

# REHAB IN REVIEW

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## PROJECTED UNITED STATES HEALTHCARE EXPENDITURE

The United States healthcare sector is on a trajectory of significant growth, with spending projected to have increased by 7.5% in 2023 (from 4.1% in 2022), outpacing the national gross domestic product (GDP) growth of 6.1%. Therefore 17.6% of the GDP was allocated to healthcare in 2023. This article provides an in-depth review of the projected healthcare expenditures through 2032.

This study used economic and demographic assumptions from the 2024 Medicare Trustees Report, along with updated macroeconomic data, to project the nation's healthcare expenditure by payer.

In 2022, the National Health Expenditure (NHE) stood at \$4,464 billion. The projected expenditures beyond 2022 are: \$4,799 billion in 2023, \$5,048.8 billion in 2024, \$5,560.3 billion in 2026, and \$7,700.5 billion in 2032. As a percentage of the GDP, the NHE is projected to grow from 17.6% in 2023 to 19.7% in 2032. In dollar values, the NHE per person is expected to rise from \$14,423 in 2023 to \$21,927 in 2032.

**Conclusion:** This study projects a significant increase in the healthcare expenditures in the U.S., as a percentage of the GDP, from 17.6% to 19.7%.

Fiore, J., et al. National Health Expenditure Projections, 2023-32: Payer Trends Diverge as Pandemic-Related Policies Fade. **Health Affairs**. 2024, July;43 (7):909.

## NUTRIENTS, SUGAR AND EPIGENETIC AGE IN BLACK AND WHITE WOMEN

Epigenetic clocks can predict biological age, independent of chronological age. These clocks reflect altered gene and protein expression patterns, particularly those resulting from differential DNA methylation (DNAm). This study

examined the association between diet and epigenetic aging in a midlife cohort comprising black and white U.S. women.

This cross-sectional study used data from the 1987 to 1997 National Heart, Lung, and Blood Institute Growth and Health Study (NGHS), which examined cardiovascular health in a community cohort of black and white females, 9-10 years of age. The women were followed into midlife at 36 -43 years. Participants provided saliva samples for DNAm analysis to estimate epigenetic age using the GrimAge2 method. All subjects were asked to self-complete a three-day food record at follow-up for three nonconsecutive days. The dietary data were used to calculate the scores of two overall diet quality nutrient indices, one based on adherence to the Mediterranean diet (aMED and the Alternate Healthy Eating Index [AHEI]-2010) and the other based on nutrient intake (Epigenetic Nutrient Index). Added sugar intake (the total sugar added to foods during food preparation and commercial food processing) was also calculated.

The sample included 342 women with a mean age at follow-up 39.2 years, with 171 black and 171 white participants. A significant association was found between greater adherence to the Mediterranean diet, as well as the Epigenetic Nutrient Index and younger epigenetic age ( $p < 0.05$  for both). Conversely, each gram of increase in added sugar intake was associated with a 0.02 increase in GrimAge2, reflecting accelerated epigenetic aging.

**Conclusion:** This cross-sectional study found that healthy diets are associated with slowing of genetic aging and added sugar is associated with accelerated genetic aging.

Chiu, D., et al. Essential Nutrients, Added Sugar Intake, and Epigenetic Age in Midlife Black and White Women: NIMHD Social Epigenomics Program. **JAMA Netw Open**. 2024; 7 (7): e2422749.

## CANNABIS SMOKING AND EPIGENETIC AGE

Cannabis has been designated as a controlled substance over the past century. This study explored the link between cannabis use and disease pathogenesis, using DNA methylation techniques to determine the association between cannabis smoking and genetic aging.

Subjects were participants within the Canadian Cohort of Obstructive Lung Disease (CanCOLD) cohort. The subjects were grouped based on cannabis use history, including never smokers ( $n=51$ ), former smokers ( $n=32$ ), and current smokers ( $n=10$ ). Tobacco use was also documented and noted in 25%, 59%, and 40% of the never, former, and current cannabis smokers, respectively. All subjects were assessed for epigenetic age using DNAmGrimAge, and DNAmPhenoAge. The epigenetic age was compared to cannabis use.

Compared to former smoking and never smoking, current cannabis smoking was significantly associated with higher DNAmGrimAge ( $p=0.005$  and  $p=0.001$  respectively) and DNAmPhenoAge acceleration ( $p=0.002$  and  $p=0.004$  respectively). No significant differences were seen in either DNAmGrimAge or DNAmPhenoAge acceleration between the former and never cannabis smoking groups. In comparison to cannabis smoking, cigarette smoking had a more significant effect on epigenetic aging. The mean differences in age acceleration based on DNAmGrimAge between the current and never cigarette smoking group was 8.86 years, while the difference between current and never cannabis smoking was 4.19 years.

**Conclusion:** This study found that cannabis smoking accelerates genetic aging, and that quitting cannabis smoking normalizes this process.

Cordero, A., et al. Cannabis Smoking is Associated with Advanced

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Epigenetic Age. *Euro Resp J.* 2024, April; 63: 240-0458.

