

# REHAB IN REVIEW

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Volume 33 Number 5

Published by Physicians  
In Physical Medicine and Rehabilitation

May 5, 2025

## HERPES ZOSTER VACCINATION AND DEMENTIA

Previous studies have suggested a potential association between the herpes zoster vaccine and a reduced risk of dementia. This study was designed to better understand the potential role of neurotropic herpesviruses in the pathogenesis of dementia.

This Welsh study compared the records of 282,541 adults who were too old to be eligible for the herpes vaccine (born before Sept 2, 1933), to those who fit the age requirement. Focusing on those without prior dementia diagnoses, the groups were compared for new onset dementia over seven years.

Vaccination rates increased from 0.01% among patients who were merely one week too old to be eligible, to 47.2% among those who were one week younger ( $p < 0.001$ ). Over seven years of follow-up, those receiving the vaccine experienced a reduced probability of a new dementia diagnoses by 3.5 percentage points ( $p=0.019$ ), a 20.0% relative reduction. The findings were robust across analytical variations and were confirmed in the broader population, suggesting a dementia-preventing or dementia-delaying effect of the zoster vaccine.

**Conclusion:** This large population study in Wales found that those who received a herpes zoster vaccination had a reduced risk of developing dementia.

Eyting, M., et al. A Natural Experiment on the Effect of Herpes Zoster Vaccination on Dementia. *Nature*. 2025. <https://doi.org/10.1038/s41586-025-08800-x%5B>.

## DARK CHOCOLATE BEFORE HIGH INTENSITY RESISTANCE EXERCISE

According to the 2020 report of the World Health Organization, cardiovascular disease was ranked as the leading cause of death globally

and is the cause of substantial morbidity. As previous studies have demonstrated a negative correlation between the consumption of dark chocolate (DC) and the risk of cardiovascular disease, this study reviewed the effects of pre-exercise supplement with DC on specific cardiovascular measurements.

The subjects were 31 healthy women, 20 to 30 years of age, randomized to a treatment or a control group. All underwent testing to identify the early follicular and mid luteal phases of each participant. It was during these phases that the study was conducted. Before the formal experiment, the women determined their one repetition maximum (1RM) for the deadlift, bench press, and squat exercises. The treatment group received supplemental DC (1 g/kg body weight), while the control group received an equal dose of milk chocolate two hours before resistance training. During training, isotonic resistance exercises were performed with the intensity set at 75% of the 1RM performed for five sets of six repetitions, with a three-minute rest between sets. At rest and up to two hours after training, measurements included pulse wave velocity (ftPWV), arterial stiffness, blood pressure, and plasma nitrous oxide (NO levels). These were compared between the treatment and control groups.

Compared to controls, the DC group demonstrate significantly increased NO levels and reduced systolic blood pressure (SBP), ftPWV, and arterial pressure volume index (API) ( $p < 0.05$ ) across both menstrual phases. During the early follicular phase, DC also attenuated exercise-induced increases in arterial stiffness and blood pressure ( $p < 0.05$ ).

**Conclusion:** This study of young women demonstrates that dark chocolate supplementation prior to resistance training results in significantly lower systolic blood pressure, arterial stiffness, and

increased plasma nitrous oxide levels.

Wang, et al. The Cardiovascular Benefits of Dark Chocolate Supplementation before High-Intensity Resistance Exercise in the Early Follicular and Mid-Luteal Phases of the Menstrual Cycle. *Sports Med Open*. 2025, Apr 18;11(1):39. doi: 10.1186/s40798-025-00850-9.

## METFORMIN AND KNEE OSTEOARTHRITIS

Obesity related knee osteoarthritis (OA) is mediated by excess weightbearing on joints, inflammation, and impaired glucose and lipid metabolism, which promote systemic inflammation, oxidative stress, and metabolic dysfunction in joint tissues. As metformin, a first-line treatment for type 2 diabetes, has shown promise in reducing inflammation and preserving cartilage, this study was designed to determine whether metformin can reduce pain due to OA.

This community-based, randomized, double-blind, placebo-controlled trial was conducted in Victoria, Australia, from June of 2021 to February of 2024. The study enrolled 107 participants with symptomatic knee OA, BMI of 25 or more, and knee pain of 40 mm or more on a 100-mm visual analog scale (VAS). The participants were assigned to receive either metformin (2,000 mg/day,  $n=54$ ) or placebo ( $n=53$ ) for six months. The primary outcome was the change in knee pain visual analogue scale (VAS) score at six months, with secondary outcomes including WOMAC pain, stiffness, function, and quality-of-life score.

The patients assigned to the metformin group experienced significantly reduced VAS-rated knee pain at six months as compared to the placebo subjects ( $p=0.01$ ). Secondary outcomes included significantly better improvements in WOMAC scores of pain ( $p=0.045$ ),

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stiffness ( $p=0.01$ ), and function ( $p=0.009$ ).

**Conclusion:** This prospective study of patients with osteoarthritis of the knee found that metformin, 2,000 mg per day, could significantly reduce pain and stiffness and improve function.

