THE MEDICAL JOURNAL OF AHMED MAHER TEACHING HOSPITAL
VOL 1 NO 10 December, 2012
Owned and Published by the Medical Society of Ahmed Maher Teaching Hospital

Abstracts

This section presents a practical and timely updates from the world's leading medical journals. Each issue of this Journal will contain abstracts of articles in selected medical specialties. The following abstracts are prepared and compiled by Assem M. Naguib, M.D., Editor.

MEDICINE

Long-term Use of Aspirin and Age-Related Macular Degeneration

Barbara E. K. Klein, MD, MPH; Kerri P. Howard, MS; Ronald E. Gangnon, PhD; Jennifer O. Dreyer, BS; Kristine E. Lee, MS; Ronald Klein, MD, MPH *JAMA.* 2012;308(23):2469-2478.doi:10.1001/jama.2012.

ABSTRACT

Context Aspirin is widely used for relief of pain and for cardioprotective effects. Its use is of concern to ophthalmologists when ocular surgery is being considered and also in the presence of age-related macular degeneration (AMD). **Objective** To examine the association of regular aspirin use with incidence of AMD. **Design, Setting, and Participants** The Beaver Dam Eye Study, a longitudinal population-based study of age-related eye diseases conducted in Wisconsin. Examinations were performed every 5 years over a 20-year period (1988-1990 through 2008-2010). Study participants (N = 4926) were aged 43 to 86 years at the baseline examination. At subsequent examinations, participants were asked if they had regularly used aspirin at least twice a week for more than 3 months. **Main Outcome Measure** Incidence of early AMD, late AMD, and 2 subtypes of late AMD (neovascular AMD and pure geographic atrophy), assessed in retinal photographs according to the Wisconsin Age-Related Maculopathy Grading System. **Results** The mean duration of follow-up was 14.8 years. There were 512 incident cases of early AMD (of 6243 person-visits at risk) and 117 incident cases of late AMD (of 8621 person-visits at risk) over the course of the study. Regular aspirin use 10 years prior to retinal examination was associated with late AMD (hazard ratio [HR], 1.63 [95% CI, 1.01-2.63]; *P* = .05), with estimated incidence of 1.76% (95% CI, 1.17%-2.64%) in regular users and 1.03% (95% CI, 0.70%-1.51%) in nonusers. For subtypes of late AMD, regular aspirin use 10 years prior to retinal examination was significantly associated with neovascular AMD (HR, 2.20 [95% CI, 1.20-4.15]; *P* = .01) but not pure geographic atrophy (HR, 0.66 [95% CI, 0.25-1.95]; *P* = .45). Aspirin use 5 years (HR, 0.86 [95% CI, 0.71-1.05]; *P* = .13) or 10 years (HR, 0.86 [95% CI, 0.65-1.13]; *P* = .28) prior to retinal examination was not associated with incident early AMD. **Conclusions** Among an adult cohort, aspirin use 5 years prior to observed incidence was not associated with incident early or late AMD. However, regular aspirin use 10 years prior was associated with a small but statistically significant increase in the risk of incident late and neovascular AMD.

Association Between Sustained Virological Response and All-Cause Mortality Among Patients With Chronic Hepatitis C and Advanced Hepatic Fibrosis

Adriaan J. van der Meer, MD; Bart J. Veldt, MD, PhD; Jordan J. Feld, MD, PhD; Heiner Wedemeyer, MD, PhD; Jean-François Dufour, MD, PhD; Frank Lammert, MD, PhD; Andres Duarte-Rojo, MD; E. Jenny Heathcote, MD, PhD; Michael P. Manns, MD, PhD; Lorenz Kuske; Stefan Zeuzem, MD, PhD; W. Peter Hofmann, MD, PhD; Robert J. de Knegt, MD, PhD; Bettina E. Hansen, PhD; Harry L. A. Janssen, MD, PhD *JAMA.* 2012;308(24):2584-2593. doi:10.1001/jama.2012.144878.

