Estrogen has been shown to decrease collagen concentration in connective tissue supporting the urethra, and subsequently, this may contribute to urinary incontinence.

**Objective:** To determine the association of hormone therapy with urinary incontinence in women ages 37 to 54 years.

**Design/Participants:** Prospective cohort study involving 7341 postmenopausal women.

**Methods:** As part of the Nurse’s Health Study II, a subset of 7341 postmenopausal women who reported no urinary incontinence was followed for the development of urinary incontinence. Questions about urinary frequency and quantity were completed in full-length questionnaires. Postmenopausal hormone use was determined by questions directed at postmenopausal hormone therapy over the previous 2 years, including hormone type and self-reported information on the estrogen dosage. A multivariate logistic regression analysis was then used to calculate odds ratios associated with either the use or nonuse of hormone therapy in the development of urinary incontinence in women 37 through 54 years of age.

**Results:** Of the 7341 women who reported no urinary incontinence in 2001, the investigators identified 1026 women who subsequently developed urinary incontinence over the following 2 years. When compared with women who had never used hormone therapy, women currently using hormone therapy had a 1.39-fold increased odds for the incidence of urinary incontinence. Women who were currently using oral estrogen alone had an odds ratio of 1.35 (95% CI, 1.03 to 1.78), and women who using a combination of oral estrogen and progestin had an odds ratio of 1.37 (95% CI, 1.13 to 1.67).

**Conclusions:** Younger postmenopausal women using hormone therapy had an increased risk of urinary incontinence.

**Reviewer’s Comments:** All of the information in this study was self-reported, and the investigator’s definition of incontinence being leakage occurring at least once per month is liberal. This observation of increased incontinence with use of hormone therapy is counter-intuitive to the concept that genital atrophy increases urinary symptoms. (Reviewer-John C. Jennings, MD).
Intensive glucose control does not improve vascular complications or survival in long-standing type 2 diabetes.

**Background:** The effect of intensive glucose control in patients with long-standing type 2 diabetes is uncertain, but 2 recent trials produced unfavorable results. In one trial, intensive control had no effect, while the other trial was stopped early due to excess mortality.

**Objective:** To determine the effects of intensive glucose control in long-standing type 2 diabetes.

**Participants:** 1791 veterans (mean age, 60.4 years; 97% men) with uncontrolled diabetes (mean HbA1c, 9.4%). On average, patients had been diabetic for 11.5 years, and 40% had prior cardiovascular events.

**Methods:** Patients were randomly assigned to standard glucose control or intensive control. Study drugs were determined by baseline body mass index (BMI): glimepiride plus rosiglitazone if BMI <27 and metformin plus rosiglitazone if BMI ≥27. The threshold for adding insulin was HbA1c >6% in the intensive-control group and >9% in the standard-control group. Other cardiovascular risk factors were treated identically. The primary outcome was time to a first vascular event. Outcomes were adjudicated in blinded fashion.

**Results:** After 6 years of follow-up, the median HbA1c was 8.4% in the standard-control group and 6.9% with intensive therapy. Other cardiovascular risk factors were similar: mean blood pressure, 126/68; LDL, 80 mg/dL; HDL, 41 mg/dl; aspirin use, 92%; and statin use, 85%. Active smoking rates decreased from 15% at entry to 7% by study end. No difference was seen in any major cardiovascular, microvascular, or mortality outcome. Total mortality rates were 11.4% in the intensive-therapy group and 10.6% in the standard-control group (not significant). Patients in the intensive-control group experienced more severe hypoglycemic events (1333 per 100 patient-years vs 383) and gained more weight (18 kg vs 9 kg).

**Conclusions:** Intensive glucose control had no effect on vascular complications or survival in patients with long-standing type 2 diabetes.

**Reviewer's Comments:** Does the Veterans Administration Diabetes Trial prove that glucose control is unimportant in long-standing diabetes? I believe it would be premature to draw that conclusion. First, the study protocol used a very unconventional set of drugs including one (rosiglitazone) that has been removed from the market due to excess cardiovascular risk. Did this affect the results? Second, this was not a placebo-controlled trial. The key word in the conclusion is "intensive." In a very high-risk group, the overall mortality rate was 11%, roughly one-third the total mortality rate in the United Kingdom Prospective Diabetes Study. Although this trial was shorter in duration, these veterans had longer-standing, more poorly controlled diabetes; many had already suffered cardiovascular events. Rather than disproving a benefit from glucose control, the results could be interpreted as demonstrating that modest glucose control in combination with aggressive management of cardiovascular risk factors achieved impressive survival results. This trial motivates me to renew my focus on controlling blood pressure and other risk factors and accept more modest goals for glucose control.

(Reviewer-John Van Loon Sheffield, MD).

© 2009, Oakstone Medical Publishing

Keywords: Glucose Control

Print Tag: Refer to original journal article
Tight BP control is highly effective at preventing complications of type 2 diabetes.

**Background:** The United Kingdom Prospective Diabetes Study (UKPDS) demonstrated that treating hypertension to a target of <150/85 results in significantly fewer vascular complications than treating to a target of <180/105. In fact, improving blood pressure (BP) control was more effective than improving glycemic control at preventing diabetes-related complications.

**Objective:** To determine whether improved BP control achieved during the UKPDS had a sustained benefit over an additional 10-year period.

**Participants:** 884 survivors of the original 1148 UKPDS BP trial cohort of newly-diagnosed type 2 diabetics.

**Design:** Observational cohort trial.

**Methods:** At the end of the intervention trial, patients and clinicians were advised to achieve the lowest glucose and BP results possible; treatment decisions were made by patients' regular providers. Clinical outcomes were captured by annual patient questionnaires. During years 1 through 5, patients returned to research clinics for basic examinations and questionnaires; only questionnaires were completed during years 6 through 10. Vital statistics were obtained from the U.K. Office of National Statistics. Outcomes were adjudicated by UKPDS investigators in blinded fashion.

**Results:** Over 90% of available patients returned for annual examinations and completed questionnaires. During the first 2 years of follow-up, intergroup differences in BP were lost (mean BP for all patients, 145/80). By year 5, medication usage in each group was similar: taking ≥2 antihypertensives, 75%; lipid-lowering therapy, 24%; and aspirin, 44%. Weight, glycated hemoglobin, and creatinine levels were also equivalent. Baseline significant differences in rates of diabetes-related complications, microvascular complications, stroke, and diabetes-related death diminished over time and were not significantly different at the end of the follow-up period.

**Conclusions:** The benefits of previously improved BP control did not persist after the between-group difference in BP control was lost. To achieve lasting benefits, good BP control must be maintained.

**Reviewer's Comments:** When the UKPDS ended, the mean BP in the tight-treatment group was 143/79 versus 152/82 in the less-tight-control group. Although the median glycated hemoglobin level was higher in the tight-BP-control group (8.3%) than in the less-tight-control group (7.5%; \( P =0.001 \)), tight-BP control reduced the relative risk of diabetes-related end points (24%), diabetes-related death (32%), stroke (44%), and microvascular complications (37%). When the intervention trial ended and the between-group difference in BP was lost, all of these benefits were lost also. This result is completely different from the long-term follow-up of the UKPDS intensive glycemic control trial. In the case of glycemic control, the between-group difference in glycemic control was lost early in the follow-up period, but prior microvascular benefits were maintained and new macrovascular and mortality benefits emerged over time. Where blood pressure control is concerned, there is clearly no "legacy effect." You have to keep at it to continue to reap the benefits. (Reviewer-John Van Loon Sheffield, MD).