## **MUSCULOSKELETAL PAIN IN 13-YEAR-OLD CHILDREN**

Musculoskeletal skeletal pain is one of the most common health problems in children and adolescents. Physical factors such as skeletal growth and maturation are believed to be dominant reasons for musculoskeletal problems that arise in children and adolescents. This study was designed to describe the prevalence and characteristics of musculoskeletal pain in 13-year-old children in a large, population-based cohort.

This study was performed within the population-based Generation R study, a prospective cohort study focusing on growth, development, and health, from fetal life until young adulthood. At 13 years of age, the children underwent physical examinations, with questionnaire data obtained from the children and parents to evaluate physical activity and sedentary behaviors. Questions concerning pain included frequency and location.

Data were completed for 3,062 children. Of these, 23.3% reported pain within the previous six weeks, with 18.8% reporting musculoskeletal pain. Of those with musculoskeletal pain, the locations were lower limb in 75.5% and back in 17.2%. Almost half (45.8%) experienced pain daily. Of those with pain, 87.2% reported that their pain was chronic (had existed for more than three months).

A multivariable analysis found significant associations for the prevalence of musculoskeletal pain included male gender (OR 0.74), higher maternal education (OR 0.69), BMI (OR 1.19), being physically active (OR 1.41), and reporting behavioral problems (OR 1.85).

**Conclusion:** This longitudinal study of 13-year-old children found that 18.8% reported musculoskeletal pain, of which almost 90% was chronic.

Guido, V et al., Musculoskeletal Pain In 13-Year-Old Children: The Generation R Study. *Pain.* 2024, August;165(8): 1806-1813.

## **MUSCULOSKELETAL PAIN WHEN RUNNING DURING PREGNANCY**

While physical activity is beneficial during pregnancy, less than one third of pregnant women meet the

minimum recommendations of 150 minutes per week of moderate intensity activity. This study investigated the prevalence and risk factors for musculoskeletal pain when running during pregnancy.

The subjects were adult women who, before pregnancy, had regularly run at least once per week, for a minimum of 20 minutes. The women were provided an online survey focusing on the six months prior to pregnancy. Questions focused on demographic information, running habits (pre- and during pregnancy), pre-pregnancy injury, and during-pregnancy physical pain experiences.

Data were received from 3,102 women with an average age of 36.1 years. Of these, 86% experienced pain while running during pregnancy. The women reduced their mean running distance compared to pre-pregnancy by 23% (first trimester), 36% (second trimester), and 45% (third trimester). Pain was located at the pelvis/sacroiliac joint (59.4%), lower back (51.6%), abdomen (51.3%), breast (44.4%), hip (40.0%), knee (19.1%), foot (13.5%), calf (9.9%), ankle (8.5%) and thigh (5.2%).

**Conclusion:** This study of women who were habitual runners found that, during pregnancy, running distances and frequency were reduced, and that 86% experienced pain while running.

Wyatt, H., et al. Prevalence and Risk Factors for Musculoskeletal Pain when Running During Pregnancy: A Survey of 3,102 Women. *Sports Med.* 2024, July; 54 (7): 1955-1964.

## **DECOMPRESSION VERSUS DECOMPRESSION WITH FUSION FOR SPINAL STENOSIS**

In degenerative lumbar spinal stenosis, the spinal canal is constricted by bulging of the disc and hypertrophy of the ligaments and facet joints, causing compression of neural structures. Degenerative spondylolisthesis (DS), defined as slippage of a vertebral body over the vertebral body below, may be present at the level of stenosis. Traditionally, fusion has been added to decompression to prevent instability and recurrent stenosis. A recent meta-analysis found no significant difference in function at two years between those treated with a decompressive surgery and those with decompressive surgery plus fusion. This study investigated the

five-year outcomes of these two surgical options.

This multicenter, open label, clinical superiority trial included patients with pseudoclaudication in one or both legs, and back pain, with stenosis at the lumbar region of the spine. The patients were randomized to receive decompression alone (D), or decompression with fusion (D-F). The primary outcome measure was the Oswestry Disability Index (ODI) at five years' follow up.

Compared with baseline, the ODI improved by 16 units in the D group and by 14 in the D-F group ( $p=0.226$ ). The mean EQ-5D at five years was higher in the D group than in the D-F group ( $p=0.027$ ). The mean improvement in quality of life was greater in the D group than in the D-F group ( $p=0.027$ ). The relative risk for the D-F patients to report decreased leg pain was 0.71 when compared to the D group.

**Conclusion:** This study of patients with lumbar degenerative lumbar spine stenosis found that those who were treated with decompression experience greater improvement than those with decompression with fusion.

Karlsson, T., et al. Decompression Alone or Decompression with Fusion for Lumbar Spinal Stenosis: Five-Year Clinical Results from a Randomized Clinical Trial. *Bone Joint J.* 2024; 106-B(7): 705-712.

### DEPRESSIVE SYMPTOMS AND COGNITIVE DECLINE

Both depression and cognitive impairment are prevalent in older adults. This study was designed to understand the temporal relationship between depressive symptoms and cognitive decline among individuals 85 years of age or older.

