Can CT Coronary Angiography Replace Cardiac Catheterization?

Diagnostic Performance of Coronary Angiography by 64-Row CT.

Miller JM, Rochitte CE, et al:


CT coronary angiography can identify significant coronary stenoses in patients at high risk for heart disease, but it is falsely negative in 17% of patients.

**Background:** Given the high prevalence of coronary artery disease (CAD), there continues to be great interest in minimally invasive ways to evaluate for coronary stenoses. Currently, CT coronary angiography is being used with increasing frequency, but its sensitivity and specificity are still unclear.

**Objective:** To determine the accuracy of CT angiography as compared to conventional coronary angiography in patients at high risk for CAD.

**Design:** Prospective, multicenter, international diagnostic study.

**Participants:** To be eligible, patients had to be aged at least 40 years and be referred for coronary angiography for suspected symptomatic heart disease. Patients were not eligible if they had undergone cardiac surgery, had decreased renal function, or had elevated coronary calcium scoring (Agatston score >600).

**Methods:** Each patient underwent coronary calcium scoring and CT coronary angiography (with 64-row scanners) before also undergoing cardiac catheterization. For CT images, 2 independent observers quantitated the degree of stenosis, and a reading was performed with an available software program. Similar segments of artery were identified and measured with conventional coronary angiography. Obstructive lesions were considered clinically important if >50%.

**Results:** 291 patients were enrolled (median age, 59 years; 74% were male). Median time between CT study and conventional angiography was 10 hours. Overall, 56% of patients were found to have significant obstructive CAD. The sensitivity for CT angiography was 85% and specificity was 90%. For this population with a 56% prevalence, the positive-predictive value was 91% and the negative-predictive value was 83%. In a secondary analysis, CT angiography compared favorably with conventional angiography in predicting the need for coronary interventions. Only 2 patients had serious reactions to contrast dye, requiring hospitalization, and there were no cases of renal failure reported.

**Conclusions:** CT coronary angiography can identify significant coronary stenoses in patients at high risk for heart disease. However, 17% of patients with a negative study were found to have significant obstruction on conventional angiography, making it unlikely that CT has adequate accuracy to replace conventional angiography.

**Reviewer's Comments:** The accompanying editorial offers strong words on the judicious (or lack thereof) use of new technologies, offering concern over the quick adaption and use of unproven diagnostic tests. At this point, the most clearly defined role for CT angiography has been to quickly "rule out" significant disease in lower-risk patients presenting with chest symptoms (partly as a way to avoid need for hospitalization). Now we have further information on patients at higher risk. Clearly, the test has the capacity to identify many patients with CAD. However, it remains unclear to me that it has any use in this high-risk population. (Reviewer-Mark E. Pasanen, MD).

© 2009, Oakstone Medical Publishing

Keywords: Coronary Artery Disease

Print Tag: Refer to original journal article
In patients with symptomatic heart failure and preserved systolic function, the addition of an angiotensin receptor blockade does not improve important clinical outcomes.

**Background:** In patients with symptomatic heart failure (HF), nearly half have preserved left ventricular function. When hospitalized, these patients have similar outcomes to those with impaired ventricular function. Although there are proven interventions to improve outcomes in patients with systolic dysfunction, there are no proven treatments for those with preserved function. There are several theoretical reasons why an angiotensin receptor blockade (ARB) might be helpful, including beneficial effects on blood pressure and ventricular hypertrophy.

**Objective:** To determine whether irbesartan, an ARB, improves cardiovascular outcomes in patients with HF and preserved ejection fraction (EF).

**Design:** Randomized, double-blind placebo-controlled trial.

**Participants:** Patients were enrolled from 25 centers around the world. To be eligible, patients needed to be aged at least 60 years, have symptoms of HF, and have an EF of at least 45%. In addition, they needed to have been hospitalized for HF in the last 6 months or have class III or IV HF with objective evidence supporting the diagnosis. Exclusion criteria included recent acute coronary syndrome, stroke or revascularization, hypertrophic cardiomyopathy, systolic blood pressure <100 or >160 mm Hg, or creatinine >2.5 mg/dL.

**Methods:** Patients were started on irbesartan 75 mg or placebo daily, and dose was titrated up to 300 mg daily. The primary outcome was a composite of death from any cause or hospitalization for cardiovascular reasons. Multiple secondary outcomes were tracked, including HF, quality-of-life measures, and B-type natriuretic peptide.

**Results:** 4128 patients were enrolled; approximately 60% were female, and average age was 72 years. Mean EF was 60%, with the most common cause of HF being hypertension (64%). By the study’s completion, many patients were also treated with an angiotensin-converting enzyme (ACE) inhibitor (39% to 40%), spironolactone (28% to 29%), or β-blockers (73%). At a mean follow-up of 4 years, there were no significant differences between irbesartan and placebo with respect to the composite cardiovascular outcome, death, worsening HF, or hospitalization. Adverse event rates were similar in both groups.

**Conclusions:** In patients with symptomatic HF and preserved systolic function, the addition of an ARB does not improve important clinical outcomes.

**Reviewer’s Comments:** Unfortunately, this is another negative study in the management of patients with HF and reasonable ventricular function. At this point, it does not appear that inhibiting the renin-angiotensin-aldosterone system has a significant effect on clinically relevant outcomes in this patient population. It is important to realize, however, that these patients at baseline had good blood pressure control (137/79 mm Hg) and were aggressively managed, as exhibited by rates of spironolactone, β-blockers, and concomitant ACE inhibitors. Therefore, I think it is still very important to manage blood pressure and volume status. (Reviewer-Mark E. Pasanen, MD).

© 2009, Oakstone Medical Publishing

**Keywords:** Diastolic Heart Failure

**Print Tag:** Refer to original journal article
Perioperative β-Blockers: Use With Caution

Perioperative β Blockers in Patients Having Non-Cardiac Surgery: A Meta-Analysis.
Bangalore S, Wetterslev J, et al:


Perioperative β-blockers don't help most patients; save them for those at highest risk for cardiac events.

**Background:** β-blockers are often used in the perioperative setting, even though data to support them are scant.

**Objective:** To consolidate available data on perioperative β-blockers.

**Design:** Systematic review and meta-analysis.

**Methods:** All trials combined included 12,000 patients. The authors divided the trials into 2 groups, on the basis of whether or not blinding and randomization were thought to be adequate. Trials with good blinding and randomization were thought to be at low risk of bias, and trials with problems in these areas were thought to be at high risk of bias.

**Results:** Most trials that showed benefit were in the high-risk group, and they were also fairly small in numbers. Trials at low risk for bias were much less likely to show improved outcomes, particularly in all-cause mortality. There were considerable differences among the various trials in the risk profile of patients, as well as the choice of β-blocker and dose. In the aggregate, the meta-analysis suggests that use of β-blockers leads to a decrease in risks for nonfatal myocardial infarction and perioperative ischemia, at the expense of increased risks for nonfatal stroke, hypotension, and bradycardia. There is a trend toward increased overall mortality, but nothing definitive.

**Reviewer's Comments:** A few things seem evident: β-blockers should be avoided in patients at low risk for cardiac events who are far more likely to suffer complications than to see benefit. Also, long-acting β-blockers, particularly metoprolol succinate, are probably not good choices. There may be some benefit to β-blockers for patients at high risk, and patients who have independent indications for β-blockers should continue them at the time of surgery. For everyone else, the role of perioperative β-blockers remains questionable. Whether or not to use them will continue to be a matter of judgment based on individual patient risk factors. However, measuring use of perioperative β-blockers as a marker of quality care should probably be discouraged until indications and contraindications become clearer. (Reviewer-Christopher L. Knight, MD).

