# REHAB IN REVIEW

TM

*WWW.REHABINREVIEW.COM*

Volume 30 Number 6 | Published by Physicians In Physical Medicine and Rehabilitation | June 5, 2022

## COLLEGE AMERICAN FOOTBALL AND LONG-TERM HEALTH

Despite research focusing on the later-life effects of playing professional American football, the long-term effects of college football remain largely unknown. This study examined the prevalence of self-reported health conditions in older, former college football players.

Subjects were 447 former University of Notre Dame (UND) football players, 59 to 75 years of age at the time of the study. Those participants were administered a health survey addressing general health conditions including, but not limited to, diagnoses and/or treatments for cognitive, other neurologic, psychiatric, cardiovascular, orthopedic, and sleep conditions. For comparison with the general population, data were obtained from the Health and Retirement Study (HRS), a longitudinal study of a representative sample of U.S. adults over 50 years of age. The living UND players were matched to HRS participants.

Of the 406 players, 234 responded, including 216 former players and 18 next of kin of deceased players. Compared to the HRS group, the UND group had lower all-cause mortality (p=0.02), including death due to cancer (p=0.02) and diseases of the heart (p=0.02). Compared to the HRS group, the UND group reported a higher prevalence of cognitive impairment (p=0.02), headaches (p=0.001), cardiovascular disease (p=0.001), hypercholesteremia (p=0.001), alcohol use (p=0.02), and a lower prevalence of diabetes (p=0.001).

**Conclusion:** This study found that former college football players had significantly lower mortality than the general population, but self-reported higher levels of cognitive impairment, recurrent headaches, and cardiovascular disease than the general population.

Phelps, A., et al. Association of Playing College American Football with Long-term Health Outcomes and Mortality. **JAMA Netw Open**. 2022 Apr 1;5(4):e228775. doi: 10.1001/jamanetworkopen.2022.8775. PMID: 35442450; PMCID: PMC9021915.

## MEDITERRANEAN DIET VERSUS LOW-FAT DIET FOR SECONDARY PREVENTION OF CARDIOVASCULAR DISEASE

The Mediterranean diet is characterized by a relatively high proportion of fruits, vegetables, legumes, and cereals, with white meat and fish the primary sources of protein, and olive oil the main source of fat. This study compared the efficacy of a low-fat diet and a Mediterranean diet for secondary cardiovascular prevention.

The CORonary Diet Intervention with Olive Oil and Cardiovascular PREVention (CORDIOPREV) study was a single-center, randomized trial involving patients 20 to 75 years of age, with a diagnosis of coronary heart disease. Eligible subjects had been diagnosed with acute myocardial infarction, hospitalized for unstable angina, or diagnosed with chronic high-risk ischemic heart disease. The participants were randomized to receive a Mediterranean diet or a low-fat diet. The subjects were engaged through individual face-to-face visits every six months, group sessions every three months, and telephone calls every two months. The primary outcome variable was a composite of major cardiovascular events, including myocardial infarction, revascularization, ischemic stroke, documented peripheral artery disease, and cardiovascular death occurring within seven years.

During year seven, the study was discontinued after registering primary events in 17.3% of the Mediterranean diet group and 22.2% in the low-fat diet group, with an unadjusted hazard ratio (HR) of 0.745. In all models of the multivariable-adjusted Cox HRs, the Mediterranean diet was superior to the low-fat diet, with HRs ranging from 0.719 to 0.753.

**Conclusion:** This double-blind, prospective, secondary prevention trial found the Mediterranean diet superior to a low-fat diet for reducing the risk of major cardiovascular events, with a relative decrease of 26%.

Delgado-Lista, J., et al. Long-Term, Secondary Prevention of Cardiovascular Disease with a Mediterranean Diet and a Low-Fat Diet: A Randomized, Controlled Trial. **Lancet**. 2022, May; 399: 1876-1885.

## PHENTERMINE PLUS TOPIRAMATE FOR WEIGHT LOSS IN OBESE ADOLESCENTS

Orlistat and liraglutide are the only anti-obesity medications currently approved by the U.S. Food and Drug Administration (FDA) for chronic use in adolescents. This randomized, double-blind, placebo-controlled, clinical trial evaluated the efficacy and safety of two doses of phentermine/topiramate (PHEN/TPM) as an adjunct to lifestyle therapy for weight management in adolescents with obesity.

This multicenter, randomized, double-blind, placebo-controlled, clinical trial recruited subjects 12 to 17 years of age with body mass indices (BMIs) at or greater than the 95$^{th}$ percentile. The subjects followed a 500-kilocalorie/day deficit diet and a family-based lifestyle modification program and were randomized to receive a once-daily placebo, mid-dose PHEN/TPM at a dose (7.5 mg/46 mg) or top-dose (15 mg/92 mg). The primary endpoint was the mean percent change in BMI.