The Leiden 85-Plus Study is a prospective, cohort study, investigating the health, function, and well-being of the oldest old population during five years of follow-up. The subjects reached the age of 85 between September 1997 and September 1999. Cognitive function was determined using the Mini-Mental State Examination (MMSE). Those with baseline dementia were excluded. Depression was measured with the Geriatric Depression Scale (GDS). The data were analyzed to determine whether depressive symptoms preceded cognitive decline or vice versa.

At baseline, 6.8% of the participants had GDS depression

scores of five or higher, indicating possible depression. A novel method, dynamic time warping analysis, was employed to model temporal dynamics within individuals. This analysis found that depressive symptoms preceded most of the metrics of cognitive impairment. Of the GDS-15 symptoms, those with the greatest association with subsequent cognitive decline were worthlessness, hopelessness, low happiness, dropping activities/interests, and low satisfaction with life ( $p<0.01$  for all).

**Conclusion:** This longitudinal study indicates that depressive symptoms precede cognitive decline.

Van Der Slot, A., et al. Temporal Dynamics of Depressive Symptoms and Cognitive Decline in the Oldest Old: Dynamic Time Warp Analysis of the Leiden 85-Plus Study. *Age Aging.* 2024, July: 53(7): afae130.

### CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND BRAIN CORTICAL STRUCTURE

Chronic obstructive pulmonary disease (COPD) is the third leading cause of mortality worldwide, and a leading cause of disability adjusted life years. Previous studies have found that COPD patients may have a higher risk of cognitive impairment and neurological complications than the general population. As the predicted preserved ratio (PRISm), defined as forced expiratory volume in one second (FEV1),  $<80\%$  FEV1/forced vital capacity (FVC) ratio  $\geq 0.70$ , has been linked to a higher risk of developing COPD, this study investigated the causal relationship between PRISm and brain cortical structure.

Data were obtained from FinnGen, a national repository in Finland of data on genetic factors. In addition, data were extracted from the U.K. Biobank and the SpiroMeta consortium. Data concerning brain cortical structure were obtained from the ENIGMA Consortium. Data from 20,066 patients with COPD were compared to that of 350,359 controls. A Mendelian randomization (MR) analysis was used to determine the causal effects of COPD, PRISm and lung function to global brain cortical surface area (SA) / cortical thickness (TH) as well as 34 functional regions (with or without global controls).

A causal relationship was identified between COPD, PRISm and structural changes in certain cortical regions. Genetic-predicted

PRISm was negatively associated with the surface area (SA) of the paracentral gyrus ( $p=0.014$ ), but positively associated with SA of the precuneus gyrus ( $p<0.001$ ). Genetic predicted PRISm was associated with TH of inferior parietal gyrus ( $p=0.016$ ) and temporoparietal gyrus ( $p=0.016$ ). The FEV1 had significant causal effects on the SA of caudal middle frontal ( $p= 0.047$ ), frontal pole ( $p= 0.04$ ), lingual ( $p= 0.022$ ), and pericalcarine gyrus ( $p=0.048$ ).

**Conclusion:** This study establishes a causal relationship between COPD, PRISm, lung function indices, and changes in brain cortical structure.

Fang, C., et al. COPD, PRISm, and Lung Function Reduction Affect the Brain Cortical Structure: A Mendelian Randomization Study. *BMC Pulm Med.* 2024; 24(1): 341.

### ALTERNATING CURRENT STIMULATION FOR WORKING MEMORY

Working memory (WM) allows for the temporary storage and modification of information. Studies have shown that WM is affected by brain oscillations. Transcranial alternating current stimulation (tACS) is a technique used to target WM, although the effects appear to depend upon the timing with ongoing brain oscillations. This study explored the efficacy of tACS for WM when the stimulation was coordinated with the oscillations (Closed-Loop Amplitude-Modulated (CLAM) tACS).

The subjects were fifteen healthy adults, randomly assigned to a placebo or active group. At baseline all participants performed a visual WM task for 7.5 min while monitored with real time EEG. The same tasks were then performed for 45 min with placebo or active CLAM-tACS. During the active conditions, a new phase lag between CLAM-tACS and endogenous alpha oscillations was chosen out of six different phase angles ( $30^\circ$ ,  $90^\circ$ ,  $150^\circ$ ,  $210^\circ$ ,  $270^\circ$ , and  $330^\circ$ ) for each WM trial. The WM accuracy was compared between conditions.

Compared with baseline, WM accuracy improved in a phase lag dependent manner ( $p=0.035$ ), with the best WM performance found when the phase lag was  $330^\circ$  ( $p<0.0027$ ). This enhanced WM accuracy was accompanied by suppressed frontoparietal alpha synchrony during stimulation.

**Conclusion:** This study found that the benefits of transcranial alternating current stimulation for working memory could be enhanced when the stimulation is timed to ongoing brain alpha oscillations.

Haslacher, D., et al. Working Memory Enhancement Using Real Time Phase Tuned Transcranial Alternating Current Stimulation. **Brain Stimul.** 2024, July-August; 17(4): 850-859.

