For the first time in more than 20 years, the life expectancy of Americans has declined due to an increase in eight of the 10 leading causes of death, including heart disease and strokes.

Centers for Disease Control and Prevention.  
Dec 8, 2016  
Xu J et al

“Prevention is better than the cure”

Desiderius Erasmus  
Fifteenth-century philosopher

Cardiovascular Disease Prevention 2017: Overview

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Disclosures

- Medical Director, Center for Prevention & Wellness, Baptist Health South Florida
- Scientific Advisory Board:  
  Life Extension Foundation  
  Nordic Naturals
- Speakers Bureau  
  True Health Diagnostics
- Author:  
  The Great American Heart Hoax  
  Heart Attack Proof  
  The Complete Mediterranean Diet
The Risk vs Causal Exposure Paradigm: LDL as a primary cause of vascular disease

Preventing atherosclerosis before the development of significant disease is likely to be much more effective than reducing LDL when vascular disease is advanced.

Toth P et al
Journal of Clinical Lipidology
2014; 8, 594-605

Discordance Between Apolipoprotein B and LDL-Cholesterol in Young Adults Predicts Coronary Artery Calcification
The CARDIA Study

- Background: High levels of apolipoprotein B (apoB) have been shown to predict atherosclerotic cardiovascular disease (CVD) in adults even in the context of low levels of low-density lipoprotein cholesterol (LDL-C) or non–high-density lipoprotein cholesterol (non–HDL-C).
- Objectives: This study aimed to quantify the associations between apoB and the discordance between apoB and LDL-C or non–HDL-C in young adults and measured coronary artery calcium (CAC) in midlife.
- Methods: Data were derived from a multicenter cohort study of young adults recruited at ages 18 to 30 years. All participants with complete baseline CVD risk factor data, including apoB and year 25 (Y25) CAC score, were entered into the study. Presence of CAC was defined as having a positive, nonzero Agatston score as determined by computed tomography. Baseline apoB values were divided into tertiles of 4 mutually exclusive concordant/discordant groups, based on median apoB and LDL-C or non–HDL-C.
- Results: Analysis included 2,794 participants (mean age: 25 ± 3.6 years; body mass index: 24.5 ± 5 kg/m²; and 44.4% male). Mean lipid values were as follows: total cholesterol: 177.3 ± 33.1 mg/dL; LDL-C: 109.9 ± 31.1 mg/dL; non–HDL-C: 124.0 ± 33.5 mg/dL; HDL-C: 53 ± 12.8 mg/dL; and apoB: 90.7 ± 24 mg/dL; median triglycerides were 61 mg/dL. Compared with the lowest apoB tertile, higher odds of developing Y25 CAC were seen in the middle (odds ratio [OR]: 1.53) and high (OR: 2.28) tertiles based on traditional risk factor–adjusted models. High apoB and low LDL-C or non–HDL-C discordance was also associated with Y25 CAC in adjusted models (OR: 1.55 and OR: 1.45, respectively).
- Conclusions: These data suggest a dose-response association between apoB in young adults and the presence of midlife CAC independent of baseline traditional CVD risk factors.

Fourier Trial
Rationale and design of the Further cardiovascular OUtcomes Research with PCSK9 Inhibition in subjects with Elevated Risk trial

• **BACKGROUND:**
  - Despite current therapies, patients with vascular disease remain at high risk for major adverse cardiovascular events. Low-density lipoprotein cholesterol is a well-established modifiable cardiovascular risk factor. Evolocumab is a fully human monoclonal antibody inhibitor of proprotein convertase subtilisin/kexin type 9 that reduces low-density lipoprotein cholesterol by approximately 60% across various populations.