Pan, F., et al. Metformin for Knee Osteoarthritis in Patients with Overweight or Obesity: A Randomized, Clinical Trial. **JAMA**. 2025. Advance online publication. <https://doi.org/10.1001/jama.2025.3471>.

### **EXTENSOR EXERCISE PROTECTS AGAINST MUSCLE DAMAGE FROM SUBSEQUENT FLEXOR EXERCISE**

Eccentric exercise is known to induce muscle damage, but the protective effects of antagonist muscle eccentric exercise on subsequent damage remain unclear. This study investigates whether eccentric exercise of antagonist muscles can confer a protective effect against muscle damage in the elbow and knee flexors.

Sedentary young men ( $N=72$ , aged 20-28) were randomly assigned to six groups for arm or leg exercises. The subjects performed two bouts of 30 maximal eccentric contractions (30MaxEC) of the elbow flexors (EF) or 60 maximal eccentric contractions (60MaxEC) of the knee flexors (KF) using a different arm (contra-EF-EF) or leg (contra-KF-KF) between bouts. The other two groups performed 30MaxEC of the elbow extensors (EE) or 60MaxEC of the knee extensors (KE) first followed by the 30MaxEC of EF or 60MaxEC of KF using the ipsilateral (ipsi-EE-EF, ipsi-KE-KF) or contralateral limb (contra-EE-EF, contra-KE-KF). Muscle damage markers (MVC torque, ROM, limb circumference, echo intensity, muscle soreness, plasma CK activity) were measured before and up to five days post-exercise. Changes were compared between groups.

The study found that eccentric exercise of the extensors significantly reduced muscle damage markers in subsequent eccentric exercise of the flexors. The average protective effect across the six variables was found for both ipsilateral (56-59%) and contralateral (23-25%) limbs, with ipsilateral limbs showing greater protection ( $p<0.05$ ).

**Conclusion:** This study demonstrates that the magnitude of muscle damage caused by excentric

flexion can be reduced by first performing eccentric extension exercise of the same limb.

Chen, T. C., et al. Effects of Eccentric Exercise of The Extensors on Eccentric Exercise-Induced Muscle Damage of The Flexors in Limbs. **Med Sci Sports Exerc**. 2025, May; 57(5), 970-983.

### **LITHIUM PLUS VALPROATE IMPROVES COGNITIVE OUTCOMES**

Previous studies have shown that the combination of lithium and sodium valproate may be effective in improving mood disorders and slowing the progression of neurological diseases. This study was designed to determine whether this combination of medications could be an effective treatment for mTBI-associated learning and memory impairments.

The subjects were Sprague-Dawley rats, subjected to a mild fluid percussion injury (mFPI) to evaluate the efficacy of low-dose lithium (0.5 or 1 mEq/kg) combined with valproate (20 mg/kg), administered for three days post-injury. The control groups received saline, lithium alone, or valproate alone. Cognitive and behavioral assessments included the Morris Water Maze for spatial learning, novel object recognition (NOR), social preference, and fear conditioning tasks, conducted for one to six days post-injury. Motor function was tested via beam balance and foot-fault tasks. Immunohistochemical analysis at 14 days post-injury quantified neurons (NeuN+) and microglia (Iba1+) using a convolutional neural network to assess neuroinflammation and neuronal preservation.

The combination of low-dose lithium (1 mEq/kg) and valproate significantly improved hippocampal-dependent spatial learning and memory, a finding which was not apparent with either drug alone. This combination also enhanced recognition memory, sociability, and contextual fear memory, while reducing fear generalization. Measures of neuroinflammation were reduced in the treatment group, with fewer Iba1+ microglia in cortical regions, and cortical neuron counts preserved relative to those of the control animals.

**Conclusion:** This animal model of traumatic brain injury found that the combination of lithium and valproate, administered shortly after head

trauma, could reduce cognitive impairments.

Redell, J., et al. A Combination of Low Doses of Lithium and Valproate Improves Cognitive Outcomes After Mild Traumatic Brain Injury. **J Neurotrauma**. 2025, March; 42(5): 437-453.

### TRANSCRANIAL DIRECT CURRENT STIMULATION FOR MAJOR DEPRESSION

Major depressive disorder (MDD) is a significant global health challenge, often accompanied by cognitive impairments that persist despite antidepressant treatment. As home-based transcranial direct current stimulation (tDCS) has emerged as a potential adjunctive therapy, this study explored its utility for treating MDD.

This multicenter, double-blind, randomized, controlled trial enrolled 141 adults with MDD who were receiving antidepressants. Those participants were randomized into three intervention groups, sham (n=45), low-intensity (1 mA, n=47), or high-intensity (2 mA, n=49) tDCS, self-administered daily for 30 minutes over six weeks (42 sessions). The intervention targeted the dorsolateral prefrontal cortex using a bifrontal electrode setup. Outcomes, assessed at baseline and at weeks two, four, and six, included cognitive improvement (measured by the 2-Back Task accuracy), depressive symptoms [Hamilton-Depression (HAM-D)], anxiety (HAM-A), and quality of life (QLES).

