

REHAB IN REVIEW

WWW.REHABINREVIEW.COM

TM

Volume 26 Number 11

Published by Physicians
In Physical Medicine and Rehabilitation

November 5, 2019

ELECTRONIC CIGARETTE USE IN THE UNITED STATES

The use of electronic cigarettes among US adults declined between 2014 and 2017. However, the Center For Disease Control and Prevention (CDC) reported an increase in use among US middle school and high school students between 2017 and 2018. This study updates these data for adults.

The National Health Interview Survey is conducted by the National Center For Health Statistics to provide a nationally representative sampling of the noninstitutionalized civilian US population. Subjects were queried about electronic cigarette use including frequency over time, covering 2014 through 2018.

Data were obtained from 153,177 adults. Of these, e-cigarette use decreased from 3.7% in 2014 to 2.8% in 2017, and then increased to 3.2% in 2018. The increase in prevalence from 2017-2018 was highest among adults 18-24 years of age ($p=0.02$). An increased prevalence was also observed among men ($p=0.002$), non-hispanic asians ($p=0.03$), those from family income at least four times the federal poverty level ($p=0.001$), and those who formally smoked tobacco ($p=0.01$).

Conclusion: This nationally representative sample of adult Americans found that, while declining between 2014 and 2017, electronic cigarette use increased between 2017 and 2018.

Bao, W et al. Electronic Cigarette Use Among Young, Middle-Aged, and Older Adults in the United States In 2017 and 2018. *JAMA Intern Med.* 2019:E1-E2.

THURSDAY NIGHT FOOTBALL IMPACT ON NFL INJURIES

Since the introduction of Thursday Night Football in the National Football League (NFL), players have publicly opposed the games, citing a lack of proper recovery time from the previous Sunday. As prior studies

have shown connections between lack of rest and injury, this study reviewed the effect of the shortened recovery time on injuries sustained during Thursday night games.

Using data published weekly by the NFL between 2012 and 2017, data concerning injuries were collected for every player on all 32 NFL teams. The rate of all-cause injuries was compared between Thursday night games and those played on weekends.

Data were available for 69 Thursday NFL games involving 8,480 players. The all-cause injury rate for weekend games was 7,598 per 1,000 athletic exposures, while that for Thursday night games was 6,072 per 1,000 athletic exposure. The calculated relative risk of injury during Thursday night games compared to weekend games was 0.97.

Collusion: This study found that injuries during Thursday night football games in the NFL are slightly less than those sustained during play on weekends, with an absolute risk reduction of three percent.

Baker, H., et al. Thursday Night Football's Impact on All Cause Injuries in NFL Players During 2012 to 2017. *Phys Sportsmed.* 2019; 47 (3): 350-352.

SOFT DRINK CONSUMPTION AND MORTALITY

While the regular consumption of sugar sweetened soft drinks is thought to add to the obesity epidemic, the health implications of artificially sweetened soft drinks are unknown. This study investigated the association between soft drink consumption, both sugared and artificially sweetened, with mortality.

This multicenter cohort study included 451,743 participants, recruited between 1992 and 2000 from the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort, collected in ten European countries. Data were excluded for those with a baseline report of cancer, heart disease or

diabetes. Dietary intake was assessed during the baseline enrollment visit. From these data, total soft drink consumption was determined and subdivided into sugar-sweetened and artificially sweetened soft drink consumption. In addition, data were obtained concerning vital status, as well as the cause and date of death. Patients from groups with baseline data taken from 1992 to 2000 were followed up in the period December of 2009 to 2013.

Compared with those who had low consumption (LC) of soft drinks (less than one glass per month) those with high consumption (HC) of soft drinks (two or more glasses per day) had a higher all-cause mortality ($p<0.001$). This was true for both sugar sweetened soft drinks (HR 1.11) and artificially sweetened soft drinks (HR 1.27). For specific diseases, elevated mortality was found for circulatory diseases with a high consumption of artificially sweetened soft drinks ($p<0.001$), and for digestive diseases with sugar-sweetened soft drinks ($p<0.001$).

Conclusion: This European study found that soft drinks, both sugar sweetened and artificially sweetened, are positively associated with increased mortality.

Mullee, A., et al. Association between Soft Drink Consumption and Mortality in 10 European Countries. *JAMA Intern Med.* 2019, Sept 3; doi: 10.1001/jamainternmed. 2019.2478.

UPPER EXTREMITY PERFORMANCE OVER THE FIRST 12 WEEKS AFTER STROKE

After a stroke, 80% of individuals experience some degree of upper extremity (UE) paresis. Research into the recovery of upper limb function has most often used outcomes measured in the laboratory rather than in a free-living environment. This study examined the recovery trajectory of sensor measured UE performance in the first 12 weeks after an ischemic stroke.

