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TRAJECTORIES OF SLEEP DURATION AND DEMENTIA

Several studies have explored the association between sleep patterns and dementia, although the heterogeneity of the results has hampered conclusions. This study examined the relationship between baseline and self-reported sleep parameters and the incidence of dementia.

Participants were 1,749 cognitively healthy adults, 65 years of age or older at baseline. At each follow-up, global cognitive function was assessed with the Mini-Mental Status Examination (MMSE). A diagnosis of dementia was established and verified by an independent committee of neurologists. The subjects were asked to estimate their usual bedtime, time out of bed, and length of sleep during the night and during the day. Bedtime and wake-up times were also recorded. The Epworth Sleepiness Scale was used to estimate daytime sleepiness. In addition, baseline covariates included age, gender, educational level, mobility restrictions, body mass index, hypertension, diabetes, hypercholesterolemia, and cardio-cerebral vascular disease.

During a median follow-up of 10.1 years, 10.5% of the participants developed dementia. A higher risk of dementia was found among those with longer 24-hour sleep durations, particularly for those who slept for nine or more hours. Compared with non-demented participants, those with incident dementia were more likely to have a persistent long sleep duration (8h) or a change from short/normal to long sleep duration. Those reporting a persistently late bedtime (after 11 pm) were less likely to develop dementia.

Conclusion: This study of community-dwelling older people found that the risk of dementia was increased among those who slept more than eight hours per night and those who had earlier bedtimes.

Cavailles, C., et al. Trajectories of Sleep Duration and Timing before Dementia: A 14-Year Follow-Up Study. *Age Aging*. 2022 Aug 2;51(8):afac186. doi: 10.1093/ageing/afac186.

GLOBAL PREVALENCE OF MILD COGNITIVE IMPAIRMENT

Mild cognitive impairment (MCI), the preclinical and transitional stage between healthy aging and dementia, is viewed as a potential target for intervention. This study provides an updated review of the worldwide prevalence of MCI among community dwellers 50 years of age or older.

A review of the medical literature was completed for studies involving community-dwelling persons over 50 years of age and diagnosed with MCI. For inclusion, studies were assessed for their representation of the entire population, which used validated criteria to assess for the presence or absence of disease.

Data were obtained from 66 articles comprising 242,804 participants. The mean ages of the samples ranged from 62.1 years to 86.34 years. The overall prevalence of MCI was 15.56%, increasing with age from 10.88% of those 50-59 years to 21.27% of those over 80 years. The prevalence was 19.7% for those with \leq six years and 11.33% for those with $>$ six years of education ($p=0.0185$). A subgroup analysis demonstrated that the geographic region of the study and male gender proportion per sample were significant correlates of MCI prevalence. Those studies from Latin/Caribbean and from Asia/Pacific regions had higher rates of MCI.

Conclusion: This large meta-analysis estimated the global prevalence of mild cognitive impairment among community dwellers over 50 years of age to be 15.56%.

Bai, W., et al. Worldwide Prevalence of Mild Cognitive Impairment among Community Dwellers Aged 50 Years

and Older: A Meta-Analysis and Systematic Review of Epidemiology Studies. *Age Aging*. 2022; 51: 1-14.

LIFE EXPECTANCY IN THE UNITED STATES

Large differences in life expectancy have long been observed between racial and ethnic groups. This study examined the recent trends in life expectancy among the three largest ethnic groups in the United States.

Data were obtained from the United States census to construct a time series by state, gender, and ethnic group from 1990 to 2019. Estimates of all-cause mortality were obtained from the National Vital Statistics System. Life expectancy for each group was generated for 1990, 2000, and 2019.

For all females, in 1990, the mean life expectancy was 79.3, increasing by 2019 to 81.3, a gain of two years (+2). For Hispanic females, the change was 84.8-88.1 years (+3.3). For Black females, the change was 74.2-79.3 years (+5.1). For White females, the change was 79.9-81.4 years (+1.5). For all males, the mean life expectancy in 1990 was 72.6, and in 2019 was 76.3 (+3.7). Changes over the same period were 77.2-82.8 (+5.6) for Hispanic males, 65.7-72.9 (+7.2) for Black males, and 73.5-76.6 (+3.1) for White males.

Overall, this study comparing life expectancy in 1990 to that in 2019 found that the greatest gains in life expectancy were realized by Black males and Hispanic males, though significant differences persist between groups.

Conclusion: This study found that, between 1990 and 2019 life expectancy in the US increased by a mean of two years, ranging from an increase of 7.2 years for Black males to 1.5 years for White females.

Johnson, C., et al. Life Expectancy for White, Black and Hispanic Race/Ethnicity in the U.S. States: Trends and Disparities from 1990 to 2019.

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Annals Int Med. 2022, August; 175 (8):1057-1064.