© 2009, Oakstone Medical Publishing

Keywords: Blood Pressure

Print Tag: Refer to original journal article
Continuity of care between the outpatient and inpatient settings for patients with advanced lung cancer is associated with decreased ICU admissions during the final hospitalization.

**Background:** Continuity of care between the outpatient and inpatient settings has declined over the past 2 decades. Hospitalized patients are being increasingly cared for by hospitalists and subspecialists with whom they do not have a longstanding relationship. The absence of a continuity relationship may affect appropriate medical management and resource utilization, especially at the end of life.

**Objective:** To determine if the lack of a continuity relationship between the outpatient and inpatient settings in the treatment of patients with stage IIIB or stage IV lung cancer results in increased ICU admissions.

**Methods:** 21,183 individuals age ≥65 years who were diagnosed with stage IIIB or stage IV lung cancer between 1992 and 2002 and who died within a year of diagnosis were identified from the linked Surveillance, Epidemiology, and End Results (SEER)-Medicare database. All subjects were hospitalized during the last 6 months of life and had at least 3 outpatient visits to their usual care provider (UCP) during the year before their final hospitalization. Continuity of care was defined as having a visit by the UCP during the final hospitalization. Patient socioeconomic, demographic, and disease characteristics were obtained from the SEER database. ICU use during the last hospitalization was the primary outcome of interest.

**Results:** In 1992, 60.1% of patients were visited by a UCP during their final hospitalization compared to 51.5% in 2002, \(P < 0.001\). Over the same time period, the number of patients who were cared for by hospitalists during their final admission increased from 8.0% to 16.1% \(P < 0.001\). After adjusting for patient characteristics, those who were visited by a UCP were 25% less likely to be admitted to an ICU. ICU admissions increased by 5.8% per year from 1992 to 2002. Men, African Americans, patients of low socioeconomic status, unmarried patients, patients who were cared for in teaching hospitals, and those cared for by a hospitalist were less likely to experience outpatient-to-inpatient continuity.

**Reviewer’s Comments:** The absence of a UCP at the end of life increased the likelihood of an ICU admission among patients with advanced lung cancer. The results of this study imply that patients who are cared for by a physician they trust and with whom they have discussed their values with are less likely to be admitted to the ICU near the end of life. Since 2002, continuity of care has continued to decrease due to increasing numbers of subspecialists and hospitalists and decreasing numbers of primary care physicians. Further studies are needed to better understand the impact of continuity of care on appropriate resource utilization and strategies to increase continuity of care. (Reviewer-Elaine F. Sachter, MD).

© 2009, Oakstone Medical Publishing

Keywords: End of Life

Print Tag: Refer to original journal article
Triptans are frequently effective in sinus headache sufferers.

**Background:** Many patients are convinced that their recurrent headaches are due to problems with their sinuses. Several studies in the past few years have shown that >80% of patients with self-proclaimed or physician-diagnosed sinus headaches meet International Headache Society criteria for migraine headaches. **Objective:** To determine the response rate to triptans in alleviating "sinus headaches" in patients with a negative work-up for sinus disease. **Design:** Prospective clinical trial of patients presenting to a tertiary care ear, nose, and throat department with self- or physician-diagnosed "sinus headaches." **Methods:** Patients enrolled in the study underwent history, physical examination, headache questionnaire, nasal endoscopy, and sinus CT scans. Patients who had a negative work-up for sinus pathology underwent headache treatment with a triptan (eletriptan). If the patients did not have a response to eletriptan at the follow-up visit, they were switched to sumatriptan or rizatriptan. At repeat follow-up, those with a response to triptans were continued on this treatment, and those who did not have a response were referred to a headache specialist. **Results:** 54 patients were enrolled; 38 patients (69%) completed follow-up, with 31 patients (82%) having a significant reduction in headache pain with triptan use. An additional 3 patients had response to migraine-directed therapy, for a total of 92% of patients having a response to migraine treatment. **Conclusions:** Sinus headaches are often migraine headaches that respond to migraine treatment. **Reviewer’s Comments:** This study confirms what several other studies have shown, that sinus headaches are most likely migraine headaches. This study goes a step further to show that there is an excellent response rate in this population to triptan medications. The relatively high dropout rate in this study was due to patients who were frustrated because they were told that their "sinus headaches" were not due to their sinuses. Unless patients have features that truly suggest ongoing sinus disease (eg, fever and copious drainage), then up-front treatment of "sinus headaches" with a triptan is a reasonable approach. (Reviewer-Douglas S. Paauw, MD).
Vasectomy Not Associated With Prostate Cancer

Vasectomy and the Risk of Prostate Cancer.

Holt SK, Salinas CA, Stanford JL:

J Urol 2008; 180 (December): 2565-2568

There is no association between prostate cancer and age at vasectomy or years since vasectomy.

**Background:** Most of the literature has shown no association between vasectomy and prostate cancer. The effect of vasectomy on men with a family history of prostate cancer or on those who underwent a vasectomy at a young age or had an extended period of time since the procedure has been poorly studied due to small sample sizes and short study follow-up.

**Objective:** To assess the risk of prostate cancer in men by age and length of time to exposure from vasectomy to disease.

**Design:** Population-based, prostate cancer, case-controlled study.

**Participants:** 1327 men aged 35 to 74 years residing in King County, Washington, with a diagnosis of prostate cancer.

**Methods:** Cases of prostate cancer were identified from the SEER database for this population. Structured in-person interviews were conducted. Eligible controls were identified by random digit telephone dialing. Analysis based on prostate cancer Gleason score and stage was performed. Analysis was also performed based on demographics, age, prostate cancer screening history (within the last 5 years), family history of prostate cancer, and vasectomy parameters.

**Results:** 1327 men were eligible for study from the SEER database; 1001 completed the personal questionnaire. In total, 1340 controls were identified, of which 942 were interviewed. The control population showed that men who had undergone vasectomy were older, white, married, nonsmokers with higher income and education, and had undergone prostate-specific antigen (PSA) screening. Of men with prostate cancer and controls, 36% had undergone a vasectomy. The mean number of years since vasectomy in cases and controls was 21.1 years. No significant association was seen between prostate cancer and vasectomy status, age at vasectomy, years since vasectomy, or year of vasectomy. There was no evidence of risk estimates across vasectomy parameters. Risk did not change if men with prostate cancer within 2 years of vasectomy and controls with no PSA screening within 5 years (n=136) were excluded.

**Conclusions:** No association was found between prostate cancer and vasectomy, even in men who had a vasectomy performed at a young age or had an extended period of time since vasectomy.

**Reviewer's Comments:** This paper is a well-conducted, large case-control study that answers the concern about possible limitations of previous work that reported the lack of association between prostate cancer and vasectomy. This criticism often indicated inadequate follow-up since vasectomy to make this claim. In this study, average time since vasectomy in cases of prostate cancer and controls was 21 years. Multiple variables were looked at including vasectomy in the face of prostate cancer family history and screening. This large study should end the criticism on previous work that did not answer the question of prostate cancer and time from vasectomy. (Reviewer-Ajay K. Nangia, MBBS).

© 2009, Oakstone Medical Publishing

Keywords: Vasectomy

Print Tag: Refer to original journal article
Although long-term implications of early exposure to TV are yet unclear, there are negative short-term effects on development, cognition, and attention.

**Background:** 30% of preschoolers have a television (TV) in their bedroom; young children spend 30% to 40% of their waking hours watching TV. The average age at which children began watching TV is now 5 months, because parents believe that watching TV or videos (such as “Baby Einstein”) will make the baby smarter. The American Academy of Pediatrics (AAP) discourages TV viewing in the first 2 years of life.