ABSTRACT

Context Chronic hepatitis C virus (HCV) infection outcomes include liver failure, hepatocellular carcinoma (HCC), and liver-related death. **Objective** To assess the association between sustained virological response (SVR) and all-cause mortality in patients with chronic HCV infection and advanced hepatic fibrosis. **Design, Setting, and Patients** An international, multicenter, long-term follow-up study from 5 large tertiary care hospitals in Europe and Canada of 530 patients with chronic HCV infection who started an interferon-based treatment regimen between 1990 and 2003, following histological proof of advanced hepatic fibrosis or cirrhosis (Ishak score 4-6). Complete follow-up ranged between January 2010 and October 2011. **Main Outcome Measures** All-cause mortality. Secondary outcomes were liver failure, HCC, and liver-related mortality or liver transplantation. **Results** The 530 study patients were followed up for a median (interquartile range [IQR]) of 8.4 (6.4-11.4) years. The baseline median (IQR) age was 48 (42-56) years and 369 patients (70%) were men. The Ishak fibrosis score was 4 in 143 patients (27%), 5 in 101 patients (19%), and 6 in 286 patients (54%). There were 192 patients (36%) who achieved SVR; 13 patients with SVR and 100 without SVR died (10-year cumulative all-cause mortality rate, 8.9% [95% CI, 3.3%-14.5%] with SVR and 26.0% [95% CI, 20.2%-28.4%] without SVR; *P* < .001). In time-dependent multivariate Cox regression analysis, SVR was associated with reduced risk of all-cause mortality (hazard

ratio [HR], 0.26; 95% CI, 0.14-0.49; $P < .001$) and reduced risk of liver-related mortality or transplantation (HR, 0.06; 95% CI, 0.02-0.19; $P < .001$), the latter occurring in 3 patients with SVR and 103 without SVR. The 10-year cumulative incidence rate of liver-related mortality or transplantation was 1.9% (95% CI, 0.0%-4.1%) with SVR and 27.4% (95% CI, 22.0%-32.8%) without SVR ($P < .001$). There were 7 patients with SVR and 76 without SVR who developed HCC (10-year cumulative incidence rate, 5.1%; 95% CI, 1.3%-8.9%; vs 21.8%; 95% CI, 16.6%-27.0%; $P < .001$), and 4 patients with SVR and 111 without SVR experienced liver failure (10-year cumulative incidence rate, 2.1%; 95% CI, 0.0%-4.5%; vs 29.9%; 95% CI, 24.3%-35.5%; $P < .001$). **Conclusion** Among patients with chronic HCV infection and advanced hepatic fibrosis, sustained virological response to interferon-based treatment was associated with lower all-cause mortality.

Association of an Intensive Lifestyle Intervention With Remission of Type 2 Diabetes

Edward W. Gregg, PhD; Haiying Chen, PhD; Lynne E. Wagenknecht, DrPH; Jeanne M. Clark, MD, MPH; Linda M. Delahanty, MS, RD; John Bantle, MD; Henry J. Pownall, PhD; Karen C. Johnson, MD, MPH; Monika M. Safford, MD; Abbas E. Kitabchi, MD, PhD; F. Xavier Pi-Sunyer, MD; Rena R. Wing, PhD; Alain G. Bertoni, MD, MPH; for the Look AHEAD Research Group *JAMA.* 2012;308(23):2489-2496. doi:10.1001/jama.2012.67929.