GUILLAIN-BARRE AFTER INFLUENZA VACCINATION

In 25% of cases, Guillain-Barre syndrome (GBS) is preceded by an infection that may induce an aberrant immunological response. This study assessed the risk of GBS after receiving a seasonal influenza (flu) vaccination.

This Danish study identified all patients diagnosed with GBS between 2002 and 2016. The Danish civil registration system was used to randomly select 10 controls for each case, matched for age and gender. Logistic regression analysis was used to compute the odds ratios (OR) of GBS within one month of vaccination.

Data were reviewed for 1,295 GBS cases and 12,814 matched controls. Among those with GBS, 34.4% had had an infection within the previous five months, as compared to 17% in the control group. Among those with GBS, 1.5% were vaccinated within one month of the index date, as compared with 0.9% of the controls (adjusted OR 1.9). The increased GBS risk was confined to within one month of the influenza vaccination.

Conclusion: This Danish study found that influenza vaccination resulted in a 1.9-fold increased risk of GBS within the first month after the vaccination.

Levison, L., et al. Guillain-Barre Syndrome following Influenza Vaccination: A 15-Year, Nationwide, Population-Based, Case-Control Study. *Europ J Neurol.* 2022. doi.org/10.1111/ene.15516.

COLCHICINE AND COVID-19 VACCINATION

Previous studies have suggested a possible connection between vaccines against the COVID-19 virus and flares of gout. This study was designed to clarify this relationship and the effect that colchicine may have.

This Chinese, population-based, observation and cross-sectional study included patients with a diagnosis of gout. All subjects completed a gout assessment questionnaire, a history of COVID vaccines, and data regarding flares of gout. Gout-specific health quality of life was assessed by the Gout Impact Scale of the Gout Assessment Questionnaire (GAQ).

The type and date of each vaccine were recorded.

Data were reviewed for 549 participants with a median age of 39 years. Of these, 462 received a COVID-19 vaccine with 400 receiving two doses. Of those who received the vaccine, 203 (43.9%) developed at least one gout flare within three months of any vaccine. Of these, 83.2% had symptoms within the first month. Compared to those unvaccinated, the risk of a flare in the first three months was significantly higher, with an odds ratio (OR) of 6.02. Of those who received a vaccine, those who had received a prescription of colchicine were 47% less likely to experience gout flare (OR 0.53).

Conclusion: This Chinese study found that a COVID-19 vaccination is associated with an increased risk of gout flares, with colchicine reducing this risk.

Lu, J., et al. Colchicine Prophylaxis is Associated with Fewer Gout Flares after COVID-19 Vaccination. *Ann Rheumatic Dis.* 2022, Aug; 81(8): 1189-1193.

STRUCTURAL CHANGES AFTER MENISCAL TEAR AND OSTEOARTHRITIS

Osteoarthritis (OA) affects more than 15 million adults in the United States. Over 90% of patients with symptomatic OA of the knee have meniscal tears. This study examined the risk of structural changes in the knee among individuals with a meniscal tear and knee OA.

Data were obtained from the Meniscal Tear and Osteoarthritis Research Trial (METEOR). Subjects were 45 years of age or older at baseline, had experienced knee pain for four or more weeks, had a meniscal tear extending to the surface of the meniscus, and had radiographic evidence of OA. Those randomized to a Physical Therapy (PT) group underwent a standardized, strengthening-based PT protocol involving weekly sessions with a physical therapist and home-based exercises. The surgical group underwent arthroscopic surgery to trim the damaged portion of the meniscus to a stable rim. The MRIs were scored using the MRI OA Knee Score (MOAKS), with baseline scores compared to those of MRIs at 18 and 60 months.

Data were analyzed for 302 participants, with 154 randomized to the surgical group and 148 to the PT

group. Compared to the PT group, changes in MOAKS scores between baseline and 18 months were worse in the surgical group ($p=0.0309$). Similar differences in groups were found in assessments of cartilage surface area and effusion-synovitis scores ($p=0.006$).

Conclusion: This prospective study of patients with osteoarthritis of the knee and meniscal tears found that compared to physical therapy, those treated with surgery had a worsening of MOAKS scores of structural damage.

Collins, J., et al. Five-Year Structural Changes in the Knee Among Patients with Meniscal Tear and Osteoarthritis: Data from a Randomized Controlled Trial of Arthroscopic Partial Meniscectomy Versus Physical Therapy. 2022, August; 74(8): 1333-1342.

AMERICAN FOOTBALL-RELATED INJURIES 2010-2019

American football is one of the most popular sports in the United States among youth and high school athletes. The Sport and Fitness Industry Association (SFIA) reported that the number of participants between the ages of six and 12 years has dropped by 18.7% since 2010. This decline coincides with a public debate over the safety of the sport. This study reviewed the risk of football-related injuries in the U.S. between 2010 and 2019.

