Am J Cardiol (2004);93:1030-2
Effect of carotid atherosclerosis screening on risk stratification during primary cardiovascular disease prevention
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We investigated the effect that carotid plaque area (CPA) and intima media thickness (IMT) measurements have on risk stratification in 95 patients with intermediate Framingham scores (6% to 19%). The risk status of each patient was adjusted to be low, intermediate, or high based on the results of carotid ultrasound. After carotid testing, 44% (IMT) and 45% (CPA) of the intermediate-risk patients were stratified as low risk, and 22% (IMT) and 40% (CPA) were stratified as high risk. Using the threshold values derived from our laboratory, 28% (IMT) and 45% (CPA) of patients were stratified as low risk, and 35% (IMT) and 27% (CPA) were identified as high risk. These tests adjust the risk strata of >/=63% of patients deemed as having intermediate risk by Framingham scores.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15081449

Circulation (2004);109:1536-42
Irbesartan but not amlodipine suppresses diabetes-associated atherosclerosis
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BACKGROUND: It remains controversial whether specific blockade of the renin-angiotensin system confers superior antiatherosclerotic effects over other antihypertensive agents in diabetes. Therefore, the aim of this study was to compare equihypotensive doses of the angiotensin II subtype 1 (AT1) receptor blocker irbesartan with the calcium antagonist amlodipine on diabetes-induced plaque formation in the apolipoprotein E (apoE)-null mouse and to explore molecular and cellular mechanisms linked to vascular protection. METHODS AND RESULTS: Diabetes was induced by injection of streptozotocin in 6-week-old apoE-null mice. Diabetic animals were randomized to no treatment, irbesartan, or amlodipine for 20 weeks. Diabetes was associated with an increase in plaque area and complexity in the aorta in association with a significant increase in aortic AT1 receptor expression, cellular proliferation, collagen content, macrophage- and alpha-smooth muscle actin-positive cell infiltration, as well as an increased expression of platelet-derived growth factor-B (PDGF-B), monocyte chemoattractant protein-1 (MCP-1), and vascular cell adhesion molecule-1 (VCAM-1). Irbesartan but not amlodipine treatment attenuated the development of atherosclerosis, collagen content, cellular proliferation, and macrophage infiltration as well as diabetes-induced AT1 receptor, PDGF-B, MCP-1, and VCAM-1 overexpression in the aorta despite similar blood pressure reductions by both treatments. CONCLUSIONS: Diabetes-associated atherosclerosis is ameliorated by AT1 receptor blockade but not by calcium channel antagonism, providing further evidence for the vascular renin-angiotensin system playing a pivotal role in the development and acceleration of atherosclerosis in diabetes.
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n&list_uids=15023892

N Engl J Med (2004);350:1495-504
Intensive versus moderate lipid lowering with statins after acute coronary syndromes
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BACKGROUND: Lipid-lowering therapy with statins reduces the risk of cardiovascular events, but the optimal level of low-density lipoprotein (LDL) cholesterol is unclear. METHODS: We enrolled 4162 patients who had been hospitalized for an acute coronary syndrome within the preceding 10 days and compared 40 mg of pravastatin daily (standard therapy) with 80 mg of atorvastatin daily (intensive therapy). The primary end point was a composite of death from any cause, myocardial infarction, documented unstable angina requiring rehospitalization, revascularization (performed at least 30 days after randomization), and stroke. The study was designed to establish the noninferiority of pravastatin as compared with atorvastatin with respect to the time to an end-point event. Follow-up lasted 18 to 36 months (mean, 24). RESULTS: The median LDL cholesterol level achieved during treatment was 95 mg per deciliter (2.46 mmol per liter) in the standard-dose pravastatin group and 62 mg per deciliter (1.60 mmol per liter) in the high-dose atorvastatin group (P<0.001). Kaplan-Meier estimates of the rates of the primary end point at two years were 26.3 percent in the pravastatin group and 22.4 percent in the atorvastatin group, reflecting a 16 percent reduction in the hazard ratio in favor of atorvastatin (P=0.005; 95 percent confidence interval, 5 to 26 percent). The study did not meet the prespecified criterion for equivalence but did identify the superiority of the more intensive regimen. CONCLUSIONS: Among patients who have recently had an acute coronary syndrome, an intensive lipid-lowering statin regimen provides greater protection against death or major cardiovascular events than does a standard regimen. These findings indicate that such patients benefit from early and continued lowering of LDL cholesterol to levels substantially below current target levels.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15007110

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Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial
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BACKGROUND: Type 2 diabetes is associated with a substantially increased risk of cardiovascular disease, but the role of lipid-lowering therapy with statins for the primary prevention of cardiovascular disease in diabetes is inadequately defined. We aimed to assess the effectiveness of atorvastatin 10 mg daily for primary prevention of major cardiovascular events in patients with type 2 diabetes without high concentrations of LDL-cholesterol. METHODS: 2838 patients aged 40-75 years in 132 centres in the UK and Ireland were randomised to placebo (n=1410) or atorvastatin 10 mg daily (n=1428).