ABSTRACT

Context The frequency of remission of type 2 diabetes achievable with lifestyle intervention is unclear. **Objective** To examine the association of a long-term intensive weight-loss intervention with the frequency of remission from type 2 diabetes to prediabetes or normoglycemia. **Design, Setting, and Participants** Ancillary observational analysis of a 4-year randomized controlled trial (baseline visit, August 2001–April 2004; last follow-up, April 2008) comparing an intensive lifestyle intervention (ILI) with a diabetes support and education control condition (DSE) among 4503 US adults with body mass index of 25 or higher and type2diabetes. **Interventions** Participants were randomly assigned to receive the ILI, which included weekly group and individual counseling in the first 6 months followed by 3 sessions per month for the second 6 months and twice-monthly contact and regular refresher group series and campaigns in years 2 to 4 (n=2241) or the DSE, which was an offer of 3 group sessions per year on diet, physical activity, and social support (n=2262).**Main Outcome Measures** Partial or complete remission of diabetes, defined as transition from meeting diabetes criteria to a prediabetes or nondiabetic level of glycemia (fasting plasma glucose <126 mg/dL and hemoglobin A_{1c} <6.5% with no antihyperglycemic medication) . **Results** Intensive lifestyle intervention participants lost significantly more weight than DSE participants at year 1 (net difference, −7.9%; 95% CI, −8.3% to −7.6%) and at year 4 (−3.9%; 95% CI, −4.4% to −3.5%) and had greater fitness increases at year 1 (net difference, 15.4%; 95% CI, 13.7%-17.0%) and at year 4 (6.4%; 95% CI, 4.7%-8.1%) ($P < .001$ for each). The ILI group was significantly more likely to experience any remission (partial or complete), with prevalences of 11.5% (95% CI, 10.1%-12.8%) during the first year and 7.3% (95% CI, 6.2%-8.4%) at year 4, compared with 2.0% for the DSE group at both time points (95% CIs, 1.4%-2.6% at year 1 and 1.5%-2.7% at year 4) ($P < .001$ for each). Among ILI participants, 9.2% (95% CI, 7.9%-10.4%), 6.4% (95% CI, 5.3%-7.4%), and 3.5% (95% CI, 2.7%-4.3%) had continuous, sustained remission for at least 2, at least 3, and 4 years, respectively, compared with less than 2% of DSE participants (1.7% [95% CI, 1.2%-2.3%] for at least 2 years; 1.3% [95% CI, 0.8%-1.7%] for at least 3 years; and 0.5% [95% CI, 0.2%-0.8%] for 4 years). **Conclusions** In these exploratory analyses of overweight adults, an intensive lifestyle intervention was associated with a greater likelihood of partial remission of type 2 diabetes compared with diabetes support and education. However, the absolute remission rates were modest.

GYNAECOLOGY

Effect of Maintenance Tocolysis with Nifedipine in Threatened Preterm Labor on Perinatal Outcomes A Randomized Controlled Trial

Carolien Roos, MD; Marc E. A. Spaanderman, MD, PhD; Ewoud Schuit, MSc; Kitty W. M. Bloemenkamp, MD, PhD; Antoinette C. Bolte, MD, PhD; Jérôme Cornette, MD; Johannes J. J. Duvekot, MD, PhD; Jim van Eyck, MD, PhD; Maureen T. M. Franssen, MD, PhD; Christianne J. de Groot, MD, PhD; Joke H. Kok, MD, PhD; Anneke Kwee, MD, PhD; Ashley Merién, MD; Bas Nij Bijvank, MD; Brent C. Opmeer, PhD; Martijn A. Oudijk, MD, PhD; Mariëlle G. van Pampus, MD, PhD; Dimitri N. M. Papatsonis, MD, PhD; Martina M. Porath, MD, PhD; Hubertina C. J. Scheepers, MD, PhD; Sicco A. Scherjon, MD, PhD; Krystyna M. Sollie, MD, PhD; Sylvia M. C. Vijgen, MSc; Christine Willekes, MD, PhD; Ben Willem J. Mol, MD, PhD; Joris A. M. van der Post, MD, PhD; Fred K. Lotgering, MD, PhD; for the APOSTEL-II Study Group *JAMA.* 2013;309(1):41-47. doi:10.1001/jama.2012.153817.