Yearly data were obtained from the Consumer Product Safety Commission's National Electronic Injury Surveillance System (NEISS). Using these data, national estimates were made of injuries and types of injuries.

From 2010 to 2019, the number of football participants in the U.S. decreased by 1.8% per year among those six to 12 years of age (youth), while the number among high school students decreased by an average of 1.19% ($p<0.001$ for both). From 2010 to 2019, the risk of injury for youth athletes decreased from 13.31/1,000 participants to 9.93/1,000. For high school athletes, the risk decreased from 18.63/1,000 in 2010 to 13.19/1,000 in 2019 ($p<0.001$ for both).

Conclusion: This study of youth and high school football in the United States found that, between 2010 and 2019, the number of participants fell, as did the risk of injury to those who did participate.

Hoge, C., Epidemiology of Youth and High School American Football Related Injuries Presenting to United States Emergency Departments: 2010-2019. **Physician and Sports Medicine**. 2022; 50(4): 332-337.

RESISTANCE TRAINING WITH CORTICOSTEROID INJECTIONS FOR TENNIS ELBOW

Lateral elbow tendinopathy (tennis elbow) is usually self-limiting but becomes chronic in 10-25% of patients. This study investigated the effects of 12 weeks of heavy, slow resistance training combined with a corticosteroid injection, dry needling, or placebo dry needling.

This Danish, three-arm, randomized, double-blind, placebo-control study included 60 patients, 18 to 70 years of age, with unilateral, chronic, lateral elbow tendinopathy. Baseline assessments included the Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire, the Numeric Rating Scale (NRS) for pain, and pain-free grip strength, as evaluated with a DHD-3 Digital Hand Dynamometer. A power Doppler was used to assess blood flow.

The subjects underwent progressive heavy, slow resistance training of the muscles of elbow flexion-extension, supination/pronation. Prior to the exercise training, those randomized to the corticosteroid group (CSI) received an injection of 1mL Depo-Medrol (40 mg/mL) and 1 mL of lidocaine (10 mg/mL). The tendon needling (TN) group received 1mL of 0.9% isotonic saline inserted through the tendon. The placebo needling (PN) group received a saline injection just below the skin.

Pain-free grip strength on the affected side increased from baseline to 12 weeks for all three groups ($p<0.0001$). At 12 weeks, all three groups demonstrated significant improvement in DASH scores compared with baseline, with no significant differences between groups. Hypervascularization decreased in the CSI group ($p<0.0001$) but was unchanged for the TN ($p=0.9236$) and PN ($p=0.1397$) groups from baseline to 12 weeks. After 52 weeks, DASH scores in the CSI group trended towards less improvement than those of the PN group ($p=0.0581$).

Conclusion: This study of patients with lateral epicondylitis found that adding a corticosteroid injection to a program of heavy, slow resistance training may diminish

improvements in pain and function at 52 weeks.

Coupe, C., et al. Effects of Heavy, Slow Resistance Training, Combined with Corticosteroid Injections or Tendon Needling, in Patients with Lateral Elbow Tendinopathy: A 3-Arm Randomized Double-Blinded Placebo-Controlled Study. **Am J Sports Med**. 2022, August; 50(10): 2787-2796.

GENOMIC RISK FOR ADVANCED OSTEOARTHRITIS

Osteoarthritis (OA) is a chronic disease with no known cure. Recently, large genetic studies have discovered common genetic risk loci associated with OA. These discoveries have enabled the calculation of a polygenetic risk score (PRS), suggesting a combined measure of genetic risk. This study was designed to validate the newly derived PRS for OA.

Subjects were enrolled in the Aspirin in Reducing Events in the Elderly (ASPREE) trial. This study investigated whether 100 milligrams of aspirin per day could extend disability-free survival in healthy, older adults. Knee and hip replacements during the ASPREE trial (median follow-up of 4.7 years) were identified by a review of all hospitalizations for knee and hip surgical procedures, most with the indication recorded as OA. Genotyping was performed on 14,052 DNA samples with a PRS derived. The PRS scores were analyzed as continuous variable and were also categorized into three groups based on quintiles of the PRS distribution: low-risk (quintile 1 [Q1], 0-20%), medium-risk (Q2-4, 21-80%) and high-risk (Q5, 81-100%). A regression was used to examine the associations between PRS and risk of joint replacement, adjusted for age, sex, body mass index, and socioeconomic status.

Data were completed for 12,093 participants with an average age of 75 years. During the follow-up, 11.8% had at least one knee replacement and 10.7% had at least one hip replacement. A higher PRS was associated with an increased risk of knee replacement (OR 1.13) and hip replacement (OR 1.23). Compared to those in the lowest PRS quintile, the highest risk PRS group was at a greater risk for total knee replacement (OR 1.44) and hip replacement (OR 1.88).

Conclusion: This study found that a polygenetic risk score was

associated with an increased risk of both hip and knee replacement.