At week 56, compared to the placebo group, the mean BMI changes from baseline were 10.44% in the high dose group (p<0.001) and 8.11% in the moderate dose group (p<0.001). For triglycerides and high-density lipoproteins, compared to placebo, the top dose group had reductions of 20.72% and 8.75%, respectively. The differences between moderate dose and placebo were 21.14% and 10.30%,

© Rehab in Review

**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 E. McCargo, EMBA, ALM
*Emory University, Atlanta, GA*

**Director of Global Distribution**
Jocelyn M. Smith
*Emory University, Atlanta, GA*

**Contributing Editors**
*Erin Mundy, M.D.
Miranda Ajulufoh, M.D.
Derick Davis, M.D.
Farah Hussain, M.D.
Travis Redmond, M.D.
Dayton Snyder, M.D.
Daniel Sok, M.D.
*Emory Univ. SOM, Atlanta, GA*

*Carley Trentman, M.D.
Irene Kalbian, M.D.
German Valdez, M.D.
Daniel Weng, M.D.
*Icahn SOM at Mt. Sinai, New York, NY*

*Andrew Logan, M.D.
Alex Cole, M.D.
Abhinav Arora, M.D.
Gregory Gandarillas, OMS
Zachary Kaufman, M.D.
Javier Santana, M.D.
Steven Wright, M.D.
*Jackson Memorial, Miami, FL*

* Alpha Anders, M.D.
*Thomas Grenier, M.D.
Kevin Haynes, M.D.
Michael Robbins, M.D.
*LSU, New Orleans, LA*

*Matthew Cascio, M.D.
Edwin David, D.O.
Neal Rusario, M.D.
Daniel Scura, D.O.
Corey Spector, D.O.
Hameer Thatte, D.O.
Jessica West, M.D.
*Nassau Univ., East Meadow, NY*

*Samantha Sabban-Wang, D.O.
Petra Aboulhosn, M.D.
Anusha Lekshminarayanan, M.D.
*NYMC/NYC H+H Metro, New York, NY*

*Ajay Patel, M.D.
Peyton Johnson, M.D.
Jeremy Roberts, M.D.
*NY-Presbyterian, New York, NY*

*Krupali Chokshi, M.D.
*Eric Kessler, M.D.
Krupali Chokshi, M.D.
Marie Mazzeo, M.D.
*NYU, New York, NY*

*Mitchell Burke, M.D.
*Schwab Rehab Mt. Sinai, Chicago, IL*

*Rahul Koya, D.O.
Alvin Chang, M.D.
Benjamin Drukman, M.D.
Marc Ramos Emos, M.D.
Jayne Ha, D.O.
Armaan Shah, M.D.
Nima Yazdanpanah, D.O.
*Suny Downstate, Brooklyn, NY*

*Rishi Kapoor, M.D.
Hannah Cheng, M.D.

Mary Wilson
*Temple Univ., Philadelphia, PA*

respectively. Adverse events resulting in the discontinuation of study treatment occurred in two in the placebo, and one in the top dose treatment groups.

**Conclusion:** This study of obese adolescents found that the combination of immediate-release phentermine and extended-release topiramate resulted in significant improvements in body mass index as compared to lifestyle changes alone.

Kelly, A., et al. Phentermine/ Topiramate for the Treatment of Adolescent Obesity. **NEJM Evid** 2022; 1 (6).

## INTENSITY OF LOW-DENSITY LIPOPROTEIN CHOLESTEROL REDUCTION AND SECONDARY STROKE

For patients with a history of ischemic stroke, an elevated low-density lipoprotein cholesterol (LDL-C) level is associated with an increased risk of subsequent major cardiovascular events. This systematic review and meta-analysis of randomized, clinical trials evaluated the benefits and risks associated with more intensive versus less intensive LDL-C-lowering, statin-based therapies for patients with ischemic stroke.

A literature search was conducted for trials completed between January 1, 1970, and July 31, 2021. Included studies had compared more intensive with less intensive LDL-C lowering statin-based therapies, with a primary outcome variable of recurrent stroke or major adverse cardiovascular events (MACE).

The final analysis was completed using data from 11, randomized, clinical trials, including a total of 20,163 patients with a mean age of 64.9 years. The pooled results found that more intensive LDL-C-lowering, statin-based therapies were associated with a reduced risk of recurrent stroke ($p=0.004$). More intensive LDL-C-lowering, statin-based therapies were also associated with a reduced risk of major adverse cardiovascular events MACE ($p<0.01$) and myocardial infarctions ($p=0.001$), but an increased risk of hemorrhagic stroke ($p=0.006$).

**Conclusion:** This literature review and meta-analysis found that more intensive LDL-C-lowering statin-based therapies were associated with a 12% reduction in the risk of recurrent stroke and a 17% reduction in the risk of major adverse cardiovascular events, especially for patients with evidence of atherosclerosis.

Lee, M., et al. Association between Intensity of Low--Density Lipoprotein Cholesterol Reduction with Statin-Based Therapies and Secondary Stroke Prevention: A Meta-analysis of Randomized, Clinical Trials. **JAMA Neurol**. 2022; 79(4): 349-358.

## UNITED KINGDOM CONSENSUS STATEMENT ON EXERCISE FOR OSTEOPOROSIS

Globally, an estimated 137 million women and 21 million men have a high risk of osteoporotic fracture. This is expected to double in the next 40 years. Although there is international guidance, there is no guidance in the United Kingdom (U.K.) on exercise and osteoporosis. This U.K. consensus statement was designed to provide guidance on the role of exercise and physical activity in the prevention and management of osteoporosis.

The U.K. Expert Exercise Steering Group (EESG) and the U.K. Exercise Expert Working Group (EEWG) were selected to create this consensus statement. Reviews of relevant literature were completed and circulated among the participants. The participants were asked to consider what exercise is effective in increasing bone strength and what exercise is safe and appropriate for those with, or at risk for, vertebral fractures.