No significant differences were noted between groups in changes in the HAM-D ( $p=0.609$ ), HAM-A ( $p=0.849$ ), or QLES ( $p=0.508$ ) scores. Mild adverse events, such as burning and skin redness, were more frequent in active groups ( $p<0.01$ ), but moderate-to-severe events were comparable.

**Conclusion:** This study found that home based tDCS was not effective in treating depression or working memory in patients with major depressive disorder.

Lee, C., et al. Efficacy and Safety of Home-Based Transcranial Direct Current Stimulation as Adjunct Treatment in Major Depression. **Euro Psychiatry**. 1-10. <https://doi.org/10.1192/j.eurpsy.2024.1811>.

### CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND OSTEOPOROSIS

Chronic obstructive pulmonary disease (COPD) is often linked with osteoporosis, potentially due to inflammation and corticosteroid use. This study explores the novel association between bone mineral density (BMD) and lung function in COPD patients.

This prospective cross-sectional study enrolled 85 COPD patients at Gansu Provincial People's Hospital from January to August 2024. Participants, diagnosed per GOLD guidelines with  $FEV1/FVC < 0.70$ , underwent quantitative computed tomography (QCT) to measure BMD. Exposure variables included lung function ( $FEV1/FVC\%$ ), age, sex, body mass index, smoking status, tea-drinking habits, and physical activity. Patients were grouped by BMD tertiles: low ( $\leq 80.5 \text{ mg/cm}^3$ ), moderate ( $80.6-115.7 \text{ mg/cm}^3$ ), and high ( $> 115.7 \text{ mg/cm}^3$ ). Linear regression and generalized additive models analyzed the BMD-lung function relationship, adjusting for confounders. Statistical significance was set at  $p < 0.05$ .

Linear regression showed a significant positive correlation between BMD and  $FEV1/FVC\%$  ( $p < 0.0001$ ). Non-linear analysis identified a BMD breakpoint at  $128.08 \text{ mg/cm}^3$ , with a positive correlation below this threshold ( $\beta = 0.245$ ;  $p = 0.0019$ ) and a non-significant negative trend above it ( $p = 0.0753$ ). Age, anthropometric measures, and smoking status also influenced lung function. These findings suggest  $BMD \leq 128.08 \text{ mg/cm}^3$  is a critical biomarker for assessing lung function changes in COPD, supporting the use of QCT for integrated bone and lung health evaluation.

Gao, R., et al. Novel Association Between Chronic Obstructive Pulmonary Disease and Osteoporosis: A Prospective Cross-Sectional Study. **World J Orthop**, 16 (2), 102101. <https://dx.doi.org/10.5312/wjo.v16.i2.102101>

### MINIMALLY INVASIVE LUMBAR DECOMPRESSION

Lumbar spinal stenosis (LSS) is a prevalent condition causing significant pain and disability in older adults and often requiring surgical intervention. The Minimally Invasive Lumbar Decompression (MILD) procedure, a percutaneous technique

targeting hypertrophied ligamentum flavum, lacks comprehensive evidence of its efficacy and safety, prompting this systematic review and meta-analysis.

Medical databases were reviewed using terms including "lumbar vertebrae" and "minimally invasive surgical procedures". Inclusion criteria encompassed randomized or cohort studies measuring pain (Visual Analog Scale, VAS) and disability (Oswestry Disability Index (ODI)) outcomes. Twelve trials with 500 patients were analyzed, with assessments at baseline, under six months, six months to under one year, and one year or more post-treatment.

The analysis found that MILD reduced VAS scores by 3.11 points overall ( $p < 0.00001$ ) and ODI scores by 13.61 points ( $p < 0.00001$ ), with sustained improvements for up to five years. The number of adverse events (8.2%) were lower than with traditional decompression surgeries, with no neurological deficits or dural tears reported.

**Conclusion:** This literature review and meta-analysis of lumbar spine stenosis studies found that the Minimally Invasive Lumbar Decompression (MILD) procedure is an effective treatment option.

Zhang, X-Y., et al. The Efficacy of the Minimally Invasive Lumbar Decompression (MILD®) Procedure: A PRISMA-Compliant Systemic Review and Meta-Analysis. **Pain Physician**. 2025, March; 28(1): 71-81.

### MEDITERRANEAN DIET AND COGNITIVE IMPAIRMENT: IMPACT ON MORTALITY

The aging global population is increasingly affected by cognitive impairment. The Mediterranean diet, known for cardiovascular benefits, may mitigate these risks. This study was designed to investigate the effect of the interaction of the mediterranean diet with cognitive impairment and mortality.

This study analyzed data from the National Health and Nutrition Examination Survey (NHANES) 2011–2014, involving 2,520 participants aged 60 and older, followed until December 31, 2019. Adherence to the Mediterranean diet was assessed using the alternative Mediterranean diet (aMED) index, calculated from two 24-hour dietary recalls. Cognitive impairment was determined using standardized tests (CERAD, Animal

Fluency, Digit Symbol Substitution), with the lowest quartile classified as impaired. Cox proportional hazards models evaluated the association of aMED and cognitive impairment, with all-cause and cardiovascular mortality, adjusting for confounders.

