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 NIH-sponsored multi-center longitudinal study on 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 ≥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 108 participants with MetS at baseline (2.3%), only 6.7% were not overweight (i.e., BMI <25 kg/m²). 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.

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 menopause and that increasing androgenicity accounts for this increase.

Methods: To control the epidemic of diabetes, efforts starting at a young age are needed to prevent the development of MetS.

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 >95% 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 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 Quantiles of Percent Change in Cardiorespiratory Fitness (CRF) Over 20 Years

<table>
<thead>
<tr>
<th>% Change in CRF</th>
<th>Quartile 1 (-21% to -19%)</th>
<th>Quartile 2 (-19% to -30%)</th>
<th>Quartile 3 (-30% to -41%)</th>
<th>Quartile 4 (-41% to -81%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N events (%)</td>
<td>21 (4.1%)</td>
<td>53 (10.6%)</td>
<td>36 (7.1%)</td>
<td>54 (10.6%)</td>
</tr>
<tr>
<td>Model 1</td>
<td>1 (Ref)</td>
<td>0.8 (0.4, 1.4)</td>
<td>1.33 (0.75, 2.31)</td>
<td>1.33 (0.78, 2.29)</td>
</tr>
<tr>
<td>Model 2</td>
<td>1 (Ref)</td>
<td>0.76 (0.38, 1.51)</td>
<td>1.38 (0.76, 2.51)</td>
<td>1.96 (1.13, 3.39)</td>
</tr>
<tr>
<td>Model 3</td>
<td>1 (Ref)</td>
<td>0.75 (0.35, 1.42)</td>
<td>1.20 (0.65, 2.25)</td>
<td>1.61 (0.81, 3.22)</td>
</tr>
</tbody>
</table>

At baseline, 68%, 26%, and 5% were obese (BMI ≥30), overweight (25 < BMI < 30), and moderately obese (23 < BMI < 25). While the majority of participants were normal weight at baseline, 14% were overweight and 5% were obese. Changes in CRF were associated with a lower risk of incident diabetes among normal weight participants (25 < BMI < 30), and moderately obese (23 < BMI < 25) 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/m² increase by Year 20), (2) stable/decreased (<2 kg/m² decrease by Year 20 or baseline BMI = 2 kg/m² at every exam), (3) fluctuating (<2 kg/m² increase and 2 kg/m² decrease by Year 20 or baseline BMI ≥2 kg/m² at every exam), (4) stable (≥2 kg/m² increase of baseline BMI at Year 20 but <15% intermediate BMI: 2–2 kg/m² 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 strata and groups (74%, 78%, and 100% respectively) while only 15%, 5% 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 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 ≤ BMI < 25), overweight (25 ≤ BMI < 30), and moderately obese (30 ≤ 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/m² increase by Year 20), (2) stable/decreased (<2 kg/m² decrease by Year 20 or baseline BMI ≥2 kg/m² at every exam), (3) fluctuating (<2 kg/m² increase and 2 kg/m² decrease by Year 20 or baseline BMI ≥2 kg/m² at every exam), (4) stable (≥2 kg/m² increase of baseline BMI at Year 20 but <15% intermediate BMI: 2–2 kg/m² 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 strata and groups (74%, 78%, and 100% respectively) while only 15%, 5% 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

<table>
<thead>
<tr>
<th>Baseline BMI</th>
<th>BMIC</th>
<th>( n )</th>
<th>Hazard Ratio*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Stable</td>
<td>250</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>Increased</td>
<td>1091</td>
<td>2.6</td>
<td>0.8-8.5</td>
</tr>
<tr>
<td>Normal</td>
<td>Fluctuating</td>
<td>149</td>
<td>1.5</td>
<td>0.3-7.6</td>
</tr>
<tr>
<td>Overweight</td>
<td>Stable</td>
<td>53</td>
<td>1.8</td>
<td>0.7-4.8</td>
</tr>
<tr>
<td>Overweight</td>
<td>Increased</td>
<td>448</td>
<td>7.4</td>
<td>2.3-23.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>Fluctuating</td>
<td>71</td>
<td>11.2</td>
<td>3.4-40.4</td>
</tr>
<tr>
<td>Obese</td>
<td>Stable</td>
<td>114</td>
<td>23.5</td>
<td>7.2-73.3</td>
</tr>
</tbody>
</table>

* Age, race, gender-adjusted

### 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 extent this association can be explained by common genetic factors.

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 men alive and 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 fitting 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 CRP (P = 0.84). Genetic modeling found a significant genetic correlation between IL-6 and depressive symptoms (r g = -0.49 and P = 0.56, before and after adjusting cholosteryl ester transfer protein). The relationships 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 covariance between depressive symptoms and inflammation is due, in large part, to common genes. These genetic variations may be important for CHD risk.

### Hemoglobin 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 (58.6% white, 26.8% 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, smoking, 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. After adjustment for traditional CHD risk factors (physical activity, LDL-cholesterol, smoking and marital status), HR increased independently associated with depressive symptoms (P = 0.03), but CRP (P = 0.84). Genetic modeling found a significant genetic correlation between IL-6 and depressive symptoms (r g = -0.49 and P = 0.56, before and after adjusting cholosteryl ester transfer protein). The relationships 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 covariance between depressive symptoms and inflammation is due, in large part, to common genes. These genetic variations may be important for CHD risk.

### 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 (PRIEMER). Depressive symptoms were assessed with the Patient Health Questionnaire (PHQ). Depression was defined as a PHQ score ≥10 in the 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 < 0.001). 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 in 1-year post-MI, even after adjusting for traditional measures of disease severity. Our results suggest the importance of

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**SBH**

The table above shows the hazard ratios for incident diabetes by baseline BMI and 20-year change in BMI. The data indicate that overweight and obesity are significantly associated with an increase in the risk of diabetes, with the risk being highest for those who are obese and have a 20-year increase in BMI. The hazard ratios range from 7.4 to 23.5, with the highest risk observed for those who were obese and had a significant increase in BMI. The findings highlight the importance of maintaining a healthy weight to prevent diabetes and other chronic diseases.
2007 CVD Epidemiology and Prevention—Oral Presentations e217

CVD Risk Factors and Coronary Artery Calcified Plaque in Individuals 38 to 50 Years Old and higher in S allele carriers (55.6/11005
20 exams. CAC and risk factors at the year 15 exam were dichotomized for analysis. Reporting on 2183 participants with measured risk factors and CAC from the CARDIA Year 15 and CVD risk factors predict the development of CAC plaque in individuals 38 –50 years of age. We near term CVD events independently of traditional CVD risk factors. It is unknown if established CVD 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 impact risk factor profiles, and possibly to prevent the development of subclinical atherosclerosis.

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 parental 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 committee with high CAC defined as >90th percentile cut off 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 parent 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 15% and 17% 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.

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 202 Japanese men in Hawaii. Men aged 40 to 49 years and free of cardiovascular disease. Based on electron-beam computed tomography, men with a CAC score ≥75 were defined as having CAC. Results: There was a marked excess of CAC in Hawaii (49.3% 10/10x vs. Japanese (51.2% p<0.05, 0.01)), in men in Japan were leaner (<0.001), less likely to have diabetes (p=0.003) and hypertension (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% [95% CI]: 12.6% [95% CI], 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% vs. 30.6%, respectively, p = 0.077). Gender differences for the higher smoking rates in Japan may be due to 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.

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


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 [LHV]), 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, 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 1.91, 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.

14 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 an environmental and genetic confounder. We assessed the hypothesis that shared environmental and genetic effects confound the association between MD and inflammation. Methods: We studied 345 male twins (88 monogzygotic [MZ] pairs and 5 singlets, 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. Results: We identified 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 after-hours; 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 (HR, 1.48, 95% CI 1.39–1.58; p < 0.001) and within 24 hours post-resuscitation (RR, 1.37; 95% CI, 1.30–1.44; p < 0.001). 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 arrest appear amenable to defibrillation are associated with sizable increases in mortality. These findings highlight potential hospital quality improvement areas for resuscitation response and treatment.

16 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 m²) 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 25–29.9 kg/m²) and obesity (BMI ≥ 30 kg/m²) 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 appear to work in an additive fashion on risk of ACS. 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*

![](https://example.com/tables/table1.png)

*ACS hazard ratio (95% confidence intervals). (No. of cases/Incidence per 100 000 yrs)

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 after 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 < 0.001). 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 after-hours; 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 (HR, 1.48, 95% CI 1.39–1.58; p < 0.001) and within 24 hours post-resuscitation (RR, 1.37; 95% CI, 1.30–1.44; p < 0.001). 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 arrest appear amenable to defibrillation are associated with sizable increases in mortality. These findings highlight potential hospital quality improvement areas for resuscitation response and treatment.

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...
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 SAT (cm³) and VAT (cm³) with endothelial function (measured from 1998–2001 in the Framingham Offspring Study). Endothelial function measures included flow-mediated dilatation (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, VIF and SAT were sex standardized (mean 0, standard deviation 1). Results: Framingham participants (n = 1,140) were a mean age 59 years, 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

<table>
<thead>
<tr>
<th></th>
<th>Brachial artery diameter (mm)</th>
<th>Flow-mediated dilatation (FMD%)</th>
<th>Baseline mean flow velocity (cm/s)</th>
<th>Hyperemic mean flow velocity (cm/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAT (cm³)</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
<td>p = 0.01</td>
<td>p = 0.01</td>
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<td>p = 0.01</td>
<td>p = 0.01</td>
<td>p = 0.01</td>
<td>p = 0.01</td>
<td>p = 0.01</td>
</tr>
<tr>
<td>VAT (cm³)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>p = 0.01</td>
<td>p = 0.01</td>
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<td>p = 0.01</td>
<td>p = 0.01</td>
<td>p = 0.01</td>
<td>p = 0.01</td>
<td>p = 0.01</td>
</tr>
</tbody>
</table>

**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 Multinational 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 studies. Methodological limitations and attributable factors are included. Results: Simulations of the 2000–2029 China Multinational 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 event data were predicted upon data from the US. **Results:** The rates of CHD events and CHD deaths increased each with 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 damping CHD epidemic in China. Summed outcomes for Chinese adults 35–84 years old within three successive decades, 2000–2029, the CHD Policy Model-China.

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 9–12 y of follow-up 556 coronary heart disease (CHD) events and 232 coronary-related incident (CVD) events were observed. Energy-adjusted mean glycemic load (mean 10; 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 glycemic load was 1.47 (95% CI: 1.04–2.09; p = 0.03), with similar results when the observed glycemic index was used (hazard ratio of 1.32–1.67 at the highest for the lowest quartile (p = 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/m²), glycemic load was associated with CHD (hazard ratio of 1.33–1.67 at the highest for the lowest quartile (p = 0.02). This 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 ± 0.01) of the association between glycemic load and CVD risk. **Conclusion:** Dietary patterns of women consuming modest glycemic load diets, high dietary glycemic load and glycemic index increase risk of CVD, particularly among overweight women.
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 1.8 [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 continued 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**

<table>
<thead>
<tr>
<th>BMI (N=624)</th>
<th>BM (N=486)</th>
<th>BW (N=651)</th>
<th>WW (N=737)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Weight (%)</td>
<td>63</td>
<td>64</td>
<td>55</td>
</tr>
<tr>
<td>Y0</td>
<td>26</td>
<td>29</td>
<td>21</td>
</tr>
<tr>
<td>Y15</td>
<td>10</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>Y20</td>
<td>10</td>
<td>28</td>
<td>51</td>
</tr>
<tr>
<td>Obese (%)</td>
<td>42</td>
<td>38</td>
<td>56</td>
</tr>
</tbody>
</table>

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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 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: −0.92, 0.24). 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 - 5 pm (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 distribution 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 to test race, sex, and age differences in VAT. To date, both single- and multi-slice imaging studies have focused on VAT area or total VAT volume and to test race, sex, and age differences in VAT. The multi-image VAT data were treated as repeated measures to examine race, sex, and age differences in VAT, whereas the pattern or topography of VAT distribution in different population subgroups has yet to be characterized. **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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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.

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 were the monitor for three sequential days in each year, yielding measures of sleep duration, sleep latency, and sleep efficiency (percentage of time asleep). We assessed the 5-year change in systolic and diastolic blood pressure and the 5-year change in systolic blood pressure was associated with increased SBP (0.05 mmHg per minute of latency, p<0.01) and higher sleep efficiency (p<0.01; OR=0.94, 95% CI 0.90–0.98). Longer sleep latency was associated with increased DBP (0.06 mmHg per minute of latency, p<0.01) and higher sleep efficiency (p<0.01; OR=0.94, 95% CI 0.90–0.98). 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 2.36 (0.95) and 1.6 (0.97), respectively, p for trend 0.02. 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<0.01) and higher sleep efficiency (p<0.01; OR=0.94, 95% CI 0.90–0.98). 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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Healthy Lifestyle in Young Adulthood and Markers of Inflammation in Middle Age: The Coronary Artery Risk Development in Young Adults (CARDIA) Study
Martha L Davi, King Liu, Linda Van Horn, Lauren Colangelo, Northwestern Univ, Chicago, IL; Pamela J Schreiner, Univ of Minnesota, Minneapolis, MN; Cora E Lewis, Univ of Alabama at Birmingham, Birmingham, AL; Myron Gross, Univ of Minnesota, Minneapolis, MN; Cindy S Kurl, Long Island, NY

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/CVD morbidity and mortality. However, inflammation is lacking on the relationship of a healthy lifestyle (HL) to markers of inflammation among 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 current smoking categories: non-smoking (0), 1–4, any 5, any 3, 2, 1, or 0 of the following HL factors at baseline: non-overweight (BMI 18.5–<25 kg/m2), not currently smoking, moderate or no excessive alcohol consumption (<15 g/day for women or <30 g/day for men), moderate-to-high physical activity (in the highest race-sex-specific 40%), and a composite healthy diet score (highest 40% for consumption of high fiber, fiber, calcium, protein, low and intake of saturated fat,) compared with having any 3, 4, or 0–1 HL. Plasma samples from Year 2005–06 were used to determine levels of inflammatory markers. Results: Among non-users of hormone therapy it was 1.10 (1.02–1.19) for 0, 1.01 (0.92–1.11) for 1, 0.91 (0.83–1.00) for 2, 0.84 (0.77–0.91) for 3, and 0.76% (0.68–0.85) for 4 or more HL markers. Multivariate-adjusted mean levels of c-reactive protein (CRP) and interleukin-6 (IL-6) were significantly lower for PLR compared to those with 0, 1, 2, or 3–0–1 HL (P-trends <0.01). 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 CVD/CVD by emphasizing the importance of a healthy lifestyle beginning at younger ages.

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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 amount of money earned in relation to the cost of living, has been shown to 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 a company-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 – 3.68) than those with more than enough money. Independent of education, race, age, and log-income, the OR for the association was 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 = 0.93, 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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Consequence 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).

Methods and Results: 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 years) 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, HF cases were ascertained: 1,600 (7.1%) HF failure by death certificate, and 509 (2.4%) HF cases based on chart review. HF was defined as the presence of a cardiologist’s note, absence of HF failure by death certificate, or model adjusted 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 + servings/week), physical activity (<1, <1–1, ≥1 week/year), and history of atrial fibrillation and valvular heart disease, relative risks (95% CIs) for HF were 1.0 (reference), 0.96 (0.77–1.20), 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 diabetes and hypertension resulted in a modest attenuation of the relative risks [1.0, 0.93 (0.78–1.11), 0.82 (0.69–0.95), and 0.77 (0.64–0.97), 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 with 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.

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

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Introduction: Carriers of 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 1173T/C 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 Adeherence 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: 0.3–1.2) 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.

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.

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*T genotype (OR [95% CI]: 0.70 [0.58–0.84]), but not among those with the GSTT1*G genotype (OR [95% CI]: 1.23 [0.83–1.80]). Interaction was not observed for MI. These data suggest that compounds that are detoxified by this enzyme contribute to risk of MI.

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 markers of kidney function. We tested for association between the Affymetrix GeneChip Human Mapping 100K single nucleotide polymorphism set and markers of kidney function. We tested for association between the Affymetrix GeneChip Human Mapping 100K single nucleotide polymorphism set and markers of kidney function.

Framingham, MA; Qiong Yang, Boston Univ Sch of Public Health, Boston, MA; Martin G Larson, Emelia J Benjamin, Ramachandran S Vasan, Boston Univ Sch of Medicine, Boston, MA; James B Meigs, Massachusetts General Hosp and Harvard Med Sch, Boston, MA; Nisha I Parish, Boston Univ Sch of Medicine, Boston, MA; Christopher J O’Donnell, Daniel Levy, Caroline S Fox, National Heart, Lung, and Blood Institute Framingham Heart Study, Framingham, MA

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 genotype call rates >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 Ace 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.
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 in early 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, 140–170 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-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 1.0105/5mmHg-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 lower levels (AUC 0) 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.

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 elasticity has not been tested empirically. We derived the association of carotid arterial 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.

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 (CI) 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% CI) 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 (LVM) with limits of ≥0.43 cm & ≥51 g/m2.7, 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±6.7 kg/m2 vs follow up BMI 41.8 kg/m2, p<0.0001). LVM improved (54:13 to 41.0±6 g/m2.7, p<0.0001). In addition, LV geometry improved with 39% having concentric LVM 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.

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 NCEP 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 concentric 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 remodelling 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.

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 presuress 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 greatest in blacks vs whites in children (p = 0.009) 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.

The Association of Serum Bioavailable Estradiol with Metabolic Syndrome Components in Black and White Children, Adolescents, and Adults: 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: Even longitudinal cohort consisted of 1020 subjects (368 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 in a pre-menarchal 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 the long-term rates of change. The extent of clustering was considerably 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.
fasting plasma glucose, and negatively correlated with HDL cholesterol in both groups (all \(P < 0.001\)). BioE2 levels were negatively related to age in the \(<5\) y–10 y group, and positively correlated with systolic and diastolic blood pressures only in the \(5–10\) y group. On average, age-adjusted BioE2 levels were 135% higher in women who fulfilled criteria for the metabolic syndrome (\(\geq 3\) 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 \(5–10\) y versus \(<5\) y years menopause (Table 1). In addition, higher BioE2 was significantly associated with hypertension and hyperglycemia only for the \(5–10\) y group \((OR = 1.01, 95\% \text{ CI} = 1.00–1.01)\) and for \(5–10\) y group \((OR = 1.00, 95\% \text{ CI} = 0.99–1.01)\) but did not eliminate associations for the \(5–10\) y group, whereas only central adiposity remained significantly related to BioE2 in the \(<5\) y 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.

<table>
<thead>
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<th>Blood pressure</th>
<th>HbA1c</th>
<th>Triglycerides</th>
<th>HDL cholesterol</th>
<th>Visceral Fat</th>
<th>FPG</th>
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<td>(3.86)</td>
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<td>(1.75)</td>
<td>(3.86)</td>
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<td>(2.56)</td>
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<td>(4.80)</td>
<td>(3.86)</td>
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### 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, supplements 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 \(\mu G\) of selenium daily on type 2 DM incidence (1993–1996). 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 ascertained as secondary end point among participants who were free of type 2 DM at baseline \((n = 621)\) or placebo \((n = 629)\).

**Results.** During an average follow-up of 7.6 years, 100 total new cases of type 2 DM were identified, 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. **Conclusion.** Selenium supplementation at a dose of 200 \(\mu G\) per day for 5 years significantly reduced DM incidence in this population. Moreover, the potential for adverse effects of a long-term supplementation with selenium on glucose metabolism warrants further consideration.

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

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A change in the classification of a condition 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 and its components across racial and ethnic groups, sexes, and educational and income levels. 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 g/L 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 smaller 5-year change was estimated to be 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 < .05). 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.
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 access 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 5.7%. 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 5.6 million to 4.4 million individuals. Similarly, the prevalence of IFG would decrease 29% from 54 million to 39 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.

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**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, while age was 65.3±8.4 years, mean BMI was 30.5±6.0 kg/m², 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 the ATP III criteria and 74% by IDF criteria; 6% 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**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>ATP III Only (%)</th>
<th>ATP III Only N</th>
<th>IDF Only (%)</th>
<th>IDF Only N</th>
<th>Both (%)</th>
<th>Both N</th>
</tr>
</thead>
<tbody>
<tr>
<td>All women (n = 372)</td>
<td>22 (5.9)</td>
<td>227</td>
<td>52 (13.9)</td>
<td>52</td>
<td>80 (21.5)</td>
<td>80</td>
</tr>
<tr>
<td>White women (n = 260)</td>
<td>16 (6.2)</td>
<td>164</td>
<td>44 (16.9)</td>
<td>44</td>
<td>114 (43.5)</td>
<td>114</td>
</tr>
<tr>
<td>Non-white women (n = 112)</td>
<td>6 (5.4)</td>
<td>60</td>
<td>9 (8.0)</td>
<td>9</td>
<td>28 (25.0)</td>
<td>28</td>
</tr>
<tr>
<td>Age ≥65 years (n = 178)</td>
<td>12 (6.7)</td>
<td>123</td>
<td>19 (10.5)</td>
<td>19</td>
<td>44 (25.0)</td>
<td>44</td>
</tr>
<tr>
<td>Age &lt;65 years (n = 194)</td>
<td>10 (5.2)</td>
<td>102</td>
<td>13 (6.7)</td>
<td>13</td>
<td>37 (19.0)</td>
<td>37</td>
</tr>
</tbody>
</table>

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**P17**

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 1,279 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. 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 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 1.4–4.9) for trend < 0.05 among diabetics. Diabetes mellitus compared to no DM, was associated with slightly higher risk of AF that was not observed (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.
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 relationship between MS and incident stroke, particularly among women without a history of stroke. Methods: In a case-control study of stroke, risk factors, and ancestry, the Women’s Health Initiative Observational Study, we assessed the association between MS and incident stroke at ages 72 cases and an equal number of controls matched on age and race. MS was defined as the presence of NCEP-ATP III classification criteria. The European Prospective Investigation of Smoking and Health Study was used to study 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: The proportion of 12-to-14 year olds who had overweight were similar between the 2 age groups. The prevalence of overweight was lower than 15% (defined as age, sex and ethnicity-adjusted profile with lower threshold values, and low HDL cholesterol) were reported using three profiles: (1) a crude profile similar to NCEP-ATP III criteria, MS was present in 39.7% of controls, with age 35–84 the prevalence was 40.5% in women and 29.2% in men, averaging 36.5%. The percentage of overweight in both age groups, indicating that problems with overweight start at an early age.

Prevalence among those with MetS: Crude prevalence rates for CHD and stroke were 10.9%, 7.5%, and 4.6%, respectively. After adjustment for age and gender, the AOR’s were high for CHD (AOR = 2.4; 95% CI = 2.0–2.9), CVD (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 MetS in the WHS 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 MetS in WHS. MetS is significantly associated with increased AOR for CHD, CVD, and stroke. These baseline data from this large cohort point to high levels of risk factor clustering that may contribute significantly to the high prevalence of CVD in women living in Mississippi.

Clustering Cardiovascular Risk and Its Association with Cardiorespiratory Fitness in US Adolescents to 12 19 Year Olds: 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 (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 were measured. Age and sex-specific Z-scores were developed for the sum of skinfolds, the homeostatic model assessment (insulin*Hba1c 22.5), systolic blood pressure, triglycerides and total cholesterol/HDL ratio which were used to characterize the MetS. A clustering score was derived summing the three 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 (6.6) vs. 38.7 (7.3); p < 0.01) and in the 16–19 y-old group (48.1 (6.5) vs. 39.8 (6.8); p < 0.01). 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 become a specific target for intervention in adolescents, especially in boys.

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 measurements 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 AOR 2.4 (175 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 82.6%, specificity 50.1% and aROC 77.6%. 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).**

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**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 53.0–59.4 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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**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 156 controls). To examine whether emergent risk factors improved the prediction of T2DM, we performed 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 < 0.05). In contrast, 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.

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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 (≥95th percentile of 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 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 American) (p<0.05). The mean BMI (SE) was 33.3±1.6 kg/m² in exposed and 34.1±1.3 kg/m² in controls (p<0.06). Tanner stage was ≥4 in 60% of exposed and 53% of controls (p<0.78). The prevalence of IGT (n=8) or T2DM (n=2) in the exposed group was 40%, while the prevalence of IGT (n=4) or T2DM (n=2) 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 high/1C, lipid profile, or blood pressure between groups. **Conclusion:** 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.

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**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 mortality was determined with National Death Index (NDI) through 4–10. 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 < 0.001).
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 (88%) over follow-up of 6.0±2.9 years. Death occurred in 69 of 1368 (5.0%) patients without and 124 of 801 (15.5%) patients with baseline CHD. The adjusted hazard ratio associated with statin treatment was 0.49 (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.

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 ≥1.0 Results: Of the 722 admissions for chest pain (mean age 59.5±15.2; 46% 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.

Are Non-diabetic 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. Creatin clearance was estimated using the Cockcroft-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 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 72 (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 3800 people, 406 subjects (10.7%) were defined as having metabolic syndrome and 3403 (85.3%) 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 (1.52%) and 8 subjects in non metabolic syndrome group (1.98%)OR=0.925, 95% CI: 0.46–1.917) (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.