For all people with osteoporosis, the group recommended muscle-strengthening exercise two to three times per week, including progressive muscle resistance training, with the load set at the maximum that could be lifted eight to 12 times. For those with osteoporosis without vertebral fractures or multiple low-trauma fractures, it was recommended that moderate exercise on most days include at least 50 impacts per session. For those with osteoporosis who have vertebral fractures or multiple low trauma fractures, impact exercise on most days at a level up to brisk walking was recommended, aiming for 150 minutes over the week. For those with osteoporosis who are frail and/or less able to exercise, the authors noted that fall prevention should be a priority, through strength and balance exercise.

To reduce falls, recommendations included specific and highly challenging balance and muscle-strengthening exercises three hours a week over at least four months.

Further, it was recommended that progression occur from strength and balance to higher impact exercise, with focused exercise including back muscles to improve posture.

For those with vertebral fractures, the exercise should focus on endurance by exercising at low intensity, using Yoga and Pilates or similar programs, to help with posture and pain. The risk of these exercise recommendations was thought to be low.

**Conclusion:** This consensus statement, endorsed by the Royal Osteoporosis Society Clinical and Scientific Committee of the United Kingdom, provides specific recommendations for those with, or at risk of, osteoporosis.

Brooke-Wavell, K., et al. Strong, Steady and Straight: U.K. Consensus Statement on Physical Activity and Exercise for Osteoporosis. **Br J Sports Med**. 2022, May 16: 104634.

## INTENSIVE VERSUS STANDARD BLOOD PRESSURE CONTROL AND CEREBRAL BLOOD FLOW

Hypertension is a major risk factor for cardiovascular and cerebrovascular diseases. The Systolic Blood Pressure (SBP) Intervention Trial (SPRINT) trial studied hypertensive patients, demonstrating that a target systolic blood pressure of <120mmHg, was superior to that of a target SBP of <140mmHg for cardiovascular mortality and morbidity, as well as cerebrovascular health. This substudy of SPRINT assessed the effect of intensive blood pressure lowering, on the volume of blood flowing through brain parenchyma per unit time (CBF).

Subjects were 9,061 participants with hypertension, 50 years of age or older, with systolic blood pressure (SBP) at a baseline of 130 mmHg to 180 mmHg. The subjects were randomized to a group with a target of <140mmHg or a target of <120mmHg. Brain MRIs were obtained at baseline and at 48 months after randomization to assess for changes in whole-brain CBF (WB-CBF) from baseline. Secondary outcomes were changes in gray matter (GM-CBF), white matter (WM-CBF), and periventricular white matter CBF (PWM-CBF).

The mean SBP was 120.5 mm Hg in the intensive treatment group and 134.4 mmHg in the standard treatment group. At a mean of four-year follow-up, the increase in mean WB-CBF in the intensive treatment group was significantly greater than that in the standard treatment (p=0.02). Gray, white, and periventricular white matter CBF showed similar changes. Greater changes in CBF were found in the participants with a history of cardiovascular disease.

**Conclusion:** This study of hypertensive patients found that the volume of blood flowing through brain parenchyma per unit time was more improved among those with a systolic blood pressure target of <120mmHg compared to those with a target of <140mmHg.

Dolui, S., et al. Association of Intensive vs Standard Blood Pressure Control with Cerebral Blood Flow. Secondary Analysis of the Sprint Mind Randomized, Clinical Trial. **JAMA Neurol.** 2022, April 1; 79(4): 380-389.

## CREUTZFELDT-JAKOB DISEASE AND MICROBIOTA

Creutzfeldt-Jakob Disease (CJD) is a common form of human prion disease with an incidence of one to two cases per million per year. This disease causes cerebral spongiform formation, neural loss, and astrogliosis, often with rapidly progressive dementia. This study investigated the association between gut microbiota and CJD.

Subjects were 10 patients with CJD and 10 gender and age-matched controls. Stool samples were collected for all patients, with DNA analysis completed. The subjects were assessed with the Mini Mental State Examination and the Beijing version of the Montreal Cognitive Assessment (MoCA). Cerebral spinal fluid was taken the morning after a 12 -hour fast to assess for 14-3-3 protein.

At the phylum level, Actinobacteria (p=0.03) and Fusobacteria (p=0.01) were in greater abundance in the CJD group than in the healthy controls. At the class level, increases in Fusobacteriia (p=0.01), Actinobacteria (p=0.03), and Alphaproteobacteria (p<0.01), and, conversely, decreases in Negativicutes (p=0.02) were noted in the CJD group as compared to healthy controls. At the family level, there was a higher abundance of Fusobacteriaceae (p=0.01), Succinivibrionaceae (p<0.01), and Enterococcaceae (p<0.01) in the CJD group. Further, Bifidobacteriaceae was greater in the CJD group (p=0.05).

At the genus level, enrichment in the abundance of Fusobacterium (p=0.01), Succinivibrio (p=0.02), Enterococcus (p<0.01), Ruminococcus gnavus (p< 0.01), Tyzzerella 4 (p=0.03) was seen in the CJD group. Conversely, decreases were observed in the abundance of Coprococcus 1, Lachnospiraceae ND3007, Roseburia, and Holdemanella in the CJD group as compared to the controls. Aeromonadales (p=0.02), its family Succinivibrionaceae (p=0.02), and genus Succinivibrio (p=0.02) were positively related to MoCA scores. The iron-reducing bacterium (clone HN70) was negatively related to patient survival time (p=0.03).

**Conclusion:** This study of patients with Creutzfeldt-Jakob disease found that the gut microbiota is altered in these patients as compared to controls.

Guo, Y., et al., Creutzfeldt-Jakob Disease: Alterations of Gut Microbiota. **Front Neurol**. 2022. Apr 15; 13:832599.