### LOW DOSE ASPIRIN AFTER TOTAL KNEE ARTHROPLASTY

Previous guidelines for the prevention of venous thromboembolism (VTE) for those undergoing total knee arthroplasty (TKA) have emphasized the importance of chemoprophylaxis. However, debate continues regarding the most effective agent to reduce the incidence of VTE while minimizing bleeding. This study examined the relative efficacy of low dose aspirin (LDA) compared to other agents.

Data were obtained from the U.S. Collaborative Network within TriNetX, a federated health research network with electronic health record (EHR) data for 88,338,842 adult patients. Records from 2012-2022 were queried for the proportion of patients at high and low risk for VTE who received only a low-dose aspirin (LDA) or an anticoagulant (AC). A temporal analysis was constructed of VTEs within 90 days after surgery.

Data were reviewed for 15,721 high risk patients in both the LDA and the AC groups. At 90 days, compared to the AC group, those in the LDA group had a reduced risk of deep venous thrombosis (Odds Ratio (OR) 0.25), pulmonary embolism (OR 0.23), hemorrhage (OR 0.19), hematoma (OR 0.70), stroke (OR 0.75), and mortality (OR 0.95). In the low-risk group, at 90 days, compared to those in the AC group, the LDA group had a reduced risk of deep venous thrombosis (OR 0.19), pulmonary embolism (OR 0.13), hemorrhage (OR 0.16), hematoma (OR 0.76), stroke (OR 0.71), and mortality (OR 0.73).

**Conclusion:** This study of patients undergoing total knee arthroplasty found that those treated with low dose aspirin had a reduced risk of venous thromboembolism and a lower risk of bleeding, as compared to other anticoagulants.

Lavu, M., et al. Low Dose Aspirin Is the Safest Prophylaxis for Prevention of Venous Thromboembolism after

Total Knee Arthroplasty across All Patient Risk Profiles. **J Bone Joint Surg Am.** 2024, Jul 17; 106(14): 1256-1267.

### RILUZOLE AND DEGENERATIVE CERVICAL MYELOPATHY

Degenerative cervical myelopathy (DCM) is an age-related, progressive spinal disorder. Despite being the most prevalent cause of non-traumatic spinal cord impairment, treatment options for DCM are sparse. As the sodium glutamate antagonist, riluzole has been shown to attenuate neurodegeneration in amyotrophic lateral sclerosis, this study assessed the efficacy of this medication for DCM.

The Cervical Spondylotic Myelopathy (CSM-PROTECT) trial included adults with DCM, each scheduled for decompressive surgery. Eligible patients had modified Japanese Orthopaedic Association (mJOA) Scale scores between eight and 14 (moderate to severe functional disability). The treatment group received oral riluzole, 50mg twice daily, for 14 days before surgery, and for 28 days after surgery. The primary outcome measure was the global treatment effect (GTE), a combination score including SF-36, PCS, neck pain NRS, arm pain NRS, ASIA motor score, and Nurick grade. The patients were followed for up to one-year.

Data were collected for 290 patients. The riluzole group demonstrated a greater probability of global improvement compared with placebo at one year follow-up (p=0.02). A better GTE was found at both 35 days and six months, though this did not reach statistical significance. The riluzole-treated patients had a 54% greater likelihood of achieving better outcomes at one year as compared with the placebo group.

**Conclusion:** This study of patients with degenerative cervical myelopathy who underwent decompressive surgery found that treatment with riluzole was associated with improved clinical outcomes.

Fehlings, M., et al. Riluzole for Degenerative Cervical Myelopathy: A Secondary Analysis of the CSM-PROTECT Trial. **JAMA Network Open.** 2024; 7(6): e2415643. doi:10.1001/jamanetworkopen.2024.15643.

### JOINT INFECTION IN MORBIDLY OBESE PATIENTS UNDERGOING ARTHROPLASTY

Studies have shown that morbid obesity is a risk factor for infection during surgery, including orthopedic surgery. This study was designed to identify preoperative laboratory values which may identify patients at greater risk for joint infection after total hip arthroplasty (THA) or total knee arthroplasty (TKA).

Using the Premier Healthcare Database, patients undergoing primary elective TKA or THA were identified. Data were extracted from the charts of those who were morbidly obese (BMI of  $\geq 40$  kg/m<sup>2</sup>) and had pre-operative laboratory data, including a complete blood count (CBC). From the data, CBC-based ratios (CBRs) were obtained, including the platelet-lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR), monocyte-lymphocyte ratio (MLR), and systemic immune-inflammation index (SII). Those with a periprosthetic joint infection (PJI) at ninety days were compared to those without an infection.

Of the 6,780 patients identified for this analysis, 47 (0.69%) developed a PJI within 90 days. Multivariable analysis revealed that a post-operative infection was associated with an abnormal NLR (aOR: 2.38, p=0.039), PLR (aOR: 4.86, p<0.001), SII (aOR: 2.44, p=0.029), platelet count (aOR: p=0.032), and hemoglobin level (aOR: 2.62, p=0.038).