Cognitive impairment was identified in 632 (25.1%). In an adjusted analysis, higher aMED scores were associated with lower all-cause mortality (Hazard Ratio (HR) 0.65;  $p < 0.001$ ) and lower cardiovascular mortality (HR 0.73;  $p = 0.003$ ). In addition, cognitive impairment was associated with an increased risk of long-term all-cause mortality ( $p < 0.001$ ) and cardiovascular mortality ( $p = 0.003$ ). A subgroup analysis found that, only in the cognitive impairment subgroup, was a higher Mediterranean diet score associated with a reduced risk of cardiovascular mortality.

**Conclusion:** This study, using data from NHANES, found that adherence to the Mediterranean diet significantly reduces the risk of all-cause as well as cardiovascular mortality.

Li, L., et al. Correlation of Cognitive Impairment with Mediterranean Diet and Mortality: A Prospective Cohort Study. *Front Aging Neurosci.* 2025, April 9; 17: 1556608.

### PLASMA PROTEIN RISK SCORES FOR ALZHEIMERS

The increasing prevalence of Alzheimer's disease (AD) and mild cognitive impairment (MCI) underscores the need for accessible diagnostic tools. This study investigated whether plasma protein risk scores (PPRSs) can help predict the risk of MCI and AD.

This study utilized data from 1,515 participants in the Framingham Heart Study's offspring cohort. From these, plasma AD biomarkers (p-tau181, t-tau, A $\beta$ 40, and A $\beta$ 42) were measured at different exams (nine, eight, and seven), and 1,128 plasma proteins measured at exam five. The participants were categorized as cognitively normal ( $n = 1,258$ ), with MCI ( $n = 129$ ), or with AD ( $n = 128$ ). A Cox proportional hazard (PH) model was used to analyze the association of plasma proteins with the incidence of MCI and AD. This analysis produced an aggregated plasma protein risk score (PPRS). The results identified 36 proteins for MCI PPRS and 50 for AD PPRS. Associations with cognitive changes, brain volume, and plasma AD biomarkers (p-

tau181, t-tau, A $\beta$ 40, A $\beta$ 42) were assessed.

The results showed the predictive value for developing MCI or AD, with MCI PPRS demonstrating a hazard ratio (HR) of 6.97 and AD PPRS an HR of 5.74. Both of these were significantly associated with cognitive decline, brain atrophy, and elevated plasma AD biomarkers.

**Conclusion:** This study identified plasma proteins which can assist in predicting the onset of mild cognitive impairment or Alzheimer's disease.

Rehman, H., et al. Alzheimer's Disease Neuroimaging Initiative. Plasma Protein Risk Scores for Mild Cognitive Impairment and Alzheimer's Disease in The Framingham Heart Study. *Alzheimer's and Dementia.* 2025; 21, e70066. <https://doi.org/10.1002/alz.70066>.

### TELENEUROREHABILITATION IN PARKINSON'S DISEASE

Parkinson's disease (PD) is the second most common neurodegenerative disorder worldwide. As telemedicine is beneficial for patients in low-income and middle-income countries (LMICs), where transportation costs and regular hospital visits are limiting factors, this study assessed the efficacy and safety of teleneurorehabilitation (TNR), as compared to in-person (IP) rehabilitation, among patients in India.

The TELEPARK randomized, clinical trial enrolled 63 patients with mild to moderate PD, randomly assigning them to either a TNR group or an in-person rehabilitation group. Both interventions lasted 12 weeks and followed the same protocol, twice-weekly sessions involving physiotherapy, aerobic activity, balance exercises, and guided breathing techniques. The participants were assessed pre- and post-intervention using multiple validated tools, including the MDS-UPDRS II and III for motor symptoms, the Non-Motor Symptoms Scale (NMSS), the PDQ-8 Summary Index (PDQ8-SI) for quality of life, the Six-Minute Walk Test, and the Functional Reach Test. Statistical analyses included paired and unpaired t-tests to assess intra-group and inter-group differences.

Significant improvement was found in both groups across motor and non-motor symptom scores, functional mobility, and quality of life,

with no statistically significant differences in outcomes between the TNR and in-person groups post-intervention.

**Conclusion:** This study of patients with Parkinson's disease found that treatment outcomes were similar between those who received in-person therapy and those who received remote therapy using telemedicine.

Dhamija, R. K., Teleneurorehabilitation and Motor and Nonmotor Symptoms and Quality of Life in Parkinson's Disease: The TELEPARK Randomized, Clinical Trial. *JAMA Neurol.* 2025, April; 82 (4): 376-383. <https://doi.org/10.1001/jamaneurol.2024.5387>

### GREATER COGNITIVE-MOTOR INTERFERENCE IN PATIENTS AFTER ACL RECONSTRUCTION

Cognitive-motor interference (CMI) refers to the decrease in performance of either a cognitive or motor task when performed together compared to when they are performed separately. Research has demonstrated that CMI is increased after musculoskeletal trauma, including anterior cruciate ligament (ACL) injury. This study investigated CMI in patients after ACL reconstruction (ACLR).