Editor-in-Chief

David T. Burke, M.D., M.A.
Emory University, Atlanta, GA

Executive Editor

Randolph L. Roig, M.D.
Emory University, Atlanta, GA

Copy Editor

Roberta Alysoun Bell, Ph.D.
Emory University, Atlanta, GA

Assistant Copy Editor

Tracie McCargo, EMBA, ALM
Harvard Extension Sch., Cambridge, MA

Contributing Editors

*Benjamin Sirutis, M.D.
Dhruvil Brahmbhatt, M.D.
Joshua Elkin, M.D.
Bassem Hanalla, M.D.
Giorgio A. Negron, M.D.
Kelly Purcell, M.D.
Parth Vyasa, M.D.
Emory University, Atlanta, GA

*Michael Harbus, M.D.
Sofia Barchuk, M.D.
Icahn SOM at Mt. Sinai, N.Y., NY

*Allison Sidor Alessandra, D.O.
*Gavin Nixon, D.O.
LSUHSC, New Orleans, LA

*Lite Wu, D.O.
Parini Patel, D.O.
Rebecca Tamarkin, D.O.
Nassau UMC, East Meadow, NY

*Alexander Sheng, M.D.
Stephen Leb, M.D.
Ryan Nussbaum, D.O.
Punit Patel, D.O.
N.W.U. /R.I.C., Chicago, IL

*Rosa Pasculli, M.D.
*Perry Zelinger, M.D.
Haruki Ishii, M.D.
Gabe Sanchez, M.D.
NYU/Rusk Inst., New York, NY

*Kevin Machino, D.O.
Francis DeAsis, M.D.
Leigh Graziano, M.D.
Khyrie Jones, M.D.
Karan Thakkar, M.D.
Scott Vicenzi, M.D.
Schwab Rehab Hospital, Chicago, IL

*Roshan Chhatlani, D.O.
Sonny Ahluwalia, D.O.
Evan Chernoff, D.O.
Annette Lukose, M.D.
Brandon Maisel, D.O.
Sunny Downstate, Brooklyn, NY

*Ryan Hafner, M.D.
Steven Chow, M.D.
Lorena Walker, M.D.
Temple University, Philadelphia, PA

*Shane Davis, M.D.
Fady Boutros M.D.

Shane Davis, M.D.

Upper extremity performance in daily life was quantified using four accelerometer-derived variables: hours of paretic UE use, use ratio, magnitude ratio, and bilateral magnitude. Participants wore the accelerometers for 24 hours every two weeks, with the sensor data used to quantify the contribution of each limb to an activity. In addition, the patients were assessed with the Action Research Arm Test (ARAT), measures of UE strength and the Montréal Cognitive Assessment.

Subjects were 29, first-ever stroke survivors with residual UE paresis, enrolled within two weeks of the stroke. Significant improvement was noted across all four accelerometer variables over the first 12 weeks post-stroke. The patients' subjective belief, confidence and motivation did not significantly modify UE performance.

Conclusion: This study of patients with acute ischemic stroke found that performance of the upper extremity in daily life improves during the first 12 weeks.

Waddell, K., et al. Upper Limb Performance in Daily Life Improves over the First 12 Weeks Post-Stroke. **Neurorehab Neural Repair**. 2019, October; 33(10): 836-847.

RISK OF RECURRENT STROKE WITH SYMPTOMATIC CAROTID NEAR OCCLUSION

The risk of recurrent stroke in patients with symptomatic carotid near-occlusion (SCNO) has not been clearly established. Therefore, the management of SCNO remains controversial. This study assessed the risk of recurrent ipsilateral ischemic stroke in the first two years following the presenting event.

This prospective, observational, Spanish study was conducted between January of 2010 and May of 2016. Subjects were adults with an internal carotid near-occlusion, diagnosed using digital subtraction angiography. The decision to treat with medical therapy versus revascularization was based upon criteria determined at each participating center. In-person, clinical follow-up visits were performed at three, six, 12 and 24 months after the presenting event. Events, including ischemic stroke or TIA ipsilateral to the SCNO, were registered. The primary endpoint was ipsilateral ischemic stroke or retinal infarction in the first 24 months.

Of the 140 patients followed, the primary endpoint occurred in 15 cases. Seven ipsilateral strokes

occurred in the revascularization group, with two occurring before the procedure. Five patients experienced an ischemic stroke or TIA in a different artery territory. The cumulative rate of the primary endpoint at 24 months was 11.1%. The cumulative mortality was 7.5%. The occurrence of the primary endpoint did not significantly differ between the surgical and medical treatment groups.

Conclusion: This study of patients with symptomatic carotid near-occlusion found that the cumulative rate of ipsilateral ischemic stroke at 24 months was 11.1%.

Garcia-Pastor, A., et al. The Risk of Recurrent Stroke at 24 Months in Patients with Symptomatic Carotid Near-Occlusion: Results from CAOS, a Multicenter Registry Study. **Eur J Neurol**. 2019, November; 26(11): 1391-1398.

LOW DOSE RIVAROXABAN WITH OR WITHOUT ASPIRIN AND ISCHEMIC STROKE SUBTYPES

Antiplatelet therapy remains the mainstay for the secondary prevention of most non-atrial fibrillation associated ischemic stroke subtypes. The Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS) trial tested the efficacy of rivaroxaban, combined with aspirin with that of singular treatment with rivaroxaban or aspirin alone, for the secondary prevention of stroke.

The COMPASS trial is a multicenter, double-blind, randomized, placebo-controlled trial involving hospitals from 33 countries, enrolling 27,395 participants with stable atherosclerotic vascular disease. Patients were randomized into groups receiving rivaroxaban, 2.5 mg, twice daily plus aspirin, 100 mg, once daily, rivaroxaban, 5 mg, twice daily, or aspirin, 100 mg, once daily. From the data, different stroke subtypes were identified. During the study, 291 ischemic strokes occurred, including 20.3% cardioembolic, 18.6% secondary to carotid stenosis greater than 50%, 7.2% lacunar strokes secondary to small vessel disease, and 14.4% with a negative evaluation and meeting the criteria for ESUS (embolic stroke of undetermined source).

Strokes secondary to cardiac embolism, as well as strokes of unknown etiology, were significantly less frequent in the low-dose rivaroxaban plus aspirin group as compared with the aspirin group

alone ($p=0.005$ and $p=0.006$, respectively). The groups did not differ in the risk of strokes due to internal carotid stenosis greater than 50% for lacunar strokes.