Lacaze, P., et al. Genomic Risk for Advanced Osteoarthritis in Older Adults. *Arthritis Rheumat.* 2022; 74(9): 1480-1487.

EXERCISE INTERVENTION FOR HOSPITALIZED PATIENTS

Bed rest during recovery in acute care is known to play a major role in deconditioning. Exercise has been shown to diminish damage due to acute disease and hospitalization. This study involved a secondary analysis of a randomized, controlled, clinical trial completed in a geriatric, tertiary hospital.

Subjects were 75 years of age or older, each admitted to the acute care ward of a tertiary hospital. Those patients were randomized to receive usual care or to an exercise intervention (EI) group. Participants in the exercise program performed three lower extremity exercises to optimize muscle power. Resistance exercise involved two to three sets of eight to 10 repetitions at 30 to 60% of the one repetition maximum.

Evening sessions included functional, unsupervised exercise using light loads and walking in the corridor. The primary outcome variable was the change in the Frailty Index (FI). Secondary outcomes included changes in cognition, depression, quality of life, delirium, hand grip strength, length of stay, and falls.

Data were analyzed for 323 patients with a mean age of 87.1 years and a mean FI of 0.26. FI scores improved from 0.26 to 0.2 in the EI group and worsened from 0.25 to 0.27 in the control group ($p < 0.001$). In addition, the intervention group demonstrated greater improvement in the Barthel Index, the Short Physical Performance Battery, the Mini-Mental State Examination, the Geriatric Depression Scale, the EuroQol 5D Quality of Life Scale, and hand grip strength ($p < 0.05$ for all comparisons). At 58-month follow-up, the intervention group demonstrated significantly lower mortality ($p < 0.05$).

Conclusion: This study demonstrates that a multicomponent, individualized physical exercise intervention is effective in reversing frailty in acutely hospitalized older patients.

Pérez-Zepeda, M., et al. The Impact of an Exercise Intervention on Frailty Levels in Hospitalised Older Adults:

Secondary Analysis of Randomised, Controlled Trial. *Age Ageing*, 2022, August; 51(2): afac028, <https://doi.org/10.1093/ageing/afac028>.

ACUPUNCTURE PLUS AURICULAR ACUPRESSURE FOR SMOKING CESSATION

In 2017, the global prevalence of tobacco smoking among those 15 years or older was 17.5%. Although numerous trials have investigated potential interventions for those who wish to stop smoking, no single best method has been identified. This study reviewed the effect of acupuncture, combined with acupressure, as an intervention for smoking cessation.

This prospective, multicenter trial was completed between September 2020 and February of 2022. Subjects were current smokers who wanted to quit, were 18-65 years of age, had smoked for one year or more, and consumed 20 or more cigarettes per day. All participants received standardized acupuncture and auricular acupressure treatments twice weekly for eight consecutive weeks. The acupuncture points were Baihui (GV20), Yintang (GV29), bilateral Lieque (LU7), and bilateral Hegu (LI4). The auricular acupoints used were Shenmen (TF₄), Fei (CO₁₄), Wei (CO₄), Neifenmi (CO₁₈), Pizhixia (AT₄), Jiaogan (AH_{6a}), and Kou (CO₁). The primary outcome variable was the success rate of smoking cessation at week 24. Success was defined as self-reported cessation and verified by exhaled CO level.

Smoking cessation was successful 36.67% at eight weeks, 43.33% at 16 weeks, and 46.67% at 24 weeks. Changes from baseline scores in the Fagerström Test for Nicotine Dependence (FTND), improved significantly from weeks 2 to 24 ($p < 0.05$). Those who successfully quit had significantly greater improvement between weeks 8 and 24 ($P < 0.01$).

Conclusion: This pilot study involving patients who wished to quit smoking found that a combination of acupressure and acupuncture was successful in achieving cessation at 24 weeks in nearly half of the cases.

Ho, L., et al. Acupuncture Combined with Auricular Acupressure for Smoking Cessation and its Effects on Tobacco Dependence and Smoking Behavior among Hong Kong Smokers: A Multicenter, Pilot, Clinical

Study. *Chinese Med.* 2022, August; 17(92).

TARGETING RULE AND NECK INJURIES IN HIGH SCHOOL FOOTBALL

An estimated 15% of all cervical spine injuries occur during sports. Of these, American football players exhibit the highest rate compared to athletes of other sports. This study was designed to determine the effect of the 2014 National Federation of State High School Association's (NFHS) rule change on the rates of high school football neck injuries. This rule, the targeting rule, was designed to bring awareness to the action of targeting and minimizing head injuries in football players. The targeting rule is defined as an act of taking aim and initiating contact with an opponent above the shoulders with the helmet, forearm, hand, fist, elbow, or shoulders. The defenseless player rule (2.32-16) was introduced to expand the use of the targeting rule, defining a defenseless player as one who, because of his physical position and focus of concentration, is especially vulnerable to an injury.