## FECAL SHEDDING OF SARS-COV-2

Recent reports have demonstrated severe acute respiratory syndrome coronavirus 2 (COVID-19) viral replication in both the lung and intestinal tissue. However, little is known about long-term viral shedding, especially in those with mild COVID-19. This study assessed the presence of SARS-CoV-2 in the GI tract and its relevance for short- and long-term health.

Data were obtained from individuals enrolled in a randomized, controlled study of peg-interferon lambda-1a (IFN-λ) for the treatment of mild to moderate COVID-19. In this study, fecal samples were collected at days three (zero to seven), 14 (eight to 21), 28 (22 to 35), 120 (75 to 165), 210 (166 to 255), and 300 (over 255 days) post-enrollment. Daily oropharyngeal (OP) swabs and blood draws were obtained up to day 300. Clinical specimens were paired with self-reported symptom data collected through questionnaires.

Among the 113 participants who provided stool samples, at six days after their diagnosis, 49.2% were found to have fecal COVID RNA. At four months, no oropharyngeal COVID RNA shedding was detected, while fecal shedding was found in 12.7%, falling to 3.8% at seven months. During the first month of the study, those who shed viral RNA in their stool were more likely to report nausea (OR

1.61), vomiting (OR 3.20), and abdominal pain (OR 2.05).

**Conclusion:** This study found that SARS-CoV-2 infects the gastrointestinal tract and that this infection can be prolonged in a subset of individuals with COVID-19.

Natarajan, A., et al. Gastrointestinal Symptoms and Fecal Shedding of SARS-Cov-2 RNA Suggest Prolonged Gastrointestinal Infection. **Med (N Y).** 2022 Apr 13. doi: 10.1016/ j.medj.2022.04.001. Epub ahead of print.

## EPIDEMIOLOGY AND OUTCOMES OF PERTHES DISEASE

Perthes Disease is an idiopathic avascular necrosis of a developing femoral head that results in long-term deformity of the hip. The etiology and appropriate treatments of this disease are not well understood. This prospective study explored the epidemiology and treatment of Perthes disease in the United Kingdom.

This prospective study identified a national cohort of patients, up to 14 years of age, with Perthes Disease, presenting in 63 Great Britain hospitals between April of 2016 and September of 2017. Data were collected from electronic health records, clinician notes, and post-surgical outcome measures. The data were obtained through a national surveillance program, the British Orthopaedic Surgery Surveillance (BOSS) study. Clinicians were asked to give details of factors thought to be associated with prognosis. Patient-reported outcome measures (PROMs) were collected at a subset of hospitals recruiting patients to the study.

Data were analyzed for 371 children. Of these, 117 (33.4%) hips were treated surgically and 233 (66.6%) non-surgically. Of the 117 hips treated surgically, 111 involved surgery to the bone, with most undergoing a "containment" osteotomy. Indications for containment surgery included age older than eight years and increased joint stiffness. Predictors of poor outcomes include female gender, age greater than six, and greater than 50% lateral column collapse. Surgery resulted in no significant improvement in two-year Stulberg classifications. Quality of life, as measured by the Pediatric Quality of Life Inventory, was very good/excellent in 14.3% at baseline and 41.4% at follow-up.

**Conclusion:** This study of patients with Perthes Disease found no evidence of improved radiologic outcomes after containment surgery.

Perry, D., et al. The British Orthopaedic Surgery Surveillance Study: Perthes' Disease: The Epidemiology and Two-Year Outcomes from a Prospective Cohort in Great Britain. **Bone Joint J**. 2022 Apr; 104-B(4): 510-518.

## PREDICTORS OF FAVORABLE OUTCOME AFTER LAMINECTOMY OR LAMINOTOMY

In patients with lumbar spine stenosis (LSS), one in three who undergo surgery experience little to no benefit from the surgery, and slightly more than 25% require revision surgery within one year. This study was designed to identify the physical variables associated with favorable post-operative outcomes following laminectomy or laminotomy surgery in patients with central LSS.

Subjects were adults scheduled for elective decompressive surgery for central LSS. While waiting for surgery, the eligible participants were randomized to either a six-week prehabilitation program or to hospital standard care. The prehabilitation group met with a kinesiologist for 30-minute sessions, three times per week to improve trunk stabilization, posterior chain muscle strength, and lower limb and hip muscle strength. A favorable outcome was defined as a decrease of ≥30% from baseline, both in leg pain intensity, as assessed with the Numerical Rating Scale (NRS) and in low back pain-associated disability, as measured with the Oswestry Disability Index (ODI).

Of the 58 participants, 60% achieved a favorable outcome. None of the included physical variables were found to be predictors of a favorable postoperative outcome based on leg pain intensity and low back pain-associated disability (trunk flexor muscle strength; OR 0.73), lumbar extensor muscle endurance (OR 1.09), total ambulation time (OR 1.00) lumbar active range of motion in extension (OR 1.08), and knee extensors muscle strength (OR 1.02).

**Conclusion:** This study of adults undergoing surgical decompression for lumbar spine stenosis found that none of the preoperative physical variables related to low back and lower limbs physical capacity, were associated with a favorable post-operative outcome.

Marchand, A., et al. Physical Predictors of Favorable Postoperative Outcomes in Patients Undergoing Laminectomy or Laminotomy for Central Lumbar Spinal Stenosis: Secondary Analysis of a Randomized, Controlled Trial. **Front Neurol.** 2022, April; 13: 848665.

