

# REHAB IN REVIEW

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Volume 31 Number 1

Published by Physicians  
In Physical Medicine and Rehabilitation

January 5, 2023

## COVID EFFECT ON LIFE EXPECTANCY IN THE UNITED STATES

The National Center for Health Statistics (NCHS) of the US collects data through the National Vital Statistics System and publishes annual and decennial national life tables based on vital statistics data. Using these data, this study assessed the effects of excess mortality related to the COVID-19 pandemic on life expectancy.

Provisional life expectancy estimates for 2021 were based on death certificates received by the NCHS as of April 24, 2022. Using these data life expectancy estimates were calculated.

In 2021, US life expectancy at birth was 76.1 years, the lowest it has been since 1996. For males, life expectancy at birth in 2021 was 73.2 years, a decline of one year compared to 2020. For females, during that same time, life expectancy declined by 0.8 years. Excess deaths due to COVID-19 and other causes in 2020 and 2021 led to an overall decline in life expectancy between 2019 and 2021 of 2.7 years for the total population, including 3.1 years for males, and 2.3 years for females. By ethnic group, years of life expectancy in 2019 and 2021 were 71.8 and 65.2 for American Indians and Alaskan Natives, 74.8 and 70.84 for Black Americans, 78.8 and 76.4 for White Americans, 81.9 and 77.7 for Hispanic Americans, and 85.6 and 83.5 for Asian Americans.

**Conclusion:** This study demonstrates a significant decline in life expectancy in the United States between 2019 and 2021, primarily caused by excess deaths due to COVID.

Arias, E., et al. Provisional Life Expectancy Estimates for 2021. National Center for Vital Statistics (US) Vital Statistics Rapid Release. 2022. <https://stacks.cdc.gov/view/cdc/118999>.

## BRAIN NEURON AND GLIAL DAMAGE DURING THE ACUTE COVID-19 WITHOUT NEUROLOGIC MANIFESTATIONS

Several studies have suggested that, during acute COVID-19, patients with neurological manifestations may have elevated biomarkers suggestive of neuronal and glial damage. This study reviewed the prevalence of elevated levels of neurofilament light chain (sNfL) and glial fibrillar acidic protein (sGFAP) in patients with COVID-19 who do not display neurological manifestations.

This prospective study was performed at the Siena University Hospital between October, 2021 and April, 2022. The subjects were patients who were hospitalized with acute COVID-19, who had no history of neurologic diseases, and who did not develop neurologic symptoms during hospitalization. Serum samples were collected at admission with sNfL and sGFAP concentrations measured. Neurologic assessments were performed weekly. Correlations between sNfL and sGFAP levels and demographic measures and other laboratory values were assessed.

Data were analyzed for 148 hospitalized patients with COVID-19 without clinical neurological manifestations, 53 patients with interstitial pulmonary fibrosis (IPF) and 108 healthy controls (HCs). As expected, log<sub>10</sub> sNfL levels and log<sub>10</sub> sGFAP were correlated with age in all three groups. Adjusting for age and sex, levels of sNfLs and sGFAP were higher in patients hospitalized with COVID-19 who had no neurologic symptoms than in patients with IPF ( $p < 0.001$  for both comparisons) and HCs ( $p < 0.001$  for both comparisons).

**Conclusion:** This study of patients hospitalized with COVID-19 with no neurologic manifestations found that these patients had elevated biomarkers of neuronal and glial damage.

Plantone, D., et al. Brain Neuronal and Glial Damage During Acute

COVID-19 Infection in Absence of Clinical Neurological Manifestations. *J Neurol, Neurosurg Psych.* 2022, 93: 1343-1348.

## ANXIETY DISORDERS AND DEMENTIA

Previous studies have demonstrated that anxiety disorders, which are common in adults > 65 years of age, are associated with an increased risk of all-cause dementia. This study assessed the efficacy of intervention for anxiety disorders through psychological intervention for the risk of dementia.

This prospective cohort study used data from a nationally provided psychological intervention service in England (Improving Access to Psychological Therapies (IAPT)). Data from the IAPT were compared to other routinely collected health data in England. Participant inclusion criteria were  $\geq 65$  years of age, those with a probable anxiety disorder, and without a diagnosis of dementia. The primary outcome was the development of new dementia.

The study sample comprised 111,958 people with a median follow-up of 3.12 years. Of these, 4.2% were diagnosed with dementia within one year. Of those who attended, 5.1% of those with anxiety improvement after IAPT intervention were subsequently diagnosed with dementia, compared to 3.9% of those whose anxiety did not improve. In the adjusted model, improvement in anxiety symptoms during intervention was associated with a reduced risk of dementia with the hazard ratio of 0.83 ( $p < 0.0001$ ).

**Conclusion:** This English study of adults  $\geq 65$  years of age found that improvement of anxiety after psychological intervention was associated with a reduced risk of the development of dementia.

Scott, J., et al. Associations Between Psychological Intervention for Anxiety Disorders and Risk of Dementia: A Prospective Cohort Study Using National Healthcare Records Data in

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England. **Lancet Healthy Longev.** 2022: doi.org/10.1016/ S2666-7568 (22)00242-2.