© 2009, Oakstone Medical Publishing

Keywords: Non-Cardiac Surgery

Print Tag: Refer to original journal article
In patients with hypertension at high risk for cardiovascular events, the combination of an angiotensin-converting enzyme inhibitor (ACEI)/calcium-channel blocker is superior to an ACEI/diuretic in reducing cardiovascular events.

**Background:** In current hypertension guidelines, diuretics are typically encouraged as 1 of the first 2 agents used. However, the optimal choice of antihypertensive agents remains unclear.

**Objective:** The ACCOMPLISH trial sought to determine if combination of an angiotensin-converting enzyme inhibitor (ACEI) and a calcium-channel blocker (CCB) is more effective in reducing cardiovascular events than combination of an ACEI and thiazide diuretic.

**Design:** Randomized, multicenter, double-blind industry-sponsored trial.

**Participants:** 11,506 patients with hypertension at high risk for cardiovascular events. To be eligible, patients had to have coronary artery disease, stroke, impaired renal function, peripheral arterial disease, left ventricular hypertrophy, or diabetes mellitus.

**Methods:** Patients were randomized to either benazepril 20.0 mg/amlodipine 5.0 mg or benazepril 20.0 mg/hydrochlorothiazide (HCTZ) 12.5 mg. After 1 month, benazepril was increased to 40 mg. Thereafter, doses of amlodipine and HCTZ could be increased to achieve a blood pressure (BP) of <140/90 mm Hg (or 130/80 mm Hg with diabetes or kidney disease). If needed, β-blockers, clonidine, α-blockers, and spironolactone could be added. The end point of interest was time to first important cardiovascular event, including cardiovascular-related death, myocardial infarction, stroke, hospitalization for angina, revascularization, and resuscitation.

**Results:** Mean age was 68 years, and 60% were male. At entry, BP was 145/80 mm Hg (with about 25% on 0 to 1 antihypertensive agents, approximately 36% on 2 agents, and approximately 37% to 40% on ≥3 agents). More than 60% of patients had diabetes. The trial ended prematurely at 36 months when predetermined stopping rules were met. At completion, BP was 131.6/73.3 mm Hg in the ACEI/CCB group and 132.5/74.4 mm Hg in the ACEI/diuretic group. Cardiovascular events occurred in 9.6% of ACEI/CCB patients and 11.8% of ACEI/diuretic patients. Overall mortality was similar in both groups. Serious adverse reactions were rare in both groups.

**Conclusions:** In patients with hypertension at high risk for cardiovascular events, combination of an ACEI/CCB was superior to an ACEI/diuretic in reducing cardiovascular events.

**Reviewer’s Comments:** Back in 2002, the ALLHAT trial was published in which an ACEI and CCB were compared to a diuretic in patients with hypertension and at least 1 other cardiovascular risk factor. As the diuretic arm had comparable overall outcomes to both newer agents, diuretics were deemed an appropriate first-line agent. With the ACCOMPLISH trial, the combination of an ACEI and amlodipine appears to be superior to a diuretic. The primary differences between these 2 reports is that, in the ACCOMPLISH trial, there were higher-risk patients, including >60% with diabetes. As well, HCTZ was used compared with chlorthalidone in ALLHAT. Clearly, diuretics still play an important role in BP management. However, in higher-risk patients (eg, diabetics), it may be preferable to use a CCB as a second agent (after ACEI). (Reviewer-Mark E. Pasanen, MD).

© 2009, Oakstone Medical Publishing

Keywords: Antihypertensive Medications

Print Tag: Refer to original journal article
NSAIDs are associated with an increased risk of myocardial infarction, likely related to degree of cyclooxygenase-2 inhibition.

**Background:** NSAIDs are either traditional (tNSAIDs) or cyclooxygenase (COX)-2 selective agents. The selectivity for COX-1 and COX-2 is measured in vitro using whole blood, and can be used to assess pharmacologic properties of different NSAIDs. Data have raised concerns that both COX-2 and tNSAIDs increase cardiovascular (CV) risks.

**Objective:** To evaluate the association between NSAIDs and CV events, and to evaluate the degree of which COX-2 inhibitors are related to CV risk.

**Design/Methods:** Population-based, retrospective cohort study using data from The Health Improvement Network (THIN) database and performing a nested case-control study. THIN is based in the United Kingdom comprising patients aged 50 to 84 years with at least 2 years of follow-up. Patients with a recorded diagnosis of myocardial infarction (MI) were identified, and 20,000 control subjects were matched. NSAID exposure was categorized by use based on when the last NSAID prescription was filled: current, recent, past, and never. They also identified the specific NSAID, dose, and frequency of use. In vitro whole blood assays were done to assess COX-1 and COX-2 inhibition of each of the NSAIDs used. Regression analysis was done to identify the risk of CV events in users and non-users, with multiple confounders accounted for in multivariate analysis.

**Results:** There were 8852 nonfatal MIs, with an incidence of 4.1/1000 person-years. The incident rate ratio (RR) for MI with current NSAID use was 1.35 (95% CI, 1.23 to 1.48), while those who stopped NSAIDs between 3 months and 1 year in advance had a similar rate to that of non-users (1.02; 95% CI, 0.94 to 1.39). Those who used NSAIDs for >3 years had an RR of 1.53 (95% CI, 1.28 to 1.82), and those who used higher doses had a higher risk (1.28; 95% CI, 1.97 to 1.53). The degree of whole blood COX-2 inhibition was correlated with MI ($r^2 = 0.7458$), and those NSAIDs with COX-2 inhibition <90% had an MI risk of 1.18 (95% CI, 1.02 to 1.38) compared with an MI risk of 1.60 (95% CI, 1.41 to 1.81) for those taking NSAIDs with >95% COX-2 inhibition. There was not an interaction with aspirin identified.

**Conclusions:** Patients taking NSAIDs had an increased risk of MI, and this risk was dose related and increased with duration of therapy. The authors propose that the extent of COX-2 inhibition may represent a surrogate end point to assess the CV risk of NSAIDs.

**Reviewer's Comments:** This study shed some light on concerns that NSAIDs increase the risk of MI, and may be the beginning of a method to allow those patients with CV risk to find a balance between increased risk with NSAIDs and relief of pain often uniquely treated by NSAIDs. (Reviewer-Karen Stout, MD).

© 2009, Oakstone Medical Publishing

Keywords: Myocardial Infarction

Print Tag: Refer to original journal article
Consumption of ≥2 drinks per day increases a woman’s risk for atrial fibrillation.

**Background:** Moderate alcohol consumption reduces the risk coronary artery disease (CAD) and stroke. Data on the risk of atrial fibrillation (AF) from moderate alcohol consumption have been inconsistent.

**Objective:** To assess the association between moderate alcohol consumption and AF in women.

**Design:** Prospective cohort study.

**Participants/Methods:** The Women’s Health Study enrolled >39,000 healthy women aged >45 years. Participants were randomized to low-dose aspirin and vitamin E in study of primary prevention of cardiovascular disease and cancer. For this particular analysis, women with a history of AF were excluded. Women were categorized based on self-reported alcohol consumption: none, <1 drink/day, 1 to <2 drinks/day, ≥2 drinks/day. Self-reported AF was confirmed by review of medical records.