**Conclusion:** This study of morbidly obese patients who underwent knee or hip arthroplasty found that preoperative anemia, abnormal platelet count, and elevated neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, and systemic immune-inflammation index are associated with an increased risk of periprosthetic joint infection.

Telang, S., et al. Preoperative Laboratory Values Predicting Periprosthetic Joint Infection in Morbidly Obese Patients Undergoing Total Hip or Knee Arthroplasty, **J Bone Joint Surg.** 2024, July; 106 (14), 17 July 2024, p 1317-1327.

### SLEEP APNEA AND OSTEOARTHRITIS

Studies have demonstrated common risk factors associated with obstructive sleep apnea (OSA) and osteoarthritis (OA). This study

assessed the association between OSA and OA.

Data were obtained from 12,454 participants in the National Health and Nutrition Examination Survey (NHANES). The NHANES initiative evaluated the wellbeing and dietary status of individuals in the United States. This research study involved participants from four cycles of NHANES, spanning 2005 to 2018. Data collection included demographics, dietary data, physical examinations, laboratory discoveries, and questionnaires. The exposure variable was OSA, while the outcome variable was OA.

The association between OSA and OA included causality using Mendelian randomization (MR). The laboratory data included serum calcium, Alt, ALP, creatinine, white blood cell count (WBC), and HB levels. Genetic predisposition was determined using data from the genome-wide association study (GWAS) on OSA from the Finnegan dataset population.

Of the participants, 1,560 (5.28%) were diagnosed with OA and 3,628 (29.53%) with OSA. Those with OSA had a higher prevalence of OA (39.84%) than those without OSA (27.95%). A reverse MR analysis was conducted to explore bidirectional causality using the same GWAS datasets. The MR analysis found that OSA was associated with an increased likelihood of OA (odds ratio [OR]=1.13,  $p=0.001$ ), hip OA (OR=1.11,  $p=0.002$ ), and knee OA (OR=1.08,  $p=0.005$ ). Reverse MR analyses indicated evidence of a causal relationship between OSA and OA, with BMI as a mediator.

**Conclusion:** The cross-sectional observational analysis found notable associations between OSA and OA, while MR study findings suggest a causal relationship.

Yang, Z., et al. The Relationship between Obstructive Sleep Apnea and Osteoarthritis: Evidence from an Observational and Mendelian Randomization Study. *Front Neurol.* 2024, June; 15 :1425327.

### REPURPOSED DRUGS FOR OSTEOARTHRITIS

Osteoarthritis (OA) is characterized by premature destruction of articular cartilage, subchondral bone cysts and bone remodeling, osteophytosis, and synovitis that involves multiple diverse cell types. In a subset of patients with OA, chronic, low-grade

inflammation contributes to disease pathogenesis, resulting in synovitis. In these patients the synovium demonstrates elevated levels of inflammatory cytokines such as tumor necrosis factor-alpha (TNF $\alpha$ ), interleukin (IL)-1beta and IL-6. These results have prompted multiple clinical trials of repurposed RA drugs for the treatment of OA.

The authors completed a literature search of trials that focused on drugs used to treat rheumatoid arthritis (RA) and comorbidities that are commonly associated with OA, including atopic/allergic disease, osteoporosis, type 2 diabetes, and cardiovascular disease.

The medications with some effect included; methotrexate, effective for pain, interleukin one inhibitors, tumor necrosis factor inhibitors, interleukin six inhibitors, antihistamines, oral salmon calcitonin, bone homeostasis treatments, vitamin D3, bisphosphonates, as well as metabolic disease treatments including metformin, GLP-1/DPP-4 inhibitors, and cardiovascular treatments including fish oil, statins, and non-selective beta blockers.

**Conclusion:** This study outlines drugs, repurposed from the treatment of rheumatoid arthritis, for the treatment of OA, which have demonstrated success in observational cohort studies, but have not shown strong outcomes in prospective studies.

Kuswanto, W., et al. Repurposing Drugs for the Treatment of Osteoarthritis. *OA Cartilage.* 2024, August; 32 (8): 886-895.

### ASPIRIN VERSUS ENOXAPARIN AFTER SPINE SURGERY

Patients with a spinal cord injury are at an increased risk of venous thromboembolic events (VTEs). No prior comprehensive studies have compared aspirin with other anticoagulants, including enoxaparin, in patients undergoing spine surgery. This randomized, controlled trial was conducted to compare the prophylactic efficacy of these two medications.

This randomized, controlled parallel arm trial included 100 patients scheduled to undergo spinal cord surgery between February of 2023 and July of 2023. The inclusion criterion was a Caprini score greater than five for the occurrence of DVT. A control group received subcutaneous injections of enoxaparin 40 mg for DVT prevention, while an intervention group received oral aspirin 81 mg per

day. The drugs were begun 24 hours after the surgical procedure and continued for seven days. The primary outcome variables were the occurrence of DVT or hemorrhage events, as assessed with Doppler ultrasound within seven days after surgery.