**COVID-19 MODIFICATIONS FOR NFL ATHLETES AND REGULAR SEASON INJURIES**

During the COVID-19 pandemic, the National Football League (NFL) altered off-season commitments to virtual activity, with athletes forced to train with limited personal contact and resources. This study assessed the rate and severity of injuries associated with this change in policy.

The NFL public injury database was reviewed online for all injuries occurring during the 2017-2020 seasons. In addition, the 2020 injury report was pulled for all teams. Injury data were reported as injury incidents per athlete exposure, with an injury defined as a physical ailment resulting in a player's missing a game during the NFL regular season. A season-ending injury was defined as one resulting in a player's not being reactivated after being placed on the injured reserve. An athlete exposure was defined as one player participating in one game or practice.

The incidence of injuries resulting in an athlete's missing a game during the 2020 season was 9.4 injuries per 1,000 athletic exposures, as compared to 7.6 per 1,000 athletic exposures during the previous three seasons. When comparing injuries per 1,000 athletic events, the 2020 season injury rate increased until week nine when it peaked. During the 2020 season, there were 237 season-ending injuries, compared to an average of 287 during the 2017-2019 seasons.

**Conclusion:** This study of the National Football League found a 24% increase in injuries during the 2020 season when COVID-19 restrictions were in place, as compared to the previous three seasons.

Bailey, E., et al. COVID-19 Modifications of Offseason and Preseason Training for NFL Athletes Are Associated with Increased Risk of Regular Season Injuries. **Phys Sportsmed.** 2022; 50(6): 541-545.

**NEW ONSET MUSCULOSKELETAL SYMPTOMS IN SEVERE COVID-19**

Among patients infected with the COVID-19 virus, the most severe complication is pneumonia. As the musculoskeletal system is a known

target for viral infections, this study assessed the incidence of new musculoskeletal conditions among patients hospitalized with COVID-19.

Data were obtained from the Assistance Publique-Hôpitauxde Paris (AP-HP) Clinical Data Warehouse-COVID (CWD-COVID) observational database, which includes hospitalization-related data from the electronic medical records (EMR) of patients admitted to the 39 hospitals of the AP-HP. Potential subjects were patients hospitalized for acute COVID-19 between March 2020 and December 2020 with no past history of inflammatory musculoskeletal conditions. New onset musculoskeletal conditions were identified through ICD10 codes on discharge reports or electronic medical records up to 90 days after COVID-19 diagnosis.

Data were available for 15,601 patients, of whom 1,370 (8.8%) developed at least one new musculoskeletal symptom. The most prevalent of these were low back pain in 32.9%, arthralgia in 29.9%, radicular pain in 20.2%, and synovitis/ arthritis in 22.8%. The median time from COVID-19 diagnosis to musculoskeletal symptom onset was 10 days.

**Conclusion:** This study of patients hospitalized for COVID-19 found that nine percent had new onset musculoskeletal conditions in the three months following their discharge.

Molto, A., et al. Evaluation of The Prevalence of New-Onset Musculoskeletal Symptoms in Patients Hospitalized for Severe SARS Dash-CoV-2 Infection during the First Two COVID Waves in France: A Descriptive Analysis of the Clinical Data Warehouse of 39 Hospitals in France. **Joint Bone Spine.** 2022, Nov;89(6):105450.

**HEARING LOSS AND DEVELOPMENT OF DEMENTIA**

The association between hearing loss and dementia has received particular attention within the past decade. This study explored the association between hearing loss and the risk of dementia.

Data were obtained from the Mayo Clinic Study of Aging (MCSA), a prospective population-based study. The participants were 5,766 patients ≥50 years of age at the time of enrollment between 2004 and 2019 who had been referred for hearing evaluation. Of these, 1,200

underwent assessment with formal pure tone and speech audiometry in a sound attenuated booth within five years of enrollment. The patients were also evaluated with neuropsychological testing at enrollment and every 15 months. Air induction and bone conduction pure tone averages (PTAs) were calculated.

The mean age of the subjects at enrollment was 79 years. Of the 1,200 subjects, 207 developed dementia during follow-up. Hearing loss was not predictive of the development of dementia. However, both PTA and word recognition scores were associated with worse performance on cognitive testing over time. Informant-based hearing difficulties assessed by the participants' partners were also significantly associated with the development of dementia, with a hazard ratio of 1.95.

**Conclusion:** This prospective population-based study found that subjective informant-based hearing difficulties were associated with the development of dementia, while objective measures were predictive of poorer performance on cognitive testing over time.

Marinelli, J., et al. Association Between Hearing Loss and Development of Dementia Using Formal Behavioral Audiometric Testing Within the Mayo Clinic Study of Aging (MCSA): A Prospective Population-Based Study. *Lancet Healthy Longev.* 2022, December; 3 (12); e817-e824.