**Objective:** To review the evidence for and against infant TV viewing.

**Results:** Children learn better when they see something in person rather than on TV. There is also concern that the rapid pace of many TV shows may overstimulate developing brains. Finally, time spent watching TV is often time spent alone, without interaction with other people; many developmental pediatricians argue that there are many other more developmentally appropriate or important activities that have been displaced by TV viewing. Early exposure to TV can delay language acquisition in young children. One study conducted in Thailand found that infants who watched >2 hours of TV a day were 6 times more likely to have language delay. Another study showed that for every hour of TV or baby DVDs that infants 7 to 16 months old watched, there was acquisition of 6 to 8 fewer words. Although watching shows such as “Sesame Street” can be beneficial for 3- to 5-year-olds, watching the same shows can delay cognitive and language development in younger children. In one study, every hour of daily TV viewing before the age of 3 was associated with lower scores on cognitive tests. TV watching in infancy has also been associated with an increase in attention problems. One study found that each hour of TV watching per day for 1- to 2-year-olds resulted in a 10% increased risk of attentional problems. Another study demonstrated that violent and nonviolent noneducational programs were associated with significantly increased risks of attentional problems, but more slowly paced educational programming was not.

**Reviewer’s Comments:** There are limitations to the current research on TV viewing in infants. Many of the studies are laboratory based, and some argue that the lab cannot replicate what happens in real life. In addition, studies have focused on short-term outcomes. Large, population-based studies with long-term follow-up are needed. However, evidence is growing that excessive exposure to TV in the first 2 years of life can be detrimental to infant development. In fact, France has recently banned all television and media programming directed at infants. Although the AAP guidelines discouraging TV viewing in the first years of life were published in 2001 and were largely based on the opinion that TV exposure limited exposure to more developmentally appropriate activities rather than on any current research, subsequent studies support these recommendations. (Reviewer-Rachel Moon, MD).
Alternating acetaminophen and ibuprofen results in a statistically decreased fever at 4 and 5 hours compared with acetaminophen alone, but without sustained effectiveness or parental perception of differences.

**Objective:** To compare the efficacy of acetaminophen alone with alternating acetaminophen and ibuprofen in the control of fever in children.

**Design/Participants:** Prospective, randomized, double-blind, placebo-controlled study of children, (6 months to 6 years) with a temperature >38°C (rectal if <2 years, oral if >2 years).

**Methods:** Caretakers were given thermometers for home use and instructed in proper technique. Two treatments were given. The first was acetaminophen (15 mg/kg per dose) at time zero, followed by placebo at 3 hours and then by acetaminophen again at 4 hours. The other regimen was acetaminophen at time zero, followed by ibuprofen (10 mg/kg per dose) at 3 hours and placebo at 4 hours. Caretakers were told to record the child's temperature at 3, 4, 5, and 6 hours. They also completed a list of symptoms and noted whether they believed the child needed antipyretic medication at times 3 and 4 hours. Diaries were completed hourly for 6 hours that included side effects and parental perception of the antipyretic effectiveness.

**Results:** 38 patients (mean age, 32 months) participated in the study. There were no significant differences in temperature at 0, 3, and 6 hours between the acetaminophen group and the alternating group. At 4 hours, the alternating group did have a just barely minimally statistically significant lower temperature of 38°C in the acetaminophen group versus 37.4°C in the alternating group ($P=0.05$). At 5 hours, the difference was 37.1°C versus 37.9°C, which had stronger statistical significance ($P=0.0032$). No difference was noted at 6 hours. When caretakers in each group were asked if they felt their child needed additional antipyretic medication at times 3 and 4 hours, there was no difference between the 2 groups.

**Conclusions:** Use of an alternating regimen of acetaminophen and ibuprofen resulted in a significantly decreased fever at 4 and 5 hours compared with acetaminophen alone. The decrease was not sustained at 6 hours and parents did not perceive any difference in efficacy between the 2 regimens.

**Reviewer’s Comments:** While there was some statistical difference between the 2 groups, the authors concede "the difference was transient and of questionable clinical significance." Although this alternating regimen has not been shown to have clinically impressive fever reduction, 1 survey has found that up to 50% of pediatricians advise parents to alternate these 2 medications for fever. The downsides to the dual medications include the possibility of dosing errors and the emphasis on fever itself as a dangerous phenomenon, the so-called "fever phobia." The authors note that the lack of sustained effectiveness and the lack of differences in perceived efficacy by parents with dual therapy lead them to support not routinely advocating the use of alternating antipyretic schedules in the setting of fever. (Reviewer-Mark F. Ditmar, MD).
Algorithmic Approach to Chronic Cough in Children Identifies Likely Etiologies

Evaluation of Chronic Cough in Children.
Asiloy S, Bayram E, et al:
Chest 2008; 134 (December): 1122-1128

In children with chronic cough evaluated with a chest x-ray and spirometry, the most frequently identified cause is asthma-like symptoms responsive to inhaled corticosteroids.

Objective: To use the published practice guidelines from the American College of Chest Physicians (ACCP) for evaluation of chronic cough in children.

Participants/Methods: The guidelines define chronic cough as any cough lasting >4 weeks. Initial studies included a chest x-ray (CXR) and spirometry. If normal, a watch, wait, and review approach was used with re-evaluation in 2 weeks. If spirometry was abnormal and indicated airflow limitation by bronchodilator responsiveness testing, the patient was treated with inhaled corticosteroids. A positive clinical response suggested asthma-like symptoms. If a wet cough persisted, a trial of clarithromycin for 10 days was given for suspected protracted bacterial bronchitis. Patients were diagnosed with upper airway cough syndrome (previously known as postnasal drip syndrome) if they had nasal mucosal edema or hyperemia. These patients were treated with antihistamines, nasal saline solution, and/or nasal steroid therapy for 2 to 4 weeks. Some patients underwent gastroesophageal scintigraphy for suspected reflux and, if positive, were treated with lansoprazole for 2 to 4 weeks. Other diagnoses sought included bronchiectasis (diagnosed by chest CT), tuberculosis, and Mycoplasma pneumoniae infections. Patients were followed until the cough resolved.

Results: 108 patients (mean age, approximately 8.5 years) were in the study; 25% were diagnosed with asthma and asthma-like symptoms, 24% with protracted bronchitis, 20% with upper airway cough syndrome, and 5% with gastroesophageal reflux. Mycoplasmal infection was the principle diagnosis in only 1%. A likely etiology was determined for 96% of the patients. Serious illness, including bronchiectasis and congenital malformations, was discovered in 5%.

Conclusions: The 2006 ACCP guidelines are effective in establishing the underlying diagnosis responsible for chronic cough in children.

Reviewer's Comments: Since most pediatricians do not utilize in-office spirometry as part of their practice, the use of these guidelines might mean referral to a pediatric pulmonologist, which would likely necessitate a delay. Since the study does find that asthma-like symptoms are the most common etiology, there might be a temptation in the atopic child with a normal chest x-ray to try the empiric course of inhaled steroids. However, although not mentioned in this paper, the once coughing atopic child may well be a future coughing atopic child. That initial precision of diagnosis by spirometry would be valuable in the event of recurrent episodes requiring treatment. As with other recent studies in children, gastroesophageal reflux was found to be an infrequent cause of chronic cough. Reflux is a greater culprit in adults. (Reviewer-Mark F. Ditmar, MD).

© 2009, Oakstone Medical Publishing

Keywords: Chronic Cough

Print Tag: Refer to original journal article
Objective: To evaluate the concordance of simultaneous screening for chlamydial and gonococcal infections utilizing self-collected vaginal swab, first void urine, and endocervical swab.