The subjects were 40 sports-active patients at 24.9 months post-ACLR, and 40 non-injured controls, ages 15 to 36 years. The participants performed a drop vertical jump (DVJ) task with and without (control) cognitive tasks designed to target short-term memory, attention, decision-making, and inhibitory control. Outcome measures included cognitive task accuracy (letter position recall), motor task accuracy (landing or jumping), relative jump height, and peak vertical ground-reaction force (vGRF). The Cambridge Neuropsychological Test Automated Battery (CANTAB) assessed isolated cognitive performance as covariates. Multivariate analysis of variance (MANOVA) and covariance (MANCOVA) were used to compare the ACLR group and controls.

Compared to the control group, greater CMI was found in the ACLR group, with 13.3% lower cognitive task accuracy ( $p < 0.001$ ), fewer correct motor actions ( $p = 0.003$ ), and reduced relative jump height ( $p = 0.01$ ), but no difference in vGRF. Cognitive ability as measured by the CANTAB did not affect these results.

**Conclusion:** This study of sports-active individuals, 15 to 36 years of age, found that at two years post-ACL reconstruction, cognitive motor interference was greater than in controls and was unrelated to cognitive test results.

Strong, A., et al. Greater Cognitive-Motor Interference Among Patients after Anterior Cruciate Ligament Reconstruction Compared with Controls. *Am J Sports Med.* 2025, April;53(5): 1041-1049.

### **ADDUCTOR CANAL BLOCK BEFORE VERSUS AFTER TOTAL KNEE ARTHROPLASTY**

Total knee arthroplasty (TKA) is a highly effective procedure for end-stage knee osteoarthritis (OA), but is associated with significant postoperative pain, impacting recovery and patient satisfaction. Determining the optimal timing of an adductor canal block (ACB) could enhance pain management and functional outcomes, prompting this investigation.

This double-blinded, randomized, controlled trial, conducted at West China Hospital, Sichuan University, enrolled 100 Chinese patients undergoing primary, unilateral TKA from September of 2023 to April of 2024. Those subjects were randomized to receive an ACB or a placebo block either 30 minutes before general anesthesia or postoperatively. The outcome variables included postoperative morphine consumption (primary), time to first rescue analgesia, intraoperative and postoperative stress markers (cortisol, ACTH, and hypertensive episodes), pain scores (visual analog scale), functional recovery (knee motion and ambulation), chronic pain incidence, and complications.

Preoperative ACB significantly reduced morphine consumption within 24 hours ( $p=0.001$ ) and throughout hospitalization ( $p=0.002$ ). The ACB group demonstrated an extended time to first rescue analgesia (16.3 vs. 12.6 hours,  $p=0.030$ ), lowered intraoperative opioid and anesthetic use, hypertensive episodes, and postoperative stress markers (cortisol, ACTH) on day one. The ACB group also experienced decreased pain scores at rest and during motion within 12 to 24 hours, improved knee motion on postoperative day one ( $p=0.035$ ), and

a reduced incidence of chronic pain at three months ( $p=0.046$ ).

**Conclusion:** This randomized, controlled trial of patients undergoing total knee arthroplasty found that those who received an adductor canal block preoperative had less pain over three months and better range of motion during hospitalization.

Wang, Q., et al. Comparison of Adductor Canal Block before versus after Total Knee Arthroplasty in Terms of Pain, Stress, and Functional Outcomes: A Double-Blinded, Randomized, Controlled Trial. *J Bone Joint Surg.* 2025, April, 107(8): 796-804.

### **NERVE BLOCKS FOR POSTTRAUMATIC HEADACHES**

Posttraumatic headaches (PTH) are a debilitating consequence of head trauma, often resistant to conventional treatments. This study investigates the efficacy of nerve blocks in managing refractory PTH.

This retrospective cohort study, conducted at a Houston neurology clinic, included 34 patients aged 18-72 with PTH lasting over three months. Nerve blocks (bilateral third occipital, greater/lesser occipital, supraorbital, and supratrochlear nerves) were administered to 23 patients, while 11 received partial blocks based on pain distribution. The blocks involved a mix of bupivacaine, lidocaine, and dexamethasone. Pain intensity was assessed using a 0-10 Numeric Rating Scale (NRS) at baseline, immediately after, the next day, and at three- and six-months post-procedure.

All 34 patients reported pain improvement within an hour (average 88%). Twenty-one patients (75%) rated their response to nerve blocks as  $\geq 90\%$  improvement in headaches. At three months, 27 patients averaged 73% improvement, with 12 achieving  $\geq 90\%$  relief. At six months, 11 reported relief at  $\geq 90\%$ .

**Conclusion:** This retrospective review of patients with chronic, post-traumatic headaches found that nerve blocks of the occipital supraorbital and supratrochlear nerves could be effective in reducing pain.

File, C., et al. Efficacy of Nerve Blocks for Managing Refractory, Posttraumatic Headaches. *Pain Physician.* 2025, Mar; 28(2): 137-145.