**Results:** Almost 35,000 women were followed for a median of 12.4 years. Average age was 53 years, and 44.3% were non-drinkers. Of women, 6.4% consumed 1 to 2 drinks per day, and 3.9% consumed ≥2 drinks per day. Compared to non-drinkers, women consuming ≥2 drinks a day had a significant increased risk of incident AF in multivariate analysis (hazard ratio, 1.60; 95% CI, 1.13 to 2.25). Women who drank <2 drinks per day did not have an increased risk of AF compared to non-drinkers.

**Conclusions:** In healthy, middle-aged women, consumption of >14 drinks per week significantly increases the risk for AF.

**Reviewer’s Comments:** This was a large population of relatively young women in whom the risk of AF is quite low. The absolute risk increase was only 0.66 events per 1000 person-years. Despite this relatively small increased risk, AF should not be trivialized. A diagnosis at age 60 years requires medication, consideration of anticoagulation, and risk of stroke. We often discuss risks and possible benefits of alcohol consumption with our patients. This study can add to our discussion with women who are middle-aged. (Reviewer-Deborah L. Greenberg, MD).

© 2009, Oakstone Medical Publishing

Keywords: Atrial Fibrillation

Print Tag: Refer to original journal article
Be Cautious of Aspirin, Antioxidant Use in Diabetics

The Prevention of Progression of Arterial Disease and Diabetes (POPADAD) Trial: Factorial Randomised Placebo Controlled Trial of Aspirin and Antioxidants in Patients With Diabetes and Asymptomatic Peripheral Arterial Disease.

Belch J, MacCuish A, et al:

BMJ 2008; 337 (October 16): a1840

No evidence supports use of either aspirin or antioxidants in the primary prevention of cardiovascular events and mortality in diabetics. Continue aspirin use for secondary prevention in this population.

Background: Coronary artery disease (CAD) and cerebrovascular disease are major causes of morbidity and mortality in diabetes mellitus. Patients with peripheral arterial disease (PAD) have increased risks of myocardial infarction (MI) and stroke. In patients with both diabetes and cardiovascular disease, antiplatelet agents reduce future cardiovascular events. The same is true for those with PAD. In addition, free radicals increase platelet aggregation, while antioxidants decrease aggregation. Plasma vitamin E and ascorbic acid levels are lowered in diabetes, and interest has arisen in assessing antioxidant therapy.

Objective: To determine whether aspirin and antioxidant therapies, combined or alone, are more effective than placebo in primary prevention of cardiovascular events in patients with diabetes and asymptomatic PAD.

Design: Multicenter, randomized, double-blind, 2 x 2 factorial placebo-controlled trial.

Participants: 1276 subjects (aged >39 years) with diabetes (types 1 or 2) and an ankle-brachial pressure index <1.00 who do not have symptomatic CAD.

Methods: Patients were randomly assigned to: aspirin (100 mg tablet) plus placebo, aspirin plus antioxidant, antioxidant plus placebo, or double placebo for a median of 6.7 years.

Results: The 2 primary end points included (1) the composite of death from CAD or stroke, nonfatal MI or stroke, or above-ankle amputation due to ischemia, and (2) death from CAD or stroke. There was no difference among groups in the 2 primary end points. Primary events occurred in 18.2% of the aspirin groups, in 18.3% of the no-aspirin groups, in 18.3% of the antioxidant groups, and in 18.2% of the no-antioxidant groups.

Conclusions: There is no evidence that aspirin or antioxidants have an effect in diabetics for primary prevention of cardiovascular events and mortality.

Reviewer's Comments: Without evidential support, published guidelines recommend aspirin use as primary prevention of cardiovascular disease in patients with diabetes mellitus and asymptomatic PAD. This study found no evidence of benefit from either aspirin or antioxidant treatment on the composite hierarchical primary end points of cardiovascular events and cardiovascular mortality. Aspirin is one of the most commonly prescribed drugs, and it is not without side effects. Although the calculated risk of major bleeding is relatively small, the number of people taking aspirin is relatively large and, therefore, in population terms, aspirin-induced bleeding is a major problem. Recommended aspirin use without evidence to support this practice is not warranted. (Reviewer-Debra Braverman, MD).

© 2009, Oakstone Medical Publishing

Keywords: Diabetes & Peripheral Arterial Disease

Print Tag: Refer to original journal article
A Mediterranean diet supplemented by a handful of nuts per day improves triglyceride levels, hypertension, and central obesity more than a similar diet enriched with olive oil.

Background: Epidemiologic studies and a few small trials have shown that a Mediterranean diet (rich in fruits and vegetables, grains, fish, and low-fat dairy) may prevent or reverse the metabolic syndrome (MetS).

Objective: To compare a Mediterranean diet supplemented with olive oil, a similar diet supplemented with nuts, and a low-fat control diet on the incidence and prevalence of MetS.

Design: Randomized, controlled unblinded trial.

Participants: 1224 older Spanish adults with no history of cardiovascular disease but either type 2 diabetes or 3 other cardiac risk factors: smoking, elevated low-density lipoprotein or low high-density lipoprotein (HDL), hypertension, family history of premature coronary artery disease, or body mass index >25.

Methods: At enrollment, participants were each advised on a Mediterranean diet or a generic low-fat diet for the control group. The Mediterranean diet groups also went through a 1-hour presentation each quarter on menu ideas, shopping advice, etc. The olive oil group had 1 L of free virgin olive oil per week, and the nut group had 30 g of mixed nuts per day. The control group received free gifts of aprons, cookbooks, etc. Decreasing calories was not recommended to any group, and all subjects had access to study dietitians throughout the study.

Results: At baseline, 61% of participants met criteria for MetS; 95% had hypertension, 66% had hyperglycemia, and 66% had central obesity. After 1 year, there was no significant change in weight in subjects in any of the groups. However, the prevalence of MetS had decreased by 6.7% with the Mediterranean diet plus olive oil, 13.7% with the Mediterranean diet plus nuts, and 2.0% with the generic low-fat diet. The nut dieters were less likely to have hypertriglyceridemia and hypertension, and were more likely to have regression of abdominal obesity. Fasting glucose, HDL, and need for antihypertensive and antidiabetic medications were similar with all 3 diets.

Conclusions: A Mediterranean diet supplemented with nuts can reverse elements of the MetS, and is more effective than a diet enriched in olive oil in doing so.

Reviewer's Comments: Olive oil and nuts are both high in monounsaturated and polyunsaturated fats; 30 g of nuts is described as a small handful, which would be easier to incorporate into a diet than a half a cup of olive oil and, according to this study, may be better, too. Interestingly, none of the groups gained a significant amount of weight. (Reviewer-Karen A. McDonough, MD).

© 2009, Oakstone Medical Publishing

Keywords: Metabolic Syndrome

Print Tag: Refer to original journal article
Fluoroquinolones should remain the preferred empirical treatment for women with uncomplicated pyelonephritis.

**Background:** *Escherichia coli* is the most common cause of urinary tract infections. Resistance to the most common antibiotic treatments, trimethoprim (TMP)-sulfa and quinolones, have been increasing in the past decade.

**Objective:** To determine the rates of *E coli* resistance to TMP-sulfa, fluoroquinolones, and other antibiotics used to treat pyelonephritis in a population of women with uncomplicated pyelonephritis.

**Participants/Methods:** Adults presenting to 11 urban U.S. emergency departments with symptoms of pyelonephritis were recruited for the study. Patients for whom 1 pathogen grew on urine culture were analyzed. The prevalence of antibiotic resistance to *E coli* and risk factors for TMP-sulfa resistance were evaluated.