Conclusion: This secondary analysis of the COMPASS trial found that, compared to aspirin alone, low dose rivaroxaban plus aspirin was superior to aspirin alone for the prevention of ischemic strokes.

Perera K., et al. Association between Low-Dose Rivaroxaban, with or Without Aspirin, and Ischemic Stroke Subtypes: A Secondary Analysis of the COMPASS Trial. *JAMA Neurol.* 2019; doi:10.1001/jamaneurol.2019.2984.

MEDICAL MANAGEMENT VERSUS MECHANICAL THROMBECTOMY FOR MILD STROKES

The American Heart Association recommends mechanical thrombectomy (MT) for the treatment of anterior circulation emergency large vessel occlusion presenting with a National Institutes of Health Stroke Scale (NIHSS) of at least six and presenting within six hours of symptom onset. Less clear is the safety and efficacy of MT for the management of patients with mild deficits emergency large-vessel occlusion (mELVO) who have NIHSS scores of less than six.

This retrospective, multicenter study and meta-analysis of studies of patients with mELVO compared the safety and efficacy of MT with best medical management (BMM) over a five-year period from 16 centers. The efficacy outcomes were favorable functional outcome (FFO) and functional independence (FI), as defined as modified Rankin Scale scores of zero to one and zero to two, respectively.

Subjects were 251 consecutive patients with mELVO. Of these, 138 received treatment with MT and 113 with BMM. The median hospital length of stay was five days for the MT group and four days for the BMM group ($p=0.002$). At three-month follow-up, in the adjusted analysis, at three months, there was no significant difference between those in the BMM and the MT groups in the ratio of FFO, FI, mortality or functional improvement. The multivariable analysis found that MT was associated with a higher risk of asymptomatic ICH ($p=0.03$), but not of symptomatic ICH.

Conclusion: This multicenter study and meta-analysis of studies of patients with mild strokes resulting

from emergency large vessel occlusion, found no difference in three-month outcomes between those treated with the best medical practice and those treated with mechanical thrombectomy.

Goyal, N., et al. Medical Management versus Mechanical Thrombectomy for Mild Strokes: An International, Multicenter Study and Systematic Review and Meta-analysis. *JAMA Neurol.* 2019; doi: 10.1001/jamaneurol.2019.3112.

BLOOD FLOW RESTRICTION WITH PROTEIN SUPPLEMENTATION

Mobility decline in older adults results, in part, from a progressive decline of skeletal muscle mass. This study examined the effect of blood flow restriction training with collagen hydrolysate supplementation on muscle mass and function in older men at risk for sarcopenia.

Subjects were 39 healthy men, 50 years of age or older. After a baseline assessment, including physical examination, patients were randomized to a control group (CON), a blood flow restriction group (BFR) or a BFR plus protein (BFR+P) group. The BFR and BFR+P groups underwent lower extremity leg reps with 30 repetitions at 20% of their one rep max followed by three sets of 15 repetitions, three times per week for four weeks. At four weeks the repetitions were increased to 30% of the one rep max. In the BFR group, blood flow was restricted to 50% of each individual's arterial occlusion pressure. Those in the BFR+P group received a daily dose of 15 g of collagen hydrolysate within 60 minutes of completing the exercise. Muscle mass, strength and metabolic parameters were measured at baseline and at follow up.

The cross-sectional area of the thigh increased by 6.7% in the BFR+P, 5.7% in the BFR and 1.1% in the CON group. Isometric strength increased by 10.2% in the BFR+P, 4.8% in the BFR and fell by 5.3% in the CON group. Insulin-like growth factor increased by 15.3 $\mu\text{g/l}$ in the BFR+P, and 10.6 $\mu\text{g/l}$ in the BFR group, and 5.0 $\mu\text{g/l}$ in the CON group.

Conclusion: This study demonstrates that protein, added to blood flow restriction exercise, may accelerate muscle gains in elderly individuals.

Centner, C., et al. Effects of Protein Supplementation on Muscle Mass and Strength in Older Men. *J Sports*

Sci Med. 2019, September; 18 (3):471–478.

MODIC CHANGES AND LONG-TERM PAIN

Modic changes (MCs) are often found in radiographic studies of patients with low back pain (LBP). This study reviewed the association between MCs and long term physical disability, back pain, and sick leave.

This study included patients 18-60 years of age, recruited in 2004-2005 with LBP with back greater than leg pain. The original study randomized patients to cognitive training or physiotherapy, finding no difference at one year. This 13 year follow up included 170 of 207 patients from the original study. Patients were split into two groups based on lumbar MRI evidence of Modic changes; MC group ($n=67$) and non-MC ($n=122$) group. The primary outcomes were disability, using the Roland-Morris Disability Questionnaire (RMQD) an activity limitations survey, low back pain, and number of sick leave days used in the past year due to back pain.

At 13 year follow-up the RMQD scores were significantly better in +MC group than in the -MC ($p=0.024$). In addition, activity limitations were significantly lower in the +MC group ($p=0.012$), with the +MC group taking a fewer number of sick days due to back pain ($p=0.003$).

Conclusion: This study of patients with low back pain found that those with Modic changes noted on MRI had less long-term pain, disability, or sick leave than did those without Modic changes.

Udby, P., et al. Modic Changes Are Not Associated with Long-Term Pain and Disability: A Cohort Study with 13-year Follow-up. *Spine.* 2019 Sept; 44(17):1186-1192.