### **CARDIOVASCULAR HEALTH AND BIOMARKERS OF NEURODEGENERATIVE DISEASES**

The rising prevalence of neurodegenerative diseases, particularly among older adults, has prompted research into modifiable risk factors such as cardiovascular health (CVH). This study was designed to better understand the association between CVH and neurodegeneration.

This cohort study, conducted within the Chicago Health and Aging Project (CHAP), examined adults ages 65 years and older from 1993 to 2012. For all subjects CVH was assessed using the American Heart Association's Life's Simple Seven (healthy diet, regular exercise, normal BMI, nonsmoking, and absence of dyslipidemia, diabetes, and hypertension). In addition, labs were drawn to measure serum biomarkers of neurodegeneration, neurofilament light chain (NfL), and total tau (t-tau). The scores were used to place the subjects into tertiles of CVH, including low (0 to 6), moderate (7 to 9), and high (10 to 14) groups. The data were reviewed for associations and longitudinal changes over 10 years.

Data were analyzed for 1,018 adults with a mean age of 73. Those with high CVH scores (10 to 14 points) had significantly lower NfL levels (18.9% reduction) as compared to those with low scores (0 to 6 points), and a slower annual increase in NfL scores. The findings were consistent across gender, race, and APOE e4 carriers.

**Conclusion:** This study of adults over 65 years of age found that those with good cardiovascular health, as measured by Life Simple Seven, had better neurodegeneration (NfL) scores and that these worsened more slowly than did the scores of those with less favorable cardiovascular health scores.

Dhana, A., et al. Cardiovascular Health and Biomarkers of Neurodegenerative Disease in Older Adults. *JAMA Network Open.* 2025, March;8(3), e250527. <https://doi.org/10.1001/jamanetworkopen.2025.0527>

### **CAREGIVING GAPS AMONG COMMUNITY-DWELLING OLDER ADULTS**

As populations age, the need for long-term care has become a pressing public health challenge.

Projections by the World Health Organization suggest a quadrupling of older persons unable to care for themselves by the year 2050. This study investigated the global prevalence and trends of caregiving gaps among community-dwelling older adults who have dementia and functional limitations.

Data were obtained from the United States (the Health and Retirement Study), England (the English Longitudinal Study of Ageing), 18 European countries and Israel (Survey of Health, Ageing and Retirement in Europe), and China (China Health and Retirement Longitudinal Study). The analysis focused on participants 50 years of age or older with dementia and functional limitations. The data were reviewed for receipt of personal assistance for basic activities of daily living (ADLs) and instrumental activities of daily living (IADLs).

The findings revealed that at least one-fifth of individuals with dementia and functional limitations receive no personal assistance for ADLs or IADLs across all regions. Care gaps were evident for both informal and formal care, with formal care being notably absent, particularly in China, where 99.1% lacked formal ADL care. Less educated individuals were more likely to lack formal care, while those living alone often lacked informal support, leading to complete absence of care. The absence of care was associated with an increased likelihood of hospitalization and a reduced quality of life.

**Conclusion:** This large, global study of participants 50 years of age or older with dementia found that a significant portion have no personal assistance and that those who live alone are at greatest risk for a complete lack of care.

Lin, Z., et al. Absence of Care among Community-Dwelling Older Adults with Dementia and Functional Limitations. *Nat Aging*. 2025; 5: 548-557. <https://doi.org/10.1038/S43587-025-00836-Y>.

### GASTROINTESTINAL BLEEDING AFTER ACUTE ISCHEMIC STROKE

Gastrointestinal bleeding (GIB) is a significant complication following acute ischemic stroke (AIS), yet its long-term incidence remains underexplored. This study investigated the long-term incidence and risk factors of major GIB in AIS patients.

The study analyzed data from 10,818 patients with an AIS, admitted to 14 South Korean hospitals between 2011 and 2013. All were enrolled in the Clinical Research Collaboration for Stroke in Korea-

National Institute of Health registry. The participants were followed for up to six years, with major GIB events, defined as requiring at least two units of blood transfusion, tracked using National Health Insurance Service claims data. Baseline characteristics, medical history, and stroke severity were collected, and incidence rates were calculated across seven time intervals post-stroke. Multivariable analysis was used to identify predictors of GIB.

Over a median follow-up of 3.1 years, 8.8% of patients experienced 1,224 major GIB episodes, with 20% having recurrent events. The incidence peaked at 19.2 per 100 person-years in the first month post-stroke, declining to one-sixth by the second year, and stabilizing thereafter. Key predictors of GIB included anemia, estimated glomerular filtration rate  $<60$  mL/min/1.73 m<sup>2</sup>, and three-month modified Rankin Scale scores of  $\geq 4$ . Advanced age (75 years or older) was associated with an increased GIB risk over time, while moderate-to-severe anemia posed the highest risk in the first month.

**Conclusion:** This large Korean study of patients hospitalized for an acute ischemic stroke found that the risk of a gastrointestinal bleed peaks after one month, with an increased risk among those with anemia, decreased kidney function, and a three-month modified Rankin Scale score of four or more.