**Results:** 1272 patients with pyelonephritis were enrolled, of which 977 had a urine culture performed. An additional 288 patients (29%) did not grow a pathologic organism on urine culture. The final study population consisted of 689 patients. The subgroup of patients who had uncomplicated pyelonephritis consisted of 429 women, of whom 403 had an infection due to *E coli*. The mean rate of *E coli* resistance was 24% (range, 13% to 45%). Fluoroquinolone resistance was 1% to ciprofloxacin and 3% to levofloxacin. The only risk factors for TMP-sulfa resistance were exposure to TMP-sulfa within 2 days of presentation and Hispanic ethnicity.

**Conclusions:** The prevalence of TMP-sulfa resistance to *E coli* in patients presenting with uncomplicated pyelonephritis is >20% in most communities, and it is difficult to determine patients at low risk for resistance.

**Reviewer’s Comments:** This study just reaffirms what we already know, that *E coli* resistance to TMP-sulfa is extensive. It is reassuring to see that we do not have widespread resistance to fluoroquinolones in low-risk populations of uncomplicated pyelonephritis patients. In this study, the rate of fluoroquinolone resistance in complicated pyelonephritis was 6%. With these data, we should make sure to choose a fluoroquinolone or a third-generation cephalosporin as empiric treatment for pyelonephritis. It is probably still ok to use TMP-sulfa as first-line empiric therapy for uncomplicated cystitis, as the disease is much milder and has a 50% spontaneous resolution rate. (Reviewer-Douglas S. Paauw, MD.)
Background: Oral sodium phosphate (OSP)-containing bowel preparations, such as Fleet Phospho-soda, is not recommended as a bowel preparation regimen for patients with renal insufficiency, heart failure, or ascites because of the risk of hyperphosphatemia, nephrocalcinosis, and progression of renal insufficiency. This recommendation is based largely on case reports and accumulated clinical experience.

Objective: To quantify the risk of worsening renal insufficiency in patients with preexisting renal insufficiency who received OSP as a bowel preparation regimen compared with patients who received polyethylene glycol solution (PEG).

Design/Participants: Retrospective cohort study performed among patients who were members of a health maintenance organization affiliated with Henry Ford Health System in Detroit.

Methods: Subjects received either OSP or PEG prior to colonoscopy, had a baseline creatinine determination within 60 days before colonoscopy, had stage III or worse chronic kidney disease (CKD) with an estimated creatinine clearance of <60 mL/minute, and had an unexplained increase in creatinine of at least 0.5 mg/dL within 14 days of colonoscopy.

Results: The authors identified 7971 patients who received OSP and 1511 who received PEG prior to colonoscopy. Less than one third of patients who received OSP had a baseline creatinine measured within 60 days before colonoscopy. A total of 317 patients had baseline creatinine measured and had stage III or worse CKD. Eight of 126 patients who received OSP had worsened renal insufficiency within 14 days of colonoscopy (6.3%) compared with 1 of 191 PEG users (0.5%). The adjusted relative risk for worsening renal insufficiency associated with OSP was 12.6 (95% CI, 1.5 to 106.5).

Conclusions: In patients with baseline CKD, OSP as a bowel preparation regimen for colonoscopy was associated with an increased risk of worsening renal insufficiency compared with PEG.

Reviewer's Comments: This was a retrospective cohort study from a single institution. Furthermore, the number of events was small, resulting in large confidence intervals spanning the point estimate of risk. Nonetheless, use of OSP was associated with a substantially increased risk of early renal insufficiency among patients with baseline stage III or worse CKD. It is striking that only about 30% of patients had baseline measures of creatinine prior to receiving OSP. It would be prudent to consider assessing kidney function prior to prescribing OSP for bowel preparation prior to colonoscopy. This study clearly supports the current recommendation to avoid OSP in patients with CKD. (Reviewer-Paul R. Sutton, PhD, MD).
Ginkgo biloba Does Not Prevent Dementia

Ginkgo biloba for Prevention of Dementia: A Randomized Controlled Trial.
DeKosky ST, Williamson JD, et al:

JAMA 2008; 300 (November 19): 2253-2262

Ginkgo biloba taken regularly by healthy elderly patients does not prevent or delay dementia.

-Ginkgo biloba

Background: Ginkgo biloba, which may work as an antioxidant and in preventing aggregation of amyloid, is used widely as a memory aid and to prevent dementia.

Objective: To assess the safety and efficacy of G biloba for primary prevention of dementia.

Design: Randomized double-blind trial.

Methods: The Ginkgo Evaluation of Memory Study enrolled volunteers aged >74 years in 4 U.S. communities. Participants were generally healthy, as there were extensive exclusion criteria including major medical illness, use of anticoagulants or antioxidants, and a history of bleeding disorder. Patients underwent evaluation including neuropsychological testing and several memory-related clinical scales. Those with baseline dementia but not mild cognitive impairment were excluded. Subjects were randomized to receive G biloba extract 120 mg twice daily or placebo. The primary end point was the interval diagnosis of dementia based on DSM-IV criteria. Details on confirmation of dementia diagnosis are provided in the article.

Participants: 3069 patients were enrolled in the study with an average age of 79 years; 46% were women.

Results: The 2 groups were equivalent at baseline in demographic, memory, and overall health parameters. Median follow-up was 6 years. Of all patients, 523 were diagnosed with dementia (92% with Alzheimer disease) during the study. The total rate of dementia did not differ between the G biloba treatment group and the placebo group (HR, 1.12; 0.94 to 1.33), nor did the rate of Alzheimer dementia. There was also no significant difference in adverse events including death, bleeding, or cardiovascular events. More hemorrhagic strokes occurred in the G biloba group, but this did not reach statistical significance.

Conclusions: Despite plausible mechanisms by which G biloba might prevent or delay dementia in the elderly, this large randomized trial showed no clinical benefit when taken twice a day for 6 years.

Reviewer's Comments: Many patients are scared to develop dementia, especially if they have a family history of Alzheimer disease. G biloba has not been found to be effective in the treatment of dementia, and this large, well-done, randomized controlled trial shows no benefit in patients hoping to prevent dementia. Given the lack of proven efficacy, the cost and potential risk of G biloba seem unjustified in any patient. (Reviewer-Deborah L. Greenberg, MD).

© 2009, Oakstone Medical Publishing

Keywords: Dementia

Print Tag: Refer to original journal article
The addition of a long-acting β-agonist is more effective than increasing inhaled corticosteroid doses in asthma.

**Background:** There is considerable controversy over the role of long-acting β-agonists (LABA) for asthma management.

**Objective:** To assess whether adding an LABA is more effective than increasing corticosteroid doses in managing asthma.

**Design:** Post-hoc analysis of results from a randomized controlled trial.

**Participants:** 852 patients participating in the Formoterol and Corticosteroid Establishing Therapy study.

**Methods:** Patients were randomized to 100 μg of budesonide twice daily versus 400 μg of budesonide twice daily in a 2 x 2 factorial design with formoterol versus placebo.

**Results:** The authors found a statistically significant increase of 19% in time with good asthma control in the formoterol group, compared to a 2% non-significant increase in the high-dose budesonide group. However, adding formoterol to high-dose budesonide produced even more benefit (29%, which was statistically significant). The difference between formoterol and budesonide was also statistically significant.