### TINNITUS TREATMENT THROUGH NERVE BLOCKS

Recent data have demonstrated that tinnitus perception is associated with hyperactivity of the auditory cortex and altered functional connectivity in the brain. This study explored the efficacy of a treatment method combining nerve blocks and nerve stimulation.

The subjects were 63 patients with intractable or recurrent tinnitus. The subjects received either unilateral or bilateral nerve blocks with 0.5% lidocaine administered to the facial nerve (7th cranial nerve, CN VII) and auriculotemporal nerve (a branch of the trigeminal nerve—CN V). The authors then stimulated the facial and auriculotemporal nerves by placing the needles without manual or electrical stimulation for 20–40 minutes. The procedure was performed 2–3 times a week for the

first 2–3 weeks. After confirming a marked continuous decrease or disappearance of tinnitus, the treatment was reduced to 1 or 2 times per week and then once every 1 or 2 weeks. The patients were followed for one year. The primary outcome was the tinnitus VAS (T-VAS).

The T-VAS score was reduced from 7.13 at baseline to 0.6 at follow up in the subacute group and from 7.73 at baseline to 3.25 in the chronic group ( $p < 0.001$  for both). After the 4<sup>th</sup> treatment, the mean T-VAS was reduced from 7.13 at baseline to 2.4 at follow-up in the subacute group and from 7.73 at baseline to 3.25 in the chronic group ( $p < 0.001$  for both).

**Conclusion:** This study of patients with recalcitrant tinnitus found that combining modified nerve blocks in auditory and nonauditory nerve stimulation could improve the symptoms of tinnitus.

Sirth, S., et al. Integrative Treatment for Tinnitus Combining Repeated Facial and Auriculotemporal Nerve Blocks with Stimulation of Auditory and Non-Auditory Nerves. *Front Neurosci.* 2022. 10.3389/fnins.2022.758575.

### IS HIGH CHOLESTEROL ASSOCIATED WITH NECK PAIN?

Studies have shown that atherosclerosis is associated with degenerative disc disease. Other studies have shown associations between neck pain and hypercholesterolemia. This retrospective cross-sectional analysis explored the relationship between hypercholesterolemia and neck pain.

Data were obtained from the Medicare Expenditure Panel Survey (MEPS) a nationally representative survey of US adults conducted by the agency for Healthcare Research and Quality. The subjects were 1,049 adults who completed the neck pain diagnosis items on the questionnaire. Data were also recorded for participants' specific socioeconomic and lifestyle characteristics, body mass index, tobacco use, education level and occupation.

The prevalence of neck pain was 21%, with neck pain being more prevalent among current everyday smokers, those with lower median incomes, hypertension, diabetes, alcohol abuse, depression, and hypercholesterolemia. In the fully adjusted multivariate model, those with alcohol abuse (Odds Ratio (OR 1.99)), depression (OR 3.81) and

hypercholesterolemia (OR 1.46) were at an increased risk for neck pain.

**Conclusion:** This cross-sectional nationally representative study found that neck pain was associated with alcohol abuse, depression and hypercholesterolemia.

Ahorukomeye, P., et al. Association Between Hypercholesterolemia and Neck Pain in a Cross-Sectional Population-Based Study. *Spine.* 2023, Jan 15;48(2):137-142.

### FATIGUE AND INFLAMMATION IN RHEUMATOID ARTHRITIS

Previous studies involving patients with rheumatoid arthritis (RA) have suggested that higher levels of inflammation, as measured by the Disease Activity Scale (DAS-44), are associated with higher levels of fatigue. This study assessed the effect of inflammation on fatigue in the pre arthritis phase of rheumatoid arthritis (RA).

Subjects were recruited from among patients with clinically suspect arthralgia (CSA), who had arthralgia of the small joints for less than one year, and were considered suspicious for progression to RA. The 600 patients with CSA were followed for two years for the development of clinical RA. Fatigue was assessed at every visit using a scale from zero to 100 in response to the question "How tired were you the last day?". Inflammation was measured using the DAS 44- CRP. Labs were drawn to assess the anti-citrullinated protein antibody (ACPA). The patients who progressed to RA (P-RA) were analyzed separately from those who did not progress (N-RA).

At a median follow-up of 25 months, 88 of the 600 patients developed RA. Among the P-RA group, inflammation was associated with the severity of fatigue at the time of initial presentation ( $p < 0.01$ ). Significantly higher levels of fatigue were found in ACPA-negative P-RA group compared to the ACPA-positive P-RA group.

**Conclusion:** This study of patients with clinically suspect arthritis found that the complaint of fatigue was more explained by inflammation at CSA-onset than at RA-diagnosis, suggesting a phase dependent relationship between inflammation and fatigue.

Khidir, S., et al. The Course of Fatigue During the Development of Rheumatoid Arthritis and Its Relation with Inflammation: A Longitudinal

### DAILY STEP COUNT AND INCIDENT DEMENTIA

In a recent meta-analysis, 6,000 to 8,000 steps per day were found to be associated with a reduced risk of all-cause mortality. This study reviewed the association between step count and incident dementia.