Injury data were obtained from the National Electronic Injury Surveillance System (NEISS). Injury data for patients 14 to 18 years of age were collected from 2009 to 2013 (baseline) and compared to data collected after the 2014 NFHS rule change from 2015 to 2019 (post-implementation).

Between January 1, 2009, and December 31, 2019, the yearly average of football-related neck injuries was 5,278. In the post-implementation period, this declined to 3,481 ($p = 0.04$). Neck injuries sustained via other mechanisms were not affected by the 2014 rule implementation.

Conclusion: This study identified a significant decrease in the annual incidence of high school neck injuries related to American football.

Obana, K., et al. Targeting Rule Implementation Decreases Neck Injuries in High School Football: A National Injury Surveillance Study. *Physician Sports Med.* 2022, Aug; 50(4): 338-342.

GLUCOCORTICOID INJECTIONS AND KNEE OSTEOARTHRITIS

Osteoarthritis (OA) of the knee is a major source of disability. Current treatments are aimed at reducing

pain and improving functional abilities. While intraarticular glucocorticoid (IA-G) injections have been found to be effective for pain relief, the effect of repeat injections on cartilage or other joint tissues is unclear. This study was designed to better understand the effect of these injections on the structural progression of OA.

Data were obtained from the Knee and Hip Osteoarthritis Long-term Assessment (KHOALA). This multicenter, population-based cohort included patients ages 40 to 75 years of age with symptomatic knee and/or hip OA. The participants were asked whether they had received IA-G or IA hyaluronan (IAHA) injections during the previous 12 months. Patient-reported outcomes included knee-related pain scores on a visual analog scale (VAS) and function as well as pain scores on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Patients underwent knee radiographs at baseline and at years three and five.

The subjects were 564 patients with knee OA, of whom 7.8% received IA-G injection, 15.1% received IAHA injections, and 63.1% received no injection (Controls). Compared to the controls, the risk of radiographic worsening or TKR was no greater among those who received an IA-G injection ($p=0.20$).

Conclusion: This study of patients with symptomatic knee osteoarthritis found that those treated with intraarticular glucocorticoid injections were at a similar risk of total knee replacement or radiographic progression over five years when compared to untreated patients.

Latourte, A., et al. Do Glucocorticoid Injections Increase the Risk of Knee Osteoarthritis Progression over Five Years? *Arthritis Rheumatol.* 2022, Aug; 74(8): 1343-1351.

EARLY TIME-RESTRICTED EATING FOR WEIGHT LOSS

Intermittent fasting (IF) is a practice of extending the time between meals. This study examined the effect of having a daily fast of 12 hours or more.

The subjects were new patients at the Weight Loss Medicine Clinic of the University of Alabama at Birmingham. Participants were 25-75 years of age, with a body mass index (BMI) of between 30 and 60 kg/m². In a 14-week trial, the subjects were

randomized to follow an eight-hour eating window between 7:00 AM and 3:00 PM (IF) or a self-selected time designed to mimic the U.S. median mealtime habits (Control). Randomization was performed, with stratification by gender, race, and baseline physical activity. All subjects received weight-loss counseling concerning energy restriction. The primary outcomes were weight loss and fat loss. Body composition was measured using dual x-ray absorptiometry.

Subjects were 90 adults with a mean body mass index of 39.6 kg/m² and a mean age of 43 years. After the evening meal, breakfast was eaten at a mean of 7.6 hours in the control group and 12.3 hours in the IF group. The mean weight loss was 6.3 kg for the treatment group and 4.0kg for the control group ($p=0.002$). There were no between-group differences in self-reported physical activity or energy intake. Diastolic blood pressure fell in the IF by 4mmHg more than in the control group ($p=0.04$).

Conclusion: This study found that increasing the time between the evening meal and the morning meal to at least 12 hours may assist in weight loss, as compared to the traditional American fast of fewer than eight hours.

Jamshed, H., et al. Effectiveness of Early Time Restricted Eating for Weight Loss, Fat Loss, and Cardiometabolic Health in Adults with Obesity: A Randomized, Clinical Trial. *JAMA Intern Med.* 2020. doi:10.1001/jamainternmed.2022.3050.

ORAL ASPIRIN/KETAMINE VERSUS ORAL KETAMINE FOR ACUTE MUSCULOSKELETAL PAIN

Acute pain is a common reason for Emergency Department (ED) visits, often resulting from musculoskeletal (MSK) trauma. Strong efforts have been made to mitigate the use of opioid analgesics for treating acute MSK pain, instead favoring individual or combined non-opioid analgesics. Two such options are ketamine, which inhibits N-methyl-D-aspartate (NMDA)-glutamate receptor complexes, and aspirin, which inhibits prostaglandin synthesis via the cyclooxygenase system. This study assessed the efficacy of these medications, individually or combined, for the treatment of painful MSK conditions in the ED.