**Reviewer’s Comments:** This is not a perfect study: it is a post-hoc analysis of a previous dataset. However, its findings corroborate both the clinical impression and the results of other trials that LABAs help improve asthma control. The intent behind the specific design was to demonstrate that they help more than just an increase in corticosteroid dose, and the results are fairly convincing. Unfortunately, this does not help resolve controversy around LABAs; if anything, it further muddies the waters. It is clear that inhaled corticosteroids should be used prior to using an LABA. Some previous recommendations suggested that one maximize the dose of inhaled steroids prior to adding LABAs, but this study suggests that adding the second drug is more effective. However, in clinical practice, one should approach this cautiously, and discuss carefully the risks and benefits (and how much we don't know about them) with each individual patient. (Reviewer-Christopher L. Knight, MD).

© 2009, Oakstone Medical Publishing

Keywords: Asthma Control

Print Tag: Refer to original journal article
**Background:** Recent epidemiologic studies have described an association between use of proton-pump inhibitors (PPIs) and community-acquired pneumonia (CAP). However, association cannot establish causation, and the relationship may be due to confounding factors.

**Objective:** To undertake a case-control study to assess relationship between PPI usage and CAP.

**Design:** Nested case-control study.

**Participants:** Approximately 9 million participants in the General Practice Research Database (GPRD), an electronic database used in the United Kingdom.

**Methods:** The GPRD contains details from actual medical records; these include demographic characteristics, prescription data, coded diagnoses made in the clinic or hospital, and notes from subspecialists. Patients with CAP were identified by those codes; for each one, up to 10 controls were also identified. Controls had to have been followed in the same general practice site and entered into the system within 1 month of the index patient. Index date was the date when diagnosis of CAP was made. Data that were extracted for each participant included information about PPI usage (including dose and duration) as well as a variety of other potentially important medications (eg, antibiotics, H₂-receptor antagonists, corticosteroids, NSAIDs, and agents that could compromise airway protection), smoking history, other diseases, and numbers and dates of clinic visits and/or hospitalizations.

**Results:** About 80,000 cases of CAP were identified and compared to almost 800,000 controls. The CAP group was older, more likely to be male, more likely to have a variety of concurrent chronic disease states, and more frequently seen in clinics and hospitals. They were also more likely to have consumed most of the pharmaceutical agents of interest. The odds ratio for PPI use was 2.05 ($P<0.001$). However, when analysis was corrected for other confounding factors, this association disappeared. When a variety of subgroup analyses were undertaken, 1 association stood out, namely that of CAP and beginning PPI use at ≤30 days. In fact, the relationship became even stronger when PPIs were begun within 14, 7, and 2 days.

**Conclusions:** PPI therapy that was begun ≤30 days was associated with CAP, but longer-term use was not.

**Reviewer's Comments:** It is likely that there is no causative relationship between PPI use and CAP. Rather, the association with recent use represents the appearance of a clinical condition that then led to pneumonia. (Reviewer-Ronald L. Koretz, MD).

© 2009, Oakstone Medical Publishing

Keywords: Pneumonia

Print Tag: Refer to original journal article
Wernicke encephalopathy is associated with bariatric surgery.

**Background:** Beriberi is used to describe the spectrum of thiamine deficiency. Wernicke encephalopathy is the central neurologic manifestation of thiamine deficiency characterized by mental confusion, eye movement abnormalities, and gait instability. Thiamine deficiency can occur after weight loss surgery.

**Objective:** To review cases of Wernicke encephalopathy associated with bariatric surgery.

**Design:** Literature search from 1977 to 2008.

**Participants:** 104 cases were initially identified from 410 articles; 84 met inclusion criteria.

**Methods:** Mental status changes, eye movement abnormalities, and cerebellar dysfunction were the findings used to define Wernicke encephalopathy. Data retrieved included type of procedure performed, outset of symptoms, type of symptoms, and outcomes. The primary outcome was to identify how patients with Wernicke encephalopathy present after bariatric surgery.

**Interventions:** Weight loss surgical procedures.

**Results:** Gastric bypass accounted for 51% of cases, restrictive procedures for 44%, and malabsorptive procedures for 5%. Symptoms occurred within 6 months in 94% of cases (range, 3 weeks to 18 months). The most common patient complaint was persistent vomiting in 90%. Vomiting was ongoing for 4 to 90 days (median, 21 days). Eye movement abnormalities, mental status changes, peripheral neuropathy, and gait ataxia were seen in 75% to 85% of all patients. All 3 manifestations of Wernicke encephalopathy were present in 38% of patients. Stomal obstruction was documented in 18 of 41 cases. Of patients, 18% were treated with glucose before thiamine. Complete recovery occurred in 51% of cases. Residual effects included cognitive impairments, gait instability, and nystagmus. One estimate placed the incidence at 19 cases per 10,000 procedures.

**Conclusions:** Wernicke encephalopathy occurs after all types of weight loss procedures, and persistent vomiting is the most common presenting sign.

**Reviewer's Comments:** Poor nutrition associated with alcoholism is the typical scenario we are all taught when Wernicke encephalopathy is discussed. Giving B vitamins with that first glucose load is stressed over and over again. This review suggests that we need to be as careful when evaluating a patient after bariatric surgery who presents with persistent vomiting. Thiamine can be depleted in 20 days without adequate supply. Replacement with 500 mg thiamine 3 times daily for 3 days is the recommended treatment. While not common, knowing that it can occur and how it may present will hopefully allow patients with symptoms of thiamine toxicity to be recognized early. Better yet, we can recognize its possibility and avoid it completely. (Reviewer-John A. Weigelt, MD).

© 2009, Oakstone Medical Publishing

Keywords: Bariatric Surgery

Print Tag: Refer to original journal article
Aspirin Ineffective for Prevention of Cardiovascular Events in Diabetics

Low-Dose Aspirin for Primary Prevention of Atherosclerotic Events in Patients With Type 2 Diabetes: A Randomized Controlled Trial.

Ogawa H, Nakayama M, et al:

JAMA 2008; 300 (November 12): 2134-2141

Low-dose aspirin did not reduce the risk of cardiovascular events in a study of individuals with type 2 diabetes.

Objective: To examine the efficacy of low-dose aspirin as a primary preventive of atherosclerotic events in patients with type 2 diabetes mellitus.

Design/Participants: Multicenter, prospective, randomized blinded trial involving 2539 patients with type 2 diabetes and no history of atherosclerotic disease.

Methods: Patients were followed for an average of 4.37 years and were assigned to either a placebo or low-dose aspirin group (81 or 100 mg/day). Patients were followed for development of atherosclerotic events, including ischemic heart disease, stroke, and peripheral arterial disease.

Results: During the follow-up period, 100 atherosclerotic events occurred: 68 in the aspirin group and 86 in the non-aspirin group, yielding a hazard ratio of 0.80, not statistically significant.

Conclusions: Low-dose aspirin as primary prevention did not reduce the risk of cardiovascular disease in this study of patients with type 2 diabetes.

Reviewer’s Comments: This is an important study. As the authors point out, aspirin has been shown to decrease the rate of primary and secondary cardiovascular events in individuals with risk factors for coronary artery disease. Diabetes mellitus is a powerful risk factor for cardiovascular events, yet this study—prospective and randomized—showed no benefit for diabetics in reducing the risk for cardiovascular events. As the authors point out, a primary prevention trial of aspirin for diabetic patients was needed. Now that this Japanese group has performed it, it needs to be expanded and the results confirmed because, despite the large sample size, the event rate in the study was lower than anticipated and thus underpowered, perhaps owing to the short duration of follow-up. (Reviewer-Berel Held, MD).