Potential subjects were identified through the United Kingdom Biobank with 103,684 accepting an invitation to wear an activity accelerometer on their dominant wrist 24 hours a day seven days a week. Of these, 78,430 participants ages 40 to 79 years recorded at least three valid days of accelerometer wear. Eligible subjects were free of cardiovascular disease, cancer or dementia at baseline. Incident dementia was identified through linkage with inpatient hospitalization or primary care records, or when recorded as the underlying or contributory cause of death in the death registers. The data were reviewed to calculate the mean dose for maximum risk reduction of dementia, and the minimal dose at which at least a 50% reduction of risk was observed.

Over a median follow-up of 6.9 years, 866 developed dementia at a mean age of 68.3 years. A nonlinear association was found between daily steps and dementia where the optimal dose was found to be 9,826 steps (Hazard Ratio (HR) 0.49) and a minimum dose of 3,826 steps (HR, 0.75).

**Conclusion:** This prospective study of community-dwelling adults 40 to 79 years of age found that, to reduce the risk of dementia by at least 50%, 3,820 steps per day are needed with the optimal risk reduction found at 9,826 steps.

del Pozo Cruz, B., et al. Association of Daily Step Count and Intensity with Incident Dementia in 78,430 Adults Living in the UK, **JAMA Neurol.** 2022, October; 79(10): 1059-1063.

### HYALURONATE INJECTION VERSUS PHYSICAL THERAPY FOR SHOULDER TENDINOPATHY

Shoulder pain is a common and debilitating problem, for which a variety of non-surgical interventions are recommended. Studies have suggested that hyaluronic acid (HA) may reduce scar formation through

anti-fibrotic and anti-inflammatory effects. This study compared the efficacy of physical therapy (PT) with two different molecular weights of HA; low molecular weight (LMW) and high molecular weight (HMW).

This triple-blinded trial included patients with a diagnosis of shoulder tendinopathy, randomized to receive PT, LMW-HA or HMW-HA. The PT group received 20 minutes of superficial heat, followed by transcutaneous electrical nerve stimulation and pulsed ultrasonography, stretching, and progressive strengthening exercises. The LMW-HA group received 20 mg (2 mL) of HA (500-700 kDa). The HMW-HA group received 20mg (2 mL) of HA (>200 kDa). The primary outcome was a visual analog score (VAS) for pain.

Data were analyzed for 79 patients. Comparing baseline with three-month VAS scores, greater improvement was noted in the HMW-HA group than in the other two groups for pain at night ( $p < 0.001$ ), during activity ( $p < 0.001$ ), and at rest ( $p < 0.001$ ). Both HA preparations were more effective than PT for controlling pain, decreasing disability, increasing range of motion, and improving the quality of life (all  $p < 0.05$ ). At six months, the analysis of variance tests found no differences between the three groups in improvement in pain at night, and at rest. At six months, pain during activity was most improved in the HMW-HA group, with significance reached compared to PT ( $p = 0.014$ ).

**Conclusion:** This study of patients with shoulder tendinopathy found that, compared to physical therapy, low- or high-molecular weight hyaluronate preparations provided more effective pain relief.

Esmaily, H., et al. Subacromial Injections of Low- or High-Molecular-Weight Hyaluronate Versus Physical Therapy for Shoulder Tendinopathy: A Randomized Triple-Blind Controlled Trial. **Clin J Sport Med.** 2022, September; 32(5):441-450.

### MODIFIABLE RISK FACTORS IN MID TO LATE LIFE AND LONGEVITY

In the United States, life expectancy was 78.9 years in 2019, lower than that in other high-income countries. Modifiable risk factors which can be altered by specific lifestyle adjustments are known to have a major effect on mortality. This study examined the associations

between patterns of midlife to late-life modifiable risk factors and longevity.

Data were obtained from the Nurses' Health Study (NHS) starting in 1984 and the Health Professionals Follow-up Study (HPFS) starting in 1986. A self-administered questionnaire was completed, at baseline and every two years with questions about body mass index, smoking status, alcohol intake (two drinks per day for men and one per day for women), quality of diet, and physical activity, measured as energy expenditure in metabolic equivalent task hours (MET hours/ week). Scores on the Alternative Healthy Eating Index were scored from zero to 100. Longevity was defined as living  $\geq 85$  years. For each risk factor, three patterns (patterns with high, medium, and low values) and three trajectories of change in the risk factor (patterns with increase, no change, and decrease in the factor from baseline) were assumed, creating nine patterns: high-stable, high-increase, high-decrease, medium-stable, medium-increase, medium-decrease, low-stable, low-increase, and low-decrease. These were compared to longevity.

The analysis included 85,346 participants with a mean age of 56 years. Living to an age of  $\geq 85$  years was more likely among participants with a low stable pattern for body mass index, those with a medium increase pattern for physical activity, those with a medium stable pattern for alcohol intake, those who never smoke, and those with a high increased pattern for quality of diet.