Data were collected for two groups of 30 participants, each

presenting to the ED with moderate-to-severe MSK pain. The first group received both 324 mg of VTS-Aspirin (rapid-acting formulation) and 0.5mg/kg of oral ketamine, swallowed directly (A+K). The second group received 0.5mg/kg of oral ketamine, swished in the mouth before swallowing to enhance membrane absorption (K). Pain relief outcomes were measured at 60 minutes post-administration. Improvement in pain by at least two points on the numerical rating scale (NRS) of pain was considered clinically significant.

At 60 minutes, the K group had a 53% reduction in NRS scores, twice that of the 25% in the A+K group. The K group had better pain reduction at 15, 30, 60, 90, and 120 minutes ($p<0.05$ for all comparisons). There were no clinically significant adverse events.

Conclusion: This study found that, oral ketamine when swished in the mouth before swallowing may improve moderate-to-severe musculoskeletal pain more significantly than a combination of quickly swallowed ketamine combined with aspirin.

Gerges, L., et al. Oral Aspirin/Ketamine versus Oral Ketamine for Emergency Department Patients with Acute Musculoskeletal Pain. *Am J Emerg Med.* 2022, Aug; 58:298-304.

DISEASE-MODIFYING TREATMENTS AND TIME TO LAST AMBULATION IN MULTIPLE SCLEROSIS

Primary progressive multiple sclerosis (PPMS) accounts for 10% of MS cases. This study assessed the effects of disease-modifying treatments (DMTs) on the risk of becoming wheelchair-dependent.

This multicenter study used prospectively gathered information concerning patients with a clinical diagnosis of PPMS. The subjects underwent at least three evaluations using the Expanded Disability Status Scale (EDSS) and had at least three years of follow-up. A score of seven on the EDSS was considered the level indicating the need for a wheelchair.

The use of DMTs was documented, with the medications categorized as moderately effective (interferon beta-1a/1b, glatiramer acetate, dimethyl fumarate, teriflunomide, methotrexate, and azathioprine) or highly effective (ocrelizumab, rituximab, natalizumab, alemtuzumab, cyclophosphamide,

mitoxantrone, cladribine, and fingolimod). Of the 665 patients, 452 were treated with DMTs.

During a mean follow-up of 11 years, 37% reached an EDSS score of seven. The only variable associated with a decreased risk of becoming wheelchair-bound was the interaction term between DMT exposure and superimposed relapses ($p=0.04$).

Conclusion: This study of patients with relapsing-remitting multiple sclerosis found that the use of a DMT was associated with delayed time to a wheelchair, but only among those with inflammatory activity during the follow-up period.

Portaccio, E., et al. Disease-Modifying Treatments and Time to Loss of Ambulatory Function in Patients with Primary Progressive Multiple Sclerosis. *JAMA Neurol.* 2022, Jul 25: e221929.

TIMING OF DUAL PLATELET THERAPY FOR STROKE AMONG CYP2C19 CARRIERS

Patients with acute minor ischemic stroke or transient ischemic attack (TIA) experience a high short-term risk of recurrence during the first three months. While dual antiplatelet therapy (DAPT) has been shown to be an effective secondary prevention strategy, concern remains regarding the increased risk of bleeding. This study assessed the time course of benefit and risk of DAPT in patients with a minor ischemic stroke or high-risk TIA who carry *CYP2C19* LOF alleles.

This study was a secondary analysis of the CHANCE-2 trial, a randomized, double-blind, active-controlled trial enrolling 6,412 patients with at least one *CYP2C19* LOF allele, all of whom were hospitalized with a TIA or ischemic stroke. The patients received aspirin, 75 mg daily for 21 days. Those randomized to dual therapy also received Ticagrelor 90 mg twice daily.

Compared to the aspirin group, the dual therapy group had reductions in major ischemic events by 1.34% in the first week, falling to 0.11% in the second week. The absolute increased risks of any bleeding event in the dual therapy group were 0.87% in the first week, 1.21% in the second week, and 0.33% in the third week. The net clinical benefit with the composite outcome of a major ischemic event and moderate to severe bleeding

was favored ticagrelor and aspirin over the four weeks, with the greatest benefit in the first week.

Conclusion: This study of patients with acute ischemic stroke or transient ischemic attack carrying the *CYP2C19* LOF alleles found that, compared to aspirin alone, the combination of ticagrelor and aspirin had a positive net clinical effect for 90 days, with the greatest benefit in the first week.

Pan, Y., et al. Time Course for Benefit and Risk with Ticagrelor and Aspirin in Individuals with Acute Ischemic Stroke or Transient Ischemic Attack Who Carry *CYP2C19* Loss-of-Function Alleles: A Secondary Analysis of the CHANCE-2 Randomized Clinical Trial. *JAMA Neurol.* 2022, August; 79(8): 739-745.