Participants/Methods: From 2001 to 2006, adolescent females were recruited from a Baltimore adolescent clinic for this study. Patients were eligible if they were sexually active, not recently pregnant, and between 12 and 18 years of age. At the initial visit and every 6 months, 3 specimens were collected. These included a first void urine at least 1 hour after the last micturition and before the swab collection. A self-collected vaginal swab was also obtained. Finally, a pelvic examination was performed and an endocervical swab was obtained by the clinician. Each specimen was sent for nucleic acid amplification testing for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG). Results were reported as positive, negative, or intermediate. A patient was considered infected if at least 2 of the 3 specimens were positive.

Results: 342 patients were enrolled encompassing 1080 visits. The average age was 16 years, and 96% were black. The positive rates were 26% for CT and 12% (per 100 women) for NG infections. For CT, the sensitivity of the self-collected vaginal swab was 97%, first void urine was 89%, and provider-collected endocervical swab was 90%. For NG, self-collected vaginal swabs were again the most sensitive at 100%, first void urine was 87%, and endocervical swab was 96%. Specificities for each technique ranged between 95% and >99% for both infections.

Conclusions: There was strong agreement among the 3 techniques for the detection of CT and NG in adolescent females using nucleic acid amplification testing. The most sensitive test was a self-obtained vaginal swab. The least sensitive was first void urine, although it was also the least invasive method. Self-collected vaginal swabs and first void urine samples may provide reliable alternatives to pelvic examinations with endocervical specimens for sexually-transmitted disease screening.

Reviewer's Comments: The authors sought to look at 1 diagnostic method (nucleic acid amplification testing) and to determine how sampling at 3 anatomic sites compared with disease identification. In this group of adolescents with a particularly high prevalence rate, there was great value in testing that did not involve a clinical speculum examination, particularly self-collected vaginal swabs. Of note, self-collected swabs are approved by the Food and Drug Administration only for use in health care settings. Also of note, in cases of suspected sexual abuse or assault, amplification techniques (which are nonculture methods) are not admissible as forensic evidence. Cultures need to be performed in those settings. (Reviewer-Mark F. Ditmar, MD).

© 2009, Oakstone Medical Publishing

Keywords: *Chlamydia trachomatis*

Print Tag: Refer to original journal article
Healthy and Obese/Overweight? Not When It Comes to HF

Body Mass Index and Vigorous Physical Activity and the Risk of Heart Failure Among Men.

Kenchaiah S, Sesso HD:

Circulation 2009; 119 (January 6/13): 44-52

HF risk increases with increasing BMI and decreases with increasing vigorous activity.

Background: Obese individuals have an increased risk of heart failure (HF); risk increases linearly as weight increases. There are no data on the HF risk associated with overweight, therefore, the HF Society recommendations are a goal body mass index (BMI) of <30 kg/m2.

Participants/Methods: This is a substudy of the Physicians Health Study, a study of aspirin and beta carotene in 22,071 male physicians, aged 40 to 84 years at the time of enrollment. After excluding participants with missing data or prior HF, 21,094 patients were evaluated in this study. Baseline and follow-up questionnaires addressed exercise habits and other covariates. Multivariate analysis was performed.

Results: 40% were overweight, and 5% were obese. Patients who rarely exercised were older, had higher BMI, smoked more often, and had more diabetes and hypertension. Mean follow-up was 20.5 years and mean age was 53 years. A total of 1109 men developed HF, and the incidence of HF increased by 13% for each 1 kg/m2 increase in BMI. Variables were grouped as "likely not causal" (ie, age and smoking) and "likely causal" (ie, diabetes and hypertension) in the association between BMI and HF. When adjusting for "not causal" variables, overweight men had a 62% increased risk of HF and obese men had a 240% increased risk, which increased linearly with increasing BMI. When factoring in the "causal variables," the hazard ratio declined in both overweight (1.62 to 1.49) and obese (3.38 to 2.80) men. Vigorous exercise did not substantially alter the excess risk of HF related to BMI. Active men had a lower incidence of HF than inactive men, and those who engaged in vigorous physical activity at least 1 to 3 times per month had a 26% reduction in HF risk. Increasing levels of activity were associated with a decreasing risk of HF, including in patients with elevated BMI. When analyzing BMI as a continuous variable and activity as dichotomous, the risk of HF increased with BMI and inactivity: lean and inactive (19% increased risk, but nonsignificant); overweight and active (49%); overweight and inactive (78%); obese and active (168%); and obese and inactive (293%). The risk of HF related to BMI was greater in younger patients versus older patients.

Conclusions: Elevated BMI is linearly associated with increased risk of HF; vigorous physical activity is associated with a decreased risk of HF.

Reviewer's Comments: This study adds to the literature arguing against the "healthy" obesity concept and advocates further for public health measures to promote BMI <25 and increased physical activity. (Reviewer-Karen Stout, MD).

© 2009, Oakstone Medical Publishing

Keywords: Heart Failure

Print Tag: Refer to original journal article
Fish oil supplementation decreases CV mortality, but has no effect on arrhythmia.

**Background:** Over the last decade, there has been great interest in the possible cardioprotective effect of fish oil. The interest started in the mid 1970s when a study from Greenland showed that a diet high in fish oil was associated with low cardiovascular (CV) mortality. Other studies over the years, including the large GISSI-Prevenzione trial showed decreased CV mortality, sparking interest in the possibility that part of the CV protection was due to an antiarrhythmic property of fish oil.

**Objective:** To evaluate the literature on the effects of fish oil on mortality and arrhythmias.

**Methods:** Randomized controlled trials of fish oil supplementation were reviewed using the usual data sources available. The primary outcomes of interest were arrhythmic outcomes in patients with defibrillators and sudden cardiac death. The secondary outcomes were all-cause mortality and death from cardiac causes.

**Results:** 12 studies were included involving 32,779 patients. The studies did not show a decrease in arrhythmias, either in the 3 studies with implantable defibrillators or in the 6 studies for sudden cardiac death. A total of 11 studies looked at deaths from cardiac causes, with a significant decrease noted in cardiac deaths of 20%, (OR, 0.80; 0.69 to 0.92). There was no significant decrease in all-cause mortality.

**Conclusions:** Fish oil supplementation was associated with a significant reduction in deaths from cardiac causes, but there was no reduction in arrhythmias or all-cause mortality.

**Reviewer's Comments:** There have been many studies touting the benefits of fish oil. This analysis shows a small benefit in cardiac deaths, but no benefit in all-cause mortality or in the frequency of malignant arrhythmias. What should we advise our patients? If patients eat fish 2 or more times per week, they probably get no benefit from fish oil. If they do not eat fish, there is probably a small benefit to fish oil, but not on mortality. (Reviewer-Douglas S. Pauuw, MD).

© 2009, Oakstone Medical Publishing

Keywords: Arrhythmias

Print Tag: Refer to original journal article
Patients with high-normal thyroid function are at an increased risk of atrial fibrillation.

**Background:** In the elderly population, atrial fibrillation (AF) is the most common cardiac arrhythmia. It is associated with significant morbidity and mortality, including a higher risk of stroke and peripheral embolism. Overt and subclinical hyperthyroidism has been shown to be independent risk factors for AF.

**Design/Objective:** To prospectively investigate the association of high-normal thyroid function with the development of AF. This study is part of the population-based Rotterdam Study, which is designed to assess the occurrence and progression of chronic disease and their risk factors in the elderly.