**Conclusion:** This longitudinal study found that maximum longevity was achieved among those who maintained a normal body index, never smoked, ate a healthy diet, had physical activity levels that met public health recommendations through midlife and late life, and adhered to alcohol consumption recommendations.

Ding, M., et al. Associations Between Patterns of Modifiable Risk Factors in Midlife to Late Life Longevity: 36-Year Prospective Cohort Study. **BMJ Med.** 2023;1(1): <http://dx.doi.org/10.1136/bmjmed-2021-000098>.

### THROMBOLYSIS FOR ISCHEMIC STROKE IN NONAGENARIANS

Current intravenous thrombolysis (IVT) guidelines recommend IVT for patients 80 years of age or older with ischemic stroke. However, the

probability of receiving this treatment decreases with increasing age and is lowest among patients 90 years of age or older. This study focused on this oldest age group to determine the safety and efficacy of IV thrombolysis.

Data for this study were prospectively collected for the Thrombolysis in Ischemic Stroke Patients (TRIST) study, conducted at 20 separate centers. Subjects were patients presenting to the hospital with symptoms of acute ischemic stroke, with data collection including the National Institute of Health Stroke Scale (NIHSS) score before treatment, as well as medical and functional outcomes. Intracranial hemorrhage was monitored by follow-up using computed tomography or magnetic resonance imaging. Early functional improvement was a secondary outcome defined as any decrease in the NIHSS score after 24 hours as compared to baseline.

Data were available for 16,974 patients including 978 patients  $\geq 90$  years of age. After adjusting for potential confounders, the probability of sICH and the probability of early functional improvement did not differ significantly between patients  $\geq 90$  years of age and those in the younger cohort. The probability of death and poor functional outcome remained significantly higher in patients  $\geq 90$  years or older, though this was not correlated with IVH.

**Conclusion:** This study of patients admitted with acute ischemic stroke did not find that age should be a reason for withholding intravenous thrombolysis.

Altersberger, V., et al. Intravenous Thrombolysis in Patients with Ischemic Stroke Aged  $\geq 90$  Years: A Cohort Study from The TRISP Collaboration. *Stroke*. 2022, December; 53 (12): 3557-3563.

### PREVALENCE OF NEUROLOGIC COMPLAINTS IN US EMERGENCY DEPARTMENTS

Data concerning the prevalence of neurologic complaints at the population level are scarce. This study reviewed the number and characteristics of patients presenting to emergency departments (EDs) in the United States (US) with neurologic symptoms.

Data were obtained from the National Hospital Ambulatory Medical Care Survey (NHAMCS) from 2016 to 2019. This cross-sectional annual survey is a nationally representative sample of EDs and nonfederal

hospitals, constituting 10% of US EDs. From these data were identified all patients 18 years of age or older with a neurologic complaint as their primary symptom and reason for visiting the ED. Data gathered also included demographic, clinical regional, and facility-level variables.

From 7,264 sampled cases, it was estimated that 55.8 million patients presented to EDs of the US from 2016 to 2019. Of these, 60% were female and 40% were younger than 45 years of age. The most common complaints were nonspecific, including headache, vertigo/dizziness, and general weakness. A serious neurologic condition was suspected in 10.1%, with stroke being the most frequent suspicion.

**Conclusion:** This study, using a representative sample of emergency department visits in the US from 2016 to 2019, found that 8.4% of the visits were for neurologic complaints, with headaches being the most frequent of these.

Lieberman, A., et al. Prevalence of Neurological Complaints in US Emergency Departments, 2016-2019. *JAMA Neurol*. Published online December 12, 2022. doi:10.1001/jamaneurol.2022.4531.

### ENDOVASCULAR THROMBECTOMY VERSUS MEDICAL MANAGEMENT BEYOND 24 HOURS OF LAST KNOWN WELL

Endovascular thrombectomy (EVT) has revolutionized the management of acute ischemic stroke (AIS) due to large vessel occlusion. However, no randomized trial evidence exists for the effectiveness of EVT beyond 24 hours. This retrospective study assessed the functional and safety outcomes of EVT compared with medical management (MM) in patients presenting beyond 24 hours of their last known well (LKW).

This retrospective, observational, cohort study included adults with AIS due to large vessel occlusion in the internal carotid artery or M1 or M2 segments of the middle cerebral artery who received treatment beyond 24 hours of stroke onset. Endovascular therapy was administered by a stent retriever, aspiration device, or a combination. Best MM was provided to all patients. The primary outcome variable was functional independence, defined as a modified Rankin Scale (mRS) score of zero to

two at 90-day follow-up. Safety outcomes included symptomatic intracranial hemorrhage (sICH).

Data were analyzed for 301 patients with a median age of 69 years in the EVT group and 68.5 years in the MM group. Functional independence was achieved by 38 of the EVT group and 10% and of the MM group ( $p < 0.001$ ). The EVT group had a higher incidence of sICH ( $p = 0.003$ ) than the MM group. Mortality occurred in 26% of the EVT group and 41% of the MM group ( $p = 0.02$ ).