ASSOCIATIONS WITH BRAIN AGE

The concept of brain age examines biological aging from a neuroanatomical perspective. Using machine learning to compare magnetic resonance imaging of an individual with a larger reference database of healthy brains allows for the prediction of biological brain age. This age can be subtracted from the chronological age to determine the brain-predicted age differences (brain-PADs). This study was designed to assess factors that influence brain-PAD.

Data were obtained from the Medical Research Council's National Survey of Health and Development (NSHD), the world's longest continuously running birth cohort. Data were extracted concerning childhood metrics, demographics, midlife factors, and contemporaneous factors, including imaging, APOE-4 status, grip strength, and adult cognition.

Data were completed for 456 subjects, of whom 91% were without cognitive abnormality. An increase in brain-PAD was associated with increased cardiovascular risk factors at ages 36 years and 69 years, increased cerebrovascular disease burden, lower cognitive performance, and increased serum neurofilament light concentration. Early life factors did not correlate to brain-PAD. Higher brain-PAD was associated with hippocampal atrophy over the subsequent two years. No significant association was found between brain-PAD and APOE-4.

Conclusion: This study, using the 1946 British birth cohort, found that

mid-life cardiovascular disease risk, APOE-4 status, and serum neurofilament light concentration are associated with brain health.

Wagen, A., et al. Life Course, Genetic, and Neuropathological Associations with Brain Age in the 1946 British Birth Cohort: A Population-Based Study. *Lancet Healthy Longevity.* 2022. Online First. doi.org/10.1016/S2666-7568(22)00167-2.

MINOCYCLINE PLUS N-ACETYLCYSTEINE FOR TBI

Approximately 2.5 million cases of traumatic brain injury (TBI) occur every year in the United States. The primary injury results in immediate damage to neurons, glia, and vessels. This results in a rapid secondary injury to both gray and white matter that evolves for weeks to months. Previous studies have suggested that two FDA-approved drugs, minocycline (MINO) and N-acetylcysteine (NAC), may be of help in the treatment of TBI. This literature review was designed to better understand the efficacy of these medications for the treatment of acute TBI.

After a literature review identified 26 articles concerning the effects of MINO and 16 involving the effects of NAC. Preclinical studies strongly suggested that MINO has anti-inflammatory action while NAC acts as an antioxidant. The data further show that MINO prevents white matter injury while NAC is most effective on gray matter. The combination appears to have more efficacy over a wide range of therapeutic outcomes than the individual drugs, particularly when dosed at 12 to 24 hours post-injury.

Conclusion: This literature review examined preclinical trials of the effects of minocycline and N-acetylcysteine on TBI and found that benefits that are enhanced when the drugs are used together.

Lawless, S., et al. Better Together? Treating Traumatic Brain Injury with Minocycline plus N-acetylcysteine. *Neural Regen Res.* 2022, Dec; 17(12): 2589-2592.

TREMOR AS A SYMPTOM OF DEGENERATIVE CERVICAL MYELOPATHY

Degenerative cervical myelopathy (DCM) is a chronic neurologic

condition of symptomatic cervical cord compression secondary to degenerative spinal pathology. In a recent survey, tremors emerged as a symptom reported by 40% of the patients. This literature review was designed to better understand the association between tremor and DCM.

This paper reviewed studies published before July 2020. Data extracted from the papers included demographics, presenting complaint, initial diagnosis, report of tremor, onset (acute/chronic), comorbidities, past medical history, radiological findings, management, and outcomes.

From the literature review, seven papers were included in the qualitative analysis. In four cases TCM was diagnosed with tremors as a reported symptom. In two of these cases, tremors resolved following surgical management. In four cases, patients were ultimately diagnosed with a different entity, three of which were Parkinson's disease. In all four cases, the diagnosis of TCM was made after radiologic evidence of cord compression.

Conclusion: This study describes cases of tremors resulting from degenerative cervical myelopathy.

Khoury, M., et al. Tremor as a Symptom of Degenerative Cervical Myelopathy: A Systematic Review. **Br J Neurosurg.** 2022; 36(3): 340-345.

ROSEMARY CREAM FOR WOUND HEALING

Rosemary is a medicinal plant, native to the Mediterranean region. Previous studies have suggested that this plant has antioxidant, anti-inflammatory, antibacterial, and antifungal effects. This study evaluated the effect of rosemary cream on the healing of episiotomy wounds.

This randomized, triple-blind, clinical trial used two parallel groups of intervention and placebo. The subjects were 80 primiparous women who underwent mediolateral episiotomy. Those patients were randomized to receive either rosemary cream or a placebo cream, applied to the wound twice per day for ten consecutive days. The wounds were assessed with the REEDA wound measurement scale on days four and ten, postpartum.