The rates of postoperative DVT were 4.0% in the aspirin group and 10.0% in the enoxaparin group ( $p=0.092$ ). The rates of hemorrhage were 2.0% in the aspirin group and 4.0% in the enoxaparin group ( $p=0.610$ ).

**Conclusion:** This study of patients undergoing spine surgery found low dose aspirin to be as effective as low molecular weight heparin for preventing venous thromboembolism.

Kavian, A., et al. A comparison between Enoxaparin and Aspirin in Preventing Deep Vein Thrombosis after Spine Surgery: A Randomized, Clinical Trial. *Arch Bone Jt Surg.* 2024; 12(6): 412-417.

### GENDER DIFFERENCES IN RECOVERY FROM SPORTS RELATED CONCUSSION

After the passage of title IX in 1972, there has been a substantial rise in opportunities for female athletes. While the overall effect of this has been positive, there has also been a rise in sports related injuries among female athletes, including sports related concussions (SRC). This study explored gender differences in recovery trajectories after an SRC.

The subjects were student athletes from civilian universities and cadets/midshipmen from U.S. service academies. All underwent pre-season baseline assessment. Those who experienced a concussion were reassessed within six hours and again at 24-48 hours after injury. Assessment tools at all sites (level A) included the Standardized Assessment of Concussion (SAC), Balance Error Scoring System (BESS), Brief Symptom Inventory-18 (BSI-18), Sport Concussion Assessment Tool-3 (SCAT-3) symptom evaluation, and computerized cognitive testing (ImPACT). Level B assessments, considered emerging and optional, included the Clinical Reaction Time Test, the King-Devick Test, the Vestibular Ocular Motor Screen (VOMS), the 12-Item Short-Form Health Survey (SF-12), the Hospital

Anxiety and Depression Scale and the Satisfaction with Life Scale.

Data were analyzed for 906 athletes, of whom 61% were female. Female athletes reported more symptoms and had worse ImPACT Visual Memory Scores, slower reaction times, and King Devick Total Times, and reported worse SF-12 PCS scores. During recovery, only the VOMS at 24-48 hours was different between men and women, with females having higher (worse) scores ( $p=0.005$ ). This difference resolved by the time of return to play.

**Conclusion:** This study of collegiate athletes found that, while females had worse symptoms at the time of injury, the recovery from concussion was similar to that of men, differing only in the increased vestibular symptoms in females up to 48 hours after injury.

Caccese, J., et al. Sex Differences in Recovery Trajectories of Assessments for Sport-Related Concussion among NCAA Athletes: A CARE Consortium Study. *Sports Med.* 2024; 54(6), June: 1707-1721.

### ROTTERDAM SCORING AND OUTCOME AFTER SEVERE TRAUMATIC BRAIN INJURY

Severe traumatic brain injury (TBI) has an estimated mortality rate of 20-40%. The Rotterdam Scoring System (RSS) was developed to help prognosticate for patients after a TBI, based on CT imaging findings. This study was designed to better understand the efficacy of the RSS for predicting long-term outcomes after a severe TBI.

This prospective, observational study included patients involved in the prospective longitudinal Brain Trauma Research Center database. All participants underwent multimode neural monitoring and were treated with a standardized treatment protocol. After resuscitation each subject immediately underwent non-contrast CT, which was used to calculate the RSS. The Glasgow Outcome Scale (GOS) was used to assess outcomes for up to 24 months. Outcomes were categorized as favorable (GOS=4-5) and unfavorable (GOS=1-3).

Of 168 eligible patients, 79 were lost to follow-up. Those with an RSS of three or less were more likely to have favorable outcomes than patients with an RSS of more than three at three months ( $p=0.01$ ), six months ( $p=0.0003$ ), 12 months ( $p=0.0002$ ), and 24 months ( $p=0.0004$ ). In addition, the RSS

scores correlated with survival at three, six, and 12 months ( $p<0.001$  for all) and two years ( $p=0.04$ ).

**Conclusion:** This study of patients hospitalized with a severe TBI found that initial scores on the CT-based Rotterdam Scoring System are helpful in predicting long-term outcomes.

Agarwal, N., et al. Neuroimaging with Rotterdam Scoring System and Long-Term Outcomes in Severe Traumatic Brain Injury Patients. *Br J Neurosurg.* Online ahead of print. 2024; doi.org/10.1080/02688697.2024.2349749.

### COGNITION YEARS AFTER COVID

Data suggests that more than 10% of the global population has been infected with the COVID-19 virus. Survivors have reported various cognitive deficits. This study evaluated the 2.5-year trajectory of cognition in individuals hospitalized for infection with the original COVID-19 strain.

Data were obtained from 1,245 adults  $\geq 60$  years of age hospitalized for COVID-19 in Wuhan, China, who were discharged February 2020 and April 2020. Follow-up evaluations were completed at six, 12 and 30 months after hospital discharge. Data collection included demographics, BMI, and coexisting diseases. Cognitive changes from 6 to 12 months, 12 to 30 months and 6 to 30 months were assessed by the change in Telephone Interview for Cognitive Status-40 (TICS-40) scores. Comparisons were made between severe(S) COVID-19 survivors ( $n=208$ ), non-severe (NS) COVID-19 survivors ( $n=1,037$ ) and controls (Con) chosen from spouses of patients ( $n=358$ ).