Kim, J., et al. Long-Term Incidence of Gastrointestinal Bleeding following Ischemic Stroke. *J Stroke*. 27(1): 102-112. <https://doi.org/10.5853/jos.2024.00661>.

### REGULATORY RESPONSES TO ULTRA-PROCESSED FOODS

The Nova food classification system defines ultra-processed foods (UPFs) as formulations of ingredients, mostly of exclusive industrial use, that result from a series of industrial processes. As growing evidence suggests that diets high in UPFs have a negative impact on health, this study evaluated the global scope and strength of national policies addressing UPFs.

The researchers analyzed UPF-related policy actions spanning 105 countries, using data collected in June of 2022 and updated in June of 2024. Policies were identified as UPF-related if they explicitly mentioned UPFs, food processing, or implied processing through terms such as "packaged food" or UPF examples such as "sugary drinks." Three frameworks guided the analysis: the NOURISHING framework to assess policy scope across food

environment, food system, and behavior change domains; the Nuffield Ladder to evaluate the degree of influence on consumer choice, and the Modalities of Control (MOC) framework to classify regulatory mechanisms targeting food businesses.

The study identified 417 UPF-related regulatory interventions, with only seven specifically mentioning UPF and eight mentioning highly processed foods. Of the 417 regulations, most interventions fell into the "food environment" domain, most often through nutrition labelling. Only one percent of the interventions were in the food system policy domain. Other policies for interventions to alter food environments included standards for foods in public institutions and specific settings.

**Conclusion:** This international study found that most ultra-processed related regulatory interventions are relatively weak and involve low levels of influence that are mostly informational in nature.

Northcott, T., et al. Regulatory Responses to Ultra-Processed Foods Are Skewed Towards Behaviour Change and Not Food System Transformation. *Nat Food*. 2025, Mar; 6(3): 273-282.

### IMPACT OF EPIGENETIC EDITING ON AGING

Aging is marked by distinct DNA methylation changes that underpin epigenetic clocks. This study investigated whether targeted epigenetic editing at age-associated CpG sites can modulate the epigenetic aging landscape and alter these clocks.

The researchers employed CRISPR-guided epigenetic editing to target individual, age-related CpG sites in human embryonic kidney cells (HEK293T), T cells, and mesenchymal stromal cells. The study focused on five genomic regions that either gain (hypermethylated) or lose (hypomethylated) methylation with age. Genome-wide DNA methylation was assessed via Illumina BeadChip, while 4C-sequencing mapped chromatin interactions.

The results revealed that editing single age-associated CpGs resulted in widespread bystander effects, including reproducible methylation changes at other age-related CpGs. Targeted methylation was more stable at hypermethylated sites, but both hyper- and hypomethylated edits affected the CpGs which are highly correlated with chronological age, impacting epigenetic clocks.

**Conclusion:** Using a CRISPR-guided editing process, this study identified a model wherein epigenetic modifications communicate across the genome, potentially stabilizing aging-related changes.

Liesenfelder, S., et al. Epigenetic Editing at Individual Age-Associated CpGs Affects the Genome-Wide Epigenetic Aging Landscape. *Nat Aging*. 2025. <https://doi.org/10.1038/s43587-025-00841-1>

### QUANTIFYING KNEE-ADJACENT FAT IN OSTEOARTHRITIS

Knee-adjacent subcutaneous fat (kaSCF) has emerged as a potential biomarker and risk factor for osteoarthritis (OA) progression. This study examined the relationship of kaSCF with knee structure, function, and clinical symptoms in individuals at risk for OA.

Researchers analyzed MRI data from 4,644 participants in the Osteoarthritis Initiative (OAI), to measure kaSCF. The association between kaSCF thickness was compared with cartilage thickness, cartilage T2 relaxation times (a biomarker of cartilage composition), knee pain, and isometric knee extension strength.

Increased BMI was positively associated with average kaSCF thickness ( $p < 0.001$ ). Greater kaSCF thickness was associated with lower cartilage thickness, reaching statistical significance in males ( $p = 0.01$ ). Higher kaSCF was also related to decreased knee extension strength ( $p < 0.001$ ) and to an increased odds of frequent knee pain ( $p = 0.005$ ). Notably, these associations persisted even after controlling for BMI.

**Conclusion:** This study found that knee-adjacent subcutaneous fat is associated with thinner cartilage in men, lower knee extension force, and a higher likelihood of frequent knee pain across all participants, independent of body mass index.

Joseph, G., et al. Quantifying Knee-Adjacent Subcutaneous Fat in the Entire OAI Baseline Dataset—Associations with Cartilage MRI T2, Thickness, and Pain, Independent of BMI. *Osteoarthr Cartil*. 2025, April; 33(4), 482-490.

### CHAIN FOOD STORES

The global rise in obesity and diet-related non-communicable diseases (NCDs) has been linked to transformations in food systems, particularly the dominance of large retail chains. Understanding these changes is crucial for developing

effective public health interventions to promote healthier diets.

