaturated fatty-acids, total calories and dietary fiber. BMI, WC, age and sex were found to be significant covariates however effects of these were altered by inclusion of dietary factors. Differences among models using BMI and those with WC were minimal. Estimates of heritability for HDL, LDL, TG, TC and TC:HDL C ranged between .4 and .5 when adjusted for BMI or WC, sex and age. Some Heritability estimates were affected by inclusion of dietary covariates. Heritability estimates for TG were lower with inclusion of diet variables. All estimates were statistically significant. **Conclusions**: There is a significant genetic component in serum lipid levels for this JHS cohort after adjustment for BMI or WC, sex and age. The heritability estimates observed are comparable to those previously reported for other cohorts. In particular, we found that inclusion of dietary factors affects some of these estimates, as well as the significance of non-diet covariates.

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Apolipoprotein E Polymorphism Modulates the Associations of Obesity and Insulin Resistance with C-Reactive Protein in Young Adults: The Bogalusa Heart Study

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Background: Apolipoprotein (apo E) polymorphism in known to exert pleotropic effects on several physiologic processes besides lipoprotein metabolism. Although apo E genotype is known to modulate C - reactive protein (CRP) levels, its influence on the association of obesity and insulin resistance with CRP is not known. **Methods**: This aspect was examined in a biracial (black-white) community-based sample of 929 young adults (mean age: 32.8 years, 72% whites, 44% males) who had data on apo E genotype and plasma CRP levels along with other cardiovascular risk factor variables. **Results**: The frequencies of the e2, e3, and e4 alleles differed significantly between whites and blacks (0.079, 0.770, and 0.151 for whites; 0.187, 0.656, and 0.227 for blacks). Age-, race-, and gender- adjusted mean value of CRP differed among apo E genotype groups [apo E4 (E4/4 and E4/3) $<$ apo E2 (E2/2 and E3/2) or apo E3 (E3/3), p$=$0.03–0.001]. In multivariate analysis, significant interaction effects of genotype with race, BMI, and HOMA-IR on CRP levels were noted. Significant race difference (Black$>$white, p$=$0.02–0.03) in CRP levels were observed only in apo E2 and apo E4. Further, within each genotype group, both BMI and HOMA-IR showed significant positive associations with CRP levels. However, the magnitude of these associations were least in E4 group compared to E2 or E3 groups. **Conclusion**: The associations of CRP with obesity and insulin resistance were attenuated in E4 genotype compared to E2 or E3 genotypes.

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Association of Nitric Oxide Synthase Glu298Asp Polymorphism with Serum Levels of Inflammation Biomarkers and Possible Effect Modification of Dietary Antioxidants: The Atherosclerosis Risk in Communities Study

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Background: Nitric oxide (NO) plays a major role in vascular tone by minimizing endothelial damage and scavenging free radicals. Endothelial derived NO is produced by the endothelial

nitric oxide synthase gene (eNOS). ENOS derived NO is continuously produced at low levels and maintains homeostasis within the vessel wall by vasodilatory and anti-inflammatory actions. Glu298Asp is a common eNOS polymorphism and previous research suggests that the Asp298 allele reduces vascular NO production. **Aim**: We investigated the relationship between the Glu298Asp allele and circulating levels of Factor VIII, fibrinogen, and Von Willebrand factor antigen (vWF) in the Atherosclerosis Risk in Communities Study (ARIC). We also sought to determine if dietary antioxidant consumption modifies the relationship between Glu298Asp and inflammation mediators. Antioxidant consumption decreases free radicals and may prevent increases in inflammation mediators by enhancing NO activity. **Results**: Phenotypes, genotype, and dietary intake of antioxidants, Vitamins A, C, and E, were available for 12,491 participants free of diabetes and cardiovascular disease at baseline. The Asp298 allele frequency was 12% in blacks and 32% in whites and genotype frequencies were in Hardy-Weinberg equilibrium for all race-sex groups. We found no significant associations between Glu298Asp genotype and Factor VIII, fibrinogen, or vWF after controlling for age, race, sex, and current smoking and drinking status. Dietary vitamin A consumption was significantly inversely associated with levels of Factor VIII ($p = < 0.001$) and vWF ($p = 0.003$) and dietary vitamin C consumption inversely associated with levels of vWF ($p = 0.04$). **Conclusions**: The Glu298Asp polymorphism was not associated with Factor VIII, fibrinogen, or vWF in this study sample. We observed a significant association between dietary consumption of vitamins A and C and levels of inflammation mediators.