**Methods:** The association between thyroid-stimulating hormone (TSH) levels and AF was assessed in 1426 subjects. All subjects had TSH levels in the normal range (0.4 to 4.0 mU/L) and did not have AF at baseline. It was also possible to analyze the association between free thyroxine levels within the normal range (0.86 to 1.94 ng/dL) and AF in 1177 of the 1426 subjects. During a median follow-up of 8 years, there were 105 new cases of AF identified. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated.

**Results:** The risk of AF in the study population was associated with the TSH level. Multivariate adjusted HR was 1.94 (95% CI, 1.13 to 3.34, lowest vs highest quartile; \( P \) for trend, 0.02). Also, multivariate adjusted level of free thyroxine showed the greatest association with risk of AF (HR, 1.62; 95% CI, 0.84 to 3.14, highest vs lowest quartile; \( P \) for trend, 0.06).

**Conclusions:** This is the first prospective, population-based study to report on the association between normal thyroid function and the risk of AF in the elderly population. Within the normal range of thyroid parameters, persons in the lowest quartile of the normal serum range of TSH had an approximately 2-fold increased risk of AF compared to subjects who were in the highest quartiles. This suggests that elderly persons with high-normal thyroid function are at an increased risk of AF.

**Reviewer's Comments:** Overt hyperthyroidism is a well-recognized risk factor for AF. Subclinical hyperthyroidism with a TSH level below the normal range and free thyroxine levels within the normal range has also been identified as predictive for AF. This paper, however, illustrates that elderly patients with high-normal thyroid function are at an increased risk of AF, indicating a possible age-related cardiac responsiveness to thyroid hormones. (Reviewer-Suraj Maraj, MD).

© 2009, Oakstone Medical Publishing

Keywords: Thyroid Function

Print Tag: Refer to original journal article
Ramipril at Low Dose Decreases Recurrence Rate of Lone AF

Prevention of Recurrent Lone Atrial Fibrillation by the Angiotensin-II Converting Enzyme Inhibitor Ramipril in Normotensive Patients.
Belluzzi F, Sernesi L, et al:

J Am Coll Cardiol 2009; 53 (January 6): 24-29

Ramipril is effective in preventing AF in patients without hypertension or heart disease, arguing for an antiarrhythmic effect of ACE inhibitors.

Background: Angiotensin-converting enzyme (ACE) inhibitors are associated with a lower incidence of atrial fibrillation (AF) in studies of patients with hypertension or other heart disease. The association is proposed to be related to favorable effects of ACE inhibitors on atrial pressures and atrial remodelling, rather than as a direct antiarrhythmic effect.

Objective: To evaluate the effect of ACE inhibitors, specifically ramipril, on the recurrence of lone AF in patients without clinically evident structural atrial abnormalities or conditions that would make them likely to have atrial abnormalities.

Participants/Methods: All patients admitted to a single institution with a first ever episode of AF for <12 hours were evaluated. A randomized, placebo-controlled trial of ramipril versus placebo was done; enrollment occurred after the patient underwent evaluation and was cardioverted. Once in sinus rhythm, patients were begun on ramipril 5 mg (31 patients) or placebo (31 patients). Exclusion criteria were any type of heart disease, hypertension, or underlying condition that would predictably be related to heart disease or hypertension. Patients who were dizzy or had syncope associated with AF were excluded; included patients had normal blood pressure (BP), were on no BP-lowering medications, and had a normal chest x-ray. Echocardiography was performed as was extensive laboratory evaluation. All patients were cardioverted with IV propafenone and then randomized.

Results: 469 patients were screened; 62 met inclusion criteria and agreed to participate. There were no significant differences between the 2 groups, including no significant differences in BP before or at the end of the trial. There were no echocardiographic changes during the course of the study between the groups, including assessment of the left atrium. After 3 years of follow-up, there were AF relapses in 10 placebo patients and 3 ramipril patients. No patients complained of side effects. In the 3 ramipril treated patients who had relapses of AF, 1 relapsed within 7 days of enrolment, while the other 2 relapsed 2 years after enrollment.

Conclusions: Ramipril is effective in preventing AF in patients without hypertension or heart disease, arguing for an antiarrhythmic effect of ACE inhibitors.

Reviewer’s Comments: While lone AF is associated with lower complication rates, it is often uncomfortable to patients and frequently results in hospital or ER visits. Any preventative medication that is well tolerated would have appeal to patients with lone AF, it is intriguing that ACE inhibitors may beneficially impact AF even in normotensive patients with structurally normal hearts. This also raises the possibility that there are atrial changes not otherwise identified that are beneficially impacted by ACE inhibitors. This is a small study, therefore clinical practice should not change on the basis of this trial alone. (Reviewer-Karen Stout, MD).

© 2009, Oakstone Medical Publishing

Keywords: Lone Atrial Fibrillation

Print Tag: Refer to original journal article
This consensus document evaluates reducing the gastrointestinal risk of antiplatelet therapy and NSAID use.

The following is a summary of the American College of Cardiology Foundation, the American College of Gastroenterology, and the American Heart Association 2008 expert consensus document on reducing the gastrointestinal (GI) risk of antiplatelet therapy and NSAID use. (1) Any NSAID, including COX-2 inhibitors, used with cardiac dose aspirin increases the risk of ulcer complications, such that gastroprotective therapy should be prescribed for at-risk patients. (2) Cardiac dose aspirin is associated with a 2- to 4-fold increase in upper GI events. Enteric-coated and buffered preparations do not reduce bleeding risk, so gastroprotection should be prescribed for at-risk patients. Furthermore, the risk of upper GI events increases with increasing aspirin dose, such that doses >81 mg should not be routinely prescribed. (3) The combination of aspirin and anticoagulant therapy, including unfractionated or low-molecular-weight heparin and warfarin, increases the risk of major extracranial bleeding events, the majority of which are upper GI events. When this combination is indicated, the patient should receive concomitant proton pump inhibitors (PPIs). The recommended INR when warfarin is added to aspirin plus clopidogrel is 2.0 to 2.5. (4) Substituting clopidogrel for aspirin is not recommended for reducing recurrent ulcer bleeding in high-risk patients. In addition, clopidogrel is inferior to the combination of aspirin plus a PPI. (5) Clopidogrel plus warfarin increases the incidence of major bleeding events. The combination of antiplatelet and anticoagulant therapy should be used only when indicated, and the benefits outweigh the risks. An INR of 2.0 to 2.5 is recommended when warfarin is added to aspirin plus clopidogrel. (6) PPIs are the preferred prophylactic agents for NSAID- and aspirin-associated GI events. (7) Testing for and treating Helicobacter pylori in patients with a history of ulcer disease should be performed before initiating chronic antiplatelet therapy. (8) The decision to discontinue aspirin use in the setting of an acute GI bleed must be made on an individual basis, considering cardiac versus GI risks. (9) Endoscopic therapy can be performed in high-risk cardiovascular patients on mono- or dual-antiplatelet therapy. A cardiologist and gastroenterologist should discuss the risk of bleeding versus thrombosis when considering cessation of antiplatelet therapy.

**Reviewer's Comments:** The benefits of antiplatelet therapy in both primary and secondary prevention for cardiovascular events are well recognized. It is also recognized that antiplatelet agents increase the risk of GI complications. This consensus document from the American College of Cardiology, the American College of Gastroenterology, and the American Heart Association offers physicians guidance when placing patients on mono- and dual-antiplatelet and antithrombotic therapy. (Reviewer-Vincent M. Figueredo, MD).