ABSTRACT

Importance In threatened preterm labor, maintenance tocolysis with nifedipine, after an initial course of tocolysis and corticosteroids for 48 hours, may improve perinatal outcome. **Objective** To determine whether maintenance tocolysis with nifedipine will reduce adverse perinatal outcomes due to premature birth. **Design, Setting, and participants** APOSTEL-II (Assessment of Perinatal Outcome with Sustained Tocolysis in Early Labor) is a double-blind, placebo-controlled trial performed in 11 perinatal units including all tertiary centers in the Netherlands. From June 2008 to February 2010, women with threatened preterm labor between 26 weeks (plus 0 days) and 32 weeks (plus 2 days) gestation, who had not delivered after 48 hours of tocolysis and a completed course of corticosteroids, were enrolled. Surviving infants were followed up until 6 months after birth (ended August 2010). **Intervention** Randomization

assigned 406 women to maintenance tocolysis with nifedipine orally (80 mg/d; n = 201) or placebo (n = 205) for 12 days. Assigned treatment was masked from investigators, participants, clinicians, and research nurses. **Main Outcome Measures** Primary outcome was a composite of adverse perinatal outcomes (perinatal death, chronic lung disease, neonatal sepsis, intraventricular hemorrhage >grade 2, periventricular leukomalacia >grade 1, or necrotizing enterocolitis). Analyses were completed on an intention-to-treat basis. **Results** Mean (SD) gestational age at randomization was 29.2 (1.7) weeks for both groups. Adverse perinatal outcome was not significantly different between groups: 11.9% (24/201; 95% CI, 7.5%-16.4%) for nifedipine vs 13.7% (28/205; 95% CI, 9.0%-18.4%) for placebo (relative risk, 0.87; 95% CI, 0.53-1.45). **Conclusions and Relevance** In patients with threatened preterm labor, nifedipine-maintained tocolysis did not result in a statistically significant reduction in adverse perinatal outcomes when compared with placebo. Although the lower than anticipated rate of adverse perinatal outcomes in the control group indicates that a benefit of nifedipine cannot completely be excluded, its use for maintenance tocolysis does not appear beneficial at this time.

***Neisseria gonorrhoeae* Treatment Failure and Susceptibility to Cefixime in Toronto, Canada**

Vanessa G. Allen, MD, MPH; Leo Mitterni; Christine Seah, MLT; Anuradha Rebbapragada, PhD; Irene E. Martin, BSc; Colin Lee, MD; Heather Siebert, MLT; Lynn Towns, MLT; Roberto G. Melano, PhD; Donald E. Low, MD *JAMA.* 2013;309(2):163-170.doi:10.1001/jama.2012. 176575.

ABSTRACT

Importance Although cephalosporins are the cornerstone of treatment of *Neisseria gonorrhoeae* infections, cefixime is the only oral antimicrobial option. Increased minimum inhibitory concentrations (MICs) to cefixime have been identified worldwide and have been associated with reports of clinical failure. **Objective** To assess the risk of clinical treatment failure of *N gonorrhoeae* infections associated with the use of cefixime. **Design, Setting, and Population** A retrospective cohort study of culture-positive *N gonorrhoeae* infections at a single sexual health clinic in Toronto, Canada, that routinely performs test of cure. The cohort comprised *N gonorrhoeae* culture-positive individuals identified between May 1, 2010, and April 30, 2011, treated with cefixime as recommended by Public Health Agency of Canada guidelines. **Main Outcome Measures** Cefixime treatment failure, defined as the repeat isolation of *N gonorrhoeae* at the test-of-cure visit identical to the pretreatment isolate by molecular typing and explicit denial of reexposure. **Results** There were 291 *N gonorrhoeae* culture-positive individuals identified. Of 133 who returned for test of cure, 13 were culture positive; 9 patients were determined to have experienced cefixime treatment failure, involving urethral (n = 4), pharyngeal (n = 2), and rectal (n = 3) sites. The overall rate of clinical treatment failure among those who had a test of cure was 6.77% (95% CI, 3.14%-12.45%; 9/133). The rate of clinical failure associated with a cefixime MIC of 0.12 μg/mL or greater was 25.0% (95% CI, 10.69%-44.87%; 7/28) compared with 1.90% (95% CI, 0.23%-6.71%; 2/105) of infections with cefixime MICs less than 0.12 μg/mL, with a relative risk of 13.13 (95% CI, 2.88-59.72; $P < .001$). **Conclusion and Relevance** The rate of clinical failure following treatment of *N gonorrhoeae* infections with cefixime was relatively high at a Toronto clinic and was associated with elevated MICs.