© 2009, Oakstone Medical Publishing

Keywords: Atherosclerotic Events & Diabetes

Print Tag: Refer to original journal article
The Italian experience in this study suggests there may be benefit in ECG screening of young athletes.

**Background:** Sudden cardiac death (SCD) of a young competitive athlete is a dramatic event that often has social impact beyond the athlete’s family and friends. In the Veneto region of Italy, screening of athletes has included ECG in all pre-participation evaluations for 25 years.

**Objective:** To review available data from this 25-year experience. **Summary:** The incidence of SCD in young athletes is low, but there is an estimated 2.8-fold increased risk of SCD in athletic young adults compared to non-athletes. Patients are often asymptomatic. Hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia/cardiomyopathy, long-QT syndrome, and congenital disease may all contribute to SCD. The ideal screening method for these disorders in asymptomatic patients remains controversial. Cost-effectiveness, false positives, and subsequent cardiac evaluation triggered by screening have all been issues in optimal screening. In the U.S., the American Heart Association and American College of Cardiology guidelines do not recommend an ECG as standard pre-participation screening. The Italian area of Veneto has mandatory screening of athletes with history, exam, and ECG, with exclusion from participation for those with abnormal evaluations. Any reported data from this experience are observational population-based experiences, not a comparison of screening and non-screening. Thus, comparison must be made to other areas without similar screening.

**Results:** The mortality rate of athletes in Veneto was 3.6/100,000 athlete/years prior to screening, and is now 0.4/100,000 athlete/years - a decrease of 89%. During the screening period, the rate of death in non-athletes did not change. The rate of SCD in athletes in the U.S. is estimated to be 0.75/100,000 for males and 0.13/100,000 for females. The difference in baseline rates may, in part, be due to the difference in ages; data in Italy are derived from athletes aged 12 to 35 years, while in the U.S., athletes are aged 14 to 24 years and data are incompletely recorded. There are increasing rates of SCD with increasing age from high school to college. In the Italian experience, the cost of an ECG, interpreted by an appropriately trained physician, is approximately $45, with about 9% of athletes requiring further testing.

**Conclusions:** In reviewing the Italian experience with screening young athletes with ECG in addition to history and physical exam, the authors assert that the addition of ECG appropriately screens those at high risk of SCD. This method decreases the incidence of SCD while only minimally increasing the cost of subsequent evaluation. They advocate including ECG in screening young athletes.

**Reviewer’s Comments:** The ideal screening modality remains controversial, trying to balance prevention of SCD against unnecessary exclusion from participation and expense of further evaluation. This article is an excellent review of the much-cited Italian experience, and is increasingly being discussed in the context of desires to change U.S. screening practices. (Reviewer-Karen Stout, MD).
In patients affected with Raynaud's phenomenon and digital ulcerations in systemic sclerosis, treatment with atorvastatin can be beneficial.

**Background:** Raynaud's phenomenon and digital ulcerations are prominent features of progressive systemic sclerosis (SSc). Treatment of Raynaud's and digital ulcerations in SSc can be difficult, ranging from cold avoidance to use of topical nitroglycerin and systemic calcium-channel blockers, to surgical therapy with sympathectomies.

**Objective:** To evaluate whether atorvastatin, an HMG-CoA reductase inhibitor, would be beneficial in the treatment of Raynaud's and digital ulcerations. HMG-CoA reductase inhibitors have been shown in multiple studies to not only lower lipid levels but also to decrease inflammation and improve vascular endothelial dysfunction.

**Design:** Randomized, double-blind control study.

**Participants/Methods:** 84 patients received atorvastatin 40 mg/day (n=56) or placebo (n=28) and were followed over a 4-month period. All patients also continued any ongoing vasodilator therapy. At the end of the trial period, the authors assessed the number of digital ulcerations and used various measurement scales to evaluate patients' functional status, including visual assessments by a physician and patient survey. They also measured endothelium-dependent flow-mediated dilatation via high-resolution echo-Doppler ultrasonography.

**Results:** The authors found that patients treated with atorvastatin developed fewer ulcers (mean, 1.6 vs 2.5 new digital ulcers per patient). Statistically significant improvements were also found based on patient survey and in the physician's assessment of the patient's Raynaud's phenomenon, digital ulceration, and pain. Endothelial-dependent flow-mediated dilatation was improved in the statin group as well as via ultrasonography. No patients dropped out of the study, and no major adverse events were reported.

**Conclusions:** Statins may be beneficial as adjunctive therapy for patients with Raynaud's and for digital ulcerations in patients with SSc.

**Reviewer's Comments:** Raynaud's phenomenon and digital ulcerations in SSc can be debilitating and difficult to treat. HMG-CoA reductase inhibitors (statins) are readily available with a generally mild and well-known side effect profile. In this study, promising and statistically significant improvements were demonstrated with use of statins as an adjunct to vasodilatation treatment. Statins may have led to functional improvement in Raynaud's phenomenon and decreases in ulcer development via vasodilatory and anti-inflammatory mechanisms. Further testing and evaluation in a larger group of patients, and in patients without SSc, would be valuable in the future. (Reviewer-Amy Cheng, MD).

© 2009, Oakstone Medical Publishing

Keywords: Raynaud's in Systemic Sclerosis
β-Blockers Provide Best Heart Rate Control in AF

Heart Rate Control in Patients With Atrial Fibrillation Referred for Exercise Testing.

Hilliard AA, Miller TD, et al:

Am J Cardiol 2008; 102 (September 15): 704-708

Many patients with atrial fibrillation have inadequate heart rate control, especially with exercise. β-blockers combined with other heart rate-lowering drugs are the most helpful.

**Background:** Many patients with atrial fibrillation (AF) are treated with heart rate (HR) control medications, including β-blockers (BB), digoxin, and nondihydropyridine calcium-channel blockers (CCB). The American College of Cardiology/American Heart Association/European Society of Cardiology guidelines recommend maintaining ventricular response at 60 to 80 beats per minute (bpm) at rest and at 90 to 155 bpm during moderate exercise.

**Objective:** To examine HR control at rest and during exercise in a large group of AF patients referred for exercise testing.

**Design:** Retrospective analysis.

**Participants:** 1097 patients referred for stress testing who had AF.

**Methods:** HR was evaluated at rest and at peak exercise. In a subgroup of 195 patients, HR was also recorded at the end of stage I of the Bruce protocol, which was considered moderate exercise (5 METs). Medications at the time of exercise and the time from last dose of medication were recorded (BB, 6.7 hours; CCB, 6.4 hours; digoxin, 9.6 hours). Heart rates were compared to practice guidelines.

**Results:** HR at rest exceeded the guideline goal in 50% of the population. Patients using a BB had a significantly lower HR at rest. Digoxin alone was similar to that for patients using no medication. Two thirds of patients had inadequate HR control during moderate exercise. No group using a single medication, including BBs, had an adequate median HR during moderate exercise. Groups that included a BB in combination with other rate control medications had better HR control (median HR, 117 bpm) than did those who did not include BBs as part of their regimen (median HR, 131 bpm). Groups that included a BB in combination with other rate control medications also had better HR control at maximum exercise. HR control at rest was not predictive of adequate control at moderate exercise, but it was modestly helpful in predicting adequate control at peak exercise. HR control at rest was associated with better exercise capacity.

**Conclusions:** Patients with AF frequently have inadequate HR control at rest and during exercise. Digoxin alone has no benefit. CCB alone or with digoxin was slightly more effective. The best results were in patients using BBs in combination with CCBs. Patients with adequate HR at rest exercised to a higher workload and for a longer duration.