CAUSES OF OSTEOARTHRITIS

Osteoarthritis (OA) is the most common form of arthritis in developed countries. While a number of factors are associated with OA, causal factors are less clear. Noting that Mendelian randomization (MR) can be used to test for a causal association between a risk factor and a particular outcome, this study used MR to better understand causal factors for site-specific OA in the complete UK Biobank data set.

Subjects were 502,647 individuals between the ages of 37 and 76 years

recruited from across the United Kingdom from 2006 to 2010. Baseline data included health status, demographics, and lifestyle, with physical examinations for anthropometric measures, blood pressure, and bone mineral density. The primary outcome measure was OA, defined by hospital diagnosis. To assess causal association, genetic instrument variables obtained from published genome-wide association study (GWAS) meta-analysis were used to assess the possible causality of BMI, femoral neck and lumbar spine BMD, serum HDL cholesterol, LDL cholesterol, and triglyceride levels, type 2 diabetes systolic BP and CRP levels.

The data revealed three factors (high BMI, high femoral neck BMD, and low systolic BP) that were causally associated with an increased risk of OA. High BMI was shown to be causal for knee and hip OA, but not hand OA. A high femoral neck BMD was causally associated with the risk of knee OA and hip OA. In addition, low systolic BP was causally associated with all OA.

Conclusion: This study found that high BMI, high femoral neck BMD, and low systolic BP are causally associated with an increased risk of OA.

Funck-Brentano, T., et al. Causal Factors for Knee, Hip and Hand Osteoarthritis: A Mendelian Randomization Study in the UK Biobank. *Arthritis Rheumatol.* 2019, October;71(10).1635-1641.

DISORDERED SLEEP AND LOW BACK PAIN

It has been estimated that up to 84% of all individuals will have low back pain (LBP) at some point in their lives. As sleep quality has been associated with reduced pain tolerance, this study assessed the effect of a sleep disorder on LBP and healthcare utilization.

Subjects were patients at a large US military hospital with LBP who were referred for a one-time pain self-management class. Baseline data included self-reported disability, pain intensity and sleepiness with assessments including the Oswestry Disability Index, a pain intensity question from the Oswestry Disability Index, and sleepiness using the Epworth Sleepiness Scale.

Subjects were 758 individuals who participated in the self-management class. The number of health care visits for LBP was significantly associated with pain

intensity ($p < 0.01$), disability ($p < 0.001$), and history of sleep disorder ($p < 0.001$). Health care costs for LBP were significantly associated with pain intensity ($p < 0.01$), disability ($p < 0.001$), and history of sleep disorder ($p < 0.001$). Higher disability and the presence of a sleep disorder were independently associated with higher health care visits.

Conclusion: This study of patients with low back pain found that higher disability, pain intensity, and the presence of a sleep disorder were associated with higher clinic visits and costs for LBP.

Rhon, D., et al. Does Disordered Sleep Moderate the Relationship Between Pain, Disability and Downstream Health Care Utilization in Patients with Low Back Pain? *Spine* 2019; 44(21):1481-1491.

EXTRACORPOREAL SHOCKWAVE THERAPY FOR MENISCAL TEARS

As extracorporeal shockwave therapy (ESWT) has been effective in the treatment of tendinopathies, this animal study explored the effect of ESWT in promoting the healing of meniscal tears.

Twelve-week-old male rats were divided into three groups: normal [untreated], ESWT(-), and ESWT(+). The latter two groups were subjected to full-thickness tears in the avascular region of the anterior horn. One week after surgery, the ESWT(+) group received 800 impulses of shockwave at 0.22-mJ/mm² energy flux density. At two, four, and eight weeks post-surgery, the rats were euthanized, and compared by histological and immunohistochemical analysis.

The meniscus healing scores of the ESWT+ group were significantly higher than the ESWT- group at four weeks ($p=0.009$) and eight weeks ($p=0.015$), with all rats in the ESWT+ group demonstrating bridge linking at eight weeks. The ratio of BrdU-positive cells to all cells was significantly higher in the ESWT+ group than in ESWT- groups at two weeks ($p=0.046$), four weeks ($p=0.008$), and eight weeks ($p=0.009$). Gene expression was measured for CCN2, SOX9, VEGF-a, aggrecan, collagen type 2 alpha 1 (Col1a2), and collagen type 2 alpha 1 (Col2a1). The CCN2 upregulation was greater in the ESWT+ group than in the normal and ESWT- groups ($p=0.05$ for both). The SOX9 was also significantly upregulated in the ESWT+ group to a level approximately 3.5-fold higher than

that in the normal and ESWT- groups ($p=0.002$ and $p=0.003$, respectively).

Conclusion: This animal study of meniscal tears found that extracorporeal shockwave therapy can accelerate the healing of a meniscal tear in the avascular region.

Hashimoto, et al. Extracorporeal Shockwave Therapy Accelerates the Healing of a Meniscal Tear in the Avascular Region in a Rat Model. *Am J Sports Med.* 2019, October;47(12):2937-2944.

INEBILIZUMAB FOR NEUROMYELITIS OPTICA SPECTRUM DISORDER

Neuromyelitis optica spectrum disorder (NMOSD) is a severe autoimmune, inflammatory central nervous system disease, with presentations including optic neuritis and transverse myelitis. Incomplete recovery is typical. As Inebilizumab is a humanized, anti-CD19, B cell-depleting antibody, this study assessed the effect of this medication as a monotherapy for the treatment of NMOSD.

Subjects were adults with a diagnosis of an NMOSD, with an expanded Disability Status Scale score of eight or less. Between January of 2015 and September of 2018, 230 patients were randomized, with 174 to receive Inebilizumab and 56 to receive a placebo.