**Conclusion:** This retrospective study of patients with acute ischemic stroke, presenting beyond 24 hours of their last known, well found that endovascular thrombectomy increased the likelihood of functional independence, and decreased mortality, despite an increased risk of intracerebral hemorrhage.

Sarraj, A., et al. Association of Endovascular Thrombectomy versus Medical Management with Functional and Safety Outcomes in Patients Treated Beyond 24 Hours of Last Known Well. The SELECT Late Study. *JAMA Neurol*. 2022. doi:10.1001/jamaneurol.2022.4714

### GOUT AND CARDIOVASCULAR OUTCOMES

Studies have demonstrated the benefit of urate-lowering drugs for the management of gout, with other data suggesting potential additional benefits in reducing the risk of cardiovascular disease. This study examines the effect of regular allopurinol or colchicine use on cardiovascular risk.

Subjects were residents of Aotearoa New Zealand, 20-79 years of age, identified through a linkage of national and regional health databases. Those who had been admitted with the diagnosis or had been prescribed medication for gout were identified. Serum urate values were collected, with these values categorized as  $\geq 36$  mm/L or  $< 36$  mm/L. The primary outcome measure was the time to the first fatal or nonfatal cardiovascular event.

Data were completed for 942,416 adults, of whom 31,907 had a diagnosis of gout. Compared to those without gout, those with gout had a higher rate of first cardiovascular event and a higher rate of noncardiovascular mortality. After adjusting for cardiovascular predictors, gout was associated with an increased risk of a cardiovascular

event over five years, with a hazard ratio (HR) of 1.34 in women and 1.18 in men. Among men, the risk of cardiovascular events was greater among those who were prescribed colchicine and reduced among those prescribed allopurinol.

**Conclusion:** This study found the diagnosis of gout was associated with an increased risk of incident cardiovascular events in both men and women.

Cai, K., et al. Association Between Gout and Cardiovascular Outcomes in Adults with No History of Cardiovascular Disease: Large Data Linkage Study in New Zealand. *BMJ Med.* 2022; doi:10.1136/ bmjmed-2021-000081.

### GUANFACINE AND N-ACETYLCYSTEINE FOR COGNITIVE LONG COVID

A common complaint among patients infected with COVID-19 is residual cognitive impairment, known colloquially as “brain fog.” Studies of patients with encephalomyelitis have demonstrated that guanfacine, (an  $\alpha$ -2A- adrenoceptor agonist) protects the prefrontal cortex from hypoxia and psychological stress and improves cognition. In addition, N-acetylcysteine (NAC) has been shown to protect mitochondria through several mechanisms. Taken together the authors note that NAC may help restore NMDAR neurotransmission while guanfacine may strengthen the signal by closing calcium channel blockers to strengthen prefrontal cortex connections.

This pilot study assessed the effect of extended-release guanfacine and NAC for long COVID cognitive complaints. The subjects were twelve women with symptoms of long COVID, including brain fog. The patients were prescribed extended-release guanfacine, one milligram at bedtime for the first month, increased to two milligrams after one month. In addition, the subjects received NAC 600 milligrams daily. Four patients discontinued the therapy for unknown reasons and two discontinued after episodes of hypotension and or dizziness.

The eight patients who completed the treatment reported improved working memory, concentration, and executive functions, including a resumption of normal workloads. One patient briefly stopped taking guanfacine due to a hypotensive episode and reported a return of cognitive deficits that abated with resumed guanfacine treatment.

**Conclusion:** This small pilot trial of patients with long COVID cognitive symptoms suggests that the combination of guanfacine and N-acetylcysteine may help with symptoms of brain fog.

Fesharaki-Zadeh, A., et al. Clinical Experience with the  $\alpha$ -2A-Adrenoceptor Agonist, Guanfacine, and N-Acetylcysteine for the Treatment of Cognitive Deficits in “Long-COVID19”. *Neuroimmunology Reports.* 2023; 3: 100154.

### DEGENERATIVE HIP ABDUCTOR TENDON LESIONS

Greater trochanteric pain syndrome (GTPS) is a relatively common condition with an annual incidence of 1.8 to 5.6 per thousand. Symptoms are often effectively relieved with nonoperative treatment with success rates estimated at up to 80%. For those who fail conservative treatment, surgical repair is often recommended. This study reviews the natural history of non-surgically treated hip abductor lesions over time.

The subjects were consecutive patients diagnosed with GTPS, seen between January 2003 and November 2015 at the University Hospital Balgrist in Zurich Switzerland. An MRI of the symptomatic hip was performed for patients with symptoms persisting for six or more months, despite physical therapy and focal cortisone/local anesthetic treatment. At a minimum follow-up of 36 months, the patients were invited for a clinical examination and bilateral hip MRI.

Of the 106 patients who met the criteria, 58 agreed to return for a follow-up MRI. At the initial MRI examination, 77% demonstrated a lesion of the hip abductors, and 23% had isolated trochanteric bursitis. At the final exam, at an average of 71 months, 34% of the lesions progressed from trochanteric bursitis to tendinopathy or partial tear. Of the partial tears noted on initial examination, 90% remained stable. Regression analysis demonstrated no correlations between patient demographics, radiography parameters, type and location of the initial lesion, and lesion progression.