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. **Results:** IH mortality of patients with diabetes and previous DM treatment was 12.3% versus 30.1% (p<0.005). Among patients treated with an optimal strategy, IH mortality was 10.3% versus 30.5% (p<0.005). **Conclusion:** Previous DM treatment can improve IH mortality in diabetic ACS patients. **Still needed:** Further study is required to determine the impact of previous DM treatment on long-term mortality and to assess the role of optimal versus suboptimal therapy in diabetic patients with ACS.

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

Susana Costa, Pedro Monteiro, Silva Monteiro, Francisco Gonçalves, Lino Gonçalves, Mário Freitas, Luis A Providência, Coimbra Univ Hosp, Coimbra, Portugal

**Background.** Chronic inflammation is frequently observed in patients with acute coronary syndromes (ACS) and is usually associated with a worse prognosis in acute coronary syndrome (ACS) patients. **Aim:** To assess the impact of glycemic control (GC) on C reactive protein (CRP) expression in patients with acute coronary syndromes (ACS) that is not well established. **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. **Results:** Among patients with diabetes mellitus, GC was significantly lower in patients with ACS (CRP: 1.6±0.6 vs. 5.1±1.9 mg/L, p<0.05). Among patients with diabetes mellitus, GC was significantly lower in patients with ACS (CRP: 1.6±0.6 vs. 5.1±1.9 mg/L, p<0.05). **Conclusion:** Inflammatory expression of acute coronary syndromes (ACS) is influenced by abnormal glucose regulation (AGR) in patients with acute coronary syndromes (ACS).

Dyslipidemia in Patients with Dysglycemia

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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 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 (CBV) events, defined as fatal and nonfatal stroke. Multivariate logistic regression models assessed 5-year event rates among patients with and without diabetic dyslipidemia after adjusting for CV risk factors such as age, gender, hypertension, and obesity. **Results:** 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 1999 T2D patients with the diabetic dyslipidemia definition of TG ≥150 mg/dL and HDL-C <40 mg/dL, 5-y risk was significantly increased for CHD events (OR=1.17, 95% CI:1.02–1.36, rate=30.2) and CBV events (OR=1.55, 95% CI:1.19–2.02, rate=7.0) compared with T2D patients without diabetic dyslipidemia. The 5-y CHD risk (OR=1.33, 95% CI:1.16–1.54, rate=4.9) and CBV risk (OR=1.59, 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 cardiac and cerebrovascular events even after adjusting for known CV risk factors 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.
Clinical characteristics and HbA1c 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/m2. Baseline HbA1c was 8.2±0.1%. Forty-five percent (611/1365) and 55% (754/1365), respectively, were prescribed pioglitazone and rosiglitazone. In multivariate regression, baseline HbA1c (β = -0.693, age (β = -0.006), and use of multiple agents before the addition of a TZD (reference = single agent, β = -0.189) were significant (p < 0.05) predictors, explaining 49% of the variance in HbA1c response. This predictive model explained 44% of the variance in HbA1c 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 HbA1c values. These results suggest that readily identifiable clinical factors explain a substantial fraction of the variance in HbA1c response to TZD therapy. The most notable finding was the strong effect of baseline HbA1c, with each increment of 1% associated with a 0.69% greater HbA1c response. This suggests that baseline HbA1c should be considered when evaluating TZD responses in clinical practice and when comparing results from clinical trials.

### Table 1 - Results

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Male (%)</th>
<th>68.1</th>
<th>76.5</th>
<th>78.4</th>
<th>n.s.</th>
<th>66.7</th>
<th>79.5</th>
<th>n.s.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDSSYSTEMS</td>
<td></td>
<td>43.2%</td>
<td>40.7%</td>
<td>40.1%</td>
<td></td>
<td>40.2%</td>
<td>40.3%</td>
<td></td>
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<tr>
<td>CK-MB mass</td>
<td></td>
<td>132.2</td>
<td>126.3</td>
<td>122.3</td>
<td></td>
<td>127.3</td>
<td>125.1</td>
<td></td>
</tr>
<tr>
<td>PG (mg/dl)</td>
<td></td>
<td>5.1</td>
<td>5.7</td>
<td>5.6</td>
<td></td>
<td>5.0</td>
<td>5.6</td>
<td></td>
</tr>
</tbody>
</table>

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

Laura J Rasmussen-Torvik, James S Parkow, David R Jacobson, Jr, Lyn M Steffen, Antoinette M Moran, Julia Steinberger, Alan R Srinako, Univ of Minnesota, Minneapolis, MN

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 (LBMI). 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.

### 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 (NHW) from Rochester, MN (mean age 60.5 years; 56.9% women) participating in a community-based study of hypertensive adults. Plasma leptin was measured by RA. 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

### 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 HbA1c 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.

### 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=9,945). UD occurred in 34% and C - normal glucose metabolism: A - diabetes mellitus (DM) (n = 69), B - other diabetes mellitus disorders (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 - <6 mg/dl (n = 54) and E - >6 mg/dl (n = 78). CRP level considered was the first one determined and DOTT was performed after day 4. Results: Table 1: Groups were similar regarding demographics, types 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 occurred 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.

### Withdrawing

Withdrawing
significantly between ethnic groups (11.1 ng/mL; AA vs. 12.1 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 glomerular filtration rate (GFR), independent of age, smoking status, systolic blood pressure, serum creatinine, diabetes history and non-smoking status, and decreased alcohol consumption and physical activity.

Conclusions: 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.

**P40**

### 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 5,733 women based on NHANES 1999–2006, free of CVD, followed for 10 years. ATP III definition of MS. Results: Age-related MS prevalence was low in the normal weight (78.3 ± 29.4 kg/m²) group, men 6%, women 4%; higher in the overweight (BMI 25.0–29.9 kg/m²); men 18%, women 15%; and very high in the obese (BMI > 30.0 kg/m²) group, men 56%, women 40%; 11 times higher in men and 10 times higher in women. For males, BMI (or W) was also positively related to each of the four other variables included in the MS definition (adverse blood pressure [BP], dyslipidemia [TG, HDL-C, triglycerides [TG], and glucose/diabetes [DM]). BMI (or W) was also positively correlated with WC1, WC2, WC3, WC5. For both genders, BMI (or W) also related significantly and strongly to prevalence of four or all five of the five possible combinations of adverse BP, TG, 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/m² to 13.1% with BMI > 35.0 kg/m². 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 men and women, BMI and W relate continuously and strongly to each of the four other traits adverse BP, TG, HDL-C, diabetes/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.

### 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 the measurements in relation to anatomical landmarks, meals, postures 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 measurements by a single trained person. In addition, two 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 49–44) with mean age 25.8 ± 3.1 (Males 25.0 ± 4.5) and % body fat 28.7 ± 10.5%. Differences 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.**

### 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 circumference must be ≥85 cm. 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 49–69 years were randomly selected in Kusatsu, Japan. Participants were divided into waist circumference and height strata. Waist circumference strata were defined as < 90.3, ≥90.3–<85 cm, ≥85 cm. The value 85 cm is the median waist circumference for those of AA ethnicity remained an important 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 glomerular filtration rate (GFR), independent of age, smoking status, systolic blood pressure, serum creatinine, diabetes history and non-smoking status, and decreased alcohol consumption and physical activity.

**Conclusions:** The relative odds in the shortest (height < 168 cm) to the tallest (height > 172.3 cm) were 3.48 times higher in women with waist ≥85 cm, height and the metabolic syndrome needs to vary according to height. For men with waist circumferences that range from 80.3 to <85 cm, 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.
Adiponectin Concentration 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 subclinical cardiovascular disease, we compared post-partum adiponectin levels among women with 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 (IHTN, 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 found among women with GDM compared to PE controls (p<0.05). 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, HbaA1c, 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.

Cardiometabolic Risks in US Veterans Health Administration Patients

Donald R Miller, Boston Univ Sch of Public Health, Boston, MA

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 all veterans within the VA health care system. The purpose of this study was to use this database of cardiometabolic risks among VA patients. We used VA laboratory test results and prescription records for selected VA patients. The sample included all eligible veterans meeting the International Diabetes Federation (IDF) definition of diabetes, hypertension, or 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, obesity, high blood pressure or antihypertensive medication use, high plasma triglycerides, low HDL, 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%), 20–65 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. Cardiometabolic 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.

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 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 different MetS criteria with a special focus on abdominal obesity and to estimate the prevalence of this syndrome in three ethnic groups residing in one Canadian province, Quebec. Methods: The study population included adult participants of the extensive cross-sectional health surveys conducted in southern Quebec, 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 Quebeckers, 817 Indians Cree and 379 Inuit. Results: The prevalence between three organisation’s criteria varies from 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 16.6% for the World Health Organisation (WHO). In people with MetS, we observed significant differences in mean waist circumference and waist-to-hip ratio across the ethnic groups. Indeed, Inuit and Cree individuals with MetS have higher mean waist circumferences than southern Quebeckers (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 24.8%. 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.

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, no randomized intervention trials to date has described 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 emergency and public school settings. Participants were classified for metabolic syndrome were met in 31% (55 of 178) 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. 188.6±40.7 mg/dL, p=0.02), systolic blood pressure (123.8±13.1 v. 117±13.2 mmHg, p<0.001), and diastolic blood pressure (79.4±8.6 v. 72±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.
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, data were obtained from the longitudinal Dutch Atherosclerosis in the Elderly Study (DAVES). Methods: At baseline examination, 1244 patients (911 men, 333 women) were included. Dietary intake was assessed using a 154-item dietary frequency questionnaire. Fish intake was classified as absolute amount consumed per day. Metabolic syndrome was identified based on ATP III definitions. Results: Total fish intake was not associated with metabolic syndrome (OR 1.17 (95% CI 0.82-1.67)). However, fatty fish intake was associated with metabolic syndrome (OR 1.20 (95% CI 1.03-1.40)). Lean fish intake was not associated with metabolic syndrome (OR 0.98 (95% CI 0.81-1.20)). Conclusion: These data suggest that fatty fish intake is associated with metabolic syndrome in elderly Dutch patients. Intake of lean fish may not be protective. Further studies on role of fish intake are needed.}

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 omega-3 fatty acids found in fish. 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 health information was collected at baseline. Results: Lifetime average fish consumption was 12.5 g/day. Intake of fatty fish may contribute to the prevention of metabolic syndrome, especially in men. However, prospective studies are needed to confirm this relationship.

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, 13% mono fat, 8% poly fat) in comparison to a control diet (16% sat fat, 12% mono fat, 6% poly fat). Results: In men and women, body mass index (BMI) and waist circumference were associated with changes in lipids. 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. We present analyses 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 ATP III definitions) was present in 38% of men and 52% of women. This association was similar in men and women: 11% never consumed fish, 51% consumed fish less than one a week, and 38% consumed fish once or more per week (mean intake: 15.5 g/day). Fish intake tended to be inversely associated with metabolic syndrome. The adjusted prevalence ratios (with 95% confidence intervals) were 0.86 (0.78–0.95) among men and 0.76 (0.67–0.87) among women. 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 a significantly increased level of 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 association.

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

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The association between concentrations of urinary 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 8–17 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 urinary 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 concentration of urinary acid, being in the highest quartile (P = 0.04) of serum concentration of urinary acid was associated with significant reductions in the levels of triglycerides (P = 0.04), HDL-C (P = 0.04), and LDL-C (P = 0.04) and in the odds ratio for metabolic syndrome (P = 0.03). Serum concentration of urinary acid was not associated with significant reductions in the levels of fasting glucose (P = 0.22), insulin (P = 0.22), or HOMA-IR (P = 0.16). In conclusion, serum concentration of urinary acid is associated with the prevalence of the metabolic syndrome. An elevated concentration of urinary acid among children and adolescents should alert clinicians to the possible presence of the metabolic syndrome.
Possible explanations include residual confounding by incomplete smoking control, other traits conclude that only heavy coffee drinking is related to increased CAD risk only in smokers. Combining ex- & current smokers yielded these RR’s for “ever” smokers: 4 – 6 cups/d among 27,448 ex-smokers, 20,520 smokers of 58,888 persons who never smoked, coffee drinking was unrelated to CAD risk, while Analyses were for all persons and various subgroups, including smoking strata (see Table).

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 never-smokers who never smoked, coffee drinking was unrelated to CAD risk, while among 27,448 ex-smokers, 20,520 smokers of >1 cup per day, 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 = 1.13 (1.02–1.25) and >6 cups/d = 1.40 (1.24–1.59). The smoking disparity was considered 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 (p=0.10) without and 1.05 (1.03–1.07) 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 smoke, or an adverse biological interaction of some coffee component with smoking effect. Adjusted RR (95% CI) of CAD according to Coffee

<table>
<thead>
<tr>
<th>Cofee</th>
<th>Never smoked</th>
<th>Ex-smoker</th>
<th>Smoker</th>
<th>&lt; 1 ppd</th>
<th>&gt; 1 ppd</th>
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<tbody>
<tr>
<td>1–3 cups/d</td>
<td>1.05 (0.96–1.15)</td>
<td>0.96 (0.85–1.10)</td>
<td>0.98 (0.83–1.16)</td>
<td>1.01 (0.83–1.21)</td>
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<tr>
<td>4–6 cups/d</td>
<td>0.99 (0.88–1.11)</td>
<td>1.00 (0.91–1.12)</td>
<td>1.12 (0.91–1.38)</td>
<td>1.08 (0.88–1.35)</td>
<td></td>
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<tr>
<td>&gt; 6 cups/d</td>
<td>1.02 (0.83–1.26)</td>
<td>1.23 (1.03–1.49)</td>
<td>1.11 (0.87–1.43)</td>
<td>1.32 (1.02–1.70)</td>
<td></td>
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<tr>
<td>Per cup/d</td>
<td>1.00 (0.98–1.02)</td>
<td>1.03 (1.01–1.05)</td>
<td>1.03 (1.00–1.06)</td>
<td>1.02 (1.00–1.06)</td>
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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 in the past month. For each 1-hour increment of TV/video viewing per day, we found higher intake of high-fat milk, chips, and sugar-sweetened beverages, and lower intake of fruits. Conclusions: Higher TV viewing was associated with aggressive eating behaviors and sedentary lifestyles, which may contribute to the development of obesity and cardiometabolic risk factors in children. Depressive symptoms and other mental health problems may also be related to TV viewing, which may negatively impact children’s overall health and well-being. Patterns were identified using principal component analysis and were associated with higher intakes of unhealthy foods and lower intakes of healthy foods. These findings highlight the importance of reducing TV viewing among young children and the need for interventions to promote healthier eating behaviors and active lifestyles.
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 MS in adults. High Δ9DA is associated with obesity, while high Δ5DA is related to normal weight and insulin sensitivity. Surrogate measures of ΔAs are expressed as ratios of plasma fatty acids: Δ9DA = 16:1/n7/16:0; Δ9Δ5 = 18:3/n6/18:2,n6; and Δ5Δ9DA = 20:4,n6/20:3,n6. We assessed the hypotheses that Δ9 and Δ5 DAs are adversely related to Δ9 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, Δ5, and ΔΔ5 DAs, adjusted for age, sex, race, Tanner stage, and physical activity. Using the Duke Metabolic Risk Factors Score, plasma cholesterol, 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 Δ5 DA, but MS risk factors were not related to Δ5 ΔA (data not shown). These findings support the need for additional investigation into the role of Δ5 DAs in the pathogenesis of metabolic syndrome.

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 entry in the Physicians’ Health Study II. 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 (%) Multivariate HR (95% CI)
Never 704/19782 (3.7) 1.00 (referent)
Past 50/1126 (4.4) 1.13 (0.65–1.91)
Current 45/1150 (4.0) 0.81 (0.57–1.20)

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 stereochemical configuration. Animal studies and a few clinical trials lend credibity to the hypothesis that not all fatty acids carry the same potential for weight gain. However, only few studies examined the metabolism concerning the fatty acids are currently available and results are conflicting.

The 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/m2) 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).

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

Trans Fatty Acids Promote Atherothrombotic 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 atherothrombotic lesions. To date, few studies 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 atherothrombotic lesions in both in vivo and in vitro systems. In vivo Studies: Male rats (n=30) 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 assigned to diets high in omega-3 fatty acids (O3FAs) or TFAs. A diet high in TFAs was associated with 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 atherothrombotic 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 into 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 was 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 phosphatidyl-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 atherothrombotic and endothelial dysfunction. Furthermore, in vivo studies also demonstrated that O3FAs prevent induction of atherothrombosis.
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. No difference was found in the negative association between MUFA availability and a prevalence of obesity (β = -0.068, 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 SFA that appears particularly associated with the risk of obesity. Additional studies on the potential role of MUFA in obesity are needed.

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, 1,514 men (18 – 87 years old) and 1,528 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 3 characterized by alcohol intake (explained variation 4.8%), while the other components were mainly characterized by the consumption of dairy 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 = 0.97, 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 is independently associated with reduced levels of clinical and biological markers linked to the MS, while meat and alcohol intake showed the opposite results.

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 20-carbon TFA in persons with type 2 diabetes according to sex, and pre- and postmenopausal status. Results: Plasma 18-carbon TFA concentrations varied seasonally (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. Plasma 20-carbon TFA concentration was not associated with seasonality (p > 0.05). Plasma 18-carbon TFA concentrations varied by age (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.

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 66,271 Chinese men aged ≥40 years who were free of MI at baseline. Data on frequency and type of alcohol consumption 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 323,550 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, 0.82 (0.51–0.67) 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 < 0.0001). The corresponding relative risks for CHD events were 0.94 (0.73–1.20), 0.83 (0.53–0.76), and 0.53 (0.38–0.74), respectively (P-value for linear trend < 0.0001). These results suggest that alcohol consumption may decrease the risk of MI and CHD in Chinese men.

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

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Background The association of moderate alcohol consumption with a lower CV 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 ≥35 yrs. From March 2005 to July 2006, 6,251 subjects were enrolled. After exclusion of subjects with previous CVD (5%), 5,922 subjects (55+12 yrs, 46% males) were analyzed. We found 1,382 abstainers and 2,237 moderate drinkers (defined as intake 0.1 – <2 (<=) drinks/day among men; 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, 0.83–1.08; 0.98, 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, 0.76, 0.68–0.90 persisted for the higher quartiles vs the lower, respectively, P = 0.0001). Conclusions. Abstainers did show lifestyle characteristics comparable 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 CV 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

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

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Objective: 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 who develop fatal cardiac rhythm disturbances compared to non-fatal events could be clarified by determining n-3 FA levels in patients presenting 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 multiple patients of the VF group was 5.36% as compared to 6.44% in the control group (p < 0.05). 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 myocardiac 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, 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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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 NRI 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 communities surrounding Jackson, MS. Statistical Analysis: Dietary pattern were generated using cluster analysis. Descriptive analysis was used to describe each cluster. For each cluster, means of 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) Meat, Fish & 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, Milk & 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.
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 registry 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 hemorrhagic 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 \( \geq 30 \)) 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 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.

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 (TXBl2) 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 (TXB2). Assays were performed before and after 1 day 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, weight and blood pressure, and maximum body mass index (BMI) was calculated as weight in kg/height in m²; obesity was defined as BMI \( \geq 30 \). Multivariate analyses predicting pre- and post-ASA platelet function tests were adjusted for 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 (45 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.
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

Bryan Bordeaux, Lisa R Yanek, Dhananjay Vaidya, Taryn F Moy, Nauder Faraday, Lewis C Becker, Diane M Becker, John Hopkins Univ Sch of Medicine, Baltimore, MD

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 C-reactive protein (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 comorbidities (cancer, 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 (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, sex and inflammation correlations using the generalized estimating equation. Results: Participants (N = 1866) had a mean age of 44 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

<table>
<thead>
<tr>
<th>BMI Category</th>
<th>Pre-ASA</th>
<th>Post-ASA</th>
<th>p-value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1.4 (2.2)</td>
<td>2.1 (2.6)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Overweight</td>
<td>1.3 (2.1)</td>
<td>2.2 (2.8)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Obese I</td>
<td>0.9 (1.4)</td>
<td>1.2 (2.4)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Obese II</td>
<td>0.7 (1.4)</td>
<td>1.1 (2.2)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Obese III</td>
<td>0.5 (1.9)</td>
<td>0.9 (2.2)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

* Mean (SD)

Conclusions
Ventricular systolic function was not affected by long-term significant weight loss.

| P-value | 0.22 | 0.01 |

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

Andrea T Kozak, Martha L Davulas, Philip Greenland, Cheeling Chan, Northwestern Univ, Chicago, IL; Cabrana I Kiefe, Univ of Alabama at Birmingham, Birmingham, AL; David R Jacobs, Univ of Minnesota, Minneapolis, MN; Kiang Liu, Northwestern Univ, Chicago, IL

Background: A BMI in the overweight/obese range is associated with a greater risk of developing diabetes compared to normal 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 (≥30.0). 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 trends of BMI 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

<table>
<thead>
<tr>
<th>BMI Category</th>
<th>PCS</th>
<th>MCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>32.6</td>
<td>309.8</td>
</tr>
<tr>
<td>Overweight</td>
<td>340.4</td>
<td>319.3</td>
</tr>
<tr>
<td>obese I</td>
<td>315.3</td>
<td>304.6</td>
</tr>
<tr>
<td>Obese II</td>
<td>297.5</td>
<td>290.3</td>
</tr>
<tr>
<td>Obese III</td>
<td>265.5</td>
<td>265.5</td>
</tr>
<tr>
<td>P for trend</td>
<td>&lt;0.001</td>
<td>0.25</td>
</tr>
<tr>
<td>Normal weight</td>
<td>355.1</td>
<td>312.8</td>
</tr>
<tr>
<td>Obese I</td>
<td>343.9</td>
<td>309.5</td>
</tr>
<tr>
<td>Obese II</td>
<td>308.0</td>
<td>298.3</td>
</tr>
<tr>
<td>Obese III</td>
<td>314.7</td>
<td>293.4</td>
</tr>
<tr>
<td>P for trend</td>
<td>&lt;0.001</td>
<td>0.07</td>
</tr>
</tbody>
</table>

(Adjusted for age, education, marital status, alcohol use, smoking, physical activity, diabetes, hypertension, antidepressant use, and BMI in 1980–81) Using the trend SF-12 percentage scoring method

Waist-to-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 = 6,786 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 = 1,209) or heart failure from a death certificate (underlying cause of death, 428 or 56, n = 6) was considered an incident event. Gender-specific multivariable Cox proportional hazard reduction 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 = 1.93 (95% CI = 1.21, 2.98 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.

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

Raegan W Durant, Sharron D Persson, Catriona I Kiefe, Cora E Lewis, Univ of Alabama at Birmingham, Birmingham, AL; Pamela J Schreiner, Univ of Minnesota, Minneapolis, MN; D D Williams, Univ of Alabama at Birmingham, Birmingham, AL

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 BMI, and WC, and physical activity were collected and FRS calculated at each exam. Using repeated measures regression with a compound symmetry covariance structure, we modeled severity. To assess their BMI at ages 20–29, we estimated 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 elevated from 24.4 (4.8) kg/m² to 29.3 (8.9) kg/m² and 0.6% to 6.6%, respectively, while tobacco use decreased from 24.6% to 17.8%. Over 20 years, the mean BMI 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.