An attack of NMOSD occurred in 12% of the patients in the treatment group and 39% in the placebo group ($p < 0.001$). Serious adverse events occurred in five percent of the treatment group and nine percent of the placebo group.

Conclusion: This study found that, of patients presenting with an attack of NMOSD, treatment with inebilizumab significantly reduced the recurrence of acute attacks.

Cree, B., et al. Inebilizumab for the Treatment of Neuromyelitis Optica Spectrum Disorder (N-MOMentum): A Double-blind, Randomised Placebo Controlled Phase 2/3 Trial. *Lancet.* 394: 1352-1363.

PEFICITINIB FOR RECALCITRANT RHEUMATOID ARTHRITIS

The Janus kinase (JAK) family of non-receptor protein tyrosine kinases have been found to be a promising alternative target for rheumatoid arthritis (RA) treatment. This study assessed the efficacy of a JAK

inhibitor, Peficitinib, for the treatment of RA.

This randomized, placebo controlled, double-blind study was completed at 142 sites in Japan. All participants were diagnosed with RA, with a history of a poor response to other DMARDs. The subjects were randomized to receive treatment for 52 weeks with Peficitinib, 100 mg per day, 150 mg per day, or placebo once daily, orally, in combination with a stable dose of MTX (≤ 16 mg/week) for 52 weeks. The primary efficacy endpoint was response rate at week 12, according to the ACR-20 improvement criteria, with secondary endpoints, assessed throughout the study, involving response rates to the ART 20/50/70 improvement criteria.

Five hundred nine patients completed the study. The primary efficacy variable at week 12 occurred in 57.7% of the 100 mg group, 70.4% of the 150 mg group, 83.5% of the entarcept group and 30.7% of the placebo group. Compared to placebo, significantly better outcomes were noted in the 100 mg and 150 mg groups ($p < 0.001$ for both comparisons). Compared to the placebo group, the increase in ART 20/50/70s was significantly better throughout the study in the 100 mg and 150 mg groups as well as in the entarcept group.

Conclusion: This study of patients with DMARD resistant rheumatoid arthritis found significant improvement with a novel Janus kinase inhibitor, Peficitinib.

Tanaka, Y., et al. Efficacy and Safety of Peficitinib (ASP015K) in Patients with Rheumatoid Arthritis and an Inadequate Response to Conventional DMARDs: A Randomized, Double-Blind, Placebo Controlled, Phase 3 Trial (RAJ3). *Annals Rheum Dis.* 2019, October; 78(10): 1320-1322.

INFECTION RISK WITH MULTIPLE SCLEROSIS TREATMENTS

For patients with multiple sclerosis (MS), new disease modifying therapies have been introduced, all of which modulate the patient's immune response. This raises concern about adverse events such as increased susceptibility to infectious disease. This study was designed to better understand the association between several of these drugs and the risk of infectious disease.

This nationwide cohort study included all patients in Sweden with a diagnosis of relapsing–remitting MS. Using a nationwide registry, data

were obtained from January 1, 2011 to December 31, 2017 for patients introduced to interferon beta and glatiramer acetate, fingolimod, natalizumab, or rituximab. All subjects were matched for comparison to five participants who were free of MS. The main outcome was the time until the first serious infection, defined as any infection recorded as the main reason for hospitalization.

Data were obtained for 6,421 patients with a mean age at the start of treatment of 39 years. In the adjusted analysis, using glatiramer as a reference, the hazard ratio for infectious disease was 1.81 for fingolimod, 1.53 for natalizumab, and 2.34 for rituximab. Comparing the newer DMTs with rituximab, the rate was 34% lower receiving natalizumab and 23% lower for those receiving fingolimod. Rituximab and natalizumab had the highest rate of antibiotics use.

Conclusion: This nationwide study of Swedish patients with relapsing–remitting multiple sclerosis found that this patient group is generally at an increased risk of infections with infections lowest among those treated with interferon beta and glatiramer, and highest among those using rituximab.

Luna, G., et al. Infection Risks Among Patients With Multiple Sclerosis Treated With Fingolimod, Natalizumab, Rituximab, and Injectable Therapies. *JAMA Neurol.* 2019, doi:10.1001/jamaneurol.2019.3365

PLATELET RICH PLASMA VERSUS DRY NEEDLING FOR ACHILLES TENDINOPATHY

For the treatment of tendinopathies, platelet rich plasma (PRP), and dry needling (DN) have shown some success in the reduction of pain and improvement of function. This study compared these two interventions for the treatment of non-insertional Achilles tendinopathy.

Subjects were patients with non-insertional Achilles tendinopathy for more than three months. Baseline measures including demographic and anthropomorphic data as well as pain on a visual analog scale (VAS), and an ultrasound examination of the tendon. The PRP group received five ml of mepivacaine 2% with a 21-gauge needle inserted into the tendon, with autologous PRP deposits place at the site of the most damage, and then proximal and distal for total of 4-5 mL. The three

injections were performed at one week intervals. The dry needling group used a 21-gauge needle with multiple longitudinal passes performed over the tendon once a week for three weeks. After the second procedure, eccentric training and stretching was recommended daily for at least three months. Outcome measures included the Victorian Institute of Sport Assessment-Achilles (VISA-A), and pain evaluated by means of a 0–10 cm Visual Analogue Scale (VAS).