## LOWER BODY RESISTANCE GARMENT DURING RUNNING

Wearable resistance (WR) is a method of placing an external load on the body during exercise to provide a greater training stimulus. This study examined the physiological and perceptual responses to steady-state running while wearing a novel lower body WR garment with 1-3% body mass applied resistance.

Subjects were males, 18 to 35 years of age with a body mass index of < 30 kg/m². Those assigned to the WR group received a garment which applied one to three percent body mass (BM) resistance at the hips and knees and the musculature, acting upon these joints, including the quadriceps, hamstrings, gluteals, and lower leg muscles. A crossover design was used, with subjects serving as their own controls. All participants completed a 2 × 10-minute steady-state run followed by a 10-minute passive recovery period, with concomitant monitoring of oxygen consumption ($VO_2$), heart rate (HR), and rating of perceived exertion (RPE), wearing either the resistance garment (an experimental group) or running shorts (a control group).

Compared to the control condition, during steady-state running, $VO_2$ and RPE were higher (by 4.5% and 7.7%, respectively) while wearing the resistance garment. These results did not reach statical significance. In addition, $VO_2$ and HR were reduced in the WR condition as compared to the control condition, again failing to reach significance.

**Conclusion:** This pilot study of healthy adults revealed that a wearable resistance garment increased $VO_2$ and perceived exertion during steady-state running and reduced $VO_2$ and heart rate during passive recovery, as compared to a control condition, although these differences failed to reach statistical significance.

Hoffman, S., et al. The Assessment of a Novel Lower Body Resistance Garment as a Mechanism to Increase the Training Stimulus during Running: A Randomized, Crossover Study. **BMC Sports Sci Med and Rehab.** 2022; 14: 63.

## SUBCLINICAL ATHEROSCLEROSIS AND COGNITIVE DECLINE

In 2018, dementia affected 50 million people worldwide. This is estimated to rise to 252 million people by the year 2050. Although atherosclerosis is thought to be associated with a decline in cognitive function, the association between subclinical atherosclerosis and dementia is unclear. This study investigated the association between subclinical atherosclerosis and cognitive function.

The Beijing Research on Aging and Vessel (BRAVE) is a community-based, prospective, longitudinal study investigating the contributions of vascular conditions to cognitive impairment and dementia. At baseline, in 2019, 1,554 residents, ages 40 to 80 years, were enrolled. Baseline assessments included carotid artery ultrasound (US), with intima-media thickness (IMT), carotid plaque, and brachial-ankle pulse wave velocity (ba-PWV). Global cognitive function was assessed with the Chinese version of the MoCA Basic (MoCA-BC). A verbal memory test (VMT) was used to assess memory through immediate and delayed free recall of a 10-word list.

A regression analysis found significant associations between increasing plaque numbers and all three cognitive assessment scores ($p<0.001$ for all). After adjusting for covariates, increased plaque was associated with worse MoCA ($p=0.006$) and VMT scores ($p=0.013$). Arterial stiffness was associated with MoCA-BC scores and semantic fluency.

**Conclusion:** This longitudinal study found that subclinical atherosclerosis is associated with a decline in cognitive abilities.

Lu, Y., et al. Association of Subclinical Atherosclerosis and Cognitive Decline: A Community-Based, Cross-Sectional Study. **BMJ**. 2022; 12: e059024. doi: 10.1136/ bmjopen-2021-059024.

## TENS FOR MOTOR RECOVERY AFTER STROKE

Upper limb impairment is a common sequela of stroke. A number of treatments have demonstrated some efficacy in improving the function of the affected arm. These include unilateral transcutaneous electrical stimulation (Uni-TENS) for activating the lesioned hemisphere, task-oriented training (TOT) of the affected extremity to improve arm-hand performance, and bilateral TENS (Bi-TENS) to reduce paresis. This study compared the effect of Bi-TENS+TOT with those of Uni-TENS+TOT, Placebo-TENS+TOT, and a control (C).

Subjects were 120 adults with a mean age of 61.5 years, recruited from stroke self-help groups. Those with upper extremity paresis were randomized to one of four treatment groups, including Bi-TENS+TOT, Uni-TENS+TOT, Placebo-TENS+TOT, or a control group. The subjects received 20, 60-minute treatment sessions, three sessions per week for seven weeks. The control group received no active treatment. The TENS was delivered at 100 Hz and applied in 0.2-ms square pulses at an intensity of twice the sensory threshold. The primary outcome measure was the Fugl-Meyer Assessment (FMA) of Upper Extremity (FMA-UE).

At follow-up, the Bi-TENS+TOT group showed greater improvement in FMA-UE scores than the other three groups (Uni-TENS+TOT ($p=0.004$), Placebo-TENS+TOT ($p=0.001$), and Control ($p=0.001$). In a post hoc analysis, the Bi-TENS+TOT group showed significantly greater improvement in FMA-UE scores than the Uni-TENS+TOT group at post-intervention ($p=0.005$). The between-group improvement in the Bi-TENS+TOT group was maintained at one- and three-month follow-up.

**Conclusion:** This study of patients with arm paresis due to stroke found that bilateral transcutaneous electrical nerve stimulation of the upper extremity, combined with task-oriented training, was superior to other combinations for improving upper extremity function.

Chen, P., et al. Bilateral Transcutaneous Electrical Nerve Stimulation Improves Upper Limb Motor Recovery in Stroke: A Randomized, Controlled Trial. **Stroke.** 2022, April; 53: 1134-1140.