**Conclusion:** This study of degenerative hip abductor lesions found that 1/3 progressed over time, while 90% of those with partial tears were stable over time.

Schenk, P., et al. Natural History of Degenerative Hip Abductor Tendon

Lesions. *Am J Sport Med.* 2023, January;51(1):160-168.

### QUALITY OF LIFE IN PATIENTS WAITING FOR KNEE OR HIP REPLACEMENT

During the COVID-19 pandemic, many patients scheduled to receive a total hip (THA), or knee arthroplasty (KA) experienced longer wait times. This study of patients waiting at least six months for a THA or KA assessed their change in health-related quality of life (HRQoL) during the wait.

This cross-sectional study in the United Kingdom included 326 subjects, randomly selected from among those who had been waiting six months or more for a primary THA or KA. The patients completed the EuroQol five-dimension questionnaire (EQ-5D), a visual analog scale (EQ-VAS), the Rockwood Clinical Frailty Scale (CFS), and the 36-Item Short Form Survey. The patients were asked to provide scores for that day and for six months prior to that day.

Of the 326 patients, 110 (37%) stated that their health was much worse than six months earlier. During the six months, scores worsened on the EQ-5D by a mean of 0.175 ( $p<0.001$ ) and on the EQ-VAS by a mean of 8.6 ( $p<0.001$ ). The mean scores on the CFS fell from a mean of three (managing well) to a mean of four (vulnerable) ( $p<0.001$ ). The percentage of patients who rated their quality of life as worse than death rose from 10.4% to 25.2% ( $p<0.001$ ).

**Conclusion:** This cross-sectional study found that patients who experienced more than a six-month wait for a hip or knee replacement experienced a significant deterioration in their quality of life, with 25% reporting their quality of life as worse than death.

Clement, N., et al. Significant Deterioration in Quality of Life and Increased Frailty in Patients Waiting More than Six Months for Total Hip or Knee Arthroplasty: A Cross-Sectional, Multicentre Study. *Bone Joint J.* 2022; 104-B(11): 1215-1224.

### SUMATRIPTAN AND CENTRAL SENSITIZATION

Triptans are a first-line therapy for the treatment of migraine and cluster headaches. This study explored the site of action of triptans in healthy humans and compared the differences in cephalic and extra-cephalic nociception.

Subjects were recruited from among medical students at Hamburg

University. Baseline quantitative sensory testing readings were obtained, with the participants then randomized to receive either six mg of subcutaneous sumatriptan or 0.9% normal saline. Twenty minutes after this injection, capsaicin patches were placed at the forehead (V1) and the ventral forearm (extracephalic dermatome). The test site and the contralateral site were assessed for warm detection thresholds (WDT), primary heat hyperalgesia (PHH) within the zone of capsaicin application, mechanical pain sensitivity (MPS) to pinprick stimuli, and dynamic mechanical allodynia (DMA).

After capsaicin application, the WDTs decreased at both sites ipsilateral to the application of capsaicin for both the triptan group ( $p=0.001$ ) and the placebo group ( $p=0.006$ ). After capsaicin conditioning, an increase in pain ratings to brief heat stimuli was observed at the ipsilateral V1 and forearm in the triptan group ( $p<0.001$  and  $p<0.001$ ) and in the placebo group ( $p<0.001$  and  $p<0.001$ ). No significant difference was found on the contralateral control sites. The MPS adjacent to the area of flare induced by capsaicin application increased only in the forearm but not the V1 dermatome, suggesting an attenuation of the sensitization of secondary hypoalgesia exclusively in the V1 (central) dermatome. In addition, treatment with sumatriptan reduced the size of the flare after capsaicin application exclusively in the V1 dermatome.

**Conclusion:** This study of capsaicin-induced pain found that sumatriptan prevents the central sensitization of the secondary sensory neurons without modulating peripheral sensitization.

Peng, K., et al. Sumatriptan Prevents Central Sensitization Specifically in the Trigeminal Dermatome in Humans. *Euro J Pain*. 2022, November; 26(10): 2152-2161.

### PRECUNEUS MAGNETIC STIMULATION FOR ALZHEIMER'S

Previous studies performed on healthy subjects revealed that precuneus repetitive transcranial magnetic stimulation (rTMS) can modulate long-term memory function and strengthen the connectivity between the precuneus (PC) and the temporal cortex. This study assessed the effect of rTMS on the cognitive and functional decline among patients with Alzheimer's disease (AD).

This sham-controlled, randomized

trial included patients, 50 to 85 years of age, with mild to moderate dementia due to AD. The participants were randomly assigned to receive PC-rTMS or sham-rTMS (S-rTMS), applied to the PC for 20 minutes per day, five times per week followed by a 22-week maintenance phase, with the same stimulation applied weekly. The primary outcome measure was the change from baseline to 24 weeks in the scores on the Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB) score. Secondary outcomes included changes in the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), Mini Mental State Exam (MMSE), Alzheimer's Disease Cooperative Study-Activities of Daily Living scale (ADCS), Frontal Assessment Battery, and Neuropsychiatric Inventory.