This study analyzed trends in retail food environments across 97 countries from 2009 to 2023, focusing on physical retail indicators. Data were obtained from the Euromonitor International Passport Database, with obesity prevalence obtained from the NCD Risk Factor Collaboration. Physical retail indicators included chain and non-chain outlet density, sales from chain retailers, and unhealthy food sales per capita. The data were reviewed for trends, and associations between retail environment changes and obesity prevalence.

During the study period, chain store density rose 23% (from 2.63 to 3.25 per 10,000 population) while non-chain store density decreased by 13.7% (from 31.82 to 27.47 per 10,000). Grocery sales from chain retailers, unhealthy food sales per capita, and digital grocery sales also rose, with South Asia and low- and middle-income countries experiencing the most rapid changes. A positive correlation was found between the increase in chain stores and the prevalence of obesity.

**Conclusion:** This study found an association between an increased density of food sales at chain stores and an increase in obesity of the population.

Scapin, T., et al. Global Food Retail Environments Are Increasingly Dominated by Large Chains and Linked to the Rising Prevalence of Obesity. *Nat Food*. 2025, 6: 283-295. <https://doi.org/10.1038/s43016-025-01134-x>.

### BECOMING AN ELITE ATHLETE AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION AT EARLY AGE

Anterior cruciate ligament (ACL) injuries in young athletes can significantly impact their athletic careers. This study explored the rate of return to sport (RTS) and the ability to compete at an elite level after a pediatric or adolescent ACL reconstruction.

This cohort study analyzed the records of 1,392 patients, aged 10 to 18 years, derived from the Swedish National Knee Ligament Registry (SNKLR), who underwent primary ACL reconstruction between 2005 and 2022. The patients included pediatric (female: 11 to 13 years; male: 11 to 15 years) and adolescent (female: 14 to 18 years; male: 16 to 18 years) athletes. Data were retrieved that included patient-specific, injury-related, and treatment-specific variables, along with Knee injury and Osteoarthritis Outcome

Score (KOOS) subscores, collected at baseline and at one, two, five, and 10-year follow-ups. All subjects received a survey which included the question, "What is the absolute highest level that you have been competing in after your ACL injury?"

Significant improvements in KOOS scores were noted at all follow-up times for both groups. Pediatric and adolescent patients had RTS rates of 74% and 68%, respectively, with 31% and 23% achieving elite-level status. Cartilage injuries noted at reconstruction reduced the likelihood of RTS [odds ratio (OR) 0.60;  $p = 0.001$ ]. Pediatric and adolescent patients rated their highest level of knee function after ACL reconstruction to be 87 and 84 of a maximum of 100 points, respectively.

**Conclusion:** This study of pediatric and adolescent athletes with ACL reconstruction found that 74% and 68%, respectively, were able to successfully return to sport and 31% and 23% respectively were able to become elite athletes

Thorolfsson, B., et al. The Chance to Become an Elite Athlete after Pediatric and Adolescent Anterior Cruciate Ligament Reconstruction. *Am J Sports Med*. 2025, April; 53(5): 1027-1033. <https://doi.org/10.1177/0363546523120415>.

### CLINICAL PRACTICE GUIDELINE ON INTERVENTIONAL PROCEDURES FOR CHRONIC SPINE PAIN

Chronic spine pain, a leading cause of disability, is often managed with interventional procedures despite inconsistent guideline recommendations. This study was designed to evaluate the effectiveness and safety of these procedures for non-cancer chronic axial and radicular spine pain.

An international panel, including patients, clinicians, and methodologists, developed the guideline using the GRADE approach and standards for trustworthy guidelines, supported by the MAGIC Evidence Ecosystem Foundation. The recommendations were informed by a systematic review and network meta-analysis of randomized trials and observational studies, focusing on procedures including epidural injections, joint-targeted injections, radiofrequency ablation, and intramuscular injections. The panel adopted an individual patient perspective, prioritizing patient-centered outcomes.

For chronic axial spine pain ( $\geq 3$  months duration), the panel strongly recommended against joint radiofrequency ablation, epidural

(Continued from page 2)

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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.**

injections, joint-targeted injections, and intramuscular injections of local anesthetic with or without steroids, citing little to no pain relief benefit compared to sham procedures (moderate to low certainty evidence). For chronic radicular spine pain, strong recommendations were issued against dorsal root ganglion radiofrequency and epidural injections, also showing minimal benefit. Harms included a 0.7% risk of deep infection, 1.4% risk of dural puncture, 8.6% risk of prolonged pain/stiffness, and rare catastrophic complications including paraplegia. The guideline applies to adults with chronic spine pain not associated with cancer or inflammatory arthropathy.

**Conclusion:** This clinical practice guideline recommends against the use of common interventional procedures for chronic, non-cancer spine pain.

Busse, J. W., et. Al. Commonly Used Interventional Procedures for Non-Cancer Chronic Spine Pain: A Clinical Practice Guideline. **BMJ**, 388, E079970. Doi:10.1136/Bmj.2024-079970.

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ISSN # 1081-1303



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