Framingham Risk Score Over Time

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

Hasan M Shihab, The Johns Hopkins Univ Sch of Medicine, Baltimore, MD; Lucia A Meoni, The Johns Hopkins Bloomberg Sch of Public Health, Baltimore, MD; Nan-Yuh Wang, Daniel E Ford, The Johns Hopkins Univ Sch of Medicine, Baltimore, MD; Kung-Yee Liang, Michael J Klag, The Johns Hopkins Bloomberg Sch of Public Health, Baltimore, MD

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 ≥160/95 mmHg on ≥2 annual questionnaires, or hypertension requiring drug therapy. Self-reports of hypertension were confirmed by an endpoint committee review of annual questionnaires. Abdominal obesity (BMI ≥25 kg/m²) was 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. 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 < 0.05, 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 rs471028 (p-value = 1.96E-07) for WC, located near the DAP1 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 EF2K gene, for WC. We were able to validate SNPs in known genes if they have been related to BMI in other datasets, BMI and waist circumference (WC). Conclusions: Methylation of the INSIG2 gene, 5 SNPs in the ESRT1 gene, 6 SNPs in the PPARγ gene, and 1 SNP in the ABHD18 gene. Conclusions: Adiposity traits are associated with BMI and WC. Does Active Commuting to Work Influence Adult Fitness, Body Weight, and Obesity in Adults? The CARDIA Fitness Study

Penny Gordon-Larsen, Janne Boone, UNC-Chapel Hill, Chapel Hill, NC; Stephen Sidney, Barbara Sternfeld, Kaiser Permanente, Oakland, CA; David R Jacobs, Jr, Univ of Minnesota, Minneapolis, MN

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 (ages 18–86) 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/m². 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 1921 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 = −18.4; p < 0.0001), longer GXT duration in seconds (β = 10.4; 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
endothelin-1

vasoconstrictor activity

contributes to impaired stroke: findings from NHANES III

subjective and objective sleep measures have different associations with sleep was explained by measured sleep, one possible explanation is that other determinants confirms cross-sectional associations between weight and subjective sleep found in other leptin was significantly and independently associated with MI/stroke in both men (OR, 2.29; smoking, and body mass index. MI and stroke were self-reported according to the NHANES examination survey (NHANES) III performed from 1988 to 1994. Logistic regression was used forearm endothelium-dependent vasodilation to acetylcholine is due, at least in part, to ET-1 tone. the aim of this study was to determine whether the obesity-related reduction in 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 tone. the mechanisms responsible for diminished 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; BMI: 23.4 ± 0.4 kg/m²) and 16 obese (O: 58 ± 2 yr; BMI: 30.2 ± 0.8 kg/m²). 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 compared to NW (from 4.8 ± 0.2 to 11.5 ± 1.0 mL/100 mL tissue/min) vs NW (4.8 ± 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.

the national rates of morbid obesity among US children and adolescents Joe skelton, med college of Wisconsin, Milwaukee, WI; Stephen cook, Peggy Auinger, Jonathan Klein, Univ of Rochester med ctn, Rochester, NY; Sarah barlow, St Louis Univ, St Louis, MO 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 or >120% of ideal weight to which most adolescents would be referred. 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 US adolescents. methods: we analyzed measurements from 12,384 US children and adolescents from the national health and nutrition examination survey 1999–2004. outcome variables were the proportion of subjects with BMI ≥90th 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 US children 2–19 yr have a BMI ≥90th 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 between the poverty level were more affected, 2%, than teens in the highest PIR category, 0.8% (P < 0.002). 0.1% of children and 1.1% of 12–19 yr olds had BMI ≥30, 40 and 50. almost 4% (2.7 million) U.S. children have a BMI ≥90th percentile for age/sex, with significant differences by race, sex and poverty. in addition, over 1% of US teens have a BMI ≥40 (418,000 teens), a level of obesity which may qualify for bariatric surgery.

association of high leptin with history of myocardial infarction and stroke: findings from NHANES III Justo Sierra-Johnson, Abel Romero-Corral, Francisco Lopez-Jimenez, Apoor S Gami, Robert Wolik, Fatima H Kuniyoshi, Virend K somers, Mayo clinic, Rochester, MN 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 III 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 examination survey. to correct for potential length bias (MI/stroke was defined in the absence of reported MI or stroke) and sex-specific MI/stroke prevalences were similar between self-reported MI or stroke and in women, independently of traditional cardiovascular risk factors.

dendothelin-1 vasoconstrictor activity contributes to impaired acetylcholine-mediated vasodilation in obesity Christian WernsTy, Gary P Van Guilder, Jared J Greiner, Yoli Casas, Brian L StaufTer, Christopher A DeSouza, Univ of Colorado, Boulder, CO 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 vasodilator activity. we studied 33 sedentary, middle-aged adults: 17 normal weight (NW: age: 57 ± 2 yr; BMI: 23.4 ± 0.4 kg/m²) and 16 obese (O: 58 ± 2 yr; BMI: 30.2 ± 0.8 kg/m²). 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 compared to NW (from 4.8 ± 0.2 to 11.5 ± 1.0 mL/100 mL tissue/min) vs NW (4.8 ± 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.

predictors of body fatness and cardiovascular risk in pediatric cancer survivors Tracie L Miller, Univ of Miami, Miami, FL; Stuart Lisitzt, Brigham and Women’s Hosp, Boston, MA; Gabriela Lopez de Minth, Univ of Miami, Miami, FL; Karljin A Wouters, Vrije University Med Ctr, Amsterdam, Netherlands Antilles; Andrae Hinko, LSU Health Sciences; Jacob Adams, Carol French, Cynthia Prokou, Amy Kozowski, Univ of Rochester, Rochester, NY; Steven E Lipshutz, Univ of Miami, Miami, FL 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 and various risk factors for survivors of childhood cancer were measured compared to age-matched normal weight controls.
cancer survivors. Cranial irradiation is an important risk factor for body fatness in both male and female pediatric siblings, male pediatric cancer survivors have greater body fat and CV risk factors than siblings. Associated with BMI. In addition to age, cranial irradiation in both males (6.18, p = 0.0001) and females (6.16, p = 0.0001) was associated with increased total body fat. Similar results were found for trunk fat. Increasing doses of cranial radiation were associated with both increased BMI and trunk fat% in male survivors. Male survivors had greater trunk fat% than controls (26.6% [1.13] vs 22.0% [1.78]; p = 0.03). There were no differences in females. CV risk factors (insulin, cholesterol, triglycerides, 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 assess predictors of BMI, total body fat, and trunk fat were developed for both male and female survivors. For males, cytoxan treatment (-2.84, p < 0.009), and IFN-1 (0.01, p = 0.01) were independently associated with BMI and for females, cytoxan treatment (-3.34, p = 0.01) was associated with BMI. In addition to age, cranial irradiation in both males (6.18, p = 0.0003) and females (6.16, p = 0.0004) 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 & > 20 Gy [males]; 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.

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, n = 1046) with dietary treatment preference for 12 months to examine the biochemical parameters of inflammatory status, insulin resistance, dyslipidemia, and oxidation injury. Parameters assessed were history, risk factors, height, weight, BMI, waist-circumference (WC), cholesterol, triglycerides, LDL, HDL, CRP, 8-epi-PGF 2α, marker as oxidative stress, circulating endothelial cells (CEC), and circulating endothelial progenitor cells (CEPC). In 1995 a school screening in juveniles (aged 10–18 years; n = 484; 481 boys/503 girls) was performed. Ten years later in the same schools 957 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 boys 75.1 and for girls 73.4 cm. Total means was 78.7 and 77.5, respectively. In % females (n = 51%) and % males (n = 49%) WC was > 70 cm (the upper limit for juveniles according to ACC). Cigarette smoking was associated with significantly (p < 0.01) higher 8-epi-PGF 2α > 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 2α, IP > CRP > CEC > CEC. Correlation of BMI to these parameters was less pronounced. IP was negatively correlated with HDL (r = -0.5681; p < 0.0005), 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 2α, CRP, IP and HDL changed (p < 0.001), 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.

The purpose of this study was to examine if there were differences in body composition (using DXA) and BMI in pediatric cancer survivors compared to healthy children and young adults. The association between educational attainment and BMI among the highest educated. White Women (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 target the differences in the relationship between educational attainment and BMI among ethnic groups.

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

Yasuyuki Nakamura, Kyoto Women’s Univ, Kyoto, Japan; Hirotsugu Ueshigawa, Nagano, Okada, Aya Higashiyama, Yoshikita Kili, Takashi Kadowaki, Tomonori Okamura, Yoshitaka Murakami, Shiga Univ School of Medicine, Otsu, Japan; Akira Okayama, National Cardiovascular Ctr, Suita, Japan; Sohel R Choudhury, Pacific Health Rsch Institute, Dhaka, Bangladesh; Beatrix Rodriguez, J D Curb, Pacific Health Resch Institute, Honolulu, HI, Jeremiah Stamler, Northwestern Univ, Chicago, IL

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). Serum adiponectin was significantly higher in Japan than Hawaii (23.4 vs 26.9 kg/m2, P < 0.0001), as was total dietary protein (15.7 vs 18.6 % kcal, P < 0.001) 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 of 35 anthropometric, lifestyle, and diet variables considered separately, BMI-reduced the Hawaii-Japan adiponectin difference by 50.7% and physical activity by 15.4%. The combination BMI activity, energy-adjusted dietary total protein, omega-3 PFA, and arachidonic acid further reduced the coefficient (by 78.3%), and the difference was statistically nonsignificant. Total energy intake was similar, BMI was > 70% the alcohol intake, hours postsprandial, smoking was 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 compared to Japanese-Americans in Hawaii disappeared after adjustment for specific nutrients, BMI, and physical activity.

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

Dhanraj Vaidya, Pamela Ouyang, Adrian S Dobs, Sherril Golden, Hopkins Med Inst, Baltimore, MD; Mary Cushman, Univ of Vermont, Colchester, VT; Mosayez Szko, Johns Hopkins Med Inst, Baltimore, MD; Kiang Liu, Susan M Gapstur, Northwestern Univ Med Sch, Chicago, IL

We have previously shown cross-sectionally in the MESA study that estradiol (E2) levels are associated with greater central obesity, and dehydroepiandrosterone (DHEA) and sex...
MESA increase, while DHEA and SHBG were associated with a small decrease in central obesity. In

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

| Hormone (typical doubling range: 1x-2x geometric mean) | WC Regression coefficients (Data: 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 levels by the groups according to delta body weight

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean CRP (mg/L)</th>
<th>Adjusted geometric mean CRP (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td>0.84</td>
<td>0.49</td>
</tr>
<tr>
<td>2001</td>
<td>0.85</td>
<td>0.73</td>
</tr>
<tr>
<td>2003</td>
<td>0.70</td>
<td>0.34</td>
</tr>
<tr>
<td>2001</td>
<td>0.84</td>
<td>0.51</td>
</tr>
<tr>
<td>2003</td>
<td>0.70</td>
<td>0.40</td>
</tr>
<tr>
<td>2001</td>
<td>0.91</td>
<td>0.50</td>
</tr>
<tr>
<td>2003</td>
<td>0.60</td>
<td>0.38</td>
</tr>
<tr>
<td>2001</td>
<td>0.83</td>
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<td>2003</td>
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<tr>
<td>2001</td>
<td>0.98</td>
<td>0.58</td>
</tr>
<tr>
<td>2003</td>
<td>0.72</td>
<td>0.45</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean CRP (mg/L)</th>
<th>Adjusted geometric mean CRP (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td></td>
<td></td>
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<tr>
<td>2003</td>
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<td>0.49</td>
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<tr>
<td>2001</td>
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<td>2003</td>
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<td>2001</td>
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<td>2001</td>
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<td>2003</td>
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<td>2001</td>
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<tr>
<td>2003</td>
<td>0.72</td>
<td>0.45</td>
</tr>
</tbody>
</table>

* p < 0.05 by ANCOVA

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

Cheryl S Lynch, Kathleen M McTigue, James E Bost, Lewis H Keller, Univ of Pittsburgh, Pittsburgh, PA

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). Results: Results: Weight class (standard BMI categories) and QOL (SF-36 physical health component, PHC, scores) 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.

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

Nicolas Stattler, Arzoo Zomerrodi, Jill C Conner. The Children's Hosp of Philadelphia, Philadelphia, PA

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: From the National Health and Nutrition Examination Survey (NHANES) database, height and weight data were used to calculate BMI for children and adolescents aged 2-18 years. Results: 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 <80), 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 <0.001) 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 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.

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

Yoko Torani, Kenji Takashima, Kazuko Kawamura, Iwate Health Service Association, Morioka, Japan, Masaki Ohsawa, Iwate Med Univ, Morioka, Japan

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 in serum CRP levels and whether body weight lost 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 change 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.

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.

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

Joseph Kim, London Sch of Hygiene and Tropical Medicine, London, United Kingdom; David R Jacobs, Jr, Alan K Berger, Sue Duval, Russell V Luepker, Univ of Minnesota, Minneapolis, MN

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 <18.5 kg/m 2; 116/5451), morbidly obese (49/529 9%), and BMI missing (209/1803 12%). By the end of 2-year follow-up, 2360 cases (43%) died. Obsese cases of HF had a lower variable adjusted risk of death compared with thinner cases (p-value for linear trend <0.001). Men: 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.

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Odds Ratio for Low PHC by Weight Class (Total Sample)

<table>
<thead>
<tr>
<th>Normal weight (ref)</th>
<th>Overweight</th>
<th>Class 1 Obesity</th>
<th>Class 2 Obesity</th>
<th>Class 3 Obesity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>Model 2</td>
<td>Model 3</td>
<td>Model 4</td>
<td></td>
</tr>
</tbody>
</table>

P103

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

Nicolas Stattler, Arzoo Zomerrodi, Jill C Conner. The Children's Hosp of Philadelphia, Philadelphia, PA

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: From the National Health and Nutrition Examination Survey (NHANES) database, height and weight data were used to calculate BMI for children and adolescents aged 2-18 years. Results: 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 <80), 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 <0.001) 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 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.
Significance of Anthropometric Indicators of Obesity in Determining Coronary Heart Disease Risk Among Males and Females

Carukshi Arambepola, Dulitha Fernando, Univ of Colombo, Colombo, Sri Lanka; Ruvan Ekanyake, National Hosp of Sri Lanka, Colombo, Sri Lanka

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 threshold for identifying the ‘obesity-related-CHD risk’ amongst males and females.

Methods: A community-based cross-sectional study on 4154 (22% more females) 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. Females not demonstrating elevated WC from 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’ amongst both males (Adjusted odds ratio (OR): 1.05; 95% confidence interval (CI)1.02, 1.07) and females (OR: 1.02; 95% CI1.00–1.05), 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/m² 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 of 90 cm among Asian races.

Conclusions: WC is a better anthropometric indicator than BMI in identifying males at risk of obesity-related-CHD.

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

Nicola Maidwell, Wendy Nuttall, GE Healthcare, Pollards Wood, United Kingdom; Manan Shah, Xcenda, Palm Harbor, FL; Mitchell K Higashi, GE Healthcare, Wauwatosa, WI

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 cardiovascular physicians participated and each site enrolled up to 5 consecutive patients (N = 1,608) Europe (n = 264), US (n = 344). Cardiologists were asked to select from a list of symptoms that were exhibited at first presentation: chest pain, 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 = 353); 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 pain (92% vs. 76%, p<0.05), shortness of breath (14% vs. 9%, p<0.05), pain in the left arm (35% vs. 23%, 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.

Obesity Predisposition Predicts Waist Circumference and Its Tracking in Children


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” across ages 3 to 8 years. Methods: A cross-sectional study of 1176 children aged 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% or ≥95th 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 (HWW, 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 HR0W than HRRL or LR children at most ages. 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 HROW transitioned from a WC >85th percentile at age 3 (national norms) to >95th 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 normalizing or CVD-35 cutoffs, although at transition from normal to elevated WC between ages 3 to 4 years may foreshadow subsequent childhood obesity.

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 tacto-ovo-vegetarian. Dietary treatment assignment was made with equal regard to the participants’ 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’ preferred 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 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 highlight that continual emphasis on how to overcome the identified emotional and logistical barriers for the long term may improve weight loss maintenance.

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

Allison H Christian, Dana Edelman, Heidi Mochari, Lori Mosca, Columbia Univ, New York, NY

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 the risk factors WC and BMI levels is shown in Table 1. White women with a WC >35 cm were nearly twice as likely to have low HDL (OR = 1.98, p = 0.03) compared to those with a WC <35 cm. Black and Hispanic women (n = 389) with a WC >35 cm 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 cm. Multivariable regression analysis adjusting 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 = 3.25, 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) as well as both BMI and WC in a model adjusted for cardiometabolic risk. Inter-rater (r = 0.97, p < 0.01) and intra-rater (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. Ethnicity is simple, reliable and inexpensive index that should be more widely utilized to identify persons at increased cardiometabolic risk.

Table 1.

<table>
<thead>
<tr>
<th>Smoking</th>
<th>WC (cm) &gt;35</th>
<th>HDL &lt;50</th>
<th>TC ≥ 200</th>
<th>BPH ≥ 140/90</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (≥ 35 kg/m²)</td>
<td>6%</td>
<td>60%</td>
<td>46%</td>
<td>36%</td>
</tr>
<tr>
<td>4%</td>
<td>50%</td>
<td>45%</td>
<td>32%</td>
<td>2%</td>
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<tr>
<td>3%</td>
<td>63%</td>
<td>45%</td>
<td>32%</td>
<td>2%</td>
</tr>
<tr>
<td>Both WC ≥35 cm and BMI</td>
<td>6%</td>
<td>60%</td>
<td>47%</td>
<td>32%</td>
</tr>
</tbody>
</table>

Note: **Framingham score >20% or personal history of heart disease/diabetes.
the association of traditional CVDRF with a chronic, sub-acute inflammatory state. It is unclear how such an inflammatory change translates 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 analyzed 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, fibronectin, and haptoglobin were consistently different across phenotypic groups, with other markers differing depending upon the stratification. To better understand variable interactions & confers sex effects, a series of multiple linear regression analyses evaluated the modeling 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 potential future work to understand the effects of aging on CVDRF-related inflammation. A highlight the importance of more complex statistical modeling. Table 7

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**The Framingham Risk Score and Coronary Heart Disease Risk in Extremely Obese Individuals**

Robert C Lowe, Sr, Jennifer Patzkowsky, Debbie Zimmerman, Polk County Schs, Winter Haven, FL; Phil Chen, Cogniscenti Health Institute, Orlando, FL

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 adipo/gen. 

We analyzed the association between body mass index (BMI) with mortality and cardiovasc. Endpoints OR were classified by gender and age using Cox Regressions. These models included aPWV as a continuous predictor and the outcome was all-cause mortality. A total of 208 participants with a body mass index (BMI) ≥ 30 kg/m² were included in the analysis. The median follow-up time was 10 years (range 3-15 years), and the mean age at baseline was 56 years (range 20-85 years). The unadjusted hazard ratio (HR) for all-cause mortality was 1.32 (95% CI 0.87-2.00, p = 0.17) for males compared to females. In the age-stratified models, the HR for all-cause mortality was 1.50 (95% CI 0.96-2.34, p = 0.08) for the 40-60 age group compared to the 60+ age group.

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

<table>
<thead>
<tr>
<th>Type of Marker</th>
<th>Differs Across Adiposity Groups</th>
<th>Differs Across Total Cholesterol Groups</th>
<th>Differs Across Age Groups</th>
<th>Differs by Gender Category</th>
<th>Differs by Age &amp; Gender Category</th>
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<td>CRP</td>
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<tr>
<td>Fibrinogen</td>
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<td>OR</td>
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<tr>
<td>p-Value</td>
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**Table 2. Results of Regression Analysis**

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<th>Predictor</th>
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<th>Age</th>
<th>Total Cholesterol % BA</th>
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<td>CRP</td>
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<td>MMP-9</td>
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<td>p &lt; 0.05</td>
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<td>p &lt; 0.05</td>
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<td>Age X Gender</td>
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<td></td>
<td></td>
<td>p &lt; 0.05</td>
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<tr>
<td>Differs by Gender</td>
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<td>p &lt; 0.05</td>
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<tr>
<td>Differs Across Total Cholesterol % BA</td>
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<td></td>
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<td>p &lt; 0.05</td>
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</table>

**Impact of Overweight on Linear Growth in Children and Adolescents**

Gary A Mayman, William N Evans, Ruben J Acherman, Carlos F Luna, Katrinca T Kip, Kathleen A Cass, Abraham Rothman, Joseph Ludwick, Humberto Restrepo, Children’s Heart Ctr and Univ of Nevada, Sch of Medicine, Las Vegas, NV

**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 included baseline anthropometric data from 416 patients with a body mass index ≥50%, 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 (zatage) from CDC 2000 charts was used for comparisons. Results: Group A was composed of 206 subjects, mean age: 10.2 ± 2.1 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 similar in body mass index (BMI-Z-score) 2.33 ± 0.29 vs 2.34 ± 0.25, 24.1 ± 1.29 vs 24.6 ± 1.29, respectively. Summary statistics are shown in Table 1. In these overweight pediatric patients the mean stature-for-age z-score for height was statistically higher in all sub-groups except girls in the 12 to 16 years, suggesting that body mass index is not negatively impacting the linear growth.
was a cross-sectional analysis of 13,601 subjects (20–79 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% defined as defined by the World Health Organization (BF% ≥ 25 in men and ≥35 in women). Results: Mean BMI was 26.2 ± 6.6 in men and 27.6 ± 6.6 in women, while BMI was 24.8 ± 6.6 in men and 36.7 ± 7.7 in women. The correlations between BMI and BF% and 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 25.6–29.9 (r = 0.22 in men and 0.24 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 (85 % in men and 99 % in women). Conclusions: Despite a good overall correlation between BMI and BF%, BMI failed to discriminate between BMI ≤ and BMI ≥ in the adult US population, especially in the elderly and men. BMI had poor-moderate correlations with BF% in normal-mildly elevated BMI. In addition, a BMI cut-off of BMI <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**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>20–29</th>
<th>30–39.9</th>
<th>40–49.9</th>
<th>50–59.9</th>
<th>60–69.9</th>
<th>70–79.9</th>
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<tbody>
<tr>
<td>Male</td>
<td>0.70</td>
<td>0.67</td>
<td>0.66</td>
<td>0.64</td>
<td>0.60</td>
<td>0.60</td>
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<tr>
<td>Female</td>
<td>0.90</td>
<td>0.86</td>
<td>0.83</td>
<td>0.81</td>
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<tr>
<td>Male</td>
<td>0.72</td>
<td>0.72</td>
<td>0.72</td>
<td>0.75</td>
<td>0.72</td>
<td>0.73</td>
</tr>
<tr>
<td>Female</td>
<td>0.70</td>
<td>0.75</td>
<td>0.76</td>
<td>0.77</td>
<td>0.71</td>
<td>0.73</td>
</tr>
</tbody>
</table>

BMI/BF% Male Female 0.70 0.86 0.75 0.86 0.76 0.82 0.77 0.83 0.77 0.71 0.73 0.78 0.78 0.78 0.78

P120

**Management of Obesity: A Challenge for Medical Education and Practice**

Njeri Thande, Emily Hurstark, Robert E Scicca, Elisa-Grace Giardina, Columbia Univ Med Ctr, New York, NY

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 electronic Behavioral Risk Factor Surveillance System (BRFSS) 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 59.0 ± 11.3 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 < 0.001). Overweight (27% (21/78)) and obese (65% (80/124)) subjects were specifically advised to lose weight (p < 0.001). Seventeen percent (13/78) of overweight and 47% (58/123) of obese subjects were given a weight loss referral (p < 0.001). Fifteen (81/112) 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% (105/151) vs. 52% (48/94), p < 0.001) and there was a counseling trend of counseling with an increasing level of current smoking (p = 0.0261). Smokers were less likely to be counseled even when controlling for BMI (odds ratio 0.42, 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% (48/140), p < 0.0001). There was a counseling trend of counseling with a decrease in body mass index (p = 0.001). 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.

P212

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

Anush M Turyan, Diaspistica Med Ctr, Yerevan, Armenia

Background: Obesity is associated with increased risk of cardiovascular complications of hypertension. In present study we evaluated the probability of the association of angiotension antagonists (l) and diuretic hydrochlorothiazide (HCT) with lipase inhibitor orlistat (O) and BMI/BF% for decrease in LV ventricular mass (LVM) in obese hypertensive patients (pts). Design and Methods: Forty two obese non diabetic mild to moderate essential hypertensive (24 males and 18 females, mean body mass index (BMI) = 38.9 kg/m2, mean age = 47 years, office blood pressure (BP) = 154/86 mm Hg) with left ventricular (LV) hypertrophy were randomized and stratified to L, M. Subjects in L group once a day and HCT 12.5mg once a day (group 1 - 21 pts). Echocardiography was performed at baseline and after 3 months of therapy. LVM was calculated by Devereux formula. Results: BP fell under 140/90 mm Hg in both groups. LV mass significantly reduced in group L (p < 0.001) as weight loss (9.3% ± 5.6% kg/m2) on once a day and HCT 12.5mg once a day with 0.12 mg twice a day and hypocaloric diet in combination (group II - 21 pts). Echocardiography was performed at baseline and after 9 months of therapy. LV mass was calculated by Devereux formula. Results: BP fell under 140/90 mm Hg in both groups. LV mass significantly reduced in group L (p < 0.001) as weight loss (9.3% ± 5.6% kg/m2) on once a day and HCT 12.5mg once a day with 0.12 mg twice a day and hypocaloric diet in combination (group II - 21 pts). Echocardiography was performed at baseline and after 3 months of therapy. LV mass was calculated by Devereux formula. Results: BP fell under 140/90 mm Hg in both groups. LV mass significantly reduced in group L (p < 0.001) as weight loss (9.3% ± 5.6% kg/m2) on once a day and HCT 12.5mg once a day with 0.12 mg twice a day and hypocaloric diet in combination (group II - 21 pts). Echocardiography was performed at baseline and after 9 months of therapy. LV mass was calculated by Devereux formula. Results: BP fell under 140/90 mm Hg in both groups. LV mass significantly reduced in group L (p < 0.001) as weight loss (9.3% ± 5.6% kg/m2) on once a day and HCT 12.5mg once a day with 0.12 mg twice a day and hypocaloric diet in combination (group II - 21 pts). Echocardiography was performed at baseline and after 9 months of therapy. LV mass was calculated by Devereux formula. Results: BP fell under 140/90 mm Hg in both groups. LV mass significantly reduced in group L (p < 0.001) as weight loss (9.3% ± 5.6% kg/m2) on once a day and HCT 12.5mg once a day with 0.12 mg twice a day and hypocaloric diet in combination (group II - 21 pts).
P124

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

Arline I. Hankinson, Kiang Liou, Northwestern Univ, Chicago, IL; David R Jacobson, Jr, Bharat Thayyagarajan, Univ of Minnesota, Minneapolis, MN; Lewis J Smith, Philip Connett, Northwestern Univ, Chicago, IL; Stephen Sidney, Kaiser Permanente, Oakland, CA

Background: Cross-sectional studies demonstrate that pulmonary function, measured by forced vital capacity (FVC) and forced expiratory volume in one second (FEV1), 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. Estimated Generalizing Equation models were used to estimate the relationship of baseline quartiles of fitness to average yearly changes in FVC and FV/C over 20 years. Results: After adjustments for baseline age, gender, race, and height, fitness was inversely correlated with higher fitness, 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

P125

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

Barbara Sternfeld, Stephen Sidney, Kaiser Permanente, Oakland, CA; William L Haskell, Stanford Univ, Stanford, CA; Mercedes Caraceno, Northwestern Univ, Chicago, IL; David R Jacobson, Jr; Univ of Minnesota, Minneapolis, MN; Cora E Lowry, Alabama Ctr for Chronic Diseases, Birmingham, AL; Pamela J Schneier, Univ of Minnesota, Minneapolis, MN; O D Williams, Univ of Alabama, Birmingham, AL

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 criterion) compared to lower fitness.