• **STUDY DESIGN:**
  - **FOURIER** is a randomized, placebo-controlled, double-blind, parallel-group, multinational trial testing the hypothesis that adding evolocumab to statin therapy will reduce the incidence of major adverse cardiovascular events in patients with clinically evident vascular disease. The study population consists of 27,564 patients who have had a myocardial infarction (MI), an ischemic stroke, or symptomatic peripheral artery disease and have a low-density lipoprotein ≥70 mg/dL or a non-high-density lipoprotein cholesterol ≥100 mg/dL on an optimized statin regimen. Patients were randomized in a 1:1 ratio to receive either evolocumab (either 140 mg subcutaneously every 2 weeks or 420 mg subcutaneously every month, according to patient preference) or matching placebo injections. The primary end point is major cardiovascular events defined as the composite of cardiovascular death, MI, stroke, hospitalization for unstable angina, or coronary revascularization. The key secondary end point is the composite of cardiovascular death, MI, or stroke. The trial is planned to continue until at least 1,630 patients experience the secondary end point, thereby providing 90% power to detect a relative reduction of ≥15% in this end point.

• **CONCLUSIONS:**
  - **FOURIER** will determine whether the addition of evolocumab to statin therapy reduces cardiovascular morbidity and mortality in patients with vascular disease


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The Vascular Biology of Atherosclerosis

Lipoprotein (Sub)Classes

The diagram illustrates the density and diameter of various lipoprotein subclasses, including chylomicrons, very low-density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), low-density lipoproteins (LDL), high-density lipoproteins (HDL), and Lp(a) particles. The density values range from 0.95 to 1.20 g/ml, and the diameter values range from 10 to 1000 nm.
CHD Event Associations of LDL-P versus LDL-C
Framingham Offspring Study (n=3,066)

Genomics and CHD
• Genetic variants related to LDL-C levels are consistently associated with CHD
• Genetic variants associated with TGRLs are strongly associated with CHD
• Genetic variants associated with HDL-C levels are NOT consistently associated with CHD

Triglycerides and CVD Risk
• Genetic, epidemiological, clinical trial and mechanistic studies all suggest that triglyceride rich lipoproteins are atherogenic.
• Ongoing trials will better define optimal therapy beyond statins
Clinical Question

Is there incremental benefit of adding omega-3 fatty acids to high-risk patients with elevated triglycerides who are on optimal statin therapy for LDL-C?

Ongoing Trials in High-Triglyceride Patients

- **REDUCE-IT**
  - Highly purified ethyl ester of eicosapentaenoic acid vs placebo in ~8000 men and women with CVD or high CVD risk and hypertriglyceridemia on statin
  - Incidence of CV events, such as coronary revascularization
  - Estimated completion 2017

- **STRENGTH**
  - Omega-3 carboxylic acids vs corn oil in ~13,000 men and women with CVD or high CVD risk and LDL-C <100 mg/dL, TG ≥200 and <500 mg/dL for men or HDL-C <45 mg/dL for women on statin
  - First occurrence of MACE (CVD death, nonfatal MI, nonfatal stroke, emergent/elective coronary revascularization, or hospitalization for unstable angina)
  - Estimated completion 2019


Apo C3

- Inhibits lipoprotein/hepatic lipases
- Impairs hepatic uptake of triglyceride-rich lipoproteins (such as lipoprotein remnants)
- Promotes hypertriglyceridemia.
- Contributes to insulin resistance
- Contributes to atherosclerosis.

Omega-3 free fatty acids for the treatment of severe hypertriglyceridemia: the EpanoVa for Lowering Very high triglycerides (EVOLVE) trial.