Study entrants had no documented previous history of cardiovascular disease, an LDL-cholesterol concentration of 4.14 mmol/L or lower, a fasting triglyceride amount of 6.78 mmol/L or less, and at least one of the following: retinopathy, albuminuria, current smoking, or hypertension. The primary endpoint was time to first occurrence of the following: acute coronary heart disease events, coronary revascularisation, or stroke. Analysis was by intention to treat. FINDINGS: The trial was terminated 2 years earlier than expected because the prespecified early stopping rule for efficacy had been met. Median duration of follow-up was 3.9 years (IQR 3.0-4.7). 127 patients allocated placebo (2.46 per 100 person-years at risk) and 83 allocated atorvastatin (1.54 per 100 person-years at risk) had at least one major cardiovascular event (rate reduction 37% [95% CI -52 to -17], p=0.001). Treatment would be expected to prevent at least 37 major vascular events per 1000 such people treated for 4 years. Assessed separately, acute coronary heart disease events were reduced by 36% (-55 to -9), coronary revascularisations by 31% (-59 to 16), and rate of stroke by 48% (-69 to -11). Atorvastatin reduced the death rate by 27% (-48 to 1, p=0.059). No excess of adverse events was noted in the atorvastatin group. INTERPRETATION: Atorvastatin 10 mg daily is safe and efficacious in reducing the risk of first cardiovascular disease events, including stroke, in patients with type 2 diabetes without high LDL-cholesterol. No justification is available for having a particular threshold level of LDL-cholesterol as the sole arbiter of which patients with type 2 diabetes should receive statins. The debate about whether all people with this disorder warrant statin treatment should now focus on whether any patients are at sufficiently low risk for this treatment to be withheld.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15325833

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Early intensive vs a delayed conservative simvastatin strategy in patients with acute coronary syndromes: phase Z of the A to Z trial
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CONTEXT: Limited data are available evaluating how the timing and intensity of statin therapy following an acute coronary syndrome (ACS) event affect clinical outcome. OBJECTIVE: To compare early initiation of an intensive statin regimen with delayed initiation of a less intensive regimen in patients with ACS. DESIGN, SETTING, AND PARTICIPANTS: International, randomized, doubl

the median LDL cholesterol level achieved at 1 month while taking 40 mg/d of simvastatin was 68 mg/dL (1.76 mmol/L) and was 63 mg/dL (1.63 mmol/L) at 8 months while taking 80 mg/d of simvastatin. A total of 343 patients (16.7%) in the placebo plus simvastatin group experienced the primary end point compared with 309 (14.4%) in the simvastatin only group (40 mg/80 mg) (hazard ratio [HR], 0.89; 95% confidence interval [CI] 0.76-1.04; P =.14). Cardiovascular death occurred in 109 (5.4%) and 83 (4.1%) patients in the 2 groups (HR, 0.75; 95% CI, 0.57-1.00; P =.05) but no differences were observed in other individual components of the primary end point. No difference was evident during the first 4 months between the groups for the primary end point (HR, 1.01; 95% CI, 0.83-1.25; P =.89), but from 4 months through the end of the study the primary end point was significantly reduced in the simvastatin only group (HR, 0.75; 95% CI, 0.60-0.95; P =.02). Myopathy (creatine kinase >10 times the upper limit of normal associated with muscle symptoms) occurred in 9 patients (0.4%) receiving simvastatin 80 mg/d, in no patients receiving lower doses of simvastatin, and in 1 patient receiving placebo (P =.02). CONCLUSIONS: The trial did not achieve the prespecified end point. However, among patients with ACS, the early initiation of an aggressive simvastatin regimen resulted in a favorable trend toward reduction of major cardiovascular events.
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Evaluating the impact of population and high-risk strategies for the primary prevention of cardiovascular disease
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AIMS: To estimate the potential effectiveness of different "high-risk" and "population" approaches to the primary prevention of cardiovascular disease (CVD) in middle-aged British men, after correction for regression dilution bias. METHODS AND RESULTS: We used a combination of cohort and randomised controlled trial evidence to estimate the effectiveness of high-risk strategies, based on the identification of high-risk factors or high absolute risk, and strategies based on population-wide reductions in cholesterol and blood pressure. High-risk strategies were potentially effective but would need to be used widely to have a substantial effect on CVD in the population. Aggressive pharmacological treatment (using statins, beta-blockers, ACE-inhibitors and aspirin) in individuals with a 10-year Framingham event risk of >or=30% (6% of population) would have reduced major CVD by at most 11%. This figure increased to 34% at a >or=20% treatment threshold (26% of population). In contrast, modest downwards shifts in the population distributions of serum total cholesterol and systolic blood pressure led to marked expected reductions in major CVD. Taking regression dilution bias into account, 10% reductions in long-term mean blood cholesterol and blood pressure could have reduced major CVD by 45%. CONCLUSIONS: If high-risk strategies are to have a major impact on CVD in the population, they need to be more widely used than previously envisaged. Population-wide reduction of major risk factors is needed if CVD is to be substantially reduced.
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n&list_uids=15039128

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Evidence-based guidelines for cardiovascular disease prevention in women
L. Mosca*, et al.*
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14998635