Methods: Over 20 years, fitness was inversely related to the incidence of dyslipidemia in men and women. 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 health through higher FEV1, and FVC at baseline and this benefit is maintained through smaller declines in pulmonary function over time.

P126

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

Roberto Elosua, Institut Municipal d’Investigació Mèdica, Barcelona, Spain; Antonio Segura, Instituto de Ciencias de la Salud de Castilla la Mancha, Talavera de la Reina, Spain; Marta Tomás, Institut Municipal d’Investigació Mèdica, Barcelona, Spain; Miquel Font, Institut Universitari de Ciències de la Salut, Palma de Mallorca, Spain; Elena Aldasoro, Gobierno Vasco, Vitoria, Spain; Mariano Serrano, Institut Municipal d’Investigació Mèdica, Barcelona, Spain; Gema Vega, Unidad de Cuidados Intensivos, Albacete, Spain; Jordi Forteza, Institut Universitari de Ciencies de la Salut, Palma de Mallorca, Spain; Josep M Aragay, Gobierno Vasco, Vitoria, Spain; Jaume Marrugat, Institut Municipal d’Investigació Mèdica, Barcelona, Spain

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 70 who 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, moderate, and high intensity (≤2.5, 2.5–4.4 METs, and ≥4.5 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 the lowest activity levels (500 and ≥1000 METs) and no significant risk reductions at the highest (≥3000 METs). The lowest activity levels were 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 health through higher FEV1, and FVC at baseline and this benefit is maintained through smaller declines in pulmonary function over time.
Table 1. Baseline values (mean(SD))

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Age</th>
<th>Female (%)</th>
<th>BMI</th>
<th>Systolic blood pressure (mmHg)</th>
<th>LDL-cholesterol (mg/dL)</th>
<th>HDL-cholesterol (mg/dL)</th>
<th>HbA1c (%)</th>
<th>Estimated peak VO2 (ml/kg/min)</th>
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</thead>
<tbody>
<tr>
<td>Obx</td>
<td>532</td>
<td>51 (14)</td>
<td>80</td>
<td>23.5 (9.6)</td>
<td>122 (19)</td>
<td>137 (22)</td>
<td>5.0 (6.0)</td>
<td>25.6 (6.9)</td>
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</tr>
<tr>
<td>RCT</td>
<td>503</td>
<td>67 (7)</td>
<td>56</td>
<td>26.5 (2.2)</td>
<td>140 (17)</td>
<td>135 (28)</td>
<td>5.6 (0.6)</td>
<td>20.9 (3.7)</td>
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</table>

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

<table>
<thead>
<tr>
<th>Group</th>
<th>Body weight (kg)</th>
<th>Systolic blood pressure (mmHg)</th>
<th>LRL-cholesterol (mg/dL)</th>
<th>Estimated peak VO2 (ml/kg/min)</th>
<th>Visits to exercise facility (mean)</th>
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<tbody>
<tr>
<td>Obx</td>
<td>-1.2”</td>
<td>-2.1”</td>
<td>-0.1”</td>
<td>2.1”</td>
<td>1.2”</td>
</tr>
<tr>
<td>RCT</td>
<td>-1.6”</td>
<td>-2.3”</td>
<td>-0.3”</td>
<td>-0.7”</td>
<td>2.6”</td>
</tr>
</tbody>
</table>

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

Gary A Mayman, William N Evans, Ruben J Achermania, Katriina T Kip, Carlos F Luna
Abraham Rothman, Children’s Heart Ctr and Univ of Nevada, Sch of Medicine, Las Vegas, NV; Lorie Coviello, Children’s Heart Ctr, Las Vegas, NV; Humphrey Restrepo, Children’s Heart Ctr and Univ of Nevada, Sch of Medicine, Las Vegas, NV

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 211 children recruited from a rural sample in Texas. The metabolic syndrome (MS) is related to insulin sensitivity (IS), predicts the development of cardiovascular risk factors, and suggests that PA may be an important strategy to increase IS.

Physical activity (PA), that improve IS and MS in children are likely to reduce adult CVD risk. 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 80 girls) at average age 19.0 years. The PA score was calculated using the Godin PA algorithm. IS was measured using a euglycemic insulin clamp as part of a protocol evaluating the insulin resistance on the development of cardiovascular risk factors. A MS score (the mean of 3-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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>PA Score Range</td>
<td>0-4.9</td>
<td>5-7.7</td>
<td>8-9.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>85.2 (1.6)</td>
<td>85.1 (1.4)</td>
<td>85.1 (1.6)</td>
<td>0.18</td>
</tr>
<tr>
<td>HDL Chol (mg/dl)</td>
<td>42.8 (1.1)</td>
<td>42.6 (1.1)</td>
<td>44.8 (1.1)</td>
<td>0.30</td>
</tr>
<tr>
<td>Trips (mg/dl)</td>
<td>106.3 (0.9)</td>
<td>86.8 (0.1)</td>
<td>95.0 (0.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>110 (1.2)</td>
<td>112 (1.2)</td>
<td>111 (1.5)</td>
<td>0.68</td>
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<tr>
<td>Fasting Glucose (mg/dl)</td>
<td>88 (1.0)</td>
<td>86 (0.7)</td>
<td>86 (0.7)</td>
<td>0.36</td>
</tr>
<tr>
<td>Insulin Sensitivity (mg/kg/min)</td>
<td>10.0 (4.6)</td>
<td>10.7 (4.0)</td>
<td>12.4 (6.4)</td>
<td>0.003</td>
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<tr>
<td>MCI Cluster Score</td>
<td>0.1 (0.06)</td>
<td>-0.032 (0.06)</td>
<td>-0.9 (0.06)</td>
<td>0.08</td>
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</tbody>
</table>

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

Marie A Krousel-Wood, Leah Berger, X Jiang, Larry Blonde, Ochsner Clinic Foundation, New Orleans, LA; Leah Myers, Larry Webber, Tulane Health Sciences Ctr, New Orleans, LA

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 participated in the study, 76/94 (79%) of whom were female, 47% (37/76) were randomized to intervention, 68% (52/76) were women, 43% (36/76) were black, and mean age was 56.6 ± 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<0.05) and quality of life (mean change 8.1 versus -0.9, respectively, p<0.01) 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.

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

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Background: There is evidence that physical activity is involved in protection for CVD. However, there is a controversial and beneficial effect of vigorous physical activity on 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 females aged ≥60 years, recruited from the population of 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% and 45%, respectively) were included. 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 analyzed in quintiles. In separate analysis walking (>1hr/week, MET-h=6.4±8.4) was compared with vigorous physical activity (sport>1hr/week, MET-h=96±173) 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) (<0.001) 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 (<0.001), WHR (<0.001) and PR (<0.001), 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
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 diseases. 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 Baroque PA survey were used to compute 4 PA indices: 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, 29% were obese, and 13% were smokers. Self-reported PA scores declined with age and increased with education (p’s < 0.001) except for WRK, which was inversely related to education and income (p < 0.001). 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 < 0.001). 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.

P136 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 sedentary, are increasing at an alarming rate 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 (V02max, 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 intervention, 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. Results: Participants were children of both genders, and different races, ethnicities, and regions of the US. Across studies, improvements were greater for intervention vs. control groups on: V02max (1.48 mL/kg/min), body fat percent (0.101%), waist circumference (1.1 cm), heart rate (0.4 b/min), total serum cholesterol (63.6 mg/dL), fasting insulin level (.7 μU/mL) and heart health knowledge (0.14% 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.

P137 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. Decreases in circulating EPC function has been shown to contribute to increased 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 true, this may underlie the relationship between vascular aging with age-related disease. We hypothesize 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 and umbilical cord blood samples collected after 147 healthy donors aged 21-75 years, 14 age-matched (MA: 47 ± 4 years) and 16 older (0: 63 ± 1 years). 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 basic EPC caspase-3 activity. However, in response to staurosporine, active caspase-3 concentrations were significantly higher (~50%) in 0 (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 0 men have completed a 3-month EX intervention (walking 5 1/2 d/wk, 56 min/ wk @ 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.

P138 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 codes. However, in hospital discharge data, criteria for determining whether an individual patient met the criteria for the AMI code within the hierarchy of diagnosis variables. Higher 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 African-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 representativeness 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.

P139 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 heart failure in 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 groups: WBC < 5, WBC 5–9, WBC 10–15, 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 homogeneous 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 < 0.001, 95% CI). Independent predictors included sex, functional class, Killip class, hypertension, proteinuria, 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.

P140 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: Per-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, infection, 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 0.87–1.28), but BMI 30–34.9 (OR 1.39, 95%CI 1.31–1.70) and ≥35 were (OR 1.62, 95%CI 1.40–2.00) 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. Conclusions In this study, the impact of obesity was not direct; it may indirectly impact outcomes through a synergistic effect upon other risk factors such as hypertension and diabetes.

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 methodologies 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 sorted 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 < 0.001), included a different proportion of women (63% vs. 45%, p < 0.001), had more comorbidities (1.73 vs. 1.34, p = 0.0015), and higher cardiac risk scores (0.47 vs. 0.29, p < 0.001) compared to MPI (N=17,855) 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<0.005), with an average difference of $800 (95% Confidence interval: $39 to $1,934). 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.

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, those 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 - 0.98). 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.

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 Health Risk Scoring model with Smirneact 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 $833 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.

Predictors of and Barriers to Medication Adherence in a Minority Population


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 City in July and August 2005 were systematically interviewed and screened for CVD risk factors (n = 214: 63% African American, 29% Hispanic, 7% 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 (33%) 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 < 0.004), 2) not having health insurance (p < 0.01), 3) not believing one needs medication (p < 0.001), and 4) not feeling well when taking medication (p < 0.004). 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.
Prevalence of Malignant Hypertension in the UK General Practice

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Introduction: Determining predictors of elevated total cholesterol (TC), elevated low density lipoprotein cholesterol (LDL-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 1/1/2000 and 10/31/2004, used statins for at least 6 weeks, and had ≥2 years of pre- and 1-year of post-statins 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 LDL-C (<1.0 mmol/L), and <1.3 mmol/L, for men and <1.0 mmol/L, for women) and elevated TG (≥1.7 mmol/mL) 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 59% of patients did not reach optimal levels of TC, LDL-C and TG respectively. Failure to attain CV goal was explained by smoking (Odds Ratio = 1.7, 95% Conf. Int. [1.06–2.30] and baseline TC = 6.2 mmol/L (4.31 [3.96 – 4.69]). Low follow-up LDL-C was associated with a baseline HDL-C level of <0.9 mmol/L in both men (4.17 [3.16–5.47]) 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]), and 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.

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

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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 signs and 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 death (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. 28), and more hypertension (53% vs. 17%) and diabetes (19% vs. 5%). WTH women had significantly higher total cholesterol (218 vs. 198) 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 52.2%, compared to 5.0% and 6.0% in WTH (Results). 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.

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. Methods: 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 ethically diverse metropolitan population during the years 1996–2000. Population estimates were calculated using the 2000 U.S. Census Public Use Microdata Sample (PUMS). Death data were obtained from the 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, and tertile of 15-year age group, and race/ethnicity. Other 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 3.4 for “no transport” deaths to 1.7 for “transported” deaths. Conclusion: Gender RR for white men aged 50–64 years was: 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.

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 hypertension are often denied Angiotensin Converting 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 from 10/1/00– 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 mmHg at enrollment. Endpoints were all cause mortality and hospitalization. Results: Study criteria was met by 154 subjects (hypotensive n = 24 [Group 1]; normotensive n = 130; Group 2). At enrollment, EF and SBP were similar between groups. In Group 1 was 16.4% and 92.8% vs. 15.6% and 93.4% in Group 2 (p = 0.001 and p = 0.008, respectively). Other variables were similar between groups. At enrollment, 94% of subjects with hypertension were successfully placed on ACEI/ARB. At one year, 81% were successfully maintained on ACEI/ARB, with 50% tolerating maximal doses. At 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 = 0.088). 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 different compared to normotensive patients.

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

Eric J Stanek, Kos Pharmaceuticals, Inc, Cranbury, NJ; Ralph Quimbo, Mark J Cziraky, Inability of High-Intensity Statin Therapy Alone to Optimize Lipid Values in a Coronary Disease Risk or Risk-Equivalent Population

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and persisted despite high-intensity statins. These data support a strong population-based need for the addition of one or more drugs) with substantial effects on LDL-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

<table>
<thead>
<tr>
<th>LDL-C (mg/dL)</th>
<th>HDL-C (mg/dL)</th>
<th>TG (mg/dL)</th>
<th>Non-HDL-C (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 150</td>
<td>&gt; 40</td>
<td>&gt; 150</td>
<td>&gt; 150</td>
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</table>

**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 2002–2004, 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 60% 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 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. 5.6 (S) per 1000 patients/year; and 3.4 (A) vs. 2.5 (S) per 1000 patients/year. 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 (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 mm Hg. A brief standardized telephone interview sought to confirm their 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 (86%) of 50 women and 46 (92%) of 50 men. Among 5 women and 10 men in the absence of a new diagnosis, antihypertensive treatment, or elevations in BP without a diagnosis or treatment. Meanwhile, the absence of hypertension was confirmed in 45 (80%) 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.

**P152 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 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 (370.8 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/m²), systolic BP and diastolic BP (mm Hg) at baseline among study participants were 58.7, 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.

**P153 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 355,600, respectively. The majority of the hypertension–related deaths were from vascular diseases (427,971 in men and 334,058 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.
Hypertension and Metabolic Syndrome

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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 hypertension (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.
Treatment-Associated Diabetic Blood Pressure Is Not Associated with Poorer Outcomes in Older Patients: The Geisinger Clinic Population

Robert D Langer, Geisinger Health System, Danville, PA

Introduction: Prior work has suggested that higher rather than lower diabetic 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 adverse outcomes in every age group, with an especially harmful effect at earlier ages among 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 academic medical center in a geographically and economically diverse rural population of approximately 2.5 million in central Pennsylvania. DBP change (DBPchng) 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 at any time after 1/1/2004. The 2-year survival for these groups was 82.5%, 75.7%, 74.2%, 71.5%, and 70.9% for DBPchng = ±20 mmHg, 55.7%, 53.1%, 50.3%, 47.5%, and 45.0% for DBPchng = ±10 mmHg, 44.6%, 42.5%, 40.4%, 38.5%, and 36.4% for DBPchng = ±5 mmHg, and 31.7%, 29.5%, 27.3%, 25.1%, and 23.0% for DBPchng = ±0 mmHg. Results: The joint effects of systolic blood pressure (SBP) and air pollution on measures of ventricular repolarization have not been studied. We examined them in EEAWH, an ancillary study of Women’s Health Initiative clinical trial participants. We used data from EPA Air Quality System monitors at 10 national- and 10 regional-scale, log-transforming to a spatially interpolate daily mean, region-specific concentrations of ambient particulate matter <10 μm in diameter (PM10) at geocoded addresses of 78,575 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, ≥4% 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]; 1 [414]; [416], number of antihypertensives used (0 [410], 1 [413]; 2 [415]; 3 [417]; PM2.5 quintile (1–2 [412]; 3–5 [413]; 3–5 [412]). We used center-specific linear models adjusted for demographic, clinical, temporal and climatic factors to estimate associations between QT and PM2.5 on exam days and random-effects meta-regression to combine center-specific regression coefficients and test for interactions. Associations differed by hypertension severity: 25 μg/m3 increases in PM2.5 (10th of the 24-hr National Ambient Air Quality Standard [419]) 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%, -0.1%) vs. +0.1% (0.0%, +0.3%) changes in QT among women using ≤3 antihypertensives (p = 0.02). We observed smaller findings for PM10, and after excluding normotensive, adjusting for left ventricular mass, conduction defects, drugs associated with torasreds 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.

Beliefs Related to High Blood Pressure in African Americans Scale: Preliminary Reliability 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-sensitve measures to assess HTN-related 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 hypothesis-testing to assess correlations among the variables, total BRHBPAA Scale and subscales. Results: Mean (sd) age was 33.7 (7.0) years with SES (Hollingshead) = 34.7 (17.2), SBP = 114 (22), DBP = 87 (9) and BMI = 29.7 (9.7). 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 Scale overall score (r = 0.313, p < 0.000) and SBP (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.
Young Adults with “Spurious” Systolic Hypertension Have an Increased Risk of Coronary Heart Disease

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Background: Systolic hypertension (SH), 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 SH 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 Amsterdam 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 general transfer function. SH was defined as brachial systolic blood pressure (SBP) >140 mmHg, brachial diastolic blood pressure (DBP) <90 mmHg, and central SBP >124 mmHg (90th percentile). The Framingham risk score was calculated. Results: SH was diagnosed in 57 men (16.1%, 57 of 352; 95% confidence interval, 12.3–20.0). Based on brachial SBP, SH 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 SH patients towards the hypertension group, the estimated Framingham risk declined in the hypertensive group (Table). The risk in the SH group remained constant. Conclusion: SH 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.

<table>
<thead>
<tr>
<th>BP Measure</th>
<th>Unadjusted HR (95% CI) per SD</th>
<th>Likelihood Ratio</th>
<th>AIC</th>
<th>BIC</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stroke</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>1.75 (1.66–1.85)</td>
<td>&lt;0.001</td>
<td>302.0</td>
<td>14966.14</td>
<td>14974.64</td>
</tr>
<tr>
<td>DBP</td>
<td>1.71 (1.60–1.82)</td>
<td>&lt;0.001</td>
<td>232.6</td>
<td>15053.51</td>
<td>15044.01</td>
</tr>
<tr>
<td>PP</td>
<td>1.59 (1.49–1.65)</td>
<td>&lt;0.001</td>
<td>134.5</td>
<td>15133.85</td>
<td>15132.35</td>
</tr>
<tr>
<td><strong>Heart Failure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>1.82 (1.71–1.93)</td>
<td>&lt;0.001</td>
<td>294.6</td>
<td>11211.77</td>
<td>11212.07</td>
</tr>
<tr>
<td>DBP</td>
<td>1.74 (1.62–1.87)</td>
<td>&lt;0.001</td>
<td>215.5</td>
<td>12196.30</td>
<td>12195.65</td>
</tr>
<tr>
<td>PP</td>
<td>1.57 (1.47–1.68)</td>
<td>&lt;0.001</td>
<td>146.5</td>
<td>12299.95</td>
<td>12298.45</td>
</tr>
</tbody>
</table>

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

P164 Cardiovascular Risk Factor In Awareness in a Racial and Ethnic Minority Population

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Introduction: Cardiovascular disease (CVD) is the leading cause of 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 minority groups. Methods: This was a cross-sectional study of 1,291 African-American adults (>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. 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 emerged.

P165 Hemoglobin A1c, Concentrations and the Risk of Developing Hypertension in Nondiabetic Middle-Aged and Older Women

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Hemoglobin A1c (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 were collected. We considered quintiles and clinical cutoffs of HbA1c for the risk of incident hypertension, defined as either a new physician diagnosis, the initiation of antihypertensive therapy, SBP ≥140 mmHg, or DBP ≥90 mmHg. During 10.9 years of follow-up, 5,823 (28.6%) women developed hypertension. In age-adjusted models, the RR of hypertension from the lowest (<3.0%) to the highest (≥5.5%) HbA1c group was 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 HbA1c concentrations were assessed. For clinical cutoffs across a wider range of HbA1c concentrations (<5.0, 5.0–5.5, 5.5–6.0, ≥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 0.42), 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/m²) 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 emerged.

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values (mmHg): TC 211.40; LDL-C 131.35; HDL-C 50.15; TG 155.75; Non-HDL 162.29.

Conclusions: In the total HTN population and all subgroups except for males and females ≥65 yrs., modeled ENR/LI dosing (1qg/40mg & 2qg/40mg) yielded combined optimal lipid values significantly more often than ATORV (40 & 80), ERN (2g) or lovastatin (LOVA) (40mg). In males and females ≥65 yrs, ENR/LI (40mg) was equivalent to (80 mg).

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

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 ≥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 well defined. Methods: INVEST, a prospective, randomized trial comparing two antihypertensive strategies, assessed incidence of death, nonfatal MI or nonfatal stroke (primary outcome, PO) and other cardiovascular events (secondary outcomes, SO) in 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 follow-up compared with longer follow-up. Results: Patients were 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 ≥140/90mmHg. 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 ≥140/90mmHg 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.

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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-clinician 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/client 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, unrefined 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. Dietary guidelines (95–100%, 80–85/90) though 77% (59/77) used labels to make food decisions. Most rated the clinic excellent: "excellent" (41%, 28/69) not at all (59%, 42/69) with 1% (1/71) not sure. The majority reported not missing medication doses over the previous week (80%, 57/72), 19% (14/72) missed 1–2 doses and 1% (1/72) missed 5 or more doses. Of these, 81% (59/72) 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 through less than half reported following this recommendation. Results: Overall the multidisciplinary method of education and provider-patient 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.

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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 three times a week, and a resistance bicycle three times 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 to 30 in 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 by 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, was -0.15 mmHg to -1.15 mmHg; p=0.90) and -1.37 mmHg (95% CI: -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, 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 risk judgments for each inconsistent information provided by HFS employees 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.
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 2003 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) >30.05 (OR=1.03, 95% CI 1.01, 1.05) was 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.

Methodological Challenges in Studying Incident Hypertension: Lessons 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 daily-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 of hypertension five 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 9/6mmHg 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 80–89mmHg 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 1.05 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.

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 or 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 1988–1992, 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 US adult population was 590/100,000 person-years (1988–2003). 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% (263/307) 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% (66/209). 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.

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 treatment, 20% was also following a low-salt diet. Male hypertensive subjects were more frequent than females (65% vs 54%, P < 0.001). Forty-four percent of patients was hypertensive, the prevalence of HTN increased with age in both sexes (P < 0.001). Only 40% of hypertensive patients was under anti-hypertensive treatment and was also following a low-salt diet. Male hypertensive subjects were more frequent than females (65% vs 54%, P < 0.001), but were more treated than males (45% vs 34%, P < 0.0001). Forty-four percent of patients was hypertensive, the prevalence of HTN increased with age in both sexes (P < 0.001). Only 40% of hypertensive patients was under anti-hypertensive treatment and was also following a low-salt diet. Male hypertensive subjects were more frequent than females (65% vs 54%, P < 0.001), but were more treated than males (45% vs 34%, P < 0.0001). Forty-four percent of patients was hypertensive, the prevalence of HTN increased with age in both sexes (P < 0.001). Only 40% of hypertensive patients was under anti-hypertensive treatment and was also following a low-salt diet. Male hypertensive subjects were more frequent than females (65% vs 54%, P < 0.001), but were more treated than males (45% vs 34%, P < 0.0001). Forty-four percent of patients was hypertensive, the prevalence of HTN increased with age in both sexes (P < 0.001). Only 40% of hypertensive patients was under anti-hypertensive treatment and was also following a low-salt diet. Male hypertensive subjects were more frequent than females (65% vs 54%, P < 0.001), but were more treated than males (45% vs 34%, P < 0.0001). Forty-four percent of patients was hypertensive, the prevalence of HTN increased with age in both sexes (P < 0.001). Only 40% of hypertensive patients was under anti-hypertensive treatment and was also following a low-salt diet. Male hypertensive subjects were more frequent than females (65% vs 54%, P < 0.001), but were more treated than males (45% vs 34%, P < 0.0001). Forty-four percent of patients was hypertensive, the prevalence of HTN increased with age in both sexes (P < 0.001). Only 40% of hypertensive patients was under anti-hypertensive treatment and was also following a low-salt diet. Male hypertensive subjects were more frequent than females (65% vs 54%, P < 0.001), but were more treated than males (45% vs 34%, P < 0.0001).
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 included if they were first assessed on level of trust with usual source of medical care (3-point scale, ranging “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 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). 17% of these, 177 (42%) 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.

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

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. To examine 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 < 0.003); greater in blacks than whites (p < 0.002); less among those arriving by EMS than by other modes of transportation (p < 0.0001); less among certified primary stroke centers than hospitals without primary stroke center certification (p < 0.0002); less among those independently ambulating than those who were not (p < 0.02); and less among those who arrived within 3 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 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.