At the 30-month follow-up, the scores on the TICS-40 were worse in the S group compared to the NS and Con groups ( $p<0.001$  and  $p=0.01$  respectively). Scores on the TICS-40 were worse in the NS than the Con group ( $p<0.001$ ). At 30 months follow-up, individuals in the S group had a higher proportion of progressive cognitive decline than individuals in the NS group (19.71% versus 8.87%,  $p<0.001$ ) and the Con group (19.71% versus 6.98%,  $p<0.001$ ). The risk factors for cognitive decline included severe illness, cognitive impairment at six months, delirium during hospitalization, vascular risk factors (hypertension and diabetes) and COPD.

**Conclusion:** This study of patients hospitalized with COVID-19

in Wuhan Cina found that the overall incidence of cognitive impairment among older survivors was 19.1% at 2.5 years.

Liu, Y., et al. Tracking Cognitive Trajectories in Older Survivors of COVID-19 Up to 2.5 Years Post Infection. *Nat Aging.* 2024, July; doi: 10.1038/s43587-024-00667-3.

### TWICE-YEARLY LENACAPAVIR FOR HIV PREVENTION

Global human immunodeficiency virus (HIV) infection is a significant contributor to disability adjusted life years. Women account for nearly half of the nearly 1.3 million new HIV infections that occur each year. Lenacapavir is a novel, first-in-class, multistage HIV-1 capsid inhibitor with high potency and a long half-life, allowing administration by subcutaneous injection twice yearly. This study evaluated the efficacy of this medication for HIV prevention.

This phase three, multicenter, double-blind, randomized, active-controlled trial (PURPOSE 1) recruited girls and young women (16 to 25 years of age) in South Africa and Uganda. All were sexually active with male partners with unknown HIV status. Those testing HIV negative at baseline were randomized to receive subcutaneous lenacapavir (927 mg, in two 1.5-ml injections) every 26 weeks (within a window of  $\pm 7$  days), daily oral F/TAF (200 mg of emtricitabine and 25 mg of TAF), or daily oral F/TDF (200 mg of emtricitabine and 300 mg of TDF). All were seen for follow up at 4, 8 and 13 weeks, and then every 13 weeks thereafter. The primary efficacy end point was incident HIV infection among randomly assigned participants.

The participants included 5,338 females with a median age of 21 years. The overall retention in the trial was 96.7% at week 26, 93.4% at week 52, and 91% at week 104. During follow up 55 incident HIV infections were discovered, including zero in the Lenacapavir group, 39 in the F/TAF group and 16 in the F/TDF group ( $p<0.001$ ).

**Conclusion:** This prospective double-blind study of adolescents and young women in South Africa and Uganda. found that a twice per year injection with Lenacapavir was 100% effective in preventing HIV infection.

Bekker, L., et al. Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women. *N Engl J Med.* 2024, July 24;DOI: 10.1056/NE/Moa2407001.

## ACTIVITY LIMITATIONS, ASSISTIVE DEVICES, AND MORTALITY

In the global population, the number of individuals  $\geq 60$  years of age is expected to increase from one billion in 2020 to more than two billion by 2050. This growth is almost three times more in the higher and middle-income countries than in lower income countries. The Prospective Urban Rural Epidemiological (PURE) study assessed self-reported activity limitations and assistive device use in 25 countries.

This prospective study collected information on sociodemographic comorbidities and risk factors as well as activity limitations at baseline. The activity limitation screen consisted of seven separate questions focusing on difficulty with walking, bending down, picking up an object from the floor, using fingers to grasp or handle, seeing close distances, seeing across the room, speaking and being understood, and hearing in a normal conversation.

Data were gathered from 175,660 individuals with a mean age of 50.5 years, with a mean follow up of 10.7 years. The most common activity limitations were difficulty with bending (30%), seeing close (13.4%) walking (13%) grasping (9.6%) seeing distances (7.5%) hearing normal conversations (5.5%), speaking or being understood (1.8%). At least one limitation was noted by 33.2% with 14.2% reporting two limitations.

**Conclusion:** This multinational study found that the global prevalence of activity limitations is over 30% with the availability of assistive devices lowest in the lowest income countries.

Joundi, R., et al. Activity Limitations, Use of Assistive Devices, And Mortality and Clinical Events From 25 High Income, Middle Income, and Low-Income Countries: An Analysis of The PURE Study. *Lancet*. 2024. In Press. [https://doi-org.proxy.library.emory.edu/10.1016/S0140-6736\(24\)01050-X](https://doi-org.proxy.library.emory.edu/10.1016/S0140-6736(24)01050-X).

## RISK OF STROKE AFTER A TRAUMATIC BRAIN INJURY

Traumatic brain injury (TBI) is associated with significant morbidity and mortality. While the short term behavioral, cognitive, and physical morbidity has been well established, TBI is now recognized as a chronic condition with implications for long term neurologic health. This study assesses the association between TBI and incident ischemic stroke.