**Reviewer's Comments:** Controlling HR in patients with AF is important. BBs provide the best HR control in AF and should be included whenever possible in a patient's regimen. (Reviewer-Marjorie Stanek, MD).

© 2009, Oakstone Medical Publishing

Keywords: Atrial Fibrillation

Print Tag: Refer to original journal article
Normal Vitamin D Levels Reduce Colon Cancer Risk

Optimal Vitamin D Status for Colorectal Cancer Prevention.

Gorham ED, Garland CF, et al:


Normal levels of plasma vitamin D are associated with a 50% reduction in colorectal cancer compared to low levels of plasma vitamin D.

**Background:** Recent studies have suggested that low-dose vitamin D does not protect against colorectal cancer (CRC).

**Objective:** To determine if a higher dose of vitamin D, which would be associated with higher serum levels of this vitamin, might reduce the incidence of colorectal cancer.

**Methods:** Through use of PubMed, studies were found associating the serum level of 25(OH)D and risk of CRC. Pooled data were divided into quintiles of vitamin D levels, and odds ratios (OR) were calculated by quintile regarding CRC incidence. All studies were nested and case-controlled looking at pre-diagnostic serum collected from healthy volunteers who were then followed for 2 to 25 years for incidence of CRC.

**Results:** This study demonstrated a decreasing linear gradient in the risk of CRC with increasing levels of 25(OH)D. OR for pooled data were, from lowest to highest quintile: 1.00, 0.82, 0.66, 0.59, and 0.46 ($P < 0.0001$). A serum 25(OH)D level of >33 ng/mL was associated with a 50% lower risk of CRC incidence compared with <12 ng/mL.

**Conclusions:** This study supports the theory that there is an inverse association between serum 25(OH)D and risk of CRC. The authors conclude that a daily intake of 1000 to 2000 IU/day of vitamin D3 could significantly reduce the incidence of CRC with minimal risk.

**Reviewer’s Comments:** These results should encourage physicians to determine vitamin D levels in their patients as the incidence of below-normal serum levels of this vitamin is remarkably high. Supplementation with oral vitamin D3 to bring levels to normal (ie, >33 ng/mL) may reduce their risk of developing CRC as well as improving the likelihood of maintaining normal bone density. (Reviewer-Michael M. Phillips, MD).

© 2009, Oakstone Medical Publishing

Keywords: Serum Vitamin D

Print Tag: Refer to original journal article
Exercise Prevents Ventricular Remodeling After AMI

Effects of 6 Months Exercise Training on Ventricular Remodelling and Autonomic Tone in Patients With Acute Myocardial Infarction and Percutaneous Coronary Intervention.

J Rehabil Med 2008; 40 (October): 776-779

Six months of supervised exercise therapy after acute myocardial infarction and percutaneous coronary intervention leads to improved heart rate recovery (reflects improved autonomic tone) and prevents ventricular remodeling.

**Background:** The degree of ventricular remodeling after acute myocardial infarction (AMI) is an important prognostic factor of subsequent cardiac function and is not worsened by exercise training. Improvement in impaired sympathovagal balance might be an important mechanism of this observation.

**Objective:** To study the effects of 6 months of exercise training in patients with AMI and percutaneous coronary intervention (PCI) in terms of ventricular remodeling and autonomic tone.

**Design:** Single-blinded, randomized controlled trial.

**Participants:** 60 patients who had PCI in the setting of AMI.

**Methods:** The treatment group participated in a 6-month supervised exercise program consisting of 30 minutes on a bicycle equipped with an ergometer 3 times weekly, while the control group had routine care. All subjects had Doppler echocardiography and an incremental cardiopulmonary exercise test on a bicycle equipped with an ergometer at baseline and at 6 months' follow-up. Outcome measures were exercise capacity, left ventricular (LV) geometrical size and systolic function, and heart rate recovery (HRR).

**Results:** LV end-diastolic diameter improved in the exercise group (5% reduction) compared to the control group (1% increase). Improvements were also seen in LV ejection fraction (exercise, 4.0% increase; controls, 0.004% decrease), peak VO$_2$ (exercise, 25% increase; controls, 3% increase), maximum workload (exercise, 25% increase; controls, no change), and VO$_2$ at anaerobic threshold (exercise, 38% increase; controls, 2%).

**Conclusions:** 6 months of exercise training in patients who underwent PCI in the setting of AMI leads to favorable modulation of sympathovagal balance and may be an important mechanism of the resultant prevention of ventricular remodeling seen in these patients.

**Reviewer's Comments:** Almost all studies of exercise training after AMI show an improvement in peak VO$_2$, the best measure of cardiovascular fitness and exercise capacity. Pooled data from clinical trials have shown significant improvement in LV ejection fraction after exercise training in patients after AMI. Ventricular remodeling post-AMI is characterized by increased LV wall thickness of non-infarcted LV segments and enlargement of the LV cavity. In this study, exercise reduced LV end-diastolic diameter, suggesting that exercise could prevent ventricular remodeling after AMI. Recent data demonstrated HRR, an index of vagal activity that is usually delayed after AMI, is an independent predictor of cardiovascular events and mortality. This is the first study to evaluate the effects of exercise training on ventricular remodeling in patients with AMI using HRR, an easily measured and powerful indirect index. (Reviewer-Debra Braverman, MD).

© 2009, Oakstone Medical Publishing

Keywords: Myocardial Infarction

Print Tag: Refer to original journal article
In patients for whom reasons for severe refractory iron-deficiency anemia remain unclear, evaluation for *Helicobacter pylori* infection should be considered even in the absence of gastrointestinal symptoms.

**Objective:** To describe the association of severe refractory iron-deficiency anemia with gastritis caused by *Helicobacter pylori* infection.

**Design/Participants:** A case series of 3 patients with profound microcytic anemia.

**Results:** The first case was a 15-year-old boy, with a baseline hemoglobin (Hb) of 6.9 and a mean corpuscular volume (MCV) of 56. Another was a 12-year-old girl who presented with dizzy spells; she had a baseline Hb of 6.9 and an MCV of 60. The third patient was a 14-year-old girl with a history of lethargy and dizziness who had a baseline Hb of 6.8 and an MCV of 68. All 3 adolescents had iron studies that were consistent with severe iron-deficiency anemia. Menstrual history in the 12-year-old was described as "normal" and menstrual history was commented on in the 14-year-old. Although none had gastrointestinal symptoms, in at least 1 patient, stool was guaiac positive. All had evaluations for Meckel's diverticulum and celiac disease that were negative. All failed to improve on iron supplementation. Endoscopy with biopsy revealed nodular gastritis, positive rapid urease testing of the biopsy, and small organisms consistent with *H pylori* infection. Esophageal, small intestines, and large bowel biopsies were normal. Patients received 7 days of clarithromycin, amoxicillin, and pantoprazole. After 3 months, a urea breath test was normal, indicating eradication. In each patient, Hb normalized.

**Conclusions:** In patients for whom the reasons for refractory iron-deficiency anemia remain unclear, evaluation for *H pylori* infection should be considered even in the absence of gastrointestinal symptoms.

**Reviewer's Comments:** Why does *H pylori* potentially cause this problem? It may cause upper gastrointestinal blood loss. Also, *H pylori* requires iron for its own metabolism, which may diminish the host supply. It may also interfere with iron absorption by encoding for proteins that mimic human ferritin. The authors, who are gastroenterologists, believe the initial diagnostic workup for *H pylori* should be aggressive. That is, endoscopy with biopsy should be done instead of a screening breath test because of a high false-positive and false-negative rate with breath tests. Indeed, the 14-year-old girl in this case series had a screening breath test prior to biopsy that was falsely normal. (Reviewer-Mark F. Ditmar, MD).