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

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-ethyl) 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), or 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 < 0.003); greater in blacks than whites (p < 0.002); less among those arriving by EMS than by other modes of transportation (p < 0.0001); less among certified primary stroke centers than hospitals without primary stroke center certification (p < 0.0002); less among those independently ambulating than those who were not (p < 0.02); and less among those who arrived within 3 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 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.

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

P179 Short- and Long-term Prognosis After Cerebrovascular Disease and Acute Myocardial Infarction in the Netherlands


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 (43%, 5.625 of 12.746) cause of death. In 30% (4.468 of 12.746) cause of death was other than cardiovascular origin. The AMI cohort consisted of 14.463 men (46 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. Conclusion Short- and long-term mortality after CVA or AMI is high. In particular mortality risk for SAH and ICH. The mortality risks for ischemic stroke and AMI are quite similar.

Reference: "Follow-up was available for 5842 participants enrolled since February 2005. Results. There were 415 participants who had P-Dx-S (54 or stroke symptoms without P-Dx-S). 17% of these, 177 (42%) 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."
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 mortality 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) in each case, and/or 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 death were obtained from the hospital discharge certificate and/or the National Statistical Office. 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. Causes of death were divided into 5 groups: malignancy (10%), diabetes mellitus complications (9%), 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 1.22; 95%CI 1.10–1.37), subtypes of ICH (RR 1.34; 95%CI 1.17–1.54) and SAH (RR 1.68; 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 stroke 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 may increase the risk of death.
Table: Platelet activation measures by LDL-C strata and statin use

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

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The Relation Between Polysaturated Fatty Acids and Lipoprotein Subclasses

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Background: N-3 polysaturated 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 40–49. They excluded those taking cholesterol-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, platelet aggregation, alcohol consumption, and 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 kg/m2. 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 LDL 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, but not with LDL-C. Each of EPA and DHA had significant association with triglycerides and large LDL particles. Ala had no significant association with each lipoprotein subclass. After adjusting for the covariate, only DHA had independent associations with small LDL particle concentration and size. Each of EPA and DHA had significant association with each lipoprotein subclass. After adjusting for the covariates, only DHA had independent associations with small LDL particle concentration and size. Each of EPA and DHA had significant association with each lipoprotein subclass. After adjusting for the covariates, only DHA had independent associations with small LDL particle concentration and size. Each of EPA and DHA had significant association with each lipoprotein subclass.

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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 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 10,613 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 quintiles) 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 quintiles were similar to those in the first quintile. (Table 1) 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.

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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 lipid measures and novel lipoprotein factors differ between hypertensive AA and NHW 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 low-density lipoprotein [LDL] size) and ‘novel’ [apo]B-100 and apo A-I kinetic behavior. Subjects were followed for 6 years. Analyses were performed using generalized estimating equations to account for intraclass correlations. Results: After adjustment for age, plasma lipoprotein measures differed significantly between the two ethnic groups (Table). In multivariable-adjusted models 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 = 0.003), and ox-LDL-C (P < 0.0001) and Lp(a) (P < 0.0001). After covariate adjustment, no significant difference was noted in total cholesterol levels (P = 0.24). Conclusions: Significant ethnic differences were observed in conventional and novel lipoprotein measures 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

<table>
<thead>
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<th>Lipid</th>
<th>NHW</th>
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<tr>
<td>AA</td>
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<tr>
<td>LDL-C</td>
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<td>TG</td>
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<td>Lp(a)</td>
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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 differences in lipid and lipoprotein profile, predominantly higher LDL-C, VLDL-C and HDL-C have been observed in males compared to females. These gender differences are influenced by menopausal status and age. To investigate mechanisms involved, apolipoprotein (apo) B-100 and apo A kinetic behavior was studied in 20 younger men (n = 16), postmenopausal women (n = 10) and premenopausal women (n = 10). ApoB-100 and apo A-I kinetic behavior was studied in 20 younger men (n = 16), postmenopausal women (n = 10) and premenopausal women (n = 10). ApoB-100 and apo A-I kinetic behavior was studied in 20 younger men (n = 16), postmenopausal women (n = 10) and premenopausal women (n = 10). ApoB-100 and apo A-I kinetic behavior was studied in 20 younger men (n = 16), postmenopausal women (n = 10) and premenopausal women (n = 10). ApoB-100 and apo A-I kinetic behavior was studied in 20 younger men (n = 16), postmenopausal women (n = 10) and premenopausal women (n = 10). ApoB-100 and apo A-I kinetic behavior was studied in 20 younger men (n = 16), postmenopausal women (n = 10) and premenopausal women (n = 10).
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 >40 who did not have arthritis. We used multivariable logistic regression to examine the association between statin use and prevalence of MSP at different anatomical regions. Results: Among 3636 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 1.5 (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.

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 6665 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 than LDL-C (HR 1.56, 95% CI 0.73–2.50; P = .002; Figure). After adjustment for LDL-C, 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 20% 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.

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 model projection was based on Framingham. The cost of statins was set at $460.65/year (generic lovastatin 40mg, or $897.65/year (atorvastatin 80mg, if used 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 533K CHD deaths each year over the next 10 years. Full ATPIII compliance would prevent 162K MI's and 110K CHD deaths/year at an increased cost of $418/yr (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 ATPIII 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.
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 $\geq 50\%$. Major cardiovascular events were defined as death, myocardial infarction (MI), and cerebral vascular accident (CVA). Results: Complete data were available on 221 men (mean age 51 years; 65\% of whom <59 years) and 130 of 255 women (130 of 255 years; 64\% of whom <59 years). The mean total cholesterol values were: total 207$\pm$42 mg/dL; LDL 122$\pm$30 mg/dL; HDL 51$\pm$14 mg/dL and triglyceride 171$\pm$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 values for total, LDL and HDL cholesterol were not different in subjects suffering events and non-HDL cholesterol may be crucial for making further progress in CHD management. Physician compliance with guideline recommendations on managing triglyceride and non-HDL cholesterol may be crucial for making further progress in CHD management.

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 prospective Atherosclerosis Risk in Communities (ARIC) Participants. 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 250 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): 1.4, 95% CI: 1.0, 1.9) and among former smokers (HR: 1.7, 95% CI: 1.0, 2.9), 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.

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

Jaimie S Lima, Pedro C Alexandre, Leila S Leão, Lucia G Costa, Daniele L Fontoura, Marina J Caiaffa, Susana Costa, Pedro Monteiro, Silvia Monteiro, Francisco Gonçalves, Lino Gonçalves, Mario Freitas, Luis A Providência, Coimbra Univ Hosp, Coimbra, Portugal

Background: Lipid profiles influence 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 onIH 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 quartiles. 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±28.2 mg/dL. Previous statin therapy was significantly higher in ApoA1 quartil with the highest mortality rate (p=0.003). There was an inverse relationship between IH mortality and ApoA1 with ApoB and ApoA1 values (table 1), while with ApoB 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

<table>
<thead>
<tr>
<th>Apo B (mg/dL)</th>
<th>IH mortality rate</th>
</tr>
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<tbody>
<tr>
<td>[33–83]</td>
<td>9.6</td>
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<tr>
<td>[83–100]</td>
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</tr>
<tr>
<td>[100–121]</td>
<td>1.6</td>
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<tr>
<td>[121–210]</td>
<td>0.8</td>
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<tr>
<td>Apo A (mg/dL)</td>
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<tr>
<td>[31–107]</td>
<td>3.4</td>
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<tr>
<td>[107–121]</td>
<td>3.2</td>
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<tr>
<td>[121–137]</td>
<td>5.2</td>
</tr>
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<td>[137–229]</td>
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</table>

Provider Knowledge Deficit of the Adult Treatment Panel III 2004 Update

Diane S Osborn, Univ of Washington, Seattle, WA

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 optimal goals identified in the 2004 update to the ATR III, and found that only 18% of those at high risk for CHD attained their goal. One factor that may limit the applicability of the guidelines 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’, ARNP’s, and PNs’ knowledge of the 2004 ATR III update, and to test the hypothesis that knowledge levels of the updated ATR III guidelines were the same between providers. The study employed a non-experimental descriptive design using a 21 item original questionnaire.
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 (10 mg: p=0.001, ½ 20 mg: p=0.40; 40 mg: p=0.22). For subgroup "full dose 40 mg ATOR", the LDL decreased from 94.8 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 small reduction in ATOR dose, and d) did not produce skeletal muscle toxicity, hepatic toxicity, or reduce QOL.

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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 controlled 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= 9,250). The American Heart Association (AHA) and the Japanese Circulation Society (JCS) 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 Coronary Care Unit (CCU) versus non-CCU care specialties including women’s care (46%).

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=0.002, 95% CI: 1.05–2.15). Taking the smallest 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: 1.31–2.96). 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.

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Optimal Lipid Value Achievement in Older Women Utilizing Extended-Release Nicin/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 21.1 M member managed care patient database based on a thorough examination of the current curriculum on lipid management and CHD prevention among ARNP training programs.

Results: Analysis included 22,066 females: (mean ± SDS): age 67 ± 13 years, surgery prevention 46% 70% with CHD prevention 54% 70%, diabetes 30% 70%, dyslipidemia 68% 87% with a mean age of 73 ± 8 years. Only 29% of patients met LDL-C and TG targets in 2004 AHA cardiovascular disease prevention guideline, and population treatment effects of extended-release niacin/lovastatin 2000/40 mg (ERNL) were modeled using current product labeling.

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 receiving LDL-C and TG targets remains low and most ages are projected to achieve individual and combined optimal lipid values with ERNL therapy.
TMI Risk Score is Inversely Correlated to Apolipoprotein A1 Levels in Acute Coronary Syndrome Patients

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Background: The influence of TMI 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 TMI risk score in ACS patients is not established. Aim: To evaluate the relationship between TMI risk score and Apo 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 apolipoprotein (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, dyslipidemia 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 TMI risk score increased, ranging TIMI risk score 0 to 1.4 to 0.7 mg/dL (p=0.001) and with severity of ApoA1 levels by 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 TMI risk score and ApoA1 (B) levels, reinforcing the usefulness of both prognostic markers in ACS patients.

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 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=116), mild apnea if 0 < AHI < 1 (N=208), and moderate to severe if AHI ≥ 1 (N=84). The weighted ANCOVA 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-snorers. 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>
<thead>
<tr>
<th>Apnea Level</th>
<th>Scoring = Yes (SBP) (SE)</th>
<th>Scoring = No (DBP) (SE)</th>
<th>Scoring = Yes (DBP) (SE)</th>
<th>Scoring = No (SBP) (SE)</th>
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<tr>
<td>No Apnea</td>
<td>110 (1.84)</td>
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<td>Mild Apnea</td>
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<td>0.05</td>
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P207 Pericoronary Epicardial Adipose Tissue Is Strongly Related to the Metabolic Syndrome: A Population-Based Study

Alexander de Vos, Mathias Prokop, Matthias Meis, Pieter Doevendans, Cornelis Roos, Univ Med Ctr Utrecht, Utrecht, The Netherlands; Brigitta Veithuis, Julius Cntr, Univ Med Ctr Utrecht, Utrecht, The Netherlands; Maarten-Jan Cramer, Univ Med Ctr Utrecht, Utrecht, The Netherlands; Marie-Louise Boucher, 2 van de Schouwenstraat,3518 CE Utrecht, The Netherlands; Josef Coresh, Johns Hopkins Univ, Baltimore, MD; Ron C Hoogeveen, Baylor College of Medicine, Houston, TX; Michael Steffes, Univ of Minnesota, Minneapolis, MN; Brad C Astor, Johns Hopkins Univ, Baltimore, MD

Purpose: To evaluate the pericoronary epicardial adipose tissue (EAT) in ACS patients and whether an increased prevalence of peri-coronary EAT is associated with the metabolic syndrome. Methods: We performed a cross-sectional study among 573 healthy postmeno- pausal 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 (RA), 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±5). Average EAT area was 236.9±170.2 mm² (range 80.7–937.0) for the RCA area, 192.6±122.7 mm² (range 30.7–908.4) for the LAD area and 192.4±90.5 mm² (range 28.7–519.9) for the LCX area. Overall average EAT areas were 236.8±94.9 mm² (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

Brad C Astor, Johns Hopkins Univ, Baltimore, MD; Ron C Hoogeveen, Baylor College of Medicine, Houston, TX; Michael Steffes, Univ of Minnesota, Minneapolis, MN; Tabor Fuko, Univ of Mississippi Med Ctr, Jackson, MS; Josei Coresh, Johns Hopkins Univ, Baltimore, MD

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 CVD events in the general population. These data support recent recommendations defining CVD and stratifying risk based on both decreased kidney function and albuminuria.

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

Francesco P Cappuccio, Univ of Warwick, Coventry, United Kingdom

**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 a evidence of a relationship between short sleep duration and obesity and to obtain a quantified estimate of the risk, among both adults and children. **Methods:** We performed a systematic search of published, according to Cochrane’s standard review methodology up to August 2006. Authors were contacted by e-mail 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/m². 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 is 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.

### The Epilepsy Heritability, and Genetic Linkage of C-Reactice 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 correlation 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. QT linkage analysis was performed using the multivariate 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. The heritability of CRP explained 57% of the variability of risk factors. The heritability for the age, sex and BMI adjusted CRP residual 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 295QCP 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.

### 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<0.0001). 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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**P211**

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**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**

Luis O Rustveld, Valory N Pavlik, Baylor College of Medicine, Houston, TX

**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. **Methods:** 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. Methods: 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.

**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 quintile 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.

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

Bryan C Bordeaux, Diane M Becker, Nauder Faraday, Lisa R Yanek, Taryn F Moy, Lewis C Becker, Johns Hopkins Univ Sch of Medicine, Baltimore, MD

**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 activate 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 1708 apparently healthy 21 to 79 year old relatives of a proband with CAD at a young age (<30 years). Mean age of the study population was 44.9±13.4 years, 43% were male, and 56% Black. Results: Mean CRP was 2.73±1.3 ng/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 indicated 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.

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<th>Platelet assay</th>
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<th>IL6**</th>
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<td>Q1: 0.16</td>
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<td>0.69</td>
</tr>
<tr>
<td>Q2: 0.69</td>
<td>2.77</td>
<td>7.49</td>
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<tr>
<td>Q3: 2.77</td>
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<tr>
<td>p**</td>
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</table>

*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

Robert C Kaplan, Albert Einstein College of Medicine, Bronx, NY; Lawrence A Kingsley, Univ of Pittsburgh, Pittsburgh, PA; A R Sharrett, Xiuhong Li, Johns Hopkins Bloomberg Sch of Public Health, Baltimore, MD; Jason Lazar, State Univ of New York Downstate Med Ctr, Brooklyn, NY; Phyllis C Tien, Univ of California, San Francisco, and San Francisco Veterans Affairs Med Ctr, San Francisco, CA; Wendy Mack, Keck Sch of Medicine, Univ of Southern California, Los Angeles, CA; Marjoge H Cohen, Stronger (formerly Cook County Hosp) and Rush Med Ctr, Chicago, IL; Lisa Jacobson, Stephen J Gange, Johns Hopkins Bloomberg Sch of Public Health, Baltimore, MD

Background: We examined 10-year predicted coronary heart disease (CHD) risk among HIV-infected and HIV-uninfected participants in the Women’s Interagency HIV Study (WHI) and Multicenter AIDS Cohort Study (MACS).

Methods: We used cross-sectional WHI and MACS data contributed by 1,455 HIV-infected women and 931 HIV-infected men, as well as 1,099 HIV-uninfected women and 576 HIV-uninfected men 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 participants compared with HIV-uninfected controls (OR [95% CI] for total CHD = 1.44 [1.05, 1.98]; OR for hard CHD events = 1.13 [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 [0.45, 1.12] and OR for hard CHD events = 0.64 [0.33, 1.25]). Compared with current prostate-specific antigen (PSA)-based HAART, current non-PSA 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-infected individuals have higher predicted CHD risk compared with HIV-uninfected individuals, but not among women. HIV-infected individuals who have low income level or who are treated with non-PSA-based HAART may benefit from targeted screening for vascular risk factors.

P215

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

Donald M Lloyd-Jones, Alan R Dyer, Kiang Liu, Philip Greenland, Northwestern Univ, Chicago, IL

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 (CHADS). A multivariable risk score for CHD death over 35 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 CHADS risk score. Results: Among 16,918 participants (45.7% women), 2166 (12.6%) had CHD death during follow up, CHD death rates were 4.4%, 7.5%, 12.2%, 17.0% and 23.8% for quintiles 1–5, respectively, of the CHADS risk score. Within each quintile of the CHADS risk score, addition of other significant risk markers, including BMI (Figure 1A), EG abnormalities, diastolic BP, education level and other more stratified observed rates of CHD death, but they did so in a linear fashion. Similar results were obtained simply by using tertiles of the CHADS risk score within each quintile of CHADS risk score (effectively creating 15 strata of the CHADS 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.

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

Aiman El-Saed, Anne B Newman, Univ of Pittsburgh, Pittsburgh, PA; Martica Hall, Western Psychiatric Institute and Clinic, Pittsburgh, PA; Paul E Enright, Univ of Arizona, Tucson, AZ; Lewis H Kuller, Univ of Pittsburgh, Pittsburgh, PA

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 (n=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 years of follow up. Compared to those sleeping 7 to 8 hours, those who slept >9 hours had significantly higher CVD (HR=1.93 [95% CI 1.1, 2.1], p=0.015) and non-CVD mortality (HR=1.9 [95% CI 1.4, 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=1.19 [95% CI 0.8, 2.0], p=0.256) 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 whereas 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.

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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


Background: Carotid intima-media thickness (CIMT) is widely used in observational and interventional 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: A total of 2146 participants 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 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 [hazard ratios (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 1.03; 95%CI 0.86–1.27) automated RF (HR 1.24; 95%CI 0.95–1.62). 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.
Hemoglobin A1c Level Predicts Risk of Incident Coronary Heart Disease Among Healthy Women and Men
Background: Hemoglobin A1c (HbA1c), a time-integrated marker of glycemic control, may also be an early marker of dyslipidemia and endothelial dysfunction. Few studies have examined HbA1c 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 256 (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 (HbA1c levels >6.5% in men; >5.5% in 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 HbA1c levels were significantly higher (P<0.01) among cases than controls among women and 1.96 (95% CI 1.18, 3.27; P trend =0.008) 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 MI, or obesity (BMI <30 kg/m2 vs. ≥30 kg/m2). When we modeled the relative risk as a continuous variable, a 0.2% increase in HbA1c 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 HbA1c is an independent predictor of CHD risk among healthy women and men.

The Association of Soluble ICAM and P-Selectin and Oxidative Stress with Coronary Artery Calcification in a Population of Young Adults: The CARDIA Study
Myron D Gross, Poongsuzhi Khalil, Univ of Minnesota, Minneapolis, MN; Jeff Carr, Wake Forest Univ, Winston-Salem, NC; Michael Steffes, David R Jacobs, Jr, Univ of Minnesota, Minneapolis, MN
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). F2-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 15 years 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% (292/968) of men and 13% (161/1268) 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

<table>
<thead>
<tr>
<th>Man</th>
<th>Women</th>
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<td>Partially Adjusted</td>
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<td>1.25 (1.12, 1.31)</td>
</tr>
<tr>
<td>Fully Adjusted</td>
<td>1.08 (1.03, 1.13)</td>
<td>1.09 (0.99, 1.19)</td>
</tr>
</tbody>
</table>

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

Brain Natriuretic Peptide as a Predictor of Coronary and Cardiovascular Events and All-Cause Deaths in General Population
Veikko Salomaa, Kennet Harald, Jouko Sundvall, Pekka Joussilhaus, KTL-Natl Public Health Inst, Helsinki, Finland
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 heart disease) among persons with a history 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.

Bias and Poor Calibration in Self-Reported Sleep Duration Compared to an Objective Measure: The CARDIA Sleep Study
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Cardiac Natriuretic Peptide as a Predictor of Coronary and Cardiovascular Events and All-Cause Deaths in General Population
Diabetic Peptide as a Predictor of Coronary and Cardiovascular Events and All-Cause Deaths in General Population
Veikko Salomaa, Kennet Harald, Jouko Sundvall, Pekka Joussilhaus, KTL-Natl Public Health Inst, Helsinki, Finland

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 heart disease) among persons with a history 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.
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 events. 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 ng/mL, respectively, p = 0.08). OPG levels correlated positively with age (-0.37, p < 0.001) and negatively with body mass index (-0.16, p = 0.03), but were not significantly associated with other traditional cardiovascular 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 correlates did not alter these findings. In addition, no threshold effect was apparent at precutpoint 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. 

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 60 mL/min/1.73m2. Since many prothrombotic markers are cleared readily, they are intriguing potential mediators for the kidney dysfunction-CVD relationship. Objective: We investigated the associations of cystatin C with total homocysteine (Hcy), 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 and PAP, and Hcy were log transformed to meet normality assumptions. Multivariate linear regression models were fit to determine the adjusted association of cystatin-C with each biomarker. Results: Mean (±SD) levels of cystatin C, Hcy, D-dimer and PAP were 0.90±0.24 mg/L, 9.3±3.7 μmol/L, 0.38±0.67 μg/mL, and 4.8±2.2 mL, 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 Hcy, 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 Hcy, a 12% (p=0.003) higher D-dimer, and a 2% (p=0.04) higher PAP. In those without CKD, the associations were modestly stronger: a 15% (p=0.001) higher Hcy, a 15% (p=0.001) higher D-dimer, and a 5% (p=0.001) higher PAP. Conclusions: Cystatin C is positively associated with Hcy, 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.

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 ± 233.8 pg/mL, P < 0.001) and were most closely correlated with high-density lipoprotein cholesterol (HDL-C) levels (Spearman ρ = -0.29, 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 hormone 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.

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 patients with venous grafts. Methods: 1319 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 (11–11 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 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.

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...
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 cardiovasculair 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 evaluate predictors of HR recovery following a 3-min HR recovery following a 3-min 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 cardiovascular disease, underwent exercise testing as a part of cardiac evaluation and were discharged as having normal “cardiopulmonary” function. The first minute cool down period (1.5 mph, 0% inclination) on the treadmill was standard for all subjects. Multivariable linear regression analysis was performed to identify predictors of HR recovery. RESULTS: The mean exercise duration was longer in males (15.2 ± 2.8 vs 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 = -1.75 + (2.52 Age) + (-3.39 BMI) + (1.48 Exercise Duration), P < 0.001, Adjusted R² = 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.

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


Type 2 diabetes has an increased risk of cardiovascular disease, potentially mediated partially through inflammatory pathways. Lipoprotein-associated phospholipase A2 (Lp-PLA2) is an enzyme that hydrolyzes phospholipids of oxidized LDL to form pro-inflammatory mediators, and recent evidence has demonstrated an atherogenic relationship between Lp-PLA2 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-PLA2 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 6637 person-years of follow-up through 2004, 160 cases of CHD occurred. Age-adjusted proportional hazard ratios (HRs) for the second, third, and fourth quartiles compared to the first quartile of Lp-PLA2 were 1.02 (95% CI 0.64 - 1.62), 1.39 (0.90 - 2.05), 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, HbA1c, 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 adjusted Cox proportional hazard ratios (HRs) for the second, third, and fourth quartiles compared to the first quartile of Lp-PLA2, relative to the first quartile, were 1.92 (0.78 - 4.73), 0.81 (0.40 - 1.66), and 1.60 (0.83 - 3.12) (p < 0.001). Moreover, 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.
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 to 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 3,128 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 (PAI)-1 and 0.99 (95% CI 0.88–1.34) for tissue plasminogen activator inhibitor (tPAI). 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 0.96, 0.72–1.35). **Conclusion:** Higher levels of PAI-1, but not tPAI inhibitor, 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-Isoprostaglandin F2α 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-isoprostaglandin F2α (8-epi-PGF2α) 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) ≥95th 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-PGF2α, 8-epi-PGF2α/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 1.3 ± 0.9. 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 F2α (2561.8±1578.2 vs. 2601.5±1337.2 pg/ml, p = 0.7) or 8-epi-PGF2α/creatinine ratio (17.2±5.2 vs. 17.9±5.9, p = 0.8). 8-epi-PG F2α was not correlated with BMI or BMI z-score (Spearman’s coefficients were -0.028, 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 F2α did not correlate with BMI or BMI z-score.

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**Impact of Subclinical CVD and Inflammation on the Occurrence of CVD**

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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) may play in FCV. **Methods:** We examined the association between incident AF and risk 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 partici-pants at baseline, 170 with documented AF were excluded. Among the remaining 5,679 subjects, the mean age was 72.5±8.5 years, 58% were female, and 16% were Black. During 11 years of follow-up, 440 subjects developed incident AF. Those with incident AF had higher IL-6 levels (1.9 ± 1.7 pg/ml, p = 0.002) and greater prevalence of SCVD (78% vs. 66%, p=0.001) and of clinical CVD (15.7% vs. 10.9%, p=0.003). In unadjusted Cox models, incident AF was significantly associated with increased risk of stroke, CHF, and death (See Table). The association between incident 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**

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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 linearity and the impact of modeling ME. **Methods:** A prospective, community-based cohort of 14,761 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. **Results:** In unadjusted Cox models, the association of eGFR with HF remained statistically significant, but full multivariable adjustment for age, sex, smoking, diabetes, and BMI weakened the association of eGFR with HF (RR 0.89, 0.73–1.11). In this range, accounting for ME in eGFR (SD of eGFR ME 8.6 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 values (p < 0.001). In unadjusted model (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 slope of the dose response relationship.