The Atherosclerosis Risk in Communities ARIC study is a community-based cohort study of adults 45 to 64 years of age, recruited in 1987-1989. The subjects were followed until December 31, 2019, or to the date of incident stroke. Data were collected from 12,813 individuals who had no history of TBI at enrollment. Head injuries requiring hospital care were identified using diagnostic codes. Stroke hospitalizations from 1987-2019 were identified through follow-up phone calls and community surveillance.

Of the 12,813 subjects 2,157 (16.8%) had a TBI, with 2,107 identified from hospital records and 532 that were self-reported. Over the study period, 1,141 (8.9%) incident ischemic strokes occurred, with 147 among individuals with TBIs. The hazard of ischemic stroke among those with TBIs was 1.34 times the hazard among those without a TBI. A dose-response association with ischemic stroke was noted after one TBI (hazard ratio [HR] 1.16) and for two or more TBIs (HR 1.94). The risk of stroke was also greater for those with severe TBI than for those with mild TBI or no TBI.

**Conclusion:** This study of community dwelling adults found that the risk of ischemic stroke is increased after incurring a TBI.

Elser, H., et al. Head Injury and Risk of Incident Ischemic Stroke in Community Dwelling Adults. *Stroke*. 2024, June;55(6): 1562-1571.

## SYSTOLIC BLOOD PRESSURE 120 MMHG VERSUS 140 MMHG

Elevated blood pressure is the largest modifiable contributor to cardiovascular disease, and premature death worldwide. This study compared the efficacy and safety of targeting systolic blood pressure (SBP) of  $< 120$  mm Hg to standard treatment ( $< 140$  mmHg) for adults with elevated cardiovascular risk, with or without diabetes or previous stroke.

The subjects were  $\geq 50$  years of age and with baseline SBP 130-180 mmHg, and with an elevated cardiovascular risk (established cardiovascular disease or at least two major cardiovascular risk factors, including aged  $\geq 60$  years for men or  $\geq 65$  years for women, diabetes, dyslipidemia, and current smoker). The subjects were randomly placed to receive intensive treatment (target SBP of  $< 120$  mm Hg) or standard treatment. The participants were seen at routine office visits for a median of 3.4 years. To optimize medication

use, free medications were provided, covering the five major classes of antihypertensive medications. The primary outcome measure was major vascular events.

During the follow-up the mean SBP in the intensive group was 119.1 mmHg and, in the standard group was 134.8 mm Hg. The primary outcome event occurred in 547 (9.7%) of 5,624 participants from the intensive treatment group and 623 of 5,631 (11.1%) from the standard treatment group ( $p=0.028$ ).

**Conclusion:** This study of adults with an elevated cardiac risk found that the treatment strategy of targeting systolic blood pressure of less than 120 mm Hg, as compared with that of less than 140 mm Hg, resulted in a significant reduction in the occurrence of major vascular events.

Liu, J., et al. Lowering Systolic Blood Pressure to Less than 120 mm Hg Versus less than 140 mm Hg in Patients with High Cardiovascular Risk with and Without Diabetes or Previous Stroke: An Open-Label, Blinded-Outcome, Randomized Trial. *Lancet*. 2024, July;404:245-255.

## ADULT SMOKING CESSATION 2022

Tobacco dependence is a chronic condition driven by nicotine addiction. Studies have shown that while interventions have been relatively ineffective, the likelihood of success is increased by health care provider intervention, including medications and by the use of behavioral counseling. This study provides data on the prevalence of tobacco use and attempts to quit in 2022.

The National Health Interview Survey is an annual nationally representative household survey of non-institutionalized United States citizens. The data are weighted to provide nationally representative estimates, adjusting for differences in selection probability and response. Seven smoking cessation indicators were assessed; 1) an interest in quitting, 2) attempt at quitting in the past year, 3) recent successful cessation, 4) receipt of healthcare professional advice to quit tobacco abuse, 5) receipt of health care professional assistance to quit, 6) use of counseling to quit, and 7) use of medication to quit.

In 2022, 28.8 million (11.6%) of the U.S. adults reported current cigarette smoking. Of these, 67.7% stated that they wanted to quit, 53.3% tried to quit in the past year, but only 8.8% were successful in recently



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quitting. Among adults who currently smoked or who quit in the past year, 77.6% and 83.1% respectively saw a health care provider in the past year. Among these adults, approximately 1/2 received health professional advice about quitting. Fewer than four in 10 adults who attempted to quit in the past year used evidence-based treatments. The prevalence of past-year quit attempts ranged from 74.4% among persons aged 18–24 years to 47.5% among those aged 45–64 years. Recent successful quitting ranged from 15.3% among those aged 18–24 years to 5.6% among those aged 45–64 and ≥65 years.

**Conclusion:** In 2022, of the 28.8 million Americans who smoked cigarettes, most expressed a desire to quit, but fewer than 10% who tried to quit were successful.

VanFrank, B., et al. Adult Smoking Cessation — United States, 2022. *MMWR*. 2024, July25;73(29).

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