Data were complete for 46 patients in the PRP group and 38 in the DN group. From baseline to three and six month follow up the VISA-A scores for the PRP group were 49.7, 63.7 and 68.4 respectively ($p = 0.04$) and for the DN group were 50.8, 62 and 64.8 respectively ($p = 0.13$), with no significant difference between groups at any time period. At six months, VAS pain scores and the number of patients who had satisfactory results did not differ between groups.

Conclusion: This study of patients with Achilles tendinopathy found no significant difference in outcomes between those treated with dry needling and those treated with platelet rich plasma.

Abate, M., et al. Platelet Rich Plasma Compared to Dry Needling in the Treatment of Non-Insertional Achilles Tendinopathy. *Phys Sportsmed.* 2019; 47 (2): 232–237.

STRESS INOCULATION THERAPY FOR WHIPLASH-ASSOCIATED DISORDER

Stress inoculation training is a cognitive behavioral approach incorporating problem-solving and coping strategies to manage stress related anxiety. This study assessed whether physiotherapy-led stress inoculation training could assist in the care of patients with whiplash associated disorder (WAD).

Subjects were community dwelling patients with WAD of less than four weeks' duration. The participants were randomized to receive guideline-based exercise (EX) delivered by a physiotherapist or the same intervention combined with stress inoculation training (EX+SIT). The stress inoculation training was provided in six, weekly sessions, with three phases including identifying and understanding stress, developing skills for managing stress, and applying skills in stressful situations to develop tolerance and confidence. The primary outcome measure was

the Neck Disability Index (NDI), with secondary outcome variables including scores on the Depression, Anxiety and Stress Scale (DASS), the Pain Catastrophizing Scale, the Pain Self-Efficacy Questionnaire (PSEQ), the Coping Strategies Questionnaire and a self-rated global impression of recovery.

On the NDI, the EX+SIT group improved significantly more than the EX group at each time point, including six weeks ($p<0.01$), six months ($p<0.05$) and 12 months ($p<0.01$). A significantly greater proportion of patients in the EX+SIT group reported that their condition was "improved" or "much improved" compared with those in the EX group ($p<0.05$).

Conclusion: This study of patients with acute whiplash associated disorder found that combining traditional physical therapy exercise with stress inoculation training resulted in greater improvement in neck pain-related disability than did the exercise alone.

Sterling, M., et al. Physiotherapist-Delivered Stress Inoculation Training Integrated with Exercise versus Physiotherapy Exercise Alone for Acute Whiplash-Associated Disorder (StressModex): A Randomized, Controlled Trial of a Combined Psychological/Physical Intervention. *Br J Sports Med.* 2019, September; 53(19): 1240 -1247.

PERCUTANEOUS ELECTRICAL NERVE STIMULATION FOR HEADACHE

Approximately two percent of the population in developed countries experience chronic, daily headaches. Techniques developed over the last two decades to address headaches include invasive and noninvasive neurostimulation, as well as noninvasive neuromodulation. This study explored the use of percutaneous electrical nerve stimulation (PENS) as a treatment for primary headache disorders.

This retrospective review included 36 patients with chronic, refractory headache disorders between 2012 and 2016. Of these, 25 had a primary headache diagnosis, of whom 14 had chronic migraines (CM), nine had chronic cluster headaches (CCH) and two had new, daily, persistent headache (NDPH). The PENS treatment was delivered with 21 gauge needles to the occipital nerve ipsilateral to the pain. Stimulation was delivered for 25 to 30 minutes, every 12 seconds, between two Hz and 100 Hz at three cycles/

day and between 1.2 and 2.5 volts, depending upon the individual patient tolerance.

Of those with CCH, six of nine improved significantly after the first session, with reduced frequency and/or severity lasting at least four weeks. With further treatments, four of these patients achieved similar benefits with subsequent treatments. However, only four of the patients with CM/NDPH experienced any noticeable benefit with PENS therapy. A previous response to a greater occipital nerve block did not predict the response to the PENS.

Conclusion: This retrospective study of patients with refractory primary headache disorders found that percutaneous electrical nerve stimulation may be of benefit to those who have chronic cluster headaches.

Weatherall, M., et al. Percutaneous Electrical Nerve Stimulation (PENS) Therapy for Refractory Primary Headache Disorders: A Pilot Study. *Br J Neurosurg.* 2019. doi.org/10.1080/02688697.2019.1671951.

WARMUP IN YOUTH BASEBALL VERSUS INJURY

Shoulder and elbow injuries are common in baseball players of all ages. Players 9 years of age or older have a significantly greater risk of medial elbow injury than those less than 9 years of age. Given previous studies have identified variables of physical function as risk factors for throwing injuries, this study assessed a preventative program focusing on these factors.

This prospective cluster randomized controlled study included 16 youth baseball teams in Yokohama Japan, who were block randomized into an intervention group or a control group. Players 9-12 years old were given a questionnaire concerning the position played and quantification of involvement each week. Those in the intervention group were instructed to perform stretching exercises aimed at improving range of motion at the elbow, and hip with dynamic mobility exercises focusing on the scapular and thoracic function with lower extremity balance training.

The program was completed within 10 minutes. Participants perform the program once per week under the supervision of the coaches. Those in the control group continued their usual preparations. All participants were followed for injuries to the shoulder and elbow.

Data were available for 117 participants in the intervention group and 120 in the control group. Over 12 months, 22% of the intervention group and 38.2% of the control group reported shoulder and elbow injuries of the throwing arm. Incidence of these injuries was 3.1 per 1,000 events in the control group and 1.7 per 1,000 athletic events in the treatment group ($p=0.01$).

Conclusion: This study found that a 10-minute injury prevention program reduced the incidence of throwing injuries of the shoulder and elbow among youth baseball players.