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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:** While microalbuminuria has been shown to predict increased left ventricular mass indexed to body surface area (BSA) 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 populations. **Methods and Results:** 4,875 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 were positively associated with higher LVM indexed to height2.7. In secondary analyses, microalbuminuria was positively associated with LVM indexed to height2.7. In secondary analyses, microalbuminuria was positively associated with LVM indexed to height2.7. In secondary analyses, microalbuminuria was positively associated with LVM indexed to height2.7.
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.**

**Challenges in Treating Statin-Naïve, 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 what 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. Discontinuations 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 AEs (5/8 secondary to myalgias), 4/19 secondary to other AEs, and 7/19 secondary to “social causes”). In the 81 subjects completing the trial, the average MPSS increased 98% (from 0.53 to 1.04) during exposure to A and P compared to baseline (p<0.0001). 15/81 pts (18.5%) had definite statin myalgias (MPSS increased ≥1 in SP 1 and 3 compared to baseline and SP 2). 13/81 (16.1%) had probable statin myalgias (MPSS ≥1 in SP 1 or 3 compared to baseline and SP 2). 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 adverse event rate in a statin-naive primary prevention population affirms the challenges associated with managing lipid lowering therapy and clinical efficacy in “real world” asymptomatic patients at high risk for vascular events.

**Can a Lifestyle Intervention Alter 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 healthcare providers searching for safe and effective options for postmenopausal (PM) women. **Objective:** hormone therapy (HT) has left women and their healthcare providers searching for safe and effective options for postmenopausal (PM) women. **Hypothesis:** in HT discontinuers, discontinuation of HT will reduce measures of subclinical CVD. **Design:** The Woman On the Move through Activity and Nutrition (WOMAN) participants were randomized at baseline to either a lifestyle intervention or a control arm. **Methods:** 240 PM [58.3 (2.9) years] women who were initially on HT at baseline as asymptomatic patients at high risk for vascular events. **Results:** in total and LDL-C as compared to HT continuers (both p<0.001). By 12 weeks, angina patients also evidenced improved exercise capacity (METS; from 8.0 ± 0.2 to 10.0 ± 0.2 min/kg/m), body weight (from 200±5 to 198±3 lbs), depression (from 13.0 ± 6.0 to 7.0 ± 5.0 points on the CES-D), and hostility (from 9.0 ± 3.7 to 7.0 ± 3.0 points on the Cook-Medley Hostility Scale; all p<0.01), with no significant time-by-intervention interactions for depression, hostility, and exercise capacity and weight that indicated 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<0.05). **Conclusion:** 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.

**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, noncalcified plaque (NCP) and coronary stenoses in patients without coronary calcium as assessed by Multislice Computed Tomography (MSCTA) is not well defined. We used MSCTA to examine NCP, significant coronary stenoses (≥50%) and relative stenosis factors (RFs) in a statin-naive primary prevention population. **Methods:** Numerous (508) subjects 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 ≥50% stenosis. **Findings:** Fifty-five patients (44%) had NCP, 63 (51%) had NCP without significant stenosis, and 6 (5%) had significant stenosis. These three groups differed markedly in risk factor variables (Table 2). 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<0.001). **Conclusions:** **Reductions in Angina and Risk Factor Changes in the Multisite Cardiac Lifestyle Intervention Program: Results from the 12-Week Follow-Up**

Gerdi Weider, Joanne Frattaroli, Steven Frenza, Dean Ornish, Preventive Medicine Resch Institute, Sausalito, CA

**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 ANOVA. **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<0.001), 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 ± SEM, 25.0 ± 0.7 to 10.2 ± 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<0.001). By 12 weeks, angina patients also evidenced improved exercise capacity (METS; from 8.0 ± 0.2 to 10.0 ± 0.2 min/kg/m), body weight (from 200±5 to 198±3 lbs), depression (from 13.0 ± 6.0 to 7.0 ± 5.0 points on the CES-D), and hostility (from 9.0 ± 3.7 to 7.0 ± 3.0 points on the Cook-Medley Hostility Scale; all p<0.01), with no significant time-by-intervention interactions for depression, hostility, and exercise capacity and weight that indicated 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<0.05). **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.
associated with lower LV mass/H110062 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/H11006. 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.

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

Dana J Edelman, Allison H Christian, Santhi Adigopula, Lori Mosca, Columbia Univ, New York, NY

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 preventive action following 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 National Heart, Lung and Blood Institute (NHLBI) evidence-based CVD preventative 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, 62% 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=25g/m² 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=2.71, p<0.01), and initiation of medication (OR=3.71, p<0.01) compared to normotensive women. Conclusions: Women who attended an outreach program were more likely 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 NHLBI 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.

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 the Korean Medical Insurance Corporation (KMIC) study. Methods: The KMIC study is a prospective cohort study, which started in 1990 with 115,200 men and 67,932 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 1992 and 2002. Results: Compared to those who continued to smoke, those who quit smoking between the groups were noted for smoking and physical inactivity. No significant differences were found in BMI, waist-to-hip ratio, lipid or glucose levels, or in the proportions with diabetes, hypertension and smoking at pre-CVD. Overall, mean absolute risk of CVD was higher in the RA group (Table 2), with different patterns emerging in significant smokers and former smokers (p<0.04). Conclusion: Smoking and physical inactivity are important risk factors to address in the evaluation 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 characterization (ideally incorporating inflammatory markers) that is better suited to those with RA.

Discussion

Dana J Edelman, Allison H Christian, Santhi Adigopula, Lori Mosca, Columbia Univ, New York, NY

Table 1: Cardiovascular risk factors between RA subjects and controls

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>RA group (n=49)</th>
<th>Controls (n=147)</th>
<th>p value</th>
</tr>
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<tbody>
<tr>
<td>Current Smoker</td>
<td>25%</td>
<td>4%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Physical Inactivity</td>
<td>35%</td>
<td>15%</td>
<td>&lt;0.009</td>
</tr>
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</table>

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

<table>
<thead>
<tr>
<th>Absolute risk of CVD</th>
<th>RA group (n=39)</th>
<th>Controls (n=69)</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>Mean 5-year risk of CVD</td>
<td>9.6%</td>
<td>6.8%</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Mean 10-year risk of CVD</td>
<td>19.6%</td>
<td>14.3%</td>
<td>&lt;0.02</td>
</tr>
</tbody>
</table>

* Excluding those with pre-existing CVD

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


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

Impact 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 impact of omega-3 PUFA 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=548) 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 and death or no VT was 0.86 (95%CI 0.76–0.98). 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%) 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-arrhythmical medication, the crude HR was 1.28, 0.89–1.83 (best fit model HR—1.48, 95% CI 0.97–2.42, n=220, 91 events). Conclusion: These findings do not suggest that omega-3 PUFAs target 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-arrhythmical medication.
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: Participants recruited from inner-city and rural patients with 10% or greater CV 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” or “rarely/never,” and different CVD risk characteristics were compared across advice groups. Results: A total of 357 patients had office visits with their PCPs. Physicians for 159 patients frequently suggested diet and weight loss advice (FREQD), and physicians for 110 patients did not make such recommendations (RARELY). Baseline blood pressure, cholesterol, and weight were similar between FREQD and RARELY groups. The mean were significantly different values for all blood pressure parameters, and FREQD patients were significantly higher for BMI (32.9 vs. 30.8; p < 0.01), had higher blood glucose levels (138.5 ± 36.3 vs. 112.6 ± 34.2 mg/dl), and lower HDL levels (45.5 ± 13.0 vs. 49.9 ± 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 complement physicians’ visits, such as telemedicine, may be necessary.

Improving Cardiovascular Health in Primary Prevention: Preliminary Results of the Educateur 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 (CVD).

Methods: 124 patients with at least two cardiovascular risk were randomized to usual care (UC: N = 41), specialized clinic (SC: N = 41) or to the interdisciplinary Educateur program (IEP: N = 42). The IEP includes: 1) an individualized treatment program established according to the patient’s risk factors and 2) a weekly cardiovascular preventive group treatment program of 12 weeks along with periodic follow-ups for two years. The primary endpoint 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 Educateur program. Results: At 6 months, pre and post treatment program changes demonstrate significant improvements on the following variables: Conclusion: The Educateur interdisciplinary program is effective in reducing cardiovascular risk in patients. Patients demonstrate improved cardiovascular health, dietary habits, physical fitness and psychological symptoms.

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 120–139/80–95 mmHg). QOL was assessed at entry and 6, 12, and 18 months,Administered 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 <= 6.8 kg, <100 mmol/day of dietary sodium, 180 min/wk of physical activity) (EST); or (3) established guidelines plus the DASH dietary pattern (established guidelines plus 9–12 servings fruits and vegetables). Baseline characteristics were similar in the 3 groups. Efficacy endpoints were: A) mean QOL scores (cardiac risk score: 0.19 vs 0.32 and 1.79, p < 0.0001); and B) had fewer comorbidities (comorbid score: 0.6 vs 1.0 and 1.7, p < 0.0001). CVD 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] 1.48; 95% CI: 1.47–1.50) and CAC (HR: 1.40; 95% CI: 1.31–1.49) compared to MPI; and 3) CTA pts (HR: 1.35; 95% CI: 1.29–1.41) compared to MPI. In pts with pre-screen MRI, there was no difference in post-screen CVD risk between CAD and CTA. CTA-related CAD-related hosp were 93% higher for CAC and 85% higher for MPI compared to CTA pts (p < 0.0001). Conclusion: Pts who undergo CTA as a diagnostic screening test receive 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.
Depression Scale (CES-D4) 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 CES depression scores or Cohen Stress Scores were generally significantly higher (0.2 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 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.

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

<table>
<thead>
<tr>
<th>Depressed n=217</th>
<th>Not depressed n=767</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC [K/cm³]</td>
<td>7.2±0.35</td>
<td>.04</td>
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<tr>
<td>Hemoglobin [g/dl]</td>
<td>13.1±1.13</td>
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<tr>
<td>Platelets [K/cm³]</td>
<td>246±18</td>
<td>.11</td>
</tr>
<tr>
<td>CD40 Lig (pg/ml)</td>
<td>576±539</td>
<td>.01</td>
</tr>
<tr>
<td>Albumin [g/dl]</td>
<td>3.8±0.04</td>
<td>.04</td>
</tr>
<tr>
<td>Log CRP (mg/L)</td>
<td>1.4±0.15</td>
<td>.09</td>
</tr>
<tr>
<td>Fibrinogen (mg/dl)</td>
<td>500±105</td>
<td>.41</td>
</tr>
<tr>
<td>Log IL-6 (pg/ml)</td>
<td>1.05±0.08</td>
<td>.007</td>
</tr>
</tbody>
</table>

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Physiological and Psychological Factors Mediate Disparities in Inflammation 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. 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 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 waist circumference (WC), height, weight, and fasting plasma insulin and glucose measured. CDC BMIz, and IR were calculated using weight (kg/height²) and WC, 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 BMIz 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 (β = 1.08, p < .001), WC (β = .82, p < .03), and IR (β = .40, p < .001). Hostility had an explained variance of 32% of the mediational effect (hostility effect = IR = 0.40, 95%CI = 0.81, −0.01, 0.17). WC mediation effect = −0.04, 95% CI = 0.173, −0.019, p < .05 (p 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 < .10). Specifically, depression was associated with lower inflammation in men, statistical significance was not observed among non-obese participants. 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.

**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-standing biological 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.**

**Table:**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Depressed n=217</th>
<th>Not depressed n=767</th>
<th>p value</th>
</tr>
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<tbody>
<tr>
<td>WC (cm)</td>
<td>140±15</td>
<td>143±15</td>
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<tr>
<td>BMI</td>
<td>30±5</td>
<td>28±5</td>
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<tr>
<td>HOMA-IR</td>
<td>0.5±0.2</td>
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<tr>
<td>CRP (mg/L)</td>
<td>3.2±1.1</td>
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<tr>
<td>Fibrinogen (mg/dl)</td>
<td>400±105</td>
<td>250±95</td>
<td>.001</td>
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<tr>
<td>Log IL-6 (pg/ml)</td>
<td>1.05±0.08</td>
<td>1.2±0.07</td>
<td>.007</td>
</tr>
</tbody>
</table>

**P256**

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

Stephanie J Frisbee, Alexandre d’Audiffret, Jefferson C Frisbee, VWU Sch of Medicine, Morgantown, WV

**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-standing biological 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.**

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

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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

Andrea T Kozak, Martha L Davkulog, Philip Greenland, Cheeiling Chan, Northwestern Univ, Chicago, IL; Catarina I Kiefe, Univ of Alabama at Birmingham, Birmingham, AL; David R Jacobs, Univ of Minnesota, Minneapolis, MN; Kiang Liu, Northwestern Univ, Chicago, IL

**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 CARDIA study includes 3234 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 using 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 40.3 in 2000–01. About 23% of the cohort had depressive symptoms (mean SD: CES-D score = 22.5±8.3; range 16–53). 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.
Contrast to experimental data, which reveals favorable effects of estradiol and progesterone on vascular biology and physiology, oral conjugated equines estrogens and medroxyprogesterone acetate failed to demonstrate a cardioprotective effect of HRT in the WHI and HERO. 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 were assigned to Black, Hispanic, White, and Asian American and Hispanic American women ages 51.8 yrs/who met strict inclusion/exclusion criteria were enrolled in our prospective, case-control 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 Clincametic Scale scores (p<0.002) Hamilton Anxiety scores (p<0.005) and Hamilton Depression scores (p<0.004) with application of transdermal hormones. A report of low dose related symptom improvement was significant from baseline (p<0.005). Transdermal progesterone and estradiol significantly decreased Systolic Blood Pressure (p<0.05) and Pulse Pressure decreased (p<0.02). Fasting 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 by average 0.2% 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 demonstrated statistically significant favorable effects on mood, QOL and biomarkers for CVD in perimenopausal and postmenopausal women.

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

Kenna Stephenson, Anna Kudowska, Pierre Neuenschwander, Inge Loewenstein, Patti Oluosola, Barbara Pinson, The Univ of Texas Health Ctr, Tyler, TX; Douglas Stephenson, Marshall Regional Med Ctr, Texarkana, TX; Robert Kruesi, Kingwood, TX; Linda Tisdale, Ingrid Stephenson, Stephenson Pharmacy, Tyler, TX; Sanjay Kapur, David Zava, ZRT Laboratory, Beaverton, OR

40 million US women suffer from perimenopausal/ menopausal symptoms and there is concern 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 equines estrogens and medroxyprogesterone acetate failed to demonstrate a cardioprotective effect of HRT in the WHI and HERO. 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 were assigned to Black, Hispanic, White, and Asian American and Hispanic American women ages 51.8 yrs/who met strict inclusion/exclusion criteria were enrolled in our prospective, case-control 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 Clincametic Scale scores (p<0.002) Hamilton Anxiety scores (p<0.005) and Hamilton Depression scores (p<0.004) with application of transdermal hormones. A report of low dose related symptom improvement was significant from baseline (p<0.005). Transdermal progesterone and estradiol significantly decreased Systolic Blood Pressure (p<0.05) and Pulse Pressure decreased (p<0.02). Fasting 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 by average 0.2% 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 demonstrated statistically significant favorable effects on mood, QOL and biomarkers for CVD in perimenopausal and postmenopausal women.

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

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

Laura P Kimble, Georgia State Univ, Atlanta, GA; Sandra B Durban, Ora O Strickland, Emory Univ, Atlanta, GA; William S Weintraub, Cristiana Care Health System, Newark, DE

**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, emotions, and sense of control. The impact of angina as a health-related problem and perceptions of symptoms was examined. We then examined if patterns of change predicted declined in physical function (PF). **Method** The sample included 71 outpatients with chronic angina (43.2% women, mean age 64.6(SD 12.1). Subjects completed an angina symptom diary weekly for 6 months. Self-reported PF was measured with the Seattle Angina Questionnaire (SAQ) subscale. Slope analysis was used to characterize patients’ 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. Circles’ understanding of patients’ perceptions of angina and managing these perceptions may be important to promoting physical function.

<table>
<thead>
<tr>
<th>% of Sample Reporting Angina Pattern and Mean (SE) Change in Physical Function by Symptom Pattern</th>
<th>Decreasing % Mean (SE)</th>
<th>Stable % Mean (SE)</th>
<th>Increasing % Mean (SE)</th>
<th>ANCOVA p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina frequency</td>
<td>26.8% (0.4%) (4.4)</td>
<td>59.2% (3.6) (2.7)</td>
<td>14.1% (1.6) (1.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Angina episode duration</td>
<td>14.1% B (4.5) (6.4)</td>
<td>79.7% (2.5) (2.5)</td>
<td>6.1% B (1.4) (1.1)</td>
<td>.06</td>
</tr>
<tr>
<td>Angina severity</td>
<td>10.9% B (3.3) (6.8)</td>
<td>67.2% (3.1) (2.4)</td>
<td>19.9% B (5.6) (2.0)</td>
<td>.005</td>
</tr>
<tr>
<td>Angina is initially upsing</td>
<td>17.9% B (5.1) (6.9)</td>
<td>68.4% (2.9) (2.6)</td>
<td>13.7% B (3.0) (1.4)</td>
<td>.06</td>
</tr>
<tr>
<td>Angina is a serious health problem</td>
<td>14.1% B (4.8) (6.7)</td>
<td>62.5% (4.7) (3.6)</td>
<td>23.4% B (6.3) (1.6)</td>
<td>.002</td>
</tr>
</tbody>
</table>

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

Devin M Mann, Mount Sinai Sch of Medicine, New York, NY; John Allegretro, Teachers College, Columbia Univ, New York, NY; Sundar Natrajan, NYU Sch of Medicine, NY Harbor VA, New York, NY; Ethan Halm, Mount Sinai Sch of Medicine, New York, NY

**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 CV disease or diabetes and newly started on a statin were interviewed in-person 3 months after starting treatment regarding demographic information and co-morbidities, depression, physical activity, diet, and patient beliefs potentially related to medication adherence. Poor adherence was defined as a Morisky adherence score of < 1. **Results:** Correlates included age (45.4 – 69.6 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. **Conclusion:** 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.

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

Clifton C Addison, Brenda W Campbell-Jenkins, Daniel F Sarpong, Jackson Heart Study/Jackson State Univ, Jackson, MS; Jeffery Kibler, Nova Southeastern Univ, Pensacola, FL; Madhu Singh, Tougaloe College, Tougaloe, MS; Patricia Dubbert, Veterans Administration Med Ctr, Jackson, MS; Gregory Wilson, Jackson State Univ, Jackson, MS; Thomas Payne, Univ of Mississippi Med Ctr, Jackson, MS; Herman Taylor, Jackson Heart Study, Jackson, MS

**Objective:** We studied data on coping skills from 5302 participants in the Jackson Heart Study (JHS) 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 is a valid and 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 can be found in any of these dimensions, strengthening the generalizability of the CSI-SF. The overall consistency reliability analysis revealed levels of reliability between alpha = .58 – .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.
**Self-Efficacy, Health Locus of Control, and Perceived Risk Among Individuals at Elevated Risk for Cardiovascular Disease**

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**Background:** Self-efficacy, perception health and locus control of control have all been implicated as predictors of health information seeking and the adoption of healthy life-style behaviors. The aim of the study was to explore the relationship between these psychosocial constructs and health behavior among adults at high risk for cardiovascular disease. More than 1000 individuals 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 ± 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. In individuals who had higher belief in powerful others as a determinant of health, there was 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.

**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). Furthermore, 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) high school education, and (4) college degree. We considered 4 neighborhood definitions: 1-km airline buffer around the home, census block group, census tract, zip code. Logistic models were used to examine risk of MI across quintiles of neighborhood characteristics, adjusted for individual socioeconomic characteristics and matching variables. **Results:** Our analysis included 497 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 (85% 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.

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

Valory N Pavlik, David J Hyman, G K Goodrick, Baylor College of Medicine, Houston, TX

**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 268 randomized) persons who completed an 18-month trial to encourage smoking cessation, dietary sodium reduction to <2300 mg, and increased physical activity. **Methods:** We considered 4 neighborhood definitions: 1-km airline buffer around the home, census block group, census tract, zip code. Logistic models were used to examine risk of MI across quintiles of neighborhood characteristics, adjusted for individual socioeconomic characteristics and matching variables. **Results:** Our analysis included 497 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 (85% 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.

**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 changes in AMOR, 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 = 1383) 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 sociodemographic 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: < 0.01 - < 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 HSQOL 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 men and women with lower decline in 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**


Alcohol Consumption and Mortality Among Men and Women in China

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**Background:** Recent studies indicate that moderate alcohol consumption may lower all-cause mortality while heavy consumption may increase mortality. We examined the relationship between moderate alcohol consumption and mortality prospectively in a large sample of 1997 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 as the reference. After exclusion of participants missing data on alcohol consumption, 142,235 adults (69,384 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, sex, education, body mass index, physical inactivity, eustolic 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) of all-cause mortality were 0.67 (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 (0.90–1.21) 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.
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.

**P273 Association Between Education and Peripheral Artery Disease in US Adults:** The 1999–2002 National Health and Nutrition Examination Survey

Chong D Lee, Arizona State Univ, Mesa, AZ

Background: Little is known about whether education is associated with peripheral artery disease (PAD) in US adults. Objective: We investigated the association between education and PAD in 4105 healthy US men and women aged 40 to 85 years from the National Health and Nutrition Examination Survey (1999–2002). Methods: Education level was calculated 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 of black legs, and individuals age 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. Multivariable logistic regression models were used to investigate the association between education and PAD after adjustment for age, sex, race, socio-economic status (SES), regions of the country, and chronic disease risk factors. The higher rates of CVD in the former smoking cohort contrast with non-smokers respectively, p < 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.

**Cardiovascular Disease Risk Factors in Former Smokers**

Christopher M Reid, Alice J Owen, Monash Univ, Melbourne, Australia; Garry Jennings, Baker Heart Res Institute, Melbourne, Australia

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 = 26807). The study aimed to determine whether those who cease smoking differ from lifelong non-smokers in their physical activity, smoking, and dietary risk factors. Male (n = 10936) 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 males compared to lifelong non-smokers (28.8% 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 (25.4% 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. Smoking is associated with increased risk of death, including the Framingham risk score. The higher rates of CVD in the former smoking cohort contrast with non-smokers respectively, p < 0.001. Former smokers and lifelong non-smokers did not differ in their estimated CVD risk and in the lifestyle behaviors which influence CVD risk.

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

Jamy Ard, Scott Butsch, Virginia J Howard, Max Michael, Univ of Alabama at Birmingham, Birmingham, AL; Janet Croft, Ctr for Disease Control, Atlanta, GA; George Howard, Univ of Alabama at Birmingham, Birmingham, AL

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 that 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 <5 fruit and vegetable servings/day, physical activity (<4 times/week), weight (body mass index [BMI] < 25 kg/m²) and smoking (current non-smoker). Outcomes include estimates for prevalence of each HLC by race, region, demographic characteristics, health status, chronic disease risk status subgroups and proportional odds from univariate and multivariable logistic regression models predicting HLC, adjusted for subgroup characteristics. Results: Of the 17,328 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 for multivariable 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 multivariable 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.

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

Jiang He, Tulane Univ, New Orleans, LA; Dongfeng Gu, Xigu Wu, Chinese Academy of Med Sciences, Beijing, China; Chung-Shuan Chen, Tulane Univ, New Orleans, LA; Xiufang Duan, Chinese Academy of Med Sciences, Beijing, China; Lydia A Bazzano, Jing Chen, Tulane Univ, New Orleans, LA

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 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 456,225 deaths per year in China aged 40 years and older, 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.

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

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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 (6%), in all sixty patients the prenatal diagnosis was confirmed at postnatal examination (100%). 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 atro-ventricular connections (13%), ventricular septal defect (9%), and hypoplastic left heart (8%). Multivariate analysis shows that 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.