Forty-five patients completed the treatment. Compared to the baseline, the CDR-SB scores were relatively stable (-0.25), with deterioration (-1.42) noted in the sham group ( $p=0.009$ ). Significant longitudinal differences were also noted between the two groups on the ADCS-Cog ( $p=0.035$ ), the MMSE ( $p=0.041$ ), and the ADCS-ADL scores ( $p<0.001$ ).

**Conclusion:** This study of patients with mild to moderate Alzheimer's disease found that 24 weeks of stimulation of the precuneus with rTMS may be beneficial in reducing the cognitive and functional decline of patients with Alzheimer's disease.

Koch, G., et al. Precuneus Magnetic Stimulation for Alzheimer's Disease: A Randomized, Sham-Controlled Trial. *Brain*. 2022, November; 145 (11): 3776-3786.

### FRESH OSTEOCHONDRAL TRANSPLANTATION OF THE KNEE

Fresh osteochondral allograft (FOCA) transplantation is a treatment option for focal osteochondral lesions larger than two  $\text{cm}^2$  in the knee. This procedure has been shown to improve the range of motion and the probability of returning to participation in sport. Using a new scoring system for computed tomography (CT) of the knee, the assessment computed tomography osteochondral allograft (ACTOCA), this study assessed the efficacy of the ACTOCA for predicting clinical outcomes.

The subjects were consecutive patients undergoing FOCA transplantation for osteochondral defects between August of 2017 and August of 2019. The subjects were 18

to 50 years of age with a full-thickness chondral and osteochondral defect  $\geq 2 \text{ cm}^2$  on the femoral condyle, trochlea, and/or patella. Each patient underwent progressive range of motion exercises with a continuous passive motion machine for six weeks. A gradual transition to weight bearing as tolerated was permitted after six to eight weeks. A CT was obtained at six months and scored with the ACTOCA. Clinical outcomes were assessed postoperatively and at 12 and 30 months using the International Knee Documentation Committee (IKDC) score, the Kujala score, the Tegner activity scale, and the Western Ontario Meniscal Evaluation Tool (WOMET) score. These were compared to the six month ACTOCA scores.

Data were gathered for 36 patients, with a mean postoperative follow-up of 38 months. The ACTOCA at six months was significantly correlated with the outcome scores at 12 and 30 months for the IKDC ( $p=0.001$ ,  $p=0.001$ ), Kujala ( $p=0.06$ ,  $p=0.001$ ), WOMET ( $p=0.011$ ,  $p=0.001$ ), and Tegner ( $p=0.03$ ,  $p=0.001$ ).

**Conclusion:** This study of patients undergoing fresh osteochondral transplantation of the knee found that a new scoring system for evaluating CT at six months was helpful in predicting 30 month outcomes.

Gelber, P., et al. Early Postoperative CT scan Provides Prognostic Data on Clinical Outcomes of Fresh Osteochondral Transplantation of the Knee. *Am J Sport Med*. 2022, December; 50 (14): 3812-3818.

### PROGNOSTIC VALUE OF SERUM NEUROGRANIN IN ACUTE ISCHEMIC STROKE

Neurogranin (Ng) is a calmodulin-binding protein that functions as a major postsynaptic protein. This protein regulates calmodulin availability and has been studied in progressive neurologic diseases. This study assessed the diagnostic value of Ng in patients with acute ischemic stroke (AIS).

This prospective, case-control investigation was completed over six months in 2020, involving adults with AIS and matched controls. The control group was selected from among healthy relatives of emergency department (ED) patients and hospital staff. Collected data included chief complaint, onset time, emergency department admission date and time, and admission scores on the Glasgow Coma Scale, the

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

National Institute of Health Stroke Scale, the modified Rankin Scale (mRS), cranial CT, and diffusion-weighted imaging. Blood samples were taken for quantification of Ng. The level of Ng was compared to the patients' outcome.

The median serum level of Ng of the patient group (160.00ng/mL) was significantly higher than that of the control group (121.26ng/mL;  $p < 0.001$ ). The Ng level of 25 patients admitted to the ED within the first six hours from the onset of their AIS was 177.93 ng/mL, while serum Ng level of 61 patients admitted to the ED within 6-24 hours was 131.84 ng/mL. The lesion volume, NIHSS, and mRS scores at admission had no significant relationship with Ng levels.

**Conclusion:** This study of patients with acute ischemic stroke found that serum neurogranin may be a biomarker of acute ischemic stroke but was not effective as a diagnostic tool.

Kusdogan, M., et al. The Diagnostic and Prognostic Value of Serum Neurogranin in Acute Ischemic Stroke. *J Stroke Cerebrovasc Dis.* 2023, February; 32(2): 106889.

*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.

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ISSN # 1081-1303



**REHAB IN REVIEW**



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



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