Effect of Intravenous Paracetamol on Postoperative

SURGERY

Morphine Requirements in Neonates and Infants Undergoing Major Non cardiac Surgery A Randomized Controlled Trial

Ilse Ceelie, MD, PhD; Saskia N. de Wildt, MD, PhD; Monique van Dijk, MSc, PhD; Margreeth M. J. van den Berg, MD; Gerbrich E. van den Bosch, MD; Hugo J. Duivenvoorden, PhD; Tom G. de Leeuw, MD; Ron Mathôt, PharmD, PhD; Catherijne A. J. Knibbe, PharmD, PhD; Dick Tibboel, MD, PhD *JAMA.* 2013;309(2):149-154. doi:10.1001/jama.2012.148050.

ABSTRACT

Importance Continuous morphine infusion as standard postoperative analgesic therapy in young infants is associated with unwanted adverse effects such as respiratory depression. **Objective** To determine whether intravenous paracetamol (acetaminophen) would significantly (>30%) reduce morphine requirements in neonates and infants after major surgery. **Design, Setting, and Patients** Single-center, randomized, double-blind study conducted in a level 3 pediatric intensive care unit in Rotterdam, the Netherlands. Patients were 71 neonates or infants younger than 1 year undergoing major thoracic (noncardiac) or abdominal surgery between March 2008 and July 2010, with follow-up of 48 hours. **Interventions** All patients received a loading dose of morphine 30 minutes before the end of surgery, followed by continuous morphine or intermittent intravenous paracetamol up to 48 hours postsurgery. Infants in both study groups received morphine (boluses and/or continuous infusion) as rescue medication on the guidance of the validated pain assessment instruments. **Main Outcome Measures** Primary outcome was cumulative morphine dose (study and rescue dose). Secondary outcomes were pain scores and morphine-related adverse effects. **Results** The cumulative median morphine dose in the first 48 hours postoperatively was 121 (interquartile range, 99-264) μg/kg in the paracetamol group (n = 33) and 357 (interquartile range, 220-605) μg/kg in the morphine group (n = 38), $P < .001$, with a between-group difference that was 66% (95% CI, 34%-109%) lower in the paracetamol group. Pain scores and adverse effects were not significantly different between groups. **Conclusion and Relevance** Among infants undergoing major surgery, postoperative use of intermittent intravenous

paracetamol compared with continuous morphine resulted in a lower cumulative morphine dose over 48 hours.

Effect of Citicoline on Functional and Cognitive Status Among Patients With Traumatic Brain Injury Citicoline Brain Injury Treatment Trial (COBRIT)

Ross D. Zafonte, DO; Emilia Bagiella, PhD; Beth M. Ansel, PhD; Thomas A. Novack, PhD; William T. Friedewald, MD; Dale C. Hesdorffer, PhD; Shelly D. Timmons, MD; Jack Jallo, MD, PhD; Howard Eisenberg, MD; Tessa Hart, PhD; Joseph H. Ricker, PhD; Ramon Diaz-Arrastia, MD, PhD; Randall E. Merchant, PhD; Nancy R. Temkin, PhD; Sherry Melton, MD; Sureyya S. Dikmen, PhD *JAMA.* 2012;308(19):1993-2000.doi:10.1001 /jama.2012. 13256.