Sakata, J., et al. Throwing Injuries in Youth Baseball Players: Can a Prevention Program Help? *Am J Sports Med.* 2019, September; 47 (11): 2709-2716.

EXPOSURE TO THE NATURAL ENVIRONMENT AND ARTHROPLASTY RECOVERY

Rates of hip and knee arthroplasty are rising globally and are projected to continue to rise as life expectancy and obesity rates increase. This New Zealand study assessed whether living in greener and or more walkable neighborhoods would have an effect on opioid use and mortality following hip or knee arthroplasty.

This cohort study followed patients who received total hip or knee arthroplasty [7,449 hip arthroplasties (THAs) and 6,558 knee arthroplasties (TKAs)] at a publicly-funded New Zealand hospital in 2006 and 2007. The individuals were followed longitudinally for nine plus years using healthcare records obtained from the Statistics New Zealand's Integrated Data Infrastructure. Outcomes included time to all-cause mortality and the number of post-surgical opioid prescriptions. Exposure to natural environment was assessed using greenness and walkability of patients' neighborhoods. Greenness was measured by the Normalized Difference Vegetation Index. Walkability was calculated using a previously validated Walkability Index (WI).

Patients who lived in greener neighborhoods lived longer and took fewer opioids in the 12 months following THA or TKA. These findings reached statistical significance only for THA. Walkability was not significantly associated with post-surgical longevity or opioid use.

Conclusion: This New Zealand observational study found that individuals living in greener neighborhoods lived longer and took

fewer opioids following hip arthroplasty.

Donovan, G., et al. Relationship Between Exposure to the Natural Environment and Recovery from Hip or Knee Arthroplasty: A New Zealand Retrospective, Cohort Study. **BMJ Open**. 2019; 9: e029522.

TICAGRELOR OR PRASUGREL FOR ACUTE CORONARY SYNDROMES

For patients with a first episode of an acute coronary syndrome (ACS), dual antiplatelet therapy (aspirin plus an adenosine biphosphate receptor antagonist) is the standard treatment. As the cyclopentyltriazolopyrimidine, ticagrelor, provides superior platelet inhibition than does clopidogrel, this study compared the safety and of these two medications for the treatment of patients with ACS.

Adult patients with ACS were randomized to receive either ticagrelor 90 mg BID or prasugrel 10 mg per day (5mg for those over 75 years of age). The primary endpoint was the composite of death, myocardial infarction or stroke, one year after randomization.

At one year, the primary endpoint occurred in 9.3% of the ticagrelor group and 6.8% of the prasugrel group ($p=0.006$). The composite of death from cardiovascular causes, myocardial infarction or stroke occurred in 8.1% of the ticagrelor and 6.3% of the prasugrel group (hazard ratio 1.32). The rates of death from any cause at one year were 4.5% in the ticagrelor group and 3.7% in the prasugrel group (hazard ratio 1.23).

Conclusion: This study of patients with acute coronary syndromes found that prasugrel was superior to ticagrelor in reducing death, myocardial infarction and stroke.

Schupke, S., et al. Ticagrelor or Prasugrel in Patients with Acute Coronary Syndromes. **N Engl J Med**. 2019, October 17; 381(16): 1524-1534.

HELMET USE AND TRAUMATIC BRAIN INJURY PREVENTION

Helmet use is often strongly recommended when bicycling. Although many studies have analyzed the efficacy of helmet use for preventing severe traumatic brain injury (sTBI), most have focused on patterns in the United States. This study retrospectively examined the relationship between helmet use and

sTBI among cyclists in the United Kingdom.

Data were obtained from the National Health Service (NHS) England Trauma Audit and Research (TARN) database to find individuals, 16 years of age or older, who presented to hospitals following cycling-related major injuries from March of 2012 to September of 2017. Of the 11,285 patients identified, helmet-use data were available for 6,621. Variables analyzed included age, gender, date, time, place and nature of the accident, helmet use, injury type, length of intensive care (if needed) and hospital length of stay and neurosurgical intervention need.

Patients not wearing helmets had significantly higher Injury Severity Scores and significantly higher scores on the Abbreviated Injury Scale for the face, chest, spine, upper limb and lower limb. A TBI was diagnosed in 47.6% of patients not wearing a helmet and in 19.1% of patients wearing a helmet. Patients without a helmet were more likely to have Glasgow Coma Scores of below 15, to require neurosurgical intervention, and to be admitted to intensive care.

Conclusion: This retrospective review found that, among those hospitalized for a bicycling accident, those who were wearing a helmet had fewer traumatic brain injuries and lower injury severity scores than did those who were not wearing a helmet.

Dodds, N., et al. Evaluating the Impact of Cycle Helmet Use on Severe Traumatic Brain Injury and Death in a National Cohort of Over 11,000 Pedal Cyclists: A Retrospective Study from the NHS England Trauma Audit and Research Network Dataset. **BMJ Open**. 2019 Sep 13; 9(9): e027845.

PRE-SURGERY PHYSIOTHERAPY IN DEGENERATIVE LUMBAR SPINE DISORDER

Lumbar spine stenosis and disc herniation are the most common causes of spinal surgery. This study examined the effect of physiotherapy on walking and leg strength among patients scheduled for back surgery.