- **BACKGROUND:**
  - Omega-3 fatty acids in free fatty acid form have enhanced bioavailability, and plasma levels are less influenced by food than for ethyl ester forms.
  - **OBJECTIVE:**
  - The aim was to evaluate the safety and lipid-altering efficacy in subjects with severe hypertriglyceridemia of an investigational pharmaceutical omega-3 free fatty acid (OM3-FFA) containing eicosapentaenoic and docosahexaenoic acid.
  - **METHODS:**
  - This was a multinational, double-blind, randomized, outpatient study. Men and women with triglycerides (TGs) ≥500 mg/dL, but <2000 mg/dL, took control (olive oil [OO] 4 g/d; n = 99), OM3-FFA 2 g/d (plus OO 2 g/d; n = 100), OM3-FFA 3 g/d (plus OO 1 g/d; n = 101), or OM3-FFA 4 g/d (n = 99) capsules for 12 weeks in combination with the National Cholesterol Education Program Therapeutic Lifestyle Changes diet.
  - **RESULTS:**
  - Fasting serum TGs changed from baseline by -25.9% (P < .01 vs OO), -25.5% (P < .01 vs OO), and -30.9% (P < .001 vs OO) with 2, 3, and 4 g/d OM3-FFA, respectively, compared with -4.3% with OO. Non-high-density lipoprotein cholesterol (non-HDL-C), total cholesterol-to-HDL-C ratio, very low-density lipoprotein cholesterol, remnant-like particle cholesterol, apolipoprotein CIII, lipoprotein-associated phospholipase A2, and arachidonic acid were significantly lowered (P < .05 at each OM3-FFA dosage vs OO); and plasma eicosapentaenoic acid and docosahexaenoic acid were significantly elevated (P < .001 at each OM3-FFA dosage vs OO). With OM3-FFA 2 and 4 g/d (but not 3 g/d), low-density lipoprotein cholesterol was significantly increased compared with OO (P < .05 vs OO). High-sensitivity C-reactive protein responses with OM3-FFA did not differ significantly from the OO response at any dosage. Fewer subjects reported any adverse event with OM3-FFA compared with OO at each dosage group, and discontinuation due to adverse event, primarily gastrointestinal, ranged from 5% to 7% across OM3-FFA dosage groups vs 0% for OO.
  - **CONCLUSIONS:**
  - OM3-FFA achieved the primary endpoint for TG lowering and secondary endpoint of non-HDL-C lowering at 2, 3, and 4 g/d in persons with severe hypertriglyceridemia.

Kastelein J et al; J Clin Lipidol; 2014 Jan-Feb;8(1):94-106

Omega-3 free fatty acids significantly lowered Apo C3
EPA Ethyl Esters and Apo C3

MARINE and ANCHOR trials, a 4 gram dose of EPA ethyl esters achieved reductions in Apo C-III levels of 25.1% (p < 0.0001) and 19.2% (p < 0.0001) compared to placebo.

Loss-of-Function Mutations in APOC3, Triglycerides, and Coronary Disease

- **BACKGROUND**
  - Plasma triglyceride levels are heritable and are correlated with the risk of coronary heart disease. Sequencing of the protein-coding regions of the human genome (the exome) has the potential to identify rare mutations that have a large effect on phenotype.

- **METHODS**
  - We sequenced the protein-coding regions of 18,886 genes in each of 9754 participants of European or African ancestry in the Exome Sequencing Project. We conducted tests to determine whether rare mutations in coding sequence, individually or in aggregate within a gene, were associated with plasma triglyceride levels. For mutations associated with triglyceride levels, we subsequently evaluated their association with the risk of coronary heart disease in 110,970 persons.

- **RESULTS**
  - An aggregate of rare mutations in the gene encoding apolipoprotein C3 (APOC3) was associated with lower plasma triglyceride levels. Among the four mutations that drove this result, three were loss-of-function mutations: a nonsense mutation (R19X) and two splice-site mutations (IVS2+1G→A and IVS3+1G→T). The fourth was a missense mutation (A43T). Approximately 1 in 150 persons in the study was a heterozygous carrier of at least one of these four mutations. Triglyceride levels in the carriers were 39% lower than levels in noncarriers (P=1×10$^{-20}$), and circulating levels of APOC3 in carriers were 46% lower than levels in noncarriers (P=8×10$^{-20}$). The risk of coronary heart disease among 498 carriers of any rare APOC3 mutation was 40% lower than the risk among 110,472 noncarriers (odds ratio, 0.60; 95% confidence interval, 0.47 to 0.75; P=4×10$^{-20}$).