© 2009, Oakstone Medical Publishing

Keywords: Iron-Deficiency Anemia

Print Tag: Refer to original journal article
Physicians Not Adequately Reimbursed for Vaccines

Primary Care Physician Perspectives on Reimbursement for Childhood Immunizations.

Freed GL, Cowan AE, Clark SJ:

Pediatrics 2008; 122 (December): 1319-1324

Significant dissatisfaction exists about the cost and reimbursement of vaccines in physician practices.

Background: The addition of the pneumococcal vaccine to the schedule raised the number of recommended vaccines to 23 before age 6 years. Moreover, it almost doubled the cost of immunizations for children. Inconsistent coverage has left some physicians feeling concerned. The schedule has continued to expand. No one really knows how the financial pressures of vaccine administration are affecting physicians in the United States.

Objective: To determine the behaviors and attitudes of physicians with respect to the cost of vaccines in their practice.

Methods: A random national sample of pediatricians (n=750) and family physicians (n=750) was drawn from the American Medical Association's physician master file. Physicians who lived in universal purchase states were excluded. Each eligible physician was sent a 4-page, 21-item survey. Included were questions about whether the practice purchased the HPV vaccine, MCV4, or Pediarix; if they did not, the reason was assessed. The survey also asked about other difficulties associated with vaccine purchases, including delays, losses, and questions on how to proceed in the future. Practice characteristics were also gathered. The survey was sent in July 2007 with a $5 cash incentive. Non-responders were contacted up to 2 more times.

Results: Of 1208 potential participants, surveys were received from 784, for a response rate of 65%. Those who purchased a stock of vaccines for privately insured patients were the primary aim of this analysis. Of these, 84% purchased HPV, 87% purchased MCV4, and 57% purchased Pediarix. About half reported delaying the purchase of a vaccine for financial reasons. Vaccines most often delayed were HPV (67%) and MCV4 (34%). More than half responded that their practices were making less money from vaccine administration in the last 3 years. More than 1 in 5 physicians strongly disagreed that reimbursement for vaccine purchase was adequate, and 17% strongly disagreed that reimbursement for administration was adequate. More than 10% had seriously thought about no longer providing vaccines to privately insured patients.

Conclusions: Significant dissatisfaction exists about the cost and reimbursement of vaccines. The cost for vaccine purchase and administration is a significant concern to physicians. Many practices have delayed purchasing vaccines because of these concerns. Although few report it now, the major concern is that these practices may stop providing vaccines at all.

Reviewer's Comments: Although it isn't surprising, physicians are very concerned about the poor reimbursement for vaccine purchase and administration. It's difficult to understand how we can keep increasing the number of vaccines that should be administered without adequately providing physicians the means to do so. (Reviewer-Aaron E. Carroll, MD, MS).

© 2009, Oakstone Medical Publishing

Keywords: Cost of Vaccines

Print Tag: Refer to original journal article
Objective: To examine the temporal trend in cancer mortality rates in the United States for comparing blacks and whites.

Methods: Temporal trends in cancer mortality were compared from 1975 to 2004 using the National Center for Health Statistics (NCHS). Mortality rates were examined across all cancers and were subdivided looking at smoking-related cancers (including bladder cancer) and cancers potentially affected by screening (including prostate cancer). Differences in mortality between blacks and whites were compared for all categories.

Results: The black-white disparity in cancer mortality narrowed from 1975 to 2004 overall, particularly in men. This was mainly due to a decreased disparity in cancers affected by tobacco exposure. However, for cancers potentially impacted by screening, the disparity worsened over the same period. For prostate cancer, while the overall mortality rate decreased for both, the difference in mortality rate between black and white men has steadily increased over time.

Conclusions: Further work is needed to improve coordinated screening and treatment programs for the entire population in order to further improve the mortality rate from cancer in the U.S.

Reviewer's Comments: Many researchers believe that black men are more likely to be diagnosed with prostate cancer and more likely to have aggressive disease. Whether this represents a difference in the biology of the disease or an environmental factor is not clear. This article sought to determine from the NCHS database whether there has been a change in disparity in mortality rates across different cancers between blacks and whites. Researchers found that from 1975 to 2004, mortality rates for blacks in general have been higher, but the overall disparity has narrowed somewhat, particularly for smoking-related cancers such as lung cancer and bladder cancer. On the other hand, for diseases that might be affected by screening, while the overall mortality rate is improving, the disparity is getting worse. This was especially striking for prostate cancer. Black men were more likely to die of prostate cancer, and the magnitude of the difference is getting larger. There is no particular reason to suppose that the biology of prostate cancer has changed substantially in the last 1 to 2 decades, so this strongly suggests that these trends represent environmental factors. It is certainly conceivable that the current results point to a disparity in prostate cancer screening between black and white men. It is also possible that the differences in mortality reflect other differences in access to or delivery of health care. These are all provocative points that deserve greater study and have potentially profound policy implications in how health care is delivered in this country. (Reviewer-Peter E. Clark, MD).

© 2009, Oakstone Medical Publishing

Keywords: Mortality

Print Tag: Refer to original journal article
Repeat Prostate Biopsy in Patients Eligible for Active Surveillance

Pathological Upgrading and Up Staging With Immediate Repeat Biopsy in Patients Eligible for Active Surveillance.

Berglund RK, Masterson TA, et al:


In this study of patients initially considered to be candidates for active surveillance of their prostate cancer rather than definitive treatment, 27% were upgraded and/or upstaged with an immediate repeat prostate biopsy.

Objective: To determine the results of immediate repeat biopsy in patients initially thought to be candidates for active surveillance rather than definitive treatment of their prostate cancer.

Methods: Following an initial biopsy, 104 patients were thought to be candidates for active surveillance rather than definitive therapy for their prostate cancer. Eligibility criteria consisted of a PSA <10 ng/mL, clinical stage T2a or less, Gleason pattern ≤3, ≤3 positive cores, and no single core with ≥50% cancer involvement.

Results: 26% of the 104 repeat biopsies were negative for cancer. On repeat biopsy, 27% of the 104 cases were either upgraded and/or upstaged; 16% of patients had a Gleason score of 7 on repeat biopsy. One patient had a Gleason score of 9. Ten percent of patients had ≥3 cores involved on repeat biopsy, and 12% had ≥50% involvement of at least 1 core.

Conclusions: The authors believe that a repeat biopsy in cases thought to be good candidates for active surveillance of prostate cancer showed that 27% of patients were either upgraded or upstaged. The authors recommend repeat biopsy in all patients initially thought to be good candidates for active surveillance instead of definitive therapy for their prostate cancer.

Reviewer’s Comments: Whether patients need to undergo a repeat biopsy prior to assigning them to active surveillance rather than definitive therapy for prostate cancer will quickly become a controversial topic. How many of these patients would ultimately be found to have progression of disease and how many would be harmed by delaying definitive therapy is currently unknown. To obtain meaningful data for active surveillance of prostate cancer requires that everyone agree on who should undergo active surveillance and not receive definitive therapy. Guidelines for identifying these patients are currently not uniform. (Reviewer-George S. Benson, MD).

© 2009, Oakstone Medical Publishing

Keywords: Surveillance

Print Tag: Refer to original journal article