## EFFECT OF A FOURTH DOSE OF BNT162B2 AGAINST OMICRON

During late December 2021, the prevalence of confirmed Omicron variant COVID-19 rose sharply. In response, authorities approved the administration of a fourth dose of the BNT162b2 vaccine (Pfizer–BioNTech). This study reports on the effectiveness of this fourth dose.

Subjects were 60 years of age or older and had received three or four doses of BNT162b2 vaccine (Pfizer–BioNTech). The rates of confirmed infections and severe infections were compared between participants who had received a fourth dose at least eight days prior (a four-dose group), those who had received only three doses (a three-dose group) and those who had received a fourth dose three to seven days earlier (an internal control group).

After receipt of the fourth vaccine dose, the adjusted rate of infection was lower by a factor of 2.0 as compared to the three-dose group, and lower by a factor of 1.8 compared to the internal control group. The adjusted rate of severe COVID-19 was 1.6 cases per 100,000 person-days after the fourth dose, 5.5 cases per 100,000 person-days in the three-dose group, and 3.6 cases per 100,000 person-days in the internal control group. Protection against confirmed infection with the Omicron variant of COVID-19 reached a maximum in the fourth week after vaccination.

**Conclusion:** This study found that patients who received a fourth dose of the BNT162b2 vaccine experienced added protection against confirmed infections and severe illness caused by the Omicron variant of COVID-19.

Meanar-on, Y., et al. Protection by a Fourth Dose of BNT162b2 against Omicron in Israel. **N Eng J Med.** 2022, May 5; 386(18): 1712-1720.

## AUTOMATED MONITORING OF COVID 19 AT HOME

Nearly 90% of patients with COVID-19 are asked to self-isolate and monitor their symptoms at home. This study, (COVID-Watch) assessed the efficacy of remote monitoring on the outcomes of patients with COVID-19.

This retrospective study included community-dwelling individuals who tested positive for COVID-19 as outpatients between March 23, 2020, and November 30, 2020. At the time of diagnosis, the patients were offered a chance to enroll in this study, initiated through an electronic health record order. Those who agreed, received twice-daily automated text messaging asking, “How are you feeling compared to 12 hours ago; better, same, worse?” Those replying “worse” received a follow-up question, “Is harder than usual for you to breathe; yes or no?” Those responding “yes” were

contacted within one hour by a clinician via telemedicine. The clinician provided advice for managing symptoms at home, prescribed medications, or redirected patients to the emergency department. The primary outcome variable was any-site mortality at 30 days after testing positive.

At 30 days, of the 3,488 patients enrolled in COVID-Watch, three (0.09%) died, compared to 12 of 4,377 (0.27%) who received usual care. Of the deaths, none in the COVID-Watch group occurred outside of the hospital, compared with six of those who received usual care. At 60 days, compared to the usual care group, there were 2.5 fewer deaths per 1,000 patients in the COVID-Watch group (p=0.002).

**Conclusion:** This study of outpatients diagnosed with COVID-19 found that an automated remote monitoring service reduced mortality.

Delgado, M., et al. Comparative Effectiveness of an Automated Text Messaging Service for Monitoring COVID-19 at Home. **Ann Intern Med.** 2022, Feb; 175(2): 179-190.

## FIXTTOE DEVICE FOR METATARSALGIA

Metatarsalgia is thought to result from repetitive overloading under the metatarsal heads. Multiple conservative treatments are available to treat this condition, including nonsteroidal anti-inflammatory drugs, physical therapy, plantar foot orthoses, metatarsal pads, and footwear modifications. This study assessed the efficacy of the Fixtoe Device (FTD), compared to traditional stabilizing tape (ST).

This cross-sectional study was conducted at a podiatry clinic in Madrid Spain. Subjects were 24 adults with no complaints of plantar pain. The main outcome measures were the maximal pressures assessed with a dynamic pressure measurement system, taken under four different conditions. These included barefoot, with ST of the second and third toe, and the FTD with (FTD-W) and without (FTD-W/O) a metatarsal pad.

Compared with the barefoot condition, plantar pressure decreased in all three experimental conditions ($p<0.0001$). Compared to ST, greater pressure reductions were noted in the FTD-W ($p<0.001$) and FTD-W/O ($p<0.001$). The pressure was least in the FTD-W condition, which was less than the FTD-W/O condition ($p=0.009$).

**Conclusion:** This study of healthy adults found that the Fixtoe device can reduce pressure under the metatarsal head better than traditional stabilizing tape.

Ruiz-Ramos, M., et al. Effectiveness of the Fixtoe Device in Plantar Pressure Reduction: A Preliminary Study. **BMC Musculoskelet Disord.** 2022; 23: 475.

## MEDICAL LITIGATION AND PHYSICIAN LIFE SATISFACTION

Medical negligence litigation has been criticized for being emotionally distressful for patients and doctors. Accumulating research demonstrates that poor doctor well-being adversely affects doctors' clinical performance and decision-making, which can directly affect the quality of patient care. This study assessed the relationship between self-reported medical negligence claims and doctor health and satisfaction scores.

Data were obtained from Medicine in Austrailia: Balancing Employment and Life (MABEL), a longitudinal panel survey of doctors' working conditions, job satisfaction, work-life balance, health, and life satisfaction. The study comprised 11 annual waves that were collected between 2008 and 2018. Self-rated health was determined through the survey question," In general, would you say your health is excellent, very good, good, fair, or poor?" This tool is a strong predictor of mortality. The key exposure variable was being a defendant in a medical negligence claim. The responses were adjusted for the effect of job satisfaction. The authors constructed four variables that were included in the models, high job demands, low job control, and poor social support.