- **CONCLUSIONS**
  - Rare mutations that disrupt APOC3 function were associated with lower levels of plasma triglycerides and APOC3. Carriers of these mutations were found to have a reduced risk of coronary heart disease.


Antisense Inhibition of Apolipoprotein C-III in Patients with Hypertriglyceridemia

- **BACKGROUND**
  - Apolipoprotein C-III (APOC3) is a key regulator of plasma triglyceride levels. Elevated triglyceride levels are associated with a risk of adverse cardiovascular events and pancreatitis. ISIS 304801 is a second-generation antisense inhibitor of APOC3 synthesis.

- **METHODS**
  - We conducted a randomized, double-blind, placebo-controlled, dose-ranging, phase 2 study to evaluate ISIS 304801 in untreated patients with fasting triglyceride levels between 350 mg per deciliter (4.0 mmol per liter) and 2000 mg per deciliter (22.6 mmol per liter) (ISIS 304801 monotherapy cohort), as well as in patients receiving stable fibrate therapy who had fasting triglyceride levels between 225 mg per deciliter (2.5 mmol per liter) and 1000 mg per deciliter (11.3 mmol per liter) (ISIS 304801–fibrate cohort). Eligible patients were randomly assigned to receive either ISIS 304801, at doses ranging from 100 to 305 mg, or placebo, once weekly for 13 weeks. The primary outcome was the percentage change in APOC3 level from baseline.

- **RESULTS**
  - A total of 57 patients were treated in the ISIS 304801 monotherapy cohort (45 received active agent, and 16 received placebo), and 33 patients were treated in the ISIS 304801–fibrate cohort (20 received active agent, and 13 received placebo). The mean baseline triglyceride levels in the two cohorts were 581±195 mg per deciliter (6.4±2.2 mmol per liter) and 376±188 mg per deciliter (4.2±2.1 mmol per liter), respectively. Treatment with ISIS 304801 resulted in dose-dependent and prolonged decreases in plasma APOC3 levels when the drug was administered as a single agent (decreases of 32.8±22.6% in the 100-mg group, 63.8±22.3% in the 200-mg group, and 79.6±9.3% in the 300-mg group, vs. an increase of 4.2±4.1% in the placebo group) and when it was administered as an add-on to fibrate therapy (decreases of 60.1±22.5% in the 100-mg group, 70.9±13.0% in the 200-mg group, vs. a decrease of 2.2±2.5% in the placebo group). Consistent reductions of 33.3 to 70.9% were observed in triglyceride levels. No safety concerns were identified in this short-term study.

- **CONCLUSIONS**
  - We found that treatment with ISIS 304801 was associated with significant lowering of triglyceride levels, among patients with a broad range of baseline levels, through selective antisense inhibition of APOC3 synthesis.

Antisense Inhibition of Apolipoprotein C-III in Patients with Hypertriglyceridemia

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  - We conducted a randomized, double-blind, placebo-controlled, dose-ranging, phase 2 study to evaluate ISIS 304801 in untreated patients with fasting triglyceride levels between 350 mg per deciliter (4.0 mmol per liter) and 2000 mg per deciliter (22.6 mmol per liter) (ISIS 304801 monotherapy cohort), as well as in patients receiving stable fibrate therapy who had fasting triglyceride levels between 225 mg per deciliter (2.5 mmol per liter) and 2000 mg per deciliter (ISIS 304801–fibrate cohort). Eligible patients were randomly assigned to receive either ISIS 304801, at doses ranging from 100 to 300 mg, or placebo, once weekly for 13 weeks. The primary outcome was the percentage change in APOC3 level from baseline.