ABSTRACT

Context Traumatic brain injury (TBI) is a serious public health problem in the United States, yet no treatment is currently available to improve outcome after TBI. Approved for use in TBI in 59 countries, citicoline is an endogenous substance offering potential neuroprotective properties as well as facilitated neurorepair post injury. **Objective** To determine the ability of citicoline to positively affect functional and cognitive status in persons with complicated mild, moderate, and severe TBI. **Design, Setting, and Patients** The Citicoline Brain Injury Treatment Trial (COBRIT), a phase 3, double-blind randomized clinical trial conducted between July 20, 2007, and February 4, 2011, among 1213 patients at 8 US level 1 trauma centers to investigate effects of citicoline vs placebo in patients with TBI classified as complicated mild, moderate, or severe. **Intervention** Ninety-day regimen of daily enteral or oral citicoline (2000 mg) or placebo. **Main Outcome Measures** Functional and cognitive status, assessed at 90 days using the TBI-Clinical Trials Network Core Battery. A global statistical test was used to analyze the 9 scales of the core battery. Secondary outcomes were functional and cognitive improvement, assessed at 30, 90, and 180 days, and examination of the long-term maintenance of treatment effects. **Results** Rates of favorable improvement for the Glasgow Outcome Scale–Extended were 35.4% in the citicoline group and 35.6% in the placebo group. For all other scales the rate of improvement ranged from 37.3% to 86.5% in the citicoline group and from 42.7% to 84.0% in the placebo group. The citicoline and placebo groups did not differ significantly at the 90-day evaluation (global odds ratio [OR], 0.98 [95% CI, 0.83-1.15]); in addition, there was no significant treatment effect in the 2 severity subgroups (global OR, 1.14 [95% CI, 0.88-1.49] and 0.89 [95% CI, 0.72-1.49] for moderate/severe and complicated mild TBI, respectively). At the 180-day evaluation, the citicoline and placebo groups did not differ significantly with respect to the primary outcome (global OR, 0.87 [95% CI, 0.72-1.04]). **Conclusion** Among patients with traumatic brain injury, the use of citicoline compared with placebo for 90 days did not result in improvement in functional and cognitive status.

Fish Oil and Postoperative Atrial Fibrillation the Omega-3 Fatty Acids for Prevention of Post-operative Atrial Fibrillation (OPERA) Randomized Trial

Dariush Mozaffarian, MD, DrPH; Roberto Marchioli, MD; Alejandro Macchia, MD; Maria G. Silletta, MS; Paolo Ferrazzi, MD; Timothy J. Gardner, MD; Roberto Latini, MD; Peter Libby, MD; Federico Lombardi, MD; Patrick T. O'Gara, MD; Richard L. Page, MD; Luigi Tavazzi, MD; Gianni Tognoni, MD; for the OPERA Investigators *JAMA.* 2012;308(19):2001-2011. doi:10.1001/jama.2012.28733.

ABSTRACT

Context Postoperative atrial fibrillation or flutter (AF) is one of the most common complications of cardiac surgery and significantly increases morbidity and health care utilization. A few small trials have evaluated whether long-chain n-3-polyunsaturated fatty acids (PUFAs) reduce postoperative AF, with mixed results. **Objective** To determine whether perioperative n-3-PUFA supplementation reduces postoperative AF. **Design, Setting, and Patients** The Omega-3 Fatty Acids for Prevention of Post-operative Atrial Fibrillation (OPERA) double-blind, placebo-controlled, randomized clinical trial. A total of 1516 patients scheduled for cardiac surgery in 28 centers in the United States, Italy, and Argentina were enrolled between August 2010 and June 2012. Inclusion criteria were broad; the main exclusions were regular use of fish oil or absence of sinus rhythm at enrollment. **Intervention** Patients were randomized to receive fish oil (1-g capsules containing ≥840 mg n-3-PUFAs as ethyl esters) or placebo, with preoperative loading of 10 g over 3 to 5 days (or 8 g over 2 days) followed postoperatively by 2 g/d until hospital discharge or postoperative day 10, whichever came first. **Main Outcome Measure** Occurrence of postoperative AF lasting longer than 30 seconds. Secondary end points were postoperative AF lasting longer than 1 hour, resulting in symptoms, or treated with cardioversion; postoperative AF excluding atrial flutter; time to first postoperative AF; number of AF episodes per patient; hospital utilization; and major adverse cardiovascular events, 30-day mortality, bleeding, and other adverse events. **Results** At enrollment, mean age was 64 (SD, 13) years; 72.2% of patients were men, and 51.8% had planned valvular surgery. The primary end point occurred in 233 (30.7%) patients assigned to placebo and 227 (30.0%) assigned to n-3-PUFAs (odds ratio, 0.96 [95% CI, 0.77-1.20]; $P = .74$). None of the secondary end points were significantly different between the placebo and fish oil groups, including postoperative AF that was sustained, symptomatic, or treated (231 [30.5%] vs 224 [29.6%], $P = .70$) or number of postoperative AF episodes per patient (1 episode: 156 [20.6%] vs 157 [20.7%]; 2 episodes: 59 [7.8%] vs 49 [6.5%]; ≥3 episodes: 18 [2.4%] vs 21 [2.8%]) ($P = .73$). Supplementation with n-3-PUFAs was generally well tolerated, with no evidence for increased risk of bleeding or serious adverse events. **Conclusion** In this large multinational trial among patients undergoing cardiac surgery, perioperative