Of the 15,105 doctors surveyed, 885 (5.9%) reported having been sued at least once. Both self-rated health and self-rated life satisfaction declined for all doctors over time at each wave of inquiry ($p<0.001$). However, no significant association was found between self-reported health and litigation.

**Conclusion:** The Balancing Employment and Life (MABEL) study found that life satisfaction in physicians has declined over time, with this decline unrelated to being a defendant in a lawsuit.

Bradfield, O., et al. Medical Negligence Claims and the Health and Life Satisfaction of Australian Doctors: Prospective Cohort Analysis of the MABEL Survey. **BMJ Open.** 2022; 12: e059447. doi: 10.1136/BMJ open-2021-059447.

## YOGA FOR PAIN FROM LUMBAR DISC HERNIATION

Lumbar disc herniation (LDH) is one of the most common causes of neuropathic pain. As several studies have reported that yoga may be effective in improving pain disability in individuals with LBP, this study investigated the effect of a stretch and strengthening-based yoga exercise program on neuropathic pain.

Subjects were female adults, 18 to 50 years of age, with confirmed disc herniation between L4 and S1 and with lumbar radicular pain for at least three months. Those participants were randomly assigned to a control group or a yoga group. All participated in a patient education program. Yoga exercise was taught and performed for one hour, twice weekly for 12 weeks. Outcome measures included the DN4 (Douleur Neuropathique 4), measure of neuropathic pain, the Leeds Assessment of Neuropathic Symptoms and Sign (LANSS), the Oswestry Disability Index (ODI), passive knee extension (PKE), and a visual analog scale (VAS), all administered at baseline and at one, three, and six months.

At three and six months, compared to the control group, better improvement was noted in the yoga group in scores on the DN4, LANSS, ODI, and VAS ($p<0.001$ for all comparisons).

**Conclusion:** This study of patients with lumbar disc herniation and neuropathic pain found that stretch and strength-based yoga can be effective for improving pain and function.

Yildirim, P., et al. The Effect of a Stretch and Strength-Based Yoga Exercise Program on Patients with Neuropathic Pain Due to Lumbar Disc Herniation. **Spine.** 2022, May 15; 47 (10):711-719.

## ERENUMAB IN CHRONIC MIGRAINE

Studies have shown that chronic migraine is an underdiagnosed condition, with only approximately 20% of patients having received a correct diagnosis. The identification of the role of Calcitonin Gene-Related Peptide (CGRP) in migraine has led to the development of treatments directed at the CGRP pathway. These include the small molecule

CGRP receptor antagonists, gepants and mABs. Erenumab is a CGRP mAB targeting the canonical CGRP receptor, with proven efficacy in migraine prevention. This study reviewed the outcomes of patients seen in real-world tertiary settings.

Participants were consecutive adult patients presenting with a diagnosis of chronic migraine who had failed to respond at least three other preventative therapies. Those subjects were offered monthly (every four weeks) erenumab, as a 70 mg subcutaneous injection, for three months (12 weeks). If their monthly migraine days (MMD) did not improve by 50%, they were offered erenumab, 140 mg subcutaneous monthly, for a further three months. Data collection included monthly headache days (MHDs), the Migraine Disability Assessment Scale (MIDAS), monthly migraine days (MMDs), acute treatment days (RxDs), and adverse events (AEs). A positive response was defined as an improvement in MMDs of at least 50% at month three after treatment initiation compared to baseline MMDs.

The median MMDs were significantly improved at three and six months ($p<0.001$ for both comparisons). The MMDs for 30% and 50% responder rates at three months were 53% (n=38) and 36% (n=26), respectively. Data were available for 42 patients at six months. Fifty percent (n=21) of that cohort had their monthly erenumab escalated to 140 mg. At six months, significant improvement was noted in MHDs, MMDs, and RxDs, and in HIT-6 (Head Impact Test-6) and MIDAS scores ($p<0.001$, $p<0.001$, $p<0.001$, $p=0.002$ and $p=0.004$, respectively).

**Conclusion:** This uncontrolled study of patients with chronic, recalcitrant migraine headaches found that erenumab, at 70mg or 140 mg, was effective in reducing monthly migraine days.

Khalil, M., et al. Erenumab in Chronic Migraine: Experience from a U.K. Tertiary Centre and Comparison with Other Real-World Evidence. **Euro J Neurol.** 2022 Apr 21. doi: 10.1111/ene.15364.

## TRANSCRANIAL FOCUSED ULTRASOUND FOR ALZHEIMER'S DISEASE

In patients with Alzheimer's Disease (AD), the hippocampus is known to be one of the most affected brain structures. Animal models have revealed that low-intensity transcranial focused ultrasound (tFUS) can increase the permeability of the blood-brain barrier (BBB) and allow anti-amyloid beta antibodies to reach the brain. This human study examined the efficacy of tFUS to the hippocampus on BBB disruption and cognitive function in patients with AD.

Subjects were six adults, 65 to 85 years of age, diagnosed with probable AD. Baseline assessments included cognitive assessment, brain magnetic resonance imaging (MRI), computed tomography, and positron emission tomography (PET) scans. The regional cerebral metabolic rate of glucose (rCMRglu) was measured in the hippocampus. The participants received low-intensity tFUS, applied to the right hippocampus immediately after intravenous injection of microbubble ultrasound contrast agents (MB). Immediately and one day after the sonication, MRI scans were acquired to detect transient blood-brain barrier opening and closing, respectively. Follow-up neuropsychological tests and PET scans were conducted within one month. The primary outcome variable was the change in neuropsychological test scores after sonication. Outcome measures also included associations between cognitive changes and rCMRglu.