- **RESULTS**
  - A total of 57 patients were treated in the ISIS 304801 monotherapy cohort (41 received active agent, and 16 received placebo), and 28 patients were treated in the ISIS 304801–fibrate cohort (20 received active agent, and 8 received placebo). The mean (±SD) baseline triglyceride levels in the two cohorts were 581±291 mg per deciliter (6.6±3.3 mmol per liter) and 376±188 mg per deciliter (4.2±2.1 mmol per liter), respectively. Treatment with ISIS 304801 resulted in dose-dependent and prolonged decreases in plasma APOC3 levels when the drug was administered as a single agent (decreases of 40.0±32.0% in the 100-mg group, 63.8±22.3% in the 200-mg group, and 79.6±9.3% in the 300-mg group, vs. an increase of 4.2±41.7% in the placebo group) and when it was administered as an add-on to fibrates (decreases of 60.2±12.5% in the 200-mg group and 70.9±13.0% in the 300-mg group, vs. a decrease of 2.2±25.2% in the placebo group). Concordant reductions of 31.3 to 70.9% were observed in triglyceride levels. No safety concerns were identified in this short-term study.

- **CONCLUSIONS**
  - We found that treatment with ISIS 304801 was associated with significant lowering of triglyceride levels (mean reduction up to 71%) in triglycerides, among patients with a broad range of baseline levels, through selective antisense inhibition of APOC3 synthesis.


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**Residual Risk**

**Therapeutic Lifestyle Intervention**
Genetic Risk, Adherence to a Healthy Lifestyle, and Coronary Disease

- **BACKGROUND**
  - Both genetic and lifestyle factors contribute to individual-level risk of coronary artery disease. The extent to which increased genetic risk can be offset by a healthy lifestyle is unknown.

- **METHODS**
  - Using a polygenic score of DNA sequence polymorphisms, we quantified genetic risk for coronary artery disease in three prospective cohorts—7814 participants in the Atherosclerosis Risk in Communities (ARIC) study, 21,222 in the Women’s Genome Health Study (WGHS), and 22,389 in the Malmö Diet and Cancer Study (MDCS)—and in 4090 participants in the cross-sectional BioImage Study for whom genotype and covariate data were available. We also determined adherence to a healthy lifestyle among the participants using a scoring system consisting of four factors: no current smoking, no obesity, regular physical activity, and a healthy diet.

- **RESULTS**
  - The relative risk of incident coronary events was 91% higher among participants at high genetic risk (top quintile of polygenic scores) than among those at low genetic risk (bottom quintile of polygenic scores) (hazard ratio, 1.91; 95% confidence interval [CI], 1.75 to 2.09). A favorable lifestyle (defined as at least three of the four healthy lifestyle factors) was associated with a substantially lower risk of coronary events than an unfavorable lifestyle (defined as no or only one healthy lifestyle factor), regardless of the genetic risk category. Among participants at high genetic risk, a favorable lifestyle was associated with a nearly 50% lower relative risk of coronary artery disease (hazard ratio, 0.54; 95% CI, 0.47 to 0.63). This finding corresponded to a reduction in the standardized 10-year incidence of coronary events from 10.7% for an unfavorable lifestyle to 5.1% for a favorable lifestyle in ARIC, from 4.6% to 2.0% in WGHS, and from 8.2% to 5.3% in MDCS. In the BioImage Study, a favorable lifestyle was associated with significantly less coronary-artery calcification within each genetic risk category.

- **CONCLUSIONS**
  - Across four studies involving 55,885 participants, genetic and lifestyle factors were independently associated with susceptibility to coronary artery disease. Among participants at high genetic risk, a favorable lifestyle was associated with a nearly 50% lower relative risk of coronary artery disease than was an unfavorable lifestyle.

Ami K et al. N Engl J Med 2016; 375:2349-2358

The Mediterranean Diet and the Metabolic Syndrome

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  - Both genetic and lifestyle factors contribute to individual-level risk of coronary artery disease. The extent to which increased genetic risk can be offset by a healthy lifestyle is unknown.

- **METHODS**
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- **CONCLUSION:**
  - Among participants at high genetic risk, a favorable lifestyle was associated with a nearly 50% lower relative risk of coronary artery disease than was an unfavorable lifestyle.