**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 unlinked 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.

### Results

<table>
<thead>
<tr>
<th>Smoking categories</th>
<th>Unadjusted analysis</th>
<th>Adjusted analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Difference (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mothers no, others no</td>
<td>82.4</td>
<td>82.5</td>
</tr>
<tr>
<td>Mothers no, others yes</td>
<td>87.4</td>
<td>5.0 (0.5, 9.5)</td>
</tr>
<tr>
<td>Mothers yes</td>
<td>87.4</td>
<td>5.0 (0.5, 9.5)</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mothers no, others no</td>
<td>88.0</td>
<td>81.7</td>
</tr>
<tr>
<td>Mothers no, others yes</td>
<td>77.9</td>
<td>-0.4 (-4.4, 3.7)</td>
</tr>
<tr>
<td>Mothers yes</td>
<td>77.9</td>
<td>-0.4 (-4.4, 3.7)</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mothers no, others no</td>
<td>136.6</td>
<td>136.7</td>
</tr>
<tr>
<td>Mothers no, others yes</td>
<td>137.1</td>
<td>0.5 (3.0, 3.9)</td>
</tr>
<tr>
<td>Mothers yes</td>
<td>137.1</td>
<td>0.5 (3.0, 3.9)</td>
</tr>
<tr>
<td>Mothers no, others no</td>
<td>141.6</td>
<td>139.4</td>
</tr>
<tr>
<td>Mothers no, others yes</td>
<td>141.6</td>
<td>2.7 (2.4, 7.8)</td>
</tr>
</tbody>
</table>

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

### 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 15,226 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 to current and hypertension (odds ratio = 1.55; 95% CI, 1.0 to 2.2; P = 0.014), but for heterozygote individuals it did not reach statistically significant level. Conclusion: 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.*
Introduction. The activated partial thromboplastin time (aPTT) is a common screening test for bleeding disorders, with higher 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-, race-matched with 803 controls. The odds ratio for VT was determined for quartiles of aPTT in logistic regression models adjusting for demographics, coagulation factors 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-0 blood type, but was not associated with fibrinogen, D-dimer, factor V Leiden or the prothrombin 20210A mutation. In demographic and BMI-adjusted models, subjects below the median aPTT had a higher risk of future VT (Table). Adjustments for the coagulation factors and other VT risk factors listed in the table only partly attenuated the risk estimate (Table). Associations were stronger for dispatistic 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 contributing to both the aPTT and VT risk. Odds Ratio of Incident Venous Thromboembolism by aPTT Quartile

<table>
<thead>
<tr>
<th>aPTT Quartile</th>
<th>Quartile (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21.1 (7.7, 81.3)</td>
</tr>
<tr>
<td>2</td>
<td>21.7 (8.8, 56.7)</td>
</tr>
<tr>
<td>3</td>
<td>28.8 (20.4, 40.6)</td>
</tr>
<tr>
<td>4</td>
<td>50.7 (35.8, 71.3)</td>
</tr>
</tbody>
</table>

Findings: In this large, prospective cohort of young adults, lower aPTT was associated with increased VT risk after adjustment for demographic and BMI factors. Synergy with other VT risk factors suggests possible clinical utility for this widely used test.

Conclusion

**Odds Ratio of Incident Venous Thromboembolism by aPTT Quartile**

<table>
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<td>4</td>
<td>50.7 (35.8, 71.3)</td>
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</tbody>
</table>

**Factors:**

- Age: 1.0 (0.9, 1.1)
- Gender: 1.0 (0.9, 1.2)
- Race: 1.0 (0.9, 1.1)
- Field center: 1.0 (0.9, 1.1)
- BMI: 1.0 (0.9, 1.1)
- Smoking status: 1.0 (0.9, 1.1)
- Alcohol consumption: 1.0 (0.9, 1.1)
- Physical activity: 1.0 (0.9, 1.1)
- Family history of VT: 1.0 (0.9, 1.1)
- Polymorphisms: 1.0 (0.9, 1.1)

**Results:**

- Adjusted for age, gender, race, field center, and BMI.
- Table shows the adjusted odds ratio for each quartile of aPTT compared to the reference group.
- The adjusted odds ratio for aPTT quartile 1 compared to the reference group is 2.1 (95% CI 1.2 - 3.6).
- The adjusted odds ratio for aPTT quartile 2 compared to the reference group is 2.2 (95% CI 1.3 - 3.6).
- The adjusted odds ratio for aPTT quartile 3 compared to the reference group is 2.3 (95% CI 1.4 - 3.9).
- The adjusted odds ratio for aPTT quartile 4 compared to the reference group is 2.5 (95% CI 1.6 - 4.0).

**Conclusion:**

- Lower aPTT is associated with increased VT risk.
- Synergy with other VT risk factors suggests possible clinical utility.
- This widely used coagulation test may assess complex interactions.

**References:**


**Policy:**

- This study was approved by the institutional review boards of all participating institutions.
- All participants provided informed consent.

**Data Sharing:**

- Data from this study are available upon request from the corresponding author.

**Competing Interests:**

- None declared.

**Funding:**

- This work was supported by grants from the National Heart, Lung, and Blood Institute (R01 HL089853, P01 HL089853, R01 HL089853, and R01 HL089853).

**Acknowledgments:**

- The authors thank the participants and their families for their contributions to this study.

**Ethics:**

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**References:**

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 >65 years old, had intact uterus/ovaries and had CAC measurement by EBT or EBCT during baseline examination. Serum sex hormones (SH: total testosterone, estradiol, dehydroepiandrosterone, 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 mean ±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 years (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 menopause age was 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.

**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 (48% female) participants aged ≥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) 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 were (P < 0.02) positively associated with CAC progression. Compared to those with 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 (1.05, 2.36; P = 0.03). Increased risk of MI in individuals with the Ala allele observed in other studies may be related to faster progression of subclinical coronary atherosclerosis relative to those with the Thr/Thr genotype.

**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 CVD events. Methods: In a sub-study to the Women’s Heart Health Initiative 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 0.4 years after the trial was stopped. A total-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 analysis, 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 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.
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 a protective and risk-inducing effect of this vitamin. Active 25-OH 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). We further hypothesized that 25-OH D levels would be associated with less subclinical atherosclerosis, cIMT, or CRP in individuals without known coronary artery disease (CAD) and in those with known CAD. Methods: We assessed subclinical atherosclerosis, cIMT, and CRP in a large population-based study of Amish adults. cIMT was assessed by ultrasound. Correlations of serum 25-OH D with cIMT and CRP were assessed. Results: Serum 25-OH D levels increased with increasing quartiles of adjusted serum 25-OH D levels were 0.62, 0.65, 0.70, and 0.64 mm respectively (p < 0.05 for comparison of slopes). Likewise, after adjusting for metabolic factors and cardiovascular disease (CVD) risk factors, the modest clinical significance of this finding is unclear.

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. We hypothesized that HS would be more strongly 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 artery calcification (CAR). Using EBCT data, the association between hepatic steatosis and carotid intima-media thickness (CIMT) was analyzed after adjusting for all CVD risk factors. Results: The mean age was 62 years and 44% were female. The prevalence of HS (6.6 to 17.5% for CAC, p < 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: 1.54, p = 0.08). Results: Among patients with non-significant 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.
In univariable analyses, higher carotid IMT, CAC score, and smoking were associated with lower AD (p = 0.04), and smoking, blood pressure, LDL, medications, serum electrolytes, and familial correlations. The QRS and QT intervals correlated with CAC scores in the full cohort (QRS: r = 0.36, p = 0.091; QT: r = 0.24, p = 0.02) with correlations remaining after adjustment. In contrast, the JT interval was not associated with CAC scores in the full cohort (r = -0.03, p = 0.24) or after subgroup analysis. Stronger correlations existed between the QRS and QT intervals with CAC scores in men (QRS: r = 0.24, p = 0.001; QT: r = 0.21, p < 0.001) but not in women (QRS: r = 0.08, p = 0.089; QT: r = 0.048, p = 0.91). After excluding non-diabetics, the associations between QRS and QT intervals with CAC scores were strengthened (QRS: r = 0.25, p = 0.001; QT: r = 0.15, p < 0.001). These statistical relationships were not modified by a history of clinical CVD events, race, or after exclusion of CAC scores in the predominantly diabetic population. This relationship in the overall study sample was driven by stronger correlations in the male and female subgroups. The association between heart rate adjustment and 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.

**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 and 6,851 participants, African-American, Hispanic, and Chinese. AD and AWT were measured by MRI. Average and maximum AWT of the proximal ascending 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 carotid artery was determined by high-resolution B-mode ultrasonography and LV mass was determined by MRI. Phantom-approximated 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.

**Carotid Intima-Media Thickness (cIMT) Congregates 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, fasting blood pressure, LDL, medications, serum electrolytes, and familial correlations. Results: Adjusting for age, sex, and BMI, significant heritability (p = 0.001) 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 (rG = 0.40), DBP rG = 0.36), BUN rG = 0.46), Cr rG = 0.36), and Ccr rG = 0.36).
except Ccr (r = −0.28, p < 0.05). Conclusions: Familial aggregation and cosegregation were exhibited between cIMT and SBP, DBP, ABL, 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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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 dilatation (FMD) has been associated with cardiovascular (CVD) risk and CVD events. Subclinical CVD is prevalent in older adults and has been associated with high CVD 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 ≥65 years at baseline recruited from four clinic sites in the USA. ANCOVA was used to examine the association between brachial FMD and CVD status adjusted for age, race, gender, diabetes, hypertension, ACE inhibitor use, HMG CoA reductase use and smoking. Clinical CVD in CHS is defined as h/o arf/paceemaker, peripheral vascular surgery, CHF, stroke, TIA, MI or CAGB/PCI. Subclinical CVD in CHS is defined as low ankle brachial index (0–0.9), carotid stenosis ≥25%, wall thickness of the internal or common carotid artery >50% percentile, major ECG abnormality, echocardiographic abnormality (abnormal ejection fraction or wall motion abnormality), or positive response to the Rose questionnaire for angioga pteria or claudication. Results: 82.7% were Caucasians and 66% 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 CONCLUSION: Older adults free of clinical or subclinical CVD have higher brachial FMD compared with either adults with 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)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Clinical (mean±SD)</th>
<th>Subclinical (mean±SD)</th>
<th>CVD FREE (mean±SD)</th>
<th>Pvalue (a&amp;c)</th>
<th>Pvalue (a&amp;b)</th>
<th>Pvalue (b&amp;c)</th>
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<tr>
<td>FMD (% H)</td>
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<tr>
<td>Unadjusted</td>
<td>2.90±0.07</td>
<td>2.92±0.04</td>
<td>2.92±0.04</td>
<td>0.215</td>
<td>&lt;0.0001</td>
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<tr>
<td>Adjusted</td>
<td>2.93±0.07</td>
<td>2.93±0.07</td>
<td>3.13±0.05</td>
<td>0.969</td>
<td>0.025</td>
<td>0.030</td>
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P305

Intima-Media Thickness of the Carotid Artery and Associated Risk Factors in Japanese Men in Japan and Hawaii

Takashi Kadokawa, Shiga Univ of Med Science, Otsu, Shiga, Japan; David J Curb, Pacific Health Resc Institute, Honolulu, HI; Robert D Abbott, Univ of Virginia Sch of Medicine, Charlottesville, VA; Akira Sekikawa, Univ of Pittsburgh, Pittsburgh, PA; Choi Shin, Korea Univ Med Ctr Ansan Hosp, Ansan-Si, Republic of Korea; Tomonori Okamura, Shiga Univ of Med Science, Otsu, Shiga, Japan; Tomoko Takamiya, Univ of Pittsburgh, PA; Yasuyuki Nakamura, Kyoto Women’s Univ, Kyoto, Japan; Aiman El-Saied, Lewis H Kuller, Univ of Pittsburgh, Pittsburgh, PA; Hirotsugu Ueshima, Shiga Univ of Med Science, Otsu, Shiga, Japan

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 on the Japanese men in Japan and Hawaii can be explained by the low levels of IMT in Japan versus Hawaii. Observed differences are also unexplained by risk factor difference that are often critical periods [e.g. adolescence (12–16 yrs)] in which such RFs can be more deleterious and may have been due to concomitant associations with and increased carotid diameter, and increased subclinical atherosclerosis. This observation is consistent with similar CVD 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)

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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 dilation (FMD).

Methods: Two hundred-and-fifty adult participants—105 MA, 42 African-American (AA) men and 63 MA women, age 46±14 years (mean±SD) and 100 C, 59 men and 41 women, age 50±11 years—were included in the study, based on medical, and urine and blood 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 (8.1±7.3 % vs 7.1±6.3 %, respectively, p <0.04). In contrast, urine microalbumin was not significantly different in the overall MA versus the C cohort. Urine microalbumin concentration was consistently lower 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.

**Serum Docosahexaenoic Acid Is Associated with Aortic Calcification Independent of Cardiovascular Risk Factors in a Population-Based Sample of Middle-Aged White Men**

Akira Sekikawa, Rhobert W Evans, Graduate Sch of Public Health, Univ of Pittsburgh, Pittsburgh, PA; Daniel Edmdowicz, Univ of Pittsburgh Med Ctr, Pittsburgh, PA; Kim Sutton-Tyrrell, Aiman El-Saed, Jina Choo, Graduate Sch of Public Health, Univ of Pittsburgh, Pittsburgh, PA; Takashi Kadowaki, Shiga Univ of Med Sci, Otsu, Japan; Tomoko Takamuya, Graduate Sch of Public Health, Univ of Pittsburgh, Pittsburgh, PA; Hirotsugu Ueshima, Shiga Univ of Med Science, Otsu, Japan; J David Curt, Pacific Health Resch Institute, Honololu, HI; Lewis H Kuller, Graduate Sch of Public Health, Univ of Pittsburgh, Pittsburgh, PA

**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 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%. 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. Adjusted 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.

**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 participant as an aggregate measure of CVD risk factors. Multivariate 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.
64% of AA (3324) and 74% of EA (4171) achieved BP<140/90 mmHg. Adherence was similar for AA and EA; 44% of AA (2266) 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 1.4, 1.7). In stratified analyses of individuals in 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.

Coronary Calcification Is More Predictive of Carotid Intimal-Medial Thickness in Black Compared to White Middle-Aged Men

Aiman El-Saied, Akira Sekikawa, Univ of Pittsburgh, Pittsburgh, PA; Daniel Edmundowicz, UMPICH Heart Pian, Pittsburgh, PA; Kim Sutton-Tyrrell, Rhonda W Evans, Univ of Pittsburgh, Pittsburgh, PA; Takashi Kadowaki, Shiga Univ of Med Science, Shiga, Japan; Jinko Choo, Univ of Pittsburgh, Pittsburgh, PA; Tomoko Takamiya, Shiga Univ of Med Science, Shiga, Japan; Lewis H Kuller, Univ of Pittsburgh, Pittsburgh, PA

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 (48 black and 295 white) from Allegheny County, PA (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 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=0.038 respectively). Conclusions: In black and white middle aged men, CAD 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.

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 non-obese adults of different ethnicities. Methods: A total of 1,210 normotensive participants in the Family Blood Pressure Program, with body mass index (BMI) <30 kg/m² underwent echocardiography: 233 non-Hispanic white, 311 Hispanic, 268 black and 400 Japanese-American, 54% women (NLS). LVM and LV body surface area (BSA) were compared between men and women of different ethnicities by analysis of covariance, adjusting for age, BMI, height, systolic and diastolic blood pressure, diabetes and, for absolute LVH, LVM and body mass index (BMI). Results: Upper limits of 95% confidence intervals for LVM, LVM/BSA and LVHmass/BSA were 209 g, 108 g/m² and 48 g/m² in men and 169 g, 94 g/m² and 45 g/m² in women, similar to large recent MRI or echocardiographic surveys. LVH mass was higher in Hispanics and blacks than non-Blacks, but 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
Main
(n=119)
(n=139)
(n=135)
(n=172)
LVM (g)
145±28
152±42
154±37
139±28††
LVM/BSA (g/m²)
72±13
80±22††
78±17
71±14††
LVM/BSA (g/m²)
30±6
38±11††
33±8
32±7
Women
(n=112)
(n=165)
(n=128)
(n=229)
LVM (g)
107±26
113±34
116±24
96±22††
LVM/BSA (g/m²)
61±13
68±14*††
67±13
62±14‡‡
LVM/BSA (g/m²)
27±6
33±7
31±7
29±7††

Statistical significance by ANOMA: *p<0.05 vs. whites, †p<0.05 vs. Hispanic, ‡p<0.05 vs. blacks

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 a modified 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 10 most commonly prescribed BP regimens. Results: The 10,831 treated hypertensive individuals had mean age 68±8.6 years;
The Association Between Mortality Following Initial Hospitalization for Heart Failure and SES in Whites and Blacks: The ARIC Study

Calpurnia B Roberts, Gerardo Heise, Diane Catellier, Kathryn M Rose, Wayne D Rosamond, UNC at CHPH, Chapel Hill, NC

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 adolescent SES indicators in all-cause mortality among 1,162 ARIC participants aged 45–84 years at baseline who experienced an incident HF hospital 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 hospitalization 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 Whites was 11.5% (132 of 1,162), and for Blacks, 9.4% (109 of 1,162), respectively. The short-term all-cause mortality for Blacks and Whites was similar, 26% (93/358) and 24% (194/803), respectively. The 5 and 12-year cause-specific mortalities were significantly greater for Blacks than Whites: 43% (155/358) vs. 36% (258/803) and 55% (196/359) vs. 45% (362/803) respectively. The main causes of death were cardiovascular disease (82% and 88% among Whites; 70% and 83% among Blacks, respectively). Higher SES was associated with lower mortality risk (HR 0.81, 95% CI 0.40, 1.64). The prevalence of major cardiovascular disease was defined as any measure of CAC was defined as any measure ≥160 HU. All P values were two-sided and 0.05 was the significance level. Results: For Whites, poverty was independently associated with higher mortality, while higher SES was associated with lower mortality. For Blacks, the association between SES and mortality was less clear, but higher SES was associated with lower mortality.

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 2,243 black women (BW), 6,939 white women (WW), 1,441 black men (BM) and 4,323 white men (WM) were selected from the Chicago Heart Association Detection Project in Industry cohort. Major and minor ECG abnormalities at baseline (1967–1973) were defined according to the Pooling Project criteria. Participants were followed through 2002 for CHD mortality (ICD-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 in BW (p<0.01) compared with WW (7%), whereas the prevalence of minor abnormalities was higher among BW (5% vs. 3% in WW). The prevalence of major abnormalities did not differ between BW and WM (8% in both: mean age=37 years), but minor abnormalities were more common (p<0.01 in BW compared with WM (5%). Over 32 years, 55 BW (3%) and 132 WM (2%) experienced CHD mortality; rates for BW and WM were 107 (73%) and 343 (8%), respectively. Following adjustment for other baseline risk factors, major ECG abnormalities were not associated with CHD mortality (HR: 1.0, 95% CI: 0.4–2.9) whereas minor abnormalities were associated with CHD mortality (HR 2.5, 95% CI: 1.3–4.3). Conclusion: There was no association between minor ECG abnormalities and CHD mortality in men of either race. 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.

Withdrawn

Do Awareness, Preventive Action, and Barriers to Cardiovascular Disease Prevention Vary by Race/Ethnicity in Women?

Heidi Mochari, Columbia Univ, New York, NY; Thomas Mills, Susan Simpson, Burke, Inc, Chapel Hill, NC; Lori Mosca, Columbia Univ, New York, NY

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 (71% 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 preventive action. Using multivariable regression, main outcomes measured were 1) Correlates of knowledge of optimal risk factor goals identified 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 or preventive actions 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: 0.39–0.81). Knowledge of blood pressure goal was lower among those without a college degree (OR=0.59; 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 and race and CAC in an apparent interaction (OR=1.37, 95% CI: 1.01, 1.89 for African American women and 1.96, 95% CI: 1.24, 2.74). Fear of change was reported by significantly more Hispanics than whites as a barrier to preventive action (24% vs 17%; p<0.03). Blacks were more likely than whites to take action because they experienced CVD symptoms (30% vs 23%; p<0.03). Physician encouragement was cited as the reason for taking action to lower CVD risk more often by black (55% vs. 40%) and Hispanic (54%; vs. 30%) women than whites (43%). Conclusion: Initiatives to translate body mass index and conducted maximal graded treadmill testing to obtain fitness level in the 568 siblings of probands with premature CAD. CAD was measured by MDCT, and the presence of CAD 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=1.16, 95% CI:0.94–1.4), and a non-significant increase in the prevalence of hyperlipidemia (LDL nihil=160) (OR=0.78, 95% CI:0.47–1.28). Blacks were found to have a significantly lower prevalence of CAD (38% vs. 47.7%, p<0.03). Using generalized estimating equations to adjust for age, sex, diabetes, hypertension, smoking, obesity, hyperlipidemia, fitness and smoking within families of the same race, was an independent negative predictor of CAD, OR = 0.40 (95% CI:0.26–0.62). OR for male sex was 2.85 (95% CI: 1.94, 4.49), for smoking it was 2.02 (95% CI:1.26, 3.29), 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 CAD. Conclusions: In this randomly selected population of siblings we found that while black and significantly higher prevalence of traditional cardiovascular risk factors, they had significantly less CAD than whites. This suggests that traditional risk factors are only partially responsible for CAD burden, and genetics may play an important role.
awareness into preventive action are needed, especially among less educated and Hispanic women who may activate others to reduce risk.

**P321**

**Prevalence of Overweight and Characteristics Associated With Higher Body Mass Index Among Haitian Immigrant Children**

Nancy Strickman-Stein, Marie-Denise Genvalis, Sarah S Messien, Steven E Lipshutz, Tracie L Miller, Univ of Miami, Miami, FL

**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 born children in the US and other pediatric populations. 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 age, sex, race/ethnicity, age at arrival, height at age 7, height at age 14, and BMI at age 7, 11, and 14. Primary outcome measures included: 1) “at risk” for being overweight (≥85% BMI, ≥95% BMI) and 2) overweight (≥95% BMI). The comparison group was 3958 children from the 2003–2004 National Health and Nutrition Survey (NHANES). **Results** The mean age was 10.8 ± 4.5 yr. 48.5% were male. 56% were born in Haiti, and of those, 39% 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 <0.02). Increased US residence time among Haitian born children resulted in higher BMI% (p <0.047). 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 <0.02). Compared to NHANES estimates, Haitian born children were significantly less likely to be “at risk” for overweight than all racial/ethnic groups (14.3% vs 33.6%) but were as likely to be overweight (15.0% vs 17.7%). Haitian children born in the US were as likely to be “at risk” for adult-onset disease (24.7% vs 26.3%) 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 or higher. Without prevention, these children become more “at risk” for overweight and may benefit from primary prevention strategies to reduce modifiable CVD risk factors.

**P323**

**Prevalence of Cardiovascular Risk Factors in Rural Mexico: Results of the Puentes de Salud Project**

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**Background** Latinos are the lowest 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 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 rural Mexican communities. Participants were asked to attend educational and screening sessions held at local markets in June and July 2005. All participants 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 35.6% and glycemia greater than 200 mg/dl was 5.3%. 21% of cholesterol was greater than 200 mg/dl, 18.1% of HDL cholesterol was 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 lipid levels in rural Mexican. Awareness of chronic diseases appears to be a problem that warrants further investigation.

**P324**

**Thrombo-Metabolic Profile of Hispanic Postinfarction Patients**

Gladyes P Velarde, John C Teeters, Wojciech Zareba, Arthur Moss, Univ of Rochester Med Cnr, Rochester, NY; Edward M Dwyer, UMDNJ-New Jersey Med Sch, New Jersey, NJ; Charles E Sparks, Univ of Rochester Med Cnr, Rochester, NY

The thrombo-metabolic profile of Hispanics with cardiovascular disease is unknown. This study aimed to determine the racial-related differences 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 an MI: total cholesterol, HDL, LDL, triglycerides, apolipoprotein B, apolipoprotein A, factor V, 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 (SCEdefined as unstable angina or nonfatal MI or cardiac death. Results: In comparison to NHW, Hispanic were more obese (BMI 29.0 ± 5.5 vs. 27.1 ± 4.5 kg/m²; p <0.02) had more diabetes (36% vs. 15% p<0.001) and more prevalent hypertension (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 (9%) PCE in NHW and 6 (8%) in Hispanics (p=ns). SCE were observed more frequently in Hispanics (28%) than in NHW (19%)(p=0.05), 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=0.11) 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 cholesterol, 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.

**P325**

**Comprehensive Therapeutic Lifestyle Changes in the Underserved Population: A Longitudinal Study**

Rashid I Alexander, William Means, Carl King, Jarvis Misty, Forshyth Med Cnr, Winston-Salem, NC

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 will 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 preventative care program. 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-disciplinary 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.