After tFUS, immediate recall ($p=0.03$) and recognition memory ($p=0.02$) were significantly improved. In addition, PET analysis showed an increased level of rCMRglu in the right hippocampus ($p=0.001$). These increases in hippocampal rCMRglu were significantly associated with improvement in recognition memory ($p= 0.02$).

**Conclusion:** This small study of patients with Alzheimer's Disease found that transcranial focused ultrasound directed at the hippocampus enhanced hippocampal glucose metabolism and improved memory, without adverse events.

Jeong, H., et al. Short-Term Efficacy of Transcranial Focused Ultrasound to the Hippocampus in Alzheimer's Disease: A Preliminary Study. **J Personalized Med**. 2022, 12, 250. Https://Doi.Org/10.3390/Jpm12020250.

## INTENSIVE BLOOD PRESSURE CONTROL AND MILD COGNITIVE IMPAIRMENT

The Systolic Blood Pressure Intervention Trial (SPRINT) demonstrated a significant reduction in the occurrence of MCI in adults with hypertension who were assigned to intensive systolic blood pressure (BP) control (<120 mm Hg) compared with those assigned to standard BP control (<140 mm Hg). This study examined the effects of intensive BP treatment on subtypes of MCI.

Participants had a mean age of 67.9 years and a systolic blood pressure (SBP) of between 130 mmHg and 180 mmHg. The subjects were randomized to a SBP goal of <120 mm Hg (intensive treatment, N=4,678) or a SBP goal of <140 mm Hg (standard treatment, N=4,683). Assessments at baseline and at follow-up included a test of global cognitive function with the Montreal Cognitive Assessment (MoCA), verbal learning and memory (Logical Memory I and II), and processing speed (Digit Symbol-Coding). The data were used to assign subjects to groups, including no cognitive impairment, MCI, or probable dementia.

Over a median follow-up period of five years, 640 participants progressed from normal cognition to MCI, with a greater risk in the standard treatment group (Hazard ratio (HR) 0.81). The subtypes of those converting to MCI were amnestic multi-domain (69.2%) and amnestic single domain (16.9%). Participants in the intensive treatment group less frequently transitioned from normal cognition to MCI (8.4% vs. 9.4%) and less frequently progressed from MCI to probable dementia (4.6% vs. 7.1%) than the standard treatment group.

**Conclusion:** Using data from the SPRINT trial, researchers found that blood pressure management to a goal of SBP of <120 mmHg reduced the risk of progression from normal cognition to MCI and from MCI to dementia.

Gaussoin, S., et al. Effect of Intensive Blood Pressure Control on Subtypes of Mild Cognitive Impairment and Risk of Progression from SPRINT Study. **J Am Geriatr Soc.** 2022, May; 70(5): 1384-1393.

## MUSIC BETWEEN SETS OF RESISTANCE EXERCISE

While there is evidence of the benefits of listening to music before resistance exercise, virtually no research exists that demonstrates the effect of listening to music solely during rest periods. This study examined the effects of self-selected respite music on upper-body resistance exercise.

The subjects were assessed for bench press one-repetition maximum (1RM). After a warm-up, each began 1RM bench press with the barbell weight progressively increased by 2.5 to 20.0 kg for each attempt,

(Continued from page 2)

Mary Wilson
*Temple Univ., Philadelphia, PA*

*Peter Lee, M.D.
Matthew Ibrahim, M.D.
Theodora Wong, M.D.
*UC Irvine, Irvine, CA*

*David Quan, M.D.
J Christian Belisaria, D.O.
Tejas Shah, M.D.
*Univ. of Penn, Philadelphia, PA*

*Kelsey Lau, D.O.
Ryan Flowers, D.O.
Michael Burke, M.D.
Sierra Haq, M.D.
*Univ. of TX SW Med Ctr., Dallas, TX*

*Trevor Ellico, D.O.
Daniel Nguyen, M.D.
Jessica Sher, M.D.
*Univ. of Washington, Seattle, WA*

*Peter Park, M.D.
*Alan Stupnitsky, M.D.
Brian Kang, M.D.
Amelia Ni, M.D.
*Washington Univ, 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*.**

continuing to failure. Participants were asked to move the bar at their maximum velocity. Each attempt was separated by two minutes of rest.

Ten resistance-trained males participated in two bench press trials. In a crossover design, during the rest period, the subjects either experienced no music (NM) or listened to self-selected music (M) with a tempo of ≥120 BPM. The rate of perceived exertion (RPE) and motivation were assessed with 100 mm visual analog scales. The velocity of the lifts was measured with a linear transducer.

The mean velocity was higher in the M group than in the NM group during set two ($p=0.009$) and set three ($p= 0.048$). In addition, motivation was higher in the M group than in the NM group following set two ($p=0.005$) and set three ($p<0.001$). No changes in RTF or RPE were noted between conditions ($p>0.05$).

**Conclusion:** This study found that, during resistance training, listening to music during rest periods improved the velocity of the lifts and the motivation of the participant.

Lehman, J., et al. Effects of Respite Music on Repeated, Upper-Body, Resistance Exercise. **Int J Exerc Sci.** 2022; 15 (7): 79-87.

***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 Rehabilitation 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 endorsed 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 (417) 779-9101.**

**ISSN # 1081-1303**

EXPANDING THE FRONTIER OF REHABILITATION SCIENCE IN RESEARCH, TEACHING, AND PATIENT CARE