The REEDA scores did not differ between the groups on day four ($p=0.17$) but were significantly better in the treatment group on day ten

($p<0.0001$). In addition, the treatment group demonstrated greater improvement in scores on wound discharge and approximation of wound edges ($p<0.001$ for all comparisons).

Conclusion: This study of episiotomy wound healing found that rosemary cream, applied twice per day, accelerated wound healing.

Hadizadeh-Talasaz, F., et al. The Effect of Rosemary Cream on Episiotomy Wound Healing In Primiparous Women: A Randomized, Clinical Trial. **BMC Complement Med Ther.** 2022, Aug 26; 22(1): 226.

NUTRITION AND PHYSICAL ACTIVITY TO PREVENT FRAILITY

When frailty manifests, the declining trajectory of physical function is difficult to reverse. The Staying Upright and Eating Well Research (SUPER) study, combined nutrition and physical activity, enhanced by social and cultural support, to reduce conversion to frailty.

Subjects were community-dwelling older adults living, diagnosed as pre-frail, living in Aotearoa New Zealand. The subjects were randomly allocated to one of the four intervention groups: the Senior Chef (SC) group, the Steady As You Go (SAYGO) group, the combined SC and SAYGO group, and a social (control) group. The SC group engaged in weekly sessions run by a trained facilitator for eight weeks. The SAGO program was a one-hour weekly group session run by a trained facilitator for 10 weeks, with exercises adapted from a program designed to prevent falls. The Fried test of frailty and physical assessments were completed at baseline, and up to 12 weeks after study completion.

Data were analyzed for 468 adults with a mean age of 80.3 years. At the 24-month follow-up, there were no differences in mean Fried scores between the intervention groups and the control group. No adverse events were reported.

Conclusion: This study of an indigenous sample in New Zealand did not find that combining nutrition education with exercise improved frailty scores.

Teh, R., et al. Effectiveness of a Complex Intervention of Group-Based Nutrition and Physical Activity to Prevent Frailty in Pre-Frail Older Adults (SUPER): A Randomized,

Controlled Trial. **Lancet Healthy Longevity.** 2022; 3: 519-513.

PAIN AFTER SPINAL CORD INJURY

The appropriate evaluation and treatment of pain has been recognized as one of the human rights worldwide. This study was designed to better understand the prevalence and characteristics of pain among patients hospitalized with spinal cord injury (SCI).

Subjects were diagnosed with traumatic or nontraumatic SCI who were 15 years of age or older. Information was gathered concerning pain location, pain characteristics, and associated symptoms including spasticity.

Data were analyzed concerning 385 persons from ten hospitals. Pain was experienced by 279 persons with 52% reported as nociceptive and 48% as neuropathic. The prevalence of pain was higher among older persons, with women having a higher risk of feeling pain. Pain intensity was similar in persons with incomplete and those with complete injuries. Of those reporting pain, only 59% received pain medications. Of those with nociceptive pain, 46% reported it as neck/shoulder pain. Of those reporting neuropathic pain, 67% was located below the level of the lesion.

Conclusion: This study of patients with traumatic nontraumatic spinal cord injury found that a high percentage experienced pain, equally distributed between nociceptive and neuropathic, with in large number receiving no pain medications.

Stampacchia, G., et al. Pain Characteristics in Italian People with Spinal Cord Injury: A Multicentre Study. **Spinal Cord.** 60:604–611 (2022).

SAFETY AND EFFICACY OF KETAMINE FOR NEUROPATHIC PAIN

N-Methyl-D-aspartate receptors (NMDARs) are ionotropic glutamate receptors that play a role in synaptic transmission, in neuroplasticity, learning and memory processes. Given that alterations in NMDARs are involved in a number of nervous system disorders, these have been investigated as potential therapeutic targets for pain management. This literature review and meta-analysis was designed to better understand

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the efficacy of an NMDA receptor antagonist (Ketamine) for the treatment of neuropathic pain.

A literature review was completed for randomized controlled trials (RCTs) of adults with neuropathic pain. The primary outcome was pain measured by the numerical rating scale (NRS) or visual analog scale (VAS).

Eighteen studies were included in the analysis. Results from six RCTs with a total of 212 patients found a significant reduction in pain among those treated with ketamine compared to standard treatment ($p < 0.0001$), with a mean reduction in pain of 46% compared with baseline. Data concerning the duration of the effect ranged from two weeks to two months. Among adverse effects, an increased risk of psychedelic effects ($p < 0.00001$), and general discomfort ($p = 0.03$) were found.

Conclusion: This literature review and meta-analysis of randomized controlled trials found that ketamine may be an effective treatment for patients with neuropathic pain.

Pereira, J., et al. Efficacy and Safety of Ketamine in the Treatment of Neuropathic Pain: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *J Pain Research*. 2022; 15: 1011-1037.

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