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The optimal diet for cardiovascular health?

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- **METHODS**
  - Across four studies involving 55,885 participants, genetic and lifestyle factors were independently associated with susceptibility to coronary artery disease. Among participants at high genetic risk, a favorable lifestyle was associated with a nearly 50% lower relative risk of coronary artery disease than was an unfavorable lifestyle.

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  - Across four studies involving 55,885 participants, genetic and lifestyle factors were independently associated with susceptibility to coronary artery disease. Among participants at high genetic risk, a favorable lifestyle was associated with a nearly 50% lower relative risk of coronary artery disease than was an unfavorable lifestyle.

- **CONCLUSION:**
  - Among participants at high genetic risk, a favorable lifestyle was associated with a nearly 50% lower relative risk of coronary artery disease than was an unfavorable lifestyle.

Ami K et al. N Engl J Med 2016; 375:2349-2358

The Mediterranean Diet vs control diet:

- **Significant reduction in body weight, insulin resistance, blood glucose, inflammatory markers and blood pressure.**
- **Significant improvement in lipid profile (decrease in total cholesterol and triglycerides and increase in HDL-cholesterol) and endothelial function.**
- **50% decrease in the prevalence of metabolic syndrome.**

Esposito et al. JAMA 2004; 292: 1440-1446
Sugar and Metabolic Syndrome

- Fructose (sucrose or HFCS) consumption has increased over the last 30 years, coinciding with the obesity epidemic
- Fructose is not glucose
- Hepatic fructose metabolism leads to all of the manifestations of the metabolic syndrome (obesity, insulin and leptin resistance, atherogenic dyslipidemia, inflammation, hypertension, de novo lipogenesis, hepatic steatosis)

The role of reducing intakes of saturated fat in the prevention of cardiovascular disease

The risk of coronary heart disease is reduced when saturated fatty acids are replaced with polyunsaturated fatty acids.

Astrup, Willett et al
Am J Clin Nutr; April 2011; vol. 93 no.4: 684-688

Red Meat Consumption and Mortality

- Red meat contains carnitine and choline which is taken up by intestinal bacteria and leads to TMAO
- TMAO in the blood increases the risk of atherosclerosis and thrombosis

Stanley Hazen et al
Nature Medicine
April 7, 2013

Adiposopathy (or “sick fat”) is defined as pathologic adipose tissue functional disturbances promoted by positive caloric balance and physical inactivity in genetically susceptible individuals that result in adverse endocrine and immune responses that increase cardiometabolic risk and promote cardiovascular disease.
Adipose Tissue / Fat Storage

Fat storage depots include:

- **Subcutaneous peripheral fat** (~80%)
  - Truncal
  - Gluteofemoral
  - Mammary
  - Inguinal (reported in animal studies)
  - Subcutaneous abdominal fat

- **Visceral fat** (~20%)
  - Intraperitoneal: omental, mesenteric, and umbilical
  - Extrapерitoneal: includes peripancreatic and perirenal
  - Intrapelvic: gonadal (epididymal) and urogenital
  - Intraorgan fat
    - Liver
    - Muscle
    - Pancreas?
    - Bone
  - Other periorgan fat
    - Pericardial
    - Perimuscular
    - Perivascular
    - Orbital
    - Paraosseal

Subcutaneous vs Visceral Fat

- Dysfunction of adipose cells is more common in visceral fat tissue than subcutaneous fat tissue.


Exercise

“Lack of activity destroys the good condition of every human being, while movement and methodical physical exercise save it and preserve it.”