© 2009, Oakstone Medical Publishing

Keywords: Antiplatelet/NSAID Use

Print Tag: Refer to original journal article
Are Oral Anticoagulants or Antiplatelets Better Tx for AF Patients?

Benefit of Oral Anticoagulant Over Antiplatelet Therapy in Atrial Fibrillation Depends on the Quality of International Normalized Ratio Control Achieved by Centers and Countries as Measured by Time in Therapeutic Range.

Connolly SJ, Pogue J, et al:

Circulation 2008; 118 (November): 2029-2037

The necessity of maintaining a therapeutic International Normalized Ratio cannot be overestimated when treating patients with atrial fibrillation.

Background: Patients with atrial fibrillation (AF) are at an increased risk of stroke and other vascular events. Oral anticoagulation (OAC) with warfarin has been shown to be superior to antiplatelet agents in the prevention of such events. An International Normalized Ratio (INR) in the range of 2 to 3 is the standard of care. Clinicians need to maximize their patients' time in therapeutic range (TTR) to provide them with maximum protection. Various studies have suggested that many patients spend a significant time outside that range. A low TTR has been associated with increased incidence of stroke.

Objective: To explore how variations in TTR between countries and centers affect the efficacy of OAC when compared with dual antiplatelet agents.

Methods: This was a post-hoc analysis of a subset of patients enrolled in a large study (ACTIVE W) of dual antiplatelet agents (aspirin and clopidogrel) compared to warfarin. All patients had AF with a ≥1 other risk factor for stroke. TTR was defined as percentage of days with INR of 2 to 3.

Results: 3371 patients in the OAC group were included in the current analysis. Mean TTR for all OAC patients was 63%. Patients were more likely to have a subtherapeutic rather than a supratherapeutic INR. There were considerable variations in mean TTR between the 29 participating countries (range 46% to 78%). In all, 15 countries with enough clinical events were included in analysis of OAC efficacy compared to dual antiplatelet agents. Patients were divided into quartiles based on their TTR. Relative risk of stroke or vascular events for the OAC and dual antiplatelet groups increased from the lowest to the highest quartiles. Patients in the 2 lowest TTR quartiles had more risk of such events with dual anti-platelet agents compared to warfarin. Conversely, patients in the 2 highest TTR quartiles had less risk of stroke with dual anti-platelet agents compared to warfarin. A similar outcome was noted for major hemorrhage. These effects were largely independent of baseline differences between the quartiles. More complex statistics were used to determine the minimum TTR that would be associated with benefit from OAC. That value was determined to be a TTR of 58%.

Conclusions: The success of INR control in the therapeutic range is an important determinant in achieving a benefit from OAC over antiplatelet agents. The study suggests that there is a TTR threshold (58%) below which OAC therapy may not be superior to antiplatelet therapy.

Reviewer's Comments: This study has serious implications for healthcare delivery systems. Simply placing patients on OAC is not sufficient to derive a benefit. Serious efforts must be directed at achieving and maintaining a therapeutic INR. (Reviewer-Khalid Almuti, MD).

© 2009, Oakstone Medical Publishing

Keywords: Atrial Fibrillation

Print Tag: Refer to original journal article
Sodium, Potassium Intakes Affect Risk of CVD

Joint Effects of Sodium and Potassium Intake on Subsequent Cardiovascular Disease: The Trials of Hypertension Prevention Follow-Up Study.

Cook NR, Obarzanek E, et al:

Arch Intern Med 2009; 169 (January): 32-40

Increases in the sodium to potassium excretion ratio are associated with an increased risk of subsequent cardiovascular disease.

**Background:** Various prior studies of dose-response effects of sodium and potassium intake on subsequent cardiovascular disease (CVD) have relied on sub-optimal measures of intake. Prior observational data and randomized trials have shown decreased blood pressures and a reduced risk of hypertension in those subjects with increased potassium intake and decreased sodium intake.

**Methods:** There have been 2 trials of sodium reduction and other interventions that collected 24-hour urinary excretions intermittently during 18 months from September 17, 1987, to January 12, 1990 (Trials of Hypertension Prevention [TOHP] I) and during 36 months from December 18, 1990, to April 7, 1995 (TOHP II). These trials included adults with pre-hypertension aged 30 to 54 years. Amongst those adults not assigned to an active sodium reduction intervention, the relationship of a mean of 3 to 7 urinary excretions (24 hour) of sodium and potassium and their ratio with subsequent CVD (stroke, myocardial infarction, coronary revascularization, or CVD mortality) through 10 to 15 years of post-trial follow-up were assessed.

**Results:** Among 2974 participants follow-up information was obtained on 2275 participants. There were 193 CVD events. After adjustments for baseline variables and lifestyle changes, there was a non-significant trend in CVD risk across sex-specific quartiles of urinary sodium excretion (\(P = 0.38\) for trend) and potassium excretion (\(P = 0.08\) for trend). There was, however, a significant trend across quartiles of the sodium to potassium excretion ratio (\(P = 0.04\) for trend). In those models containing both measures simultaneously, linear effects were: rate ratio (RR), 1.42; 95% CI, 0.99 to 2.04 per 100 mmol/24 hours of urinary sodium excretion (\(P = 0.05\)); and 0.67; 0.41 to 1.10 per 50 mmol/24 hours of urinary potassium excretion (\(P = 0.12\)). A single model containing the sodium to potassium excretion ratio (RR, 1.24; 95% CI, 1.05 to 1.46; \(P = 0.01\)) had the lowest Bayes information criterion (best fit). Conclusion: Increased sodium to potassium excretion ratio is associated with increased risk of subsequent CVD. This effect is stronger than that of sodium or potassium individually.

**Reviewer's Comments:** This paper is important since it highlights the importance of dietary intake and subsequent risk of CVD. Current diets are rich in salt. Prior studies have illustrated a decrease in blood pressure in subjects with an increased potassium intake and decreased sodium intake. This study illustrates that higher sodium to potassium excretion ratio is associated with an increased risk of subsequent CVD.

(Reviewer-Suraj Maraj, MD).

© 2009, Oakstone Medical Publishing

Keywords: Cardiovascular Disease

Print Tag: Refer to original journal article
Treatment with the angiotensin receptor blocker candesartan has been shown to result in regression of diabetic retinopathy in some patients.

**Objective:** To evaluate the effect of treatment with the angiotensin receptor blocker candesartan on the progression and regression of diabetic retinopathy in type 2 diabetics.

**Design:** Randomized, masked, controlled clinical trial.

**Methods:** Patients underwent a prospective evaluation including clinical examination and fundus photography. The severity of diabetic retinopathy was evaluated using the Early Treatment Diabetic Retinopathy Study (ETDRS) scale, based upon fundus photographs.

**Results:** A similarly low rate of progression of diabetic retinopathy was seen between treated and untreated patients. Treatment with candesartan was, however, associated with a higher probability of regression of diabetic retinopathy, with a 34% greater probability of having less severe retinopathy at the 5-year follow-up appointment in comparison to baseline. This result appeared to be independent of other risk factors for diabetic retinopathy, including hypertension.

**Conclusions:** Treatment with the angiotensin converting enzyme candesartan is associated with an increased probability of regression of diabetic retinopathy with long-term use.

**Reviewer's Comments:** The angiotensin receptor antagonist candesartan is already recommended for treatment of diabetics who show evidence of diabetic nephropathy. This study suggests that it may also play a role in the treatment of patients with diabetic retinopathy, as there was a significantly greater probability of experiencing a regression of retinopathy with its use. Additional studies will be needed to evaluate its effect in a larger number of patients and to determine the optimal treatment regimen for these patients. However, this study is important in that it represents a novel medical approach with a unique mechanism of action aimed directly at inducing a regression in the systemic complications of diabetes. (Reviewer-Scott D. Smith, MD, MPH).