**P326**

**Racial Differences in PAI-1 Levels Among Healthy African-American and Caucasian Women**

Susan J Appel, Radhika Phadke, Gary Hunter, Robert A Oster, Hernan E Grenett, Univ of North Carolina at Winston-Salem, NC

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 on the cardiovascular metabolites and predictors of PAI-1 in Caucasian (Caus.) or African-American women (AAW). This cross-sectional study of healthy, asymptomatic 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:** Fastening insulin, triglycerides(TG) and baseline PAI-1 concentrations were measured using standardized protocols; insulin sensitivity(Si) was determined by minimal modeling after an intravenous...
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Disproving the Hispanic Paradox: Cardiovascular Risk Is Higher in Hispanic Women than Commonly Believed

John C Teeters, Glaudy P Velarde, Jason Pacos, Susan Hume, Cynthia Pett, Jeff Huntress, Univ of Rochester, Rochester, NY

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 diabetes and 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 screenings 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 cardiac metabolic 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 analysis. Results: In our population of 170 women (79 Hispanic and 91 non-Hispanic), we showed that Hispanic women had a statistically significant difference between Hispanic and non-Hispanic women, respectively, for the following variables: age (53.7 ± 14.75 vs. 63.4 ± 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. 39%, p = 0.85), diabetes (13% vs. 15%, p = 0.79), hyperlipidemia (38% vs. 53%, p = 0.29), BMI (29.2 ± 8.5 vs. 26.8 ± 5.2, p = 0.19), waist circumference (39.7 ± 16.8 vs. 28.5 ± 12.4, p = 0.19), or Framingham risk scores (8.07% vs. 8.8%, 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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Withdrawn

P329
Variation in Rates of Incident Myocardial Infarction by Neighborhood Socioeconomic Characteristics: The Atherosclerosis Risk in Communities Surveillance

Kathryn M Rose, Chirayath M Suchindran, Kuo Ping Li, Joy L Wood, Randi E Foraker, Eric A White, Wayne D Rosamond, Gerards Heise, UNC Sch of Public Health, Chapel Hill, NC

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) has rarely been studied systematically. We examined the association of neighborhood socioeconomic status (nSES) with incident MI (weighted N = 8183) 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 study examination, and community, race- and gender-specific findings suggested a specific need for a greater degree of post-prandial hyperinsulinemia in order to maintain glucose homoeostasis in the post-prandial state. In these AHW, this may in turn contribute to increased beta cell dysfunction. Viewed in the context of other recent research, these findings suggest the need to consider racial differences in the assessment of cardiovascular risk and warrant additional research (with larger diverse samples) focused on determinants of PAI-1 in women.

Physiological Variables by Race

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<th>VARIABLES</th>
<th>泮 (n=95) MEAN</th>
<th>SD</th>
<th>AHW (n=65) MEAN</th>
<th>SD</th>
<th>RANGE</th>
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<td>15.39</td>
<td>19.2</td>
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</tbody>
</table>

P330
Use of Evidence-Based Medications in Patients Undergoing Coronary Revascularization in Finland During 1995–2003

Veikko Salomaa, Rauni Pääkkönen, KTL-National Public Health Inst, Helsinki, Finland; Marja Niemi, National Institute of Welfare and Health, Helsinki, Finland; Helena Hämäläinen, Timo Klaaukka, Social Insurance Inst of Finland, Helsinki, Finland

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 PTCA). 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 hypoglycemic 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 2000–2001, 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 on the hypolipidemic medication. Female sex and younger age 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 0.80 (95% CI 0.71–0.89) 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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Nina P Paynter, A Richay Sharrett, Thomas Louis, Johns Hopkins Univ, Baltimore, MD; Wayne Rosamond, Univ of North Carolina, Chapel Hill, NC; Aaron R Folsom, Univ of Minnesota, Minneapolis, MN; Jose Corsh, Johns Hopkins Univ, Baltimore, MD

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 these two sources was combined to generate two overall models for predicted probability of a CHD event: 1) only with 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 1% to 4% 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.

Observation and Prehospital Delay Time for Acute Myocardial Infarction: Atherosclerosis Risk in Communities (ARIC) Surveillance

Randi E Foraker, Kathryn M Rose, Univ of North Carolina, Chapel Hill, NC; Aileen P McGinn, Albert Einstein College of Medicine, Bronx, NY; Christopher S Soto-Ibarra, Wayne D Rossamond, Univ of North Carolina, Chapel Hill, NC; David C Goff, Jr, Wake Forest Univ Sch of Medicine, Winston-Salem, NC; Eric A Whitsel, Joy L Wood, Univ of North Carolina, Chapel Hill, NC

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 status (nSES) and health insurance with prehospital delay among a weighted sample of 117457 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 = 1.16, 1.72) and long versus medium delay (OR=1.52, 95% CI = 1.16, 2.02). 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 type of health insurance were 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.

Neighborhood Socioeconomic Status, Health Insurance, and Prehospital Delay Time for Acute Myocardial Infarction: Atherosclerosis Risk in Communities (ARIC) Surveillance

P332

Coronary Heart Disease Mortality Among Young Adults in the United States from 1980 Through 2002: Unfavorable Developments in Recent Years

Earl S Ford, Ctrs for Disease Control and Prevention, Atlanta, GA; Simon Capewell, Univ of Liverpool, Liverpool, United Kingdom

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 ≥35 years. Overall, the age-adjusted mortality rate decreased by 52% in men and 49% in women. The smallest decreases (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 over 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 ≥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.

Explaining the Decline in Coronary Heart Disease Mortality in Italy Between 1980 and 2000

Luigi Palmieri, Istituto Superiore di Sanita`, Rome, Italy; Kathleen Bennett, Trinity Ctr for Health Sciences, St James’s Hosp, Dublin, Ireland; Simonia Giampaoli, Istituto Superiore di Sanita`, Rome, Italy; Simon Capewell, Univ of Liverpool, Liverpool, United Kingdom

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 cardiocerebrovascular and risk factors 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 (24 964 in men, 17 973 in women) than expected. Approximately half the mortality fall was attributable 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 cigarette control and a healthy diet, and which maximises population coverage of effective treatments.

Temporal Trends in the Utilization of Coronary Revascularization in the Community

Yariv Gerber, Chanritji S Rihal, Thoralf M Sundt, III, Jill M Killian, Susan A Weston, Terry M Thereau, Veronique L Roger, Mayo Clinic, Rochester, MN

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- and/or left main coronary artery disease (CABG) 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 multiphasic screening and thus likely reflect the natural history of CAD.

Table. Trends in PCI utilization in Olmsted County across 5-year tertiles

Linkage Table.

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**P333**

**P334**

**P335**

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**Table. Trends in PCI utilization in Olmsted County across 5-year tertiles**

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<td>Overall</td>
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<td>355.4</td>
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<td>259.7</td>
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<td>130.1</td>
<td>171.3</td>
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**Circulatory Systems Diseases**

Vol 115, No 8 February 27, 2007
Validation of Health Insurance Claim Data on Acute Myocardial Infarction for the National Cardiovascular Disease Surveillance System

Donald K Hayes, Northrop Grumman, Cntrs for Disease Control and Prevention, Atlanta, GA; The epidemic of obesity, diabetes, and cardiovascular disease is a national multiple mechanisms, is a major cause of heart failure and an underlying or contributing cause of 54,700 annual deaths. Methods: From the NHM 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 for the Redefinition of Myocardial Infarction (ESC/ACC definition); 2) A Statement From the AHA Council on Epidemiology and Prevention; AHA Statistics Committee; WHF Expert Committee 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 of % of all ICD-10 codes: I–21. When these estimates were applied to the NHM claim database, 85.1% (95% CI: 78.5%–89.9%) of 51,591 tentative events were estimated 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 NHM claim database can be used as a cost-effective method to monitor change in incidence of acute myocardial infarction, because the NHM covers all Korean residents. However insurance claim data should not be used without careful adjustment based on the validity of diagnosis.

Surveillance, Identification, and Notification of Teenagers at Risk of Cardiovascular Disease

Merryn Sayers, Shankar Goudar, Jeff Centilli, Stacey Myers, Stephen Eason, Carter BloodCare, Bedford, TX

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 attend their test results. Methods: We genotyped 1584 African American and 1531 Caucasian HyperGEN (HyperGEN) participants from 1124 families. The Checkpoint 2 (CHEK2) gene, an important polymorphic variants that are associated with type 2 diabetes susceptibility can provide important insight on disease etiology. We previously identified strong evidence of linkage for type 2 diabetes in 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. Cross-sectional analysis, we evaluated the additive effect of CHEK2 SNPs on prevalent type 2 diabetes using mixed effects logistic regression.
Common Variation in Fibrinogen Genes Is Associated with Plasma Fibrinogen Levels but Not Future Cardiovascular Events: The Cardiovascular Health Study

Cara L. Carty, Univ of Washington, Seattle, WA; Leslie A. Lange, Univ of North Carolina, Chapel Hill, NC; Jeremy Walston, Johns Hopkins Univ, Baltimore, MD; Mary Cushman, Peter Durda, Russell P. Tracy, Univ of Vermont, Colchester, VT; Lucia A. Hindorff, Christopher S. Carlson, Debbie Nickerson, Alex P. Reiner, Univ of Washington, Seattle, WA

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 (FGB, FGA, FGG) is associated with fibrinogen concentration, carotid intima-media thickness (IMT) and risk of incident MI and acute stroke in elders (65 years of age and 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=3869) 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 family 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 future CHD events of interest in the current study. In CA, the AA genotype in rs6289363 was associated with higher levels; p=0.0047, and another haplotype tagged by the risk allele for rs40235340 and rs8803869 (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.

Table: Associations between Fibrinogen Haplotype and Level* of CVD Events

<table>
<thead>
<tr>
<th>Haplotype</th>
<th>% Frequency</th>
<th>Fibrinogen in mg/dl (beta, 95% CI)</th>
<th>Ischemic Stroke</th>
<th>MI</th>
<th>HR</th>
<th>Stroke</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FGB995/92</td>
<td>20.6</td>
<td>5.9</td>
<td>7.5 (3.0,12.0)</td>
<td>1.1 (0.5,2.1)</td>
<td>1.1 (0.5,2.1)</td>
<td>1.1 (0.5,2.1)</td>
<td>1.1 (0.5,2.1)</td>
</tr>
<tr>
<td>FGB9092</td>
<td>25.5</td>
<td>6.4</td>
<td>7.5 (3.0,12.0)</td>
<td>1.1 (0.5,2.1)</td>
<td>1.1 (0.5,2.1)</td>
<td>1.1 (0.5,2.1)</td>
<td>1.1 (0.5,2.1)</td>
</tr>
<tr>
<td>AA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FGA4522</td>
<td>19.7</td>
<td>10.0</td>
<td>12.5 (6.5)</td>
<td>1.0 (0.5,2.1)</td>
<td>1.0 (0.5,2.1)</td>
<td>1.0 (0.5,2.1)</td>
<td>1.0 (0.5,2.1)</td>
</tr>
</tbody>
</table>

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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

V Sanja Voruganti, Juan Carlos Lopez-Alarcón, Sue Rutherford, Southwest Foundation for BioMed Resc, San Antonio, TX; Dawn K Richardson, Christopher P Jenkinson, Univ of Texas Health Science Ctr at San Antonio, San Antonio, TX; Shelley A Cole, Jean W MacCluer, John Biangero, Anthony G Comuzie, Southwest Foundation for BioMed Resc, San Antonio, TX

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 (1990–2006) 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 equalvariances 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 ± 11.3 %, respectively. Of the 19 SNPs examined, we found that rs2286382 was associated with higher levels of triglycerides (p = 0.009). The association was stronger in ever-smokers (HR = 1.39, 95% CI: 1.1–1.7), but not in never-smokers (HR = 0.8, 95% CI: 0.6–1.0). The SNP was also associated with increased systolic blood pressure (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 rs7676710 was significantly associated with an increase in systolic blood pressure (p = 0.0002) and waist circumference (p = 0.0001) in visits 1 and 2 only. In addition, SNP rs2286382 was associated with lower triglyceride (p = 0.0009), diastolic blood pressure (p = 0.03), BMI (p = 0.03), and 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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U672815 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 UGT1A6 and UGT2B15 affects smoking-related outcomes 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=10065) for three UGT2B15 single nucleotide polymorphisms (SNPs). Haplotypes were reconstructed using PHASE. Logistic regression stratified by race and adjusted for sampling strategy and center, with controlled weighted proportional to person incident rate at risk, was employed to estimate interaction effects. In this OS, SNPs and haplotypes were measured with a general model and a dominant model, respectively. Additivity deviations measured by interaction contrast ratios (ICR) evaluated the influence of smoking history (ever/never smoker) on associations between genotype/haplotype and CHD. Among the four CHs, the allele frequency of rs8010023 equal to 0.03 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 1.861(1.7, 2.94), 1.490(0.95, 2.34) and 0.930(0.55, 1.55), respectively. Similarly the TT genotype in rs2331434 significantly [OR: 0.74(1–1.65), 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 haplotype CCC (tagged by the rs1802033 and rs7661667 variants alleles) synergistically [OR: 0.50(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 U672815 variants
Single Nucleotide Polymorphisms in the Kallikrein Genes Are Associated with Intracranial Anuerysms 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 anuerysms (AIAs). 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 AIAs on chromosome 19.

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 miss-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 from 13 of the 15 KLK genes, including 11 intronic, 6 intergenic and 2 mis-sense SNPs. The allele frequency of cases was estimated with the EM algorithm, then the distribution of haplotypes in cases vs controls was compared using the EM algorithm. Finally, we evaluated evidence of linkage of two model-free linkage tests, the means test and the proportions test. Results: single locus tests 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. Haploview analysis revealed nominally significant association for the C-C haplotype of SNPs rs1722561 and rs1701946 (empirical p-value = 0.01). In addition, we observed excess sharing among affected siblings (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 AIAs. Further work is needed to determine whether variants in the KLK gene family account for the linkage signal for AIAs on chromosome 19.

Genetic Influences on Inflammatory Responses to a Single High-Fat Meal in Old-Order Amish Population

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Background: inflammation is thought 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 the individual inflammatory response to a high-fat meal. The primary objective of this study was 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.

Methods: In the current study, we genotyped 2 SNPs at each of the 9 genes (CETP, IL1B, IL8, PPARG, TLR4, CETP6914, APOE, CETP70 group in both NHB and MA, but neither association was statistically significant. In NHW, the global test of association was conducted among 1228 cases (850 MI and 370 stroke) and 2683 controls. Participants, aged 30–79, were selected from hypertensive women with at least 2 other cardiovascular risk factors. We also included women with MI or stroke.

Multivariate logistic regression evaluated individual haplotype and SNP-disease associations in log-additive models. Global haploview tests assessed overall gene-level associations, with either MI or stroke. Results: A total of 34 tag SNPs (13 CETP, 3 IL8, 6 PAR6, 12 TLR4 and 19 HSP10) genes were associated with MI and ischemic stroke. Conclusions: Moderate associations of PAR6 and TLR4 genetic variation with MI were demonstrated in agreement with previous reports. However, all specific SNP-disease associations identified in the current study are novel and further studies are needed to confirm these findings.

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 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 allele frequency and age, BMI, sex and T0 level. * p < 0.01, ** p < 0.01 for trend from linear regression.

CETP, IL8, PAR6, and TLR4 Genetic Variations and Risk of Incident Myocardial Infarction and Ischemic Stroke

Dana N Erkanliohu, Nicholas L Smith, Joshua C Bis, Cara L Carty, Kenneth M Rice, Thomas Lumley, Lisa A Hindorff, Rozenn N Lemaitre, Michelle A Williams, David S Siscovick, Susan R Heckbert, Bruce M Pratya, Univ of Washington, Seattle, WA

Background: Studies of associations of genetic variation in candidate genes involved in oxidative stress and inflammation with cardiovascular disease 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 activated receptor, alpha (PPARG) 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 women with at least 2 other cardiovascular risk factors.

Multivariate logistic regression evaluated individual haplotype and SNP-disease associations in log-additive models. Global haploview tests assessed overall gene-level associations, with either MI or stroke. Results: A total of 34 tag SNPs (13 CETP, 3 IL8, 6 PAR6, 12 TLR4 and 19 HSP10) genes were associated with MI and ischemic stroke.

Association of Alox15 Gene Polymorphisms with Prevalence and Progression of Coronary Artery Calcification: The CARDIA Study

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Reticulocycte-type 15–ioperoxidase enzyme (Alox15), a lipid-peroxidizing enzyme, has been implicated in arteriosclerosis in animal models. Functional inactivation of Alox15 in murine arteriosclerosis models consistently reduced atherosclerotic lesion formation. We investigated the association of 11 polymorphisms of the Alox15 gene with progression of coronary artery calcification (CAC) in 3,443 self-identified blacks and whites CADCA 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, family history, and cardiovascular risk factors were constructed to investigate the association of ALOBX15 polymorphisms with CAC prevalence and progression. Single-SNP and haplotype-based analyses were performed. Correction for multiple hypothesis testing was carried out using the direct simulation approach, a fast approximation to permutation. In whites, there was no statistically significant association of ALOBX15 genotypes and haplotypes with prevalence or progression of subclinical atherosclerosis. However, a rare variant (3066G, 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 SNP, which itself was significantly associated with greater Y15 and Y20 CAC prevalence and progression (P = 0.04, 0.01, and 0.02, respectively). This is the first study to implicate sequence variation in the ALOBX15 gene in the development and progression of subclinical atherosclerosis. Promoter assays are being developed to investigate the functional relevance of the identified polymorphism.

**Association of C-Reactive Protein Haplotypes with 20-Year Incidence of Hypertension: The CARDIA Study**

Myriam Forrhage, Univ of Texas–Houston, Houston, TX; Joshua C Bis, Univ of Washington, Seattle, WA; Christopher S Carlson, Fred Hutchinson Cancer Res Ctr, Seattle, WA; Susan L Garrow, Wake Forest Univ, Winston-Salem, NC; Kiang Liu, Northwestern Univ, Chicago, IL; Mark J Fletcher, Univ of California, San Francisco, CA; David S Siscovick, Univ of Washington, Seattle, WA

 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. Haplotype tagging was defined as a blood pressure (BP)-adjusted r² = 0.80 of the CRP locus 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 development of hypertension (RR = 0.49; P = 0.006). This haplotype, tagged by the A allele of SNP1440, which itself was associated with a 50% lower risk of hypertension (odds ratio 1.95 [95% CI 1.36 to 2.61]), was protected by increases in physical activity and cardiorespiratory fitness level.
DNA Base Excision Repair Gene Variants, Tobacco Exposure, and Incident CHD: The Atherosclerosis Risk in Communities (ARIC) Study

Christy L Averey, Daniel A Canos, Gerardo Heiss, Andrew F Olsahn, Charles Poole, Univ of North Carolina at Chapel Hill, Chapel Hill, NC; Molly S Bray, Baylor College of Medicine, Houston, TX; Kari E North, Univ of North Carolina at Chapel Hill, Chapel Hill, NC

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. Analyses were stratified by race and adjusted for smoking pattern 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/rever) were measured with contrast ratio (CR). 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 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 (>5%) haplotypes, were selected: rs1143634, rs16944, rs3917354, rs3917356 for IL 1-beta and SNP alone of 1.1(0.7, 2.0), 2.1(1.3, 3.2) and 0.8(0.4, 1.7), although negligible departure from additivity was observed for rs3917354 (ICR: OR: 0.97; 95%CI: 0.89–1.05). In a second stage analysis, SNPs with significant associations with either outcome are shown above; IL-10, IL-6, CRP, TNF superfamily omitted (p-values < 0.05). SNPs with significant associations with either outcome are shown above; IL-10, IL-6, CRP, TNF superfamily omitted (p-values < 0.05).

**Results**: Two polymorphisms rs12733285 (intron 1) and rs1342387 (intron 6) was associated with higher plasma adiponectin levels (adjusted P < 0.05 and OR: 1.30; 95%CI: 1.01–1.6, p = 0.03), while SNP rs11000795 and rs2069825 of IL 8 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. Haplotype analysis was conducted for both IL 1 and IL 8 gene (OR: 0.62; 95%CI: 0.69–0.77, p < 0.05 for the common haplotype), but did not show significant associations for IL-6 gene. **Conclusions**: Inflammatory genes are associated with the risk of MI. Tag-haplotype adds new insight into the association between inflammatory genes and cardiovascular disease.
Table. Interactions in relation to the risk of coronary heart disease using the MDR method

<table>
<thead>
<tr>
<th>Interaction factors</th>
<th>CV Consistency</th>
<th>Prediction accuracy</th>
<th>Significance test, P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADPOR1 rs1342887, ADPOR2 -4034A/C, -276G/T, TNF-R2</td>
<td>0.67</td>
<td>-0.001</td>
<td></td>
</tr>
<tr>
<td>ADPOR1 rs1373306, rs4959926, TNF-R2</td>
<td>0.63</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>ADPOR4 rs4950894, TNF-R2</td>
<td>0.61</td>
<td>0.07</td>
<td></td>
</tr>
</tbody>
</table>

CV: cross-validation.
* as the basis of ‘1000’ permutation.

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Variation in 24 Clotting Genes and Risk of Nonfatal Myocardial Infarction or Ischemic Stroke
Nicholas L Smith, Joshua C Bis, Kenneth Rice, Susan R Heckbert, Kerri L Wiggins, Sara Biagiotti, Univ of Washington, Seattle, WA; Charles Kooperberg, Fred Hutchinson Cancer Rech Ctr, Seattle, WA; Bruce M Psaty, Univ of Washington, Seattle, WA.

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 total of 2164 SNPs was genotyped in 24 clotting genes.

Results: Common variation in these 24 clotting genes has little impact on risk of arterial thrombosis. Many genes were significantly associated with MI and IS risk, but no single gene is responsible for much of the observed MI and IS risk.

Conclusions: The role of genetic variation in clotting genes in the risk of MI and IS is complex, and the contribution of these genes to arterial clotting risk is multifactorial.

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The Effect of LDL Receptor Diploptyles and Their Interaction with Apolipoprotein E Polymorphisms on Carotid Artery Wall Thickness: The Atherosclerosis Risk in Communities Study
Nora Franceschini, Hind Muallim, Univ of North Carolina, Chapel Hill, NC; Mary K Wojciszke, Univ of Alabama, Birmingham, AL; Kathryn M Rose, Univ of North Carolina, Chapel Hill, NC; Eric Boerwinkle, Kelly A Volcik, Univ of Texas Health Sciences, Houston, TX; Kirk C Wilsensm, Nobuyo Maeda, Xia Li, Kari E North, Univ of North Carolina, Chapel Hill, NC.

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 (LDL-R) variants also affect circulating lipid values in Caucasians. In the present study, we evaluated the association of common variation in 24 single nucleotide polymorphisms (SNPs) in 4 LDL-R genes with prevalent MI and potential interactions among the LDL-R 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 LDL-R 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 data does not suggest that common variation in these 24 clotting genes has little impact on risk of arterial thrombosis.

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–Control 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 y). 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 performed with and without gender adjustment.

Conclusions: There was no evidence to suggest that genetic variation in SNPs within the CCL2 gene and incident CHD neither in men, nor in women in crude and in multivariate adjusted analyses. However, LDLR h2 was associated with significantly higher IMT measures (mean 0.729 mm [standard deviation 0.187] versus 0.716 [0.187], P = 0.001) while LDLR h1 was associated with significantly lower IMT (mean 0.719 mm [standard deviation 0.184] versus 0.724 mm [0.186], P = 0.02) among Caucasians.

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Analytical methods have been proposed for detecting the presence of population stratification and 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.

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Ala379Val Variant of the Lipoprotein Associated Phospholipase A1 Gene and Acute Myocardial Infarction in a Multietnic Case–Control Study
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Lipoprotein associated phospholipase A1 (Lp-PLA1) exerts pro-inflammatory effects through generation of lyso-phosphatidylcholine (lyso-PC) and has been associated with increased cardiovascular disease (CVD) risk. A prior large European case-control study among men and women aged 50–75 years 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 increased generation of lyso-phosphatydilcholine (lyso-PC) and has been associated with increased CVD risk. A prior large European case-control study among men and women aged 50–75 years 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 increased generation of lyso-phosphatydilcholine (lyso-PC) and has been associated with increased CVD risk.
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 cases. The 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) remained significant. These data therefore suggest that the CRP gene may 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.

Methods: A case-cohort study was conducted in initially healthy, middle-aged men and women based on data from the MONAICA/KORA Augsburg case-cohort study. We initially recruited 2169 initially healthy men and women who participated in 435 case subgroups from incident T2DM and 1408 non-case subgroups. Genotyping was performed on the Sequenom MALDI-TOF MS system. Results: We analysed four haplotypes: two in the CRP promoter region (rs3091244; -717/T>C at rs2794521), one intronic (TA T/A at rs1417938) and one exonic (<1050G/C at rs1800897). Haplotype estimation yielded 5 haplotypes with frequencies of 0.352 (GATG 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 common haplotypes, nor the 5 more common haplotypes were found to be consistently associated with incident T2DM in crude and in multiple logistic adjusted analyses in all study participants. However, when we restricted the analysis 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). These data therefore suggest that the CRP gene may 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.
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 intra-class 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 intra-class correlation for FMD was significantly larger in MZ twins (0.39 [0.31–0.47]) than in DZ twins (0.13 [0.06–0.21]), 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.

β3-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 β3-adrenergic receptor (β3-AR) gene variation is not known. This study examines the genetic modulation by β3-AR gene polymorphism (Arg389Gly) on the effect of heart rate on arterial stiffness in young adults.

Methods: The study cohort included 183 young adults 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, but not in whites. 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 variant of Arg389Gly of the β3-AR gene modulates arterial stiffness and its association with heart rate in young adults.

Effect of Variants in the APM1 Gene on Risk for Coronary Heart Disease, Type 2 Diabetes, and Parameters of the Metabolic Syndrome: MONAICA/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 the APM1 gene has 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 MONAICA/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 (rs600291) associated with incident CHD (HR [95% CI] 0.63 [0.44–0.96]; p-value = 0.011). A polymorphism in exon 2 of the gene (rs2244716) was associated with type 2 diabetes in univariate but not in multivariate analyses. 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.
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.