supplementation with n-3-PUFAs, compared with placebo, did not reduce the risk of postoperative AF.

ONCOLOGY

Association Between World Trade Center Exposure and Excess Cancer Risk

Jiehui Li, MBBS, MSc; James E. Cone, MD, MPH; Amy R. Kahn, MS; Robert M. Brackbill, PhD, MPH; Mark R. Farfel, ScD; Carolyn M. Greene, MD; James L. Hadler, MD, MPH; Leslie T. Stayner, PhD; Steven D. Stellman, PhD, MPH *JAMA.* 2012;308 (23): 2479-2488. doi:10.1001/ jama.2012.110980.

ABSTRACT

Context The terrorist attacks of September 11, 2001, resulted in the release of known and suspected carcinogens into the environment. There is public concern that exposures may have resulted in increased cancers. **Objective** To evaluate cancer incidence among persons enrolled in the World Trade Center Health Registry.**Design, Setting, and Participants** Observational study of 55 778 New York State residents enrolled in the World Trade Center Health Registry in 2003-2004, including rescue/recovery workers (n = 21 850) and those not involved in rescue/recovery (n = 33 928), who were followed up from enrollment through December 31, 2008. Within-cohort comparisons using Cox proportional hazards models assessed the relationship between intensity of World Trade Center exposure and selected cancers. **Main Outcome Measures** Cases were identified through linkage with 11 state cancer registries. Standardized incidence ratios (SIRs) adjusted for age, race/ethnicity, and sex were computed with 2003-2008 New York State rates as the reference, focusing on cancers diagnosed in 2007-2008 as being most likely to be related to exposure during September 11 and its aftermath. The total and site-specific incidence rate differences (RDs) per 100 000 person-years between the study population and the New York State population in 2007-2008 also were calculated. **Results** There were 1187 incident cancers diagnosed, with an accumulated 253 269 person-years (439 cancers among rescue/ recovery workers and 748 among those not involved in rescue/recovery). The SIR for all cancer sites combined in 2007-2008 was not significantly elevated (SIR, 1.14 [95% CI, 0.99 to 1.30]; RD, 67 [95% CI, −6 to 126] per 100 000 person-years among rescue/recovery workers vs SIR, 0.92 [95% CI, 0.83 to 1.03]; RD, −45 [95% CI, −106 to 15] per 100 000 person-years among those not involved in rescue/recovery). Among rescue/recovery workers, the SIRs had significantly increased by 2007-2008 for 3 cancer sites and were 1.43 (95% CI, 1.11 to 1.82) for prostate cancer (n = 67; RD, 61 [95% CI, 20 to 91] per 100 000 person-years), 2.02 (95% CI, 1.07 to 3.45) for thyroid cancer (n = 13; RD, 16 [95% CI, 2 to 23] per 100 000 person-years), and 2.85 (95% CI, 1.15 to 5.88) for multiple myeloma (n = 7; RD, 11 [95% CI, 2 to 14] per 100 000 person-years). No increased incidence was observed in 2007-2008 among those not involved in rescue/recovery. Using within-cohort comparisons, the intensity of World Trade Center exposure was not significantly associated with cancer of the lung, prostate, thyroid, non-Hodgkin lymphoma, or hematological cancer in either group. **Conclusions** Among persons enrolled in the World Trade Center Health Registry, there was an excess risk for prostate cancer, thyroid cancer, and myeloma in 2007-2008 compared with that for New York State residents; however, these findings were based on a small number of events and multiple comparisons. No significant associations were observed with intensity of World Trade Center exposures. Longer follow-up for typically long-latency cancers and attention to specific cancer sites are needed.