Subjects were consecutively recruited at a spinal clinic in Sweden between October of 2012 and March of 2015. All had a confirmed diagnoses of disc herniation, lumbar spine stenosis (LSS), degenerative disc disease (DDD) or spondylolisthesis of grade IV or greater. Patients allocated to a wait list control group (C) received usual care, including information

concerning the surgical procedure, postoperative rehabilitation and continued physical activity. The treatment group (TR) received physiotherapy twice per week for nine weeks, including exercises, behavioral interventions to decrease fear avoidance behavior and increase activity levels, with recommendations for physical activity of at least 30 minutes per day. Outcome measures included patient reported outcome and objective outcome measures at baseline and nine weeks, with the TR group compared to the C group.

At one year post-surgery, compared to the C group, patients in the TR group improved more on all variables from baseline to follow-up ($p<0.001$ to $p<0.028$). Patients adhering to ≥ 12 treatment sessions significantly improved on all variables ($p<0.001$ to $p<0.032$), while those receiving zero to 11 treatment sessions improved only in normal walking speed ($p=0.035$). For post-surgical function at one-year, pre-surgical gait speed, self-rated walking ability and quadriceps strength together explained 17.4% ($p=0.003$) of the variation in self-reported physical activity level. Adding pre-surgery physical activity level increased the explanatory value to 27.5% ($p<0.001$).

Conclusion: This study found that pre-surgical physiotherapy increased walking ability and strength, with these variables correlated with one-year postoperative physical activity.

Fors, M., et al. Effects of Pre-surgery Physiotherapy on Walking Ability and Lower Extremity Strength in Patients with Degenerative Lumbar Spine Disorder: Secondary Outcomes of the PREPARE Randomized, Controlled Trial. **BMC Musculoskelet Disord**. 2019; 20:468. <https://doi.org/10.1186/s12891-019-2850-3>.

PARENTAL ATRIAL FIBRILLATION AND STROKE IN YOUNG ADULTS

Approximately 25% of strokes or transient ischemic attacks (TIAs) are considered cryptogenic. Many of these may be associated with undiagnosed atrial fibrillation (AF). This study examined whether a parental history of AF is associated with increased risk of stroke or TIA in their offspring.

This population based historical cohort study included databases for the Canadian Province of Manitoba. Subjects were at least 18 years of age between April 1, 1972 and December 31, 2015. The index cohort for the offspring was April 1,

(Continued from page 2)

Shane Davis, M.D.
Tyler Doornink D.O.
Quinn Howard, M.D.
Courtney Mullen, M.D.
Sanket Patel, M.D.
Theodora Wong, M.D.
Jennifer Wu, M.D.
University of California/Irvine, CA

*Vanessa Wanjeri, M.D.
University of Pennsylvania, Phil, PA

*Amy Unwin, M.D.
Ashley Eaves, M.D.
Univ. of Washington, Seattle, WA

*Adem Aktas, D.O.
Sheyna Gifford, M.D.
Daniel Probst, M.D.
Andrew O'Halloran M.D.
Washington University, St. Louis, MO

Executive Editor Emeritus
Donald F. Langenbeck, Jr., M.D.

Subscription Manager
Michael P. Burke, M.S.

*Regional Managing Editors have
attested that they have no financial
conflict of interest when choosing
articles that appear in Rehab in
Review.

1972 or the date on which the
offspring turned 18 years old. The
end date for the offspring was the
date of stroke, TIA, or death. Those
who had a parent with a diagnosis of
AF (P-AF+) were compared to those
without a parent with AF (P-AF-).

Data were available for 325,333
individuals ages 18-29 years at study
entry, followed for a mean of 17.3
years. Of these, 1598 were P-AF+ at
study entry and 24,583 were P-AF+
by the end of the follow-up period.
During the follow-up, 8678 offspring
had an incident stroke or TIA. The
incident rate for stroke or TIA in the P
-AF+ group was 195 per 100,000
person years compared with 156.6
per 100,000 person years in the P-AF
- group. A diagnosis of AF was made
in 1.9% of the P-AF+ and in 0.3% of
the P-AF- group.

Conclusion: This study found
that parental AF is associated with a
higher frequency of AF, stroke/TIA
and other cardiovascular risk factors
in offspring in early adulthood.

McAlister, F., et al. Parental Atrial
Fibrillation and Stroke or Atrial
Fibrillation in Young Adults. *Stroke*,
2019; 50 (9): 2322-2328.

Rehab in Review (RIR) is produced
monthly by physicians in the field of
Physical Medicine and Rehabilitation
(PM&R), with the cooperation and
assistance of Emory University School
of Medicine, Department of Rehabilita-
tion Medicine. The summaries
appearing in this publication are
intended as an aid in reviewing the
broad base of literature relevant to this
field. These summaries are not
intended for use as the sole basis for
clinical treatment, or as a substitute for
the reading of the original research.

The Emory University School of
Medicine designates this journal based
activity for a maximum of 3 AMA PRA
Category 1 Credits™. Physicians
should only claim credit commensurate
with the extent of their participation in
the activity. The Emory University
School of Medicine is accredited by the
ACCME to provide continuing medical
education for physicians. The journals
are offered as a CME accredited activity
for 3 years from the date of original
publication.

RIR is affiliated with the Association
of Academic Physiatrists, the World
Health Organization, and the Chinese
and Indian Societies of PM&R and en-
dorsed by the International Society of
Physical and Rehabilitation Medicine.

Private subscriptions are available
by email at rehabinreview@aol.com or
by fax or phone at (800) 850-7388.
ISSN # 1081-1303



REHAB IN REVIEW

Produced by the Department of
Rehabilitation Medicine, Emory
University School of Medicine



EMORY
UNIVERSITY
SCHOOL OF
MEDICINE

Department of
Rehabilitation
Medicine

Expanding the frontier of rehabilitation sciences in research, teaching, and patient care