Plato
320 BC

Walking Lowers CVD Risk

- Among 73,000 postmenopausal women aged 50 to 79 in the Women's Health Initiative Observational Study, walking briskly for at least 2.5 hours/week was associated with a 30% reduction in cardiovascular events over 3 years
- In an 8-year follow-up of 72,000 healthy middle-aged female nurses in the Nurses' Health Study, 3 hours/week of brisk walking lowered heart attack risk 40%
- In a 7-year follow-up of 39,000 healthy middle-aged female health professionals in the Women's Health Study, walking at least 1 hour/week was associated with a 50% reduction in CHD risk
Relation between resting amygdalar activity and cardiovascular events: a longitudinal and cohort study

**Background**
- Emotional stress is associated with increased risk of cardiovascular disease. We imaged the amygdala, a brain region involved in stress, to determine whether its resting metabolic activity predicts risk of subsequent cardiovascular events.
- Methods
  - Individuals aged 30 years or older without known cardiovascular disease or active cancer disorders, who underwent fluorodeoxyglucose PET/CT at Massachusetts General Hospital (Boston, MA, USA) between Jan 1, 2005, and Dec 31, 2008, were studied longitudinally. Amygdalar activity, bone-marrow activity, and arterial inflammation were assessed with validated methods. In a separate cross-sectional study we analysed the relation between perceived stress, amygdalar activity, arterial inflammation, and C-reactive protein. Image analyses and cardiovascular disease event adjudication were done by mutually blinded researchers. Relations between amygdalar activity and cardiovascular disease events were validated methods. In a separate cross-sectional study we analysed the relation between perceived stress, amygdalar activity, and C-reactive protein.
- Findings
  - 293 patients (median age 55 years [IQR 45·0–65·5]) were included in the longitudinal study, 22 of whom had a cardiovascular disease event during median follow-up of 3·7 years (IQR 2·7–4·8). Amygdalar activity was associated with increased bone-marrow activity (r=0·47; p<0·0001), arterial inflammation (r=0·83; p=0·0210), and risk of cardiovascular disease events (standardised hazard ratio 1·59, 95% CI 1·27–1·98; p<0·0001), a finding that remained significant after multivariate adjustments. The association between amygdalar activity and cardiovascular disease events seemed to be mediated by increased bone-marrow activity and arterial inflammation in series. In the separate cross-sectional study of 18 patients who underwent psychometric analysis (n=13), amygdalar activity was significantly associated with arterial inflammation (r=0·49; p<0·0001). Perceived stress was associated with amygdalar activity (r=0·56; p=0·0485), arterial inflammation (r=0·83; p=0·0210), and C-reactive protein (r=0·47; p<0·0001).
- Interpretation
  - Emotional stress is associated with increased risk of cardiovascular disease. We imaged the amygdala, a brain region involved in stress, to determine whether its resting metabolic activity predicts risk of subsequent cardiovascular events. These findings provide novel insights into the mechanism through which emotional stressors can lead to CVD.
Smoking marijuana:

- Can precipitate coronary vasospasm
- Is associated with a dose-dependent increase in heart rate (20% - 100%) and an increase in supine BP
- Can lead to an increase in carboxyhemoglobin, resulting in decreased oxygen-carrying capacity
- Among patients with chronic stable angina, the anginal threshold is acutely diminished by 48% after smoking a single marijuana cigarette.


Cannabis Use: Signal of Increasing Risk of Serious Cardiovascular Disorders

Increased reporting of cardiovascular complications related to cannabis (mortality 25%) indicate cannabis as a possible risk factor for cardiovascular disease in young adults. Given that cannabis is perceived to be harmless by the general public and that legalization of its use is debated, data concerning its danger must be widely disseminated. Practitioners should be aware that cannabis may be a potential triggering factor for cardiovascular complications in young people.

Jouaninis Emile et al; J Am Heart Assoc April 23, 2014
Obstructive Sleep Apnea as a Risk Factor for Stroke and Death

H. Klar Yaggi, M.D., M.P.H., John Concato, M.D., M.P.H., Walter N. Kernan, M.D., Judith H. Lichtman, Ph.D., M.P.H., Lawrence M. Brass, M.D., and Vahid Mohsenin, M.D.

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November 10, 2005