© 2009, Oakstone Medical Publishing

Keywords: Diabetic Retinopathy

Print Tag: Refer to original journal article
Statins are effective in the primary prevention of cardiovascular events.

**Background:** Statins have been proven to be beneficial in secondary prevention of cardiovascular disease (CVD). However, its role in primary prevention of CVD is less clear.

**Objectives:** The authors, using a systematic review of literature, aimed to study the effects of statins in primary prevention of CVD.

**Methods:** A comprehensive literature review was performed using 10 major databases, and all randomized clinical trials of statins that were at least 12 months in duration were evaluated. Only studies of primary prevention (ie, >50% of the population had no CVD) were included. Studies looking at surrogate end points like lipid levels were excluded. Also, studies enrolling high-risk diabetic patients were excluded. **Results:** A total of 20 clinical trails were selected, enrolling 65,261 patients. No studies of rosuvastatin or simvastatin met inclusion criteria. All-cause mortality was assessed in 19 trials and found a RR of 0.93 ($P=0.03$). Seventeen trials assessed CVD deaths and found a RR of 0.89 ($P=0.02$). Nine trials studied myocardial infarction (MI)-attributable mortality, and found a RR of 0.46 ($P=0.005$). Major cardiovascular events in 17 trails had a RR of 0.85 ($P=0.004$), effect on MI in 17 trials had a RR of 0.77 ($P=0.01$), and incidence of all-strokes had a RR of 0.88 ($P=0.05$). Pooled analysis of stroke mortality in 11 trials found a RR of 1.05 ($P=0.72$), noncardiovascular deaths in 18 trials had a RR of 0.98 ($P=0.62$), effect on revascularization had a RR of 0.84 ($P=0.18$), and effect on angina was also nonsignificant. Effect on cancer incidence in 10 trials and rhabdomyolysis in 9 trials had a RR of 1.02 and 0.97, respectively; both were non-significant.

**Conclusions:** Statins have a role in primary prevention of CVD.

**Reviewer’s Comments:** The authors conducted a meta-analysis of more than 65000 patients followed for at least one year, and demonstrated reduction in all cause mortality, cardiovascular deaths, major cardiovascular events and myocardial infarction. It is reassuring to note that there were no increases in cancer or rhabdomyolysis. As noted in prior studies, statins were ineffective in reducing stroke mortality. No trials using rosuvastatin or the cheapest statin now available, simvastatin, were included. A large number of people would meet criteria for primary prevention and cost considerations would be a serious issue. A better understanding of the relative efficacy of various statins and their unique side effect profiles would be useful in deciding which statin to use for primary prevention; such data would need to come from head-head trials of statins.

(Reviewer-Anoop C. Parameswaran, MD).

© 2009, Oakstone Medical Publishing

Keywords: Statin Tx

Print Tag: Refer to original journal article
Despite its perceived hygienic effects, douching can predispose to harmful alterations in bacterial content and promote sexually transmitted infection.

**Objective:** To study the potential association between sexually transmitted infections and douching in adolescent patients.

**Design:** Prospective cohort study.

**Participants:** 411 females between the ages of 12 and 19 years.

**Methods:** Female subjects aged 12 to 19 years were recruited to participate in an observational study for Excellence in Adolescent Care and Health. Recruitment of individuals who were both HIV-infected and HIV-uninfected was done at 16 locations in 13 U.S. cities. Sexual risk factors and age characteristics were matched between the control HIV-uninfected and the HIV-infected adolescents. Face-to-face interviews and computer-assisted self-interviews were used to determine sexual activity and drug use. Laboratory evaluation included cervical, anal, blood, and urine samples for sexually transmitted disease including HIV, herpes simplex, chlamydia, trichomonas, and gonorrhea. Any sexually transmitted disease was treated when diagnosed and follow-up examinations were performed as a test of cure. The study of the association between douching, behavior, and sexually transmitted disease in female adolescents was classified into 2 douching categories. The first category was either never douching or intermittent douching and the second category was always douching. Douching behavior was also characterized according to whether or not the adolescent had acquired a sexually transmitted disease during the course of the study, with the hypothesis that unknown acquisition of sexually transmitted disease might change douching behavior. Analysis was then performed to determine the association of douching with the presence of sexually transmitted disease.

**Results:** In adolescents who reported that they always doused, there was a shorter time to sexually transmitted disease infection, with a hazard ratio of 2.1 (95% confidence interval [CI], 1.2 to 3.4). This compared to a hazard ratio of 1.5 (95% CI, 1.0 to 2.2) for those persons who were self described as never douchers. On adjustment of the hazard ratio, the sexually transmitted disease infection rate was 1.8 times greater for always douchers and 1.4 times greater for intermittent douching as compared with those who never douched. Adolescents who were described as always douchers had a shorter sexually transmitted infection-free time than never douchers.

**Conclusions:** Discouragement of douching in adolescents may reduce sexually transmitted infection risk in this age group.

**Reviewer’s Comments:** Although douching has long been considered a method of cleansing the vagina, in fact it has the ability to disrupt the normal vaginal flora with reduction in lactobacilli protection against endogenous and exogenous pathogens. (Reviewer-John C. Jennings, MD).

© 2009, Oakstone Medical Publishing

Keywords: Douching

Print Tag: Refer to original journal article
Pain control improves outcomes after orthopedic surgery in older adults.

**Background:** Lower-extremity orthopedic surgeries are associated with severe pain. Suboptimal analgesic therapy for older adults after hip or knee arthroplasty can lead to increased length of stay, delayed ambulation, impaired functional recovery, and greater suffering.

**Objective:** To determine the effect a multi-component intervention on pain and function after orthopedic surgery.

**Design:** Controlled, prospective, propensity score-matched clinical trial conducted in an acute rehabilitation hospital in New York City.

**Participants:** 249 patients admitted to rehabilitations after hip fracture repair or hip or knee arthroplasty.

**Methods:** Pain assessment was done at rest and with exercise by staff using numeric rating scales (1 to 5). Physicians’ protocol for standing analgesia and analgesia before physical therapy treatment were implemented on the intervention unit. Control unit patients received usual care. Pain, analgesic prescribing, gait speed, transfer time, and percentage of physical therapy (PT) sessions were completed during admission. Pain and difficulty walking were measured at 6, 12, 18, and 24 weeks after discharge.

**Results:** Intervention patients were significantly more likely than control patients to report no or mild pain at rest and with PT. On average for the first 7 days of rehabilitation, intervention patients had faster 8-foot walk times on days 4 and 7, were more than likely to receive standing orders for analgesia, and had a significantly shorter length of stay compared to controls. At 6 months, intervention patients were less likely than controls to report moderate to severe pain with walking and that pain did not interfere with walking, and they were less likely to be taking analgesics.

**Conclusions:** The analgesic program improved postoperative pain, reduced chronic pain, and improved function.

**Reviewer's Comments:** This study is one of the first clinical trials to demonstrate a significant reduction in postoperative pain and improved lower-extremity mobility acutely and at 6 months after discharge. It is the largest study to show that better pain control results in better rehabilitation for older adults after surgery and a shorter length of stay. This study also is the first to demonstrate that reducing acute postoperative pain results in a lower prevalence of chronic pain and improved walking at 6 months after discharge  (Reviewer-Soryal A. Soryal, MD).
For children with anxiety disorders, CBT and sertraline therapy (compared to placebo) reduce the severity of anxiety; combination CBT and medication has the greatest response rate.