ORTHOPEDICS

Effect of Vitamin D Supplementation on Progression of Knee Pain and Cartilage Volume Loss in Patients With Symptomatic Osteoarthritis A Randomized Controlled Trial

Timothy McAlindon, DM, MPH; Michael LaValley, PhD; Erica Schneider, PhD; Melynn Nuite, RN, BS; Ji Yeon Lee, MD, MSc; Lori Lyn Price, MAS; Grace Lo, MD, MSc; Bess Dawson-Hughes, MD *JAMA.* 2013;309(2):155-162. doi:10.1001/jama.2012.164487.

Importance Knee osteoarthritis (OA), a disorder of cartilage and periarticular bone, is a public health problem without effective medical treatments. Some studies have suggested that vitamin D may protect against structural progression. **Objective** To determine whether vitamin D supplementation reduces symptom and structural progression of knee OA. **Design, Setting, and Patients** A 2-year randomized, placebo-controlled, double-blind, clinical trial involving 146 participants with symptomatic knee OA (mean age, 62.4 years [SD, 8.5]; 57 women [61%], 115 white race [79%]). Patients were enrolled at Tufts Medical Center in Boston between March 2006 and June 2009. **Intervention** Participants were randomized to receive either placebo or oral cholecalciferol, 2000 IU/d, with dose escalation to elevate serum levels to more than 36 ng/mL **Main Outcome Measures** Primary outcomes were knee pain severity (Western Ontario and McMaster Universities [WOMAC] pain scale, 0-20: 0, no pain; 20, extreme pain), and cartilage volume loss measured by magnetic resonance imaging. Secondary end points included physical function, knee function (WOMAC function scale, 0-68: 0, no difficulty; 68, extreme difficulty), cartilage thickness, bone marrow lesions, and radiographic joint space width .**Results** Eighty-five percent of the participants completed the study. Serum 25-hydroxyvitamin D levels increased by a mean 16.1 ng/mL (95% CI, 13.7 to 18.6) in the treatment group and by a mean 2.1 mg/mL (95% CI, 0.5 to 3.7) ($P < .001$) in the placebo group. Baseline knee pain was slightly worse in the treatment group (mean, 6.9; 95% CI, 6.0 to 7.7) than

in the placebo group (mean, 5.8; 95% CI, 5.0 to 6.6) (*P* = .08). Baseline knee function was significantly worse in the treatment group (mean, 22.7; 95% CI, 19.8 to 25.6) than in the placebo group (mean, 18.5; 95% CI, 15.8 to 21.2) (*P* = .04). Knee pain decreased in both groups by a mean −2.31 (95% CI, −3.24 to −1.38) in the treatment group and −1.46 (95% CI, −2.33 to −0.60) in the placebo group, with no significant differences at any time. The percentage of cartilage volume decreased by the same extent in both groups (mean, −4.30; 95% CI, −5.48 to −3.12 vs mean, −4.25; 95% CI, −6.12 to −2.39) (*P* = .96). There were no differences in any of the secondary clinical end points. **Conclusion and Relevance** Vitamin D supplementation for 2 years at a dose sufficient to elevate 25-hydroxyvitamin D plasma levels to higher than 36 ng/mL, when compared with placebo, did not reduce knee pain or cartilage volume loss in patients with symptomatic knee OA.