**Objective**: To compare the efficacy of cognitive behavioral therapy (CBT) and selective serotonin-reuptake inhibitors (SSRIs) individually and in combination in the treatment of anxiety disorders in children.

**Design/Participants**: This randomized controlled study involved children between the ages of 7 and 17 years (recruited from 2002 to 2007) who had a primary diagnosis of anxiety disorder (either generalized, separation, or social phobia) according to DSM-IV revised criteria using the Anxiety Disorders Interview Schedule. In order to be eligible, patients were required to have substantial impairment and an IQ ≥80. Patients were enrolled in 1 of 4 groups who were followed for 3 months. One group received CBT, consisting of 14 60-minute sessions based on the Coping Cat program for anxiety management. A second group received sertraline with doses escalating from 25 mg per day up to 200 mg. A third group received combination therapy with both CBT and medication, and a fourth group received placebo. Response to therapy was monitored by 2 tools: the Clinical Global Improvement Scale, which measured impairment, and the Pediatric Anxiety Rating Scale, which measured anxiety severity.

**Results**: 488 children (mean age, approximately 10.5 years) were enrolled. Nearly 75% of patients were <13 years of age. Among the children who had combination therapy (CBT and sertraline), 81% were very much or much improved by the rating scales. This compared to 60% for CBT alone and to 55% for sertraline alone. All therapies were significantly superior to placebo, which resulted in improvement in 24%. Suicidal and homicidal ideations were no more frequent in the sertraline group than in the placebo group. There were no suicide attempts during the study.

**Conclusions**: For children with anxiety disorders, both CBT and sertraline therapy, when compared to placebo, reduced the severity of anxiety. The combination of the 2 therapies (CBT and medication) had the greatest response rate.

**Reviewer's Comments**: 6% to 20% of children, using standardized diagnostic criteria, suffer from anxiety disorders, most commonly generalized anxiety disorder, separation anxiety disorder, and social phobia. In this head-to-head trial, when used as monotherapies, both CBT and medication for anxiety were equal in effectiveness. However, when used in combination, there was a significant boost, especially when compared to placebo. One drawback of the study was that it was limited to 3 months, so the long-term remission rates are unknown. The authors note that all 3 treatment possibilities can be considered, depending on parental preferences, cost, time burden, and CBT availability. The last (counselling availability) continues to be a wild card item for most practicing pediatricians who seek mental health services for their patients. (Reviewer-Mark F. Ditmar, MD).

© 2009, Oakstone Medical Publishing

Keywords: Management Options

Print Tag: Refer to original journal article
The increase in prevalence of reported autism may be partially due to earlier age of diagnosis.

**Background:** There has been an increase in the age-specific prevalence of reported autism cases in the last 2 decades, which has raised concerns that the incidence of autism is increasing. The increased prevalence of reported cases may be caused by many factors, such as heightened public awareness, changes in referral pattern, changes in diagnostic criteria, case identification, or reporting methods.

**Objective:** To examine the effect of changing age at diagnosis on the diagnosed prevalence of autism among different birth cohorts.

**Design:** Population-based cohort study.

**Participants:** All children born in Denmark between 1994 and 1999 (n=407,458).

**Methods:** Using the Danish Medical Birth Registry and the Danish National Psychiatric Register, the age-specific prevalence, hazard ratio, and relative risk (RR) of autistic spectrum disorder by age were established.

**Results:** The age at which autism spectrum disorder (ASD) was diagnosed decreased significantly for more recent birth cohorts. For example, those born in 1994-1995 were diagnosed at mean age of 5.9 years; those born in 1996-1997 were diagnosed at age 5.8 years; and those born in 1998-1999 were diagnosed at age 5.3 years. Compared to the 1996-1997 birth cohort, those born in 1994-1995 were 1.2 times more likely to be diagnosed with an ASD at age 3 years. Similarly, the RR comparing the 1998-1999 birth cohort with the 1994-1995 birth cohort at age 3 years was 1.69. However, comparing the rates of diagnosis at age 11 years, the RR was significantly lower than that seen at age 3 years for the 2 more recent cohorts (RR, 1.10 and 1.23, respectively). A similar pattern of results (earlier age of diagnosis in more recent cohorts) was also observed for the more restricted diagnosis of autistic disorder.

**Conclusions:** This study supports the argument that the apparent increase in autism in recent years is, in part, attributable to earlier diagnosis in more recent cohorts.

**Reviewer's Comments:** The strengths of this study include a population-based birth cohort approach, a large cohort size, and all diagnostic data having been obtained from a nationwide register based on standardized diagnostic reporting. The smaller RR between cohorts when followed up to age 11 years demonstrates that shifts in age at diagnosis have probably inflated the observed prevalence of autism in young children. The rigor of diagnosis and shifts in diagnostic practices were not controlled, however. The decrease in age at diagnosis may be due to changing diagnostic abilities of doctors or an earlier onset of autism symptoms. The most recent cohort appeared to have a 1.2-fold increase in ASD cases at age 11 years, possibly representing a true increase in incidence. (Reviewer-Christopher P. Lucas, MD, MPH).
Adolescents taking virginity pledges appear to be no different than those who do not with respect to sexual activity, but they may be less likely to use condoms or birth control.

**Background:** Because early sexual initiation is associated with risk taking, sexually transmitted diseases, and pregnancy, reducing early adolescent sexual initiation is an important health concern. Some believe that abstinence-only programs, which teach only the benefits from abstaining from sexual activity, are the most effective way to accomplish this goal. Unfortunately, a randomized, controlled experiment plus a literature review have failed to detect a benefit from abstinence-only education. Virginity pledges have also been offered as a way to reduce early adolescent sexual activity. Some regression models have shown that they have promise, although others claim these models are flawed.

**Objective:** To compare adolescent virginity pledgers with nonpledgers by using more robust statistical techniques such as matching.

**Methods:** Participants for this study were drawn from the National Longitudinal Study of Adolescent Health, a representative study of students in grades 7 through 12 interviewed in 1995, 1996, and 2001. To be eligible for this study, participants had to report not taking a virginity pledge or having had sex in 1995 and had to be at least 15 years of age. In the 1996 wave, those reporting taking a virginity pledge were matched with nonpledgers on religiosity and attitudes to sex and birth control. In the 2001 wave, data were collected on sexual behaviors and positive test results for sexually transmitted diseases.

**Results:** Overall, 289 pledge takers were matched to 645 nonpledgers. Five years after having reporting taking a virginity pledge, >80% of pledgers denied ever having taken a virginity pledge. There were no significant differences between pledgers and nonpledgers with respect to reported sexual activity, including anal and oral sex, nor were there any differences in rates of sexually transmitted diseases. Pledgers and nonpledgers also had no difference in age of first sexual activity. However, pledgers were significantly less likely to report using condoms and birth control in the past year.

**Conclusions:** Adolescents taking virginity pledges appear to be no different from those who do not with respect to sexual activity, but they may be less likely to use condoms or birth control. Taking a virginity pledge seemed to have no effect on a teenager's decision to having sex. Most adolescent who reported taking virginity pledges even denied having done so 5 years later. Those taking pledges, however, were significantly less likely to use condoms or birth control.

**Reviewer's Comments:** We should be careful to interpret this study correctly. It is a study of virginity pledges, and they are, at best, ineffective. The underlying religiosity and other aspects associated with such pledges are not the focus of this study. (Reviewer-Aaron E. Carroll, MD, MS).

© 2009, Oakstone Medical Publishing

Keywords: Virginity Pledges

Print Tag: Refer to original journal article