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WORLDWIDE PHYSICAL ACTIVITY SINCE COVID 19 ONSET

Public health interventions necessary to curb disease spread during COVID-19 may have resulted in unintended consequences. This study examined worldwide trends in physical activity, before and during the COVID-19 pandemic, measured by a smart phone application.

Data were collected from the smartphones of 1,255,811 unique users of the Azumio Argus smartphone application operating in more than 200 countries. User location was determined by the smartphone IP address. The mean number of daily steps was calculated for the pre-pandemic period of Jan 1, 2019, to Dec 31, 2019, with these compared to data collected during the COVID-19 pandemic.

During the pre-pandemic period, users recorded a mean of 5,323 steps per day. The step count low point was found during the COVID surge of January 2020. From May to November of 2021, the greatest global recovery of step counts occurred, although step counts still remain 10% lower than the global pre-pandemic baseline. The changes varied by region. Compared with the 2019 baseline, the most recent data indicate that step counts have recovered to -4% in North America, -14% in Europe, -29% in South America, and -30% in Asia.

Conclusion: This study, using data from smartphones across all continents, found that worldwide physical activity declined during the COVID-19 pandemic, and has improved but has not yet returned to pre-pandemic levels.

Tison, G., et al. Worldwide Physical Activity Trends Since COVID-19 Onset. *Lancet Glob Health*. 2022 Oct;10(10):e1381-e1382.

TEA CONSUMPTION AND MORTALITY

Previous studies have suggested that tea consumption may have health benefits in populations where

drinking green tea is common. This study investigated the association of tea consumption with all-cause and cause-specific mortality in the United Kingdom, where black tea consumption is commonplace.

Data were gathered from the United Kingdom (UK) biobank study. Participants were 40 to 69 years of age and were registered with the U.K. National Health Service. A total of 498,043 persons consented to participate and completed comprehensive questionnaires assessing sociodemographic, lifestyle, and health-related data. Of those completing a dietary recall questionnaire, 79% reported drinking tea, of whom 89% drank black tea and seven percent drank green tea. Data collection also included potential confounders of health outcomes.

During a median 14-year follow-up, 29,783 deaths occurred. In the multivariate-adjusted model, compared to non-tea drinkers, the hazard ratios for death for those drinking one or fewer, two to three, four to five, six to seven, eight to nine, and 10 or more cups per day were 0.95, 0.87, 0.88, 0.88, 0.91, and 0.89, respectively. Lower risks with higher tea intake were seen in mortality from overall cardiovascular disease, ischemic heart disease, and stroke.

Conclusion: This prospective study found that greater tea consumption is associated with a modestly lower risk for all-cause mortality and mortality from cardiovascular diseases and stroke, especially among those drinking two or more cups per day.

Inoue-Choi, M., et al. Tea Consumption and All-Cause and Cause-Specific Mortality in the U.K. Biobank: A Prospective Cohort Study. *Ann Intern Med*. 2022, Sept; 175(9): 1201-1211.

RUYI ZHENBAO FOR MOTOR AND SENSORY FUNCTION AFTER STROKE

In traditional Tibetan medicine, the body has two meridians, white and black. The white meridians refer

to the nervous system. White meridian disease is thought to appear as a decline in memory, speech, facial paralysis, paralysis of the limbs, numbness, pain and incontinence. White meridian therapy combines oral Tibetan medicine and external therapy. Ruyi Zhenbao, (a combination of 30 different materials, including Concha, Chinese Eaglewood Wood, Travertine, Mica-schist Lapis, Safflower, Prepared Crab, Clove, Terminalia chebula Retz. var. tomentella Kurt., Nutmeg Seed, white cardamon fruit, Emblic leafafflower fruit, Caoguo, Cuminum cyminum L, Sandalwood, Semen Nigellaem, Rosewood Lignum, Long pepper, Medicine Terminalia Fruit, Lesser Galangal Rhizome, Licorice Root, Cassia Barkm, Frankincense, Cucklandia Root, Cassia Seed, Buffalo Horn, Hibiscus abelmoschus seeds, Lagotis brachystachya, Radix Inulae Racemosae, artificial moschus, Cow-bezoar) is often the first line of treatment. This randomized controlled trial was designed to assess the efficacy of this medication for patients with acute stroke.

Patients were adults with the diagnosis of stroke, occurring 15 days to six months before study entry. The subjects were randomized to receive either a placebo or 2 g Ruyi Zhenbao twice per day for four weeks. All received standard post-stroke treatment according to the Guidelines for the Prevention and Treatment of Cerebrovascular Diseases in China. The primary outcome was motor function using the Fugl-Meyer motor assessment (FMA-M) scale. Secondary outcomes included sensory function, activities of daily living, quality of life, balance, and pain, tested up through eight weeks of treatment.

Data was completed for 113 patients. Compared with the control group, significantly better improvement was found in the FMA-M as well as the Berg Balance Scale and FMA-Sensory after four weeks of treatment ($p < 0.05$ for all comparisons). At the 8-week follow-up, the Berg Balance Scale and Modified Barthel Index scale scores

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in the treatment group were more improved than the control group ($p < 0.05$).

Conclusion: This randomized controlled study of patients with subacute stroke found that treatment with the traditional Tibetan medicine, Ruyi Zhenbao, could improve motor and function scores.

Shan-shan, L., et al. Ruyi Zhenbao Pills for Patients with Motor and Sensory Dysfunction After Stroke: A Double-Blinded, Randomized Placebo-Controlled Clinical Trial. *Chin J Integr Med.* 2022, Oct;28 (10):872-878.

ADOLESCENT SPORT-RELATED CONCUSSION AND AEROBIC EXERCISE

The current body of relevant literature supports the use of individualized aerobic exercise programs within 10 days of injury to speed recovery from sports-related concussions (SRCs). This study investigated the relationship between adherence to an aerobic exercise prescription and recovery after an SRC.

Subjects were adolescents, 13 to 18 years of age, presenting within 10 days of an SRC. Eligible subjects were able to exercise to at least 80% of the age-appropriate maximum heart rate, without the exacerbation of concussion-like symptoms. The subjects were randomized to participate in four weeks of either a stretching program or an aerobic exercise program.

The subjects were assigned a training heart rate based on the Buffalo Concussion Treadmill Test. The aerobic group underwent 20 minutes of aerobic exercise at 90% of their heart rate target daily for six days per week. Adherence was defined as completing at least two-thirds of aerobic exercise prescriptions in any given week.

Recovery was defined as resolution of symptoms to their preinjury level as measured with the Post-Concussion Symptom Inventory. Complete data were available for 51 participants in the aerobic group. Those who were adherent to the exercise protocol were more symptomatic at baseline and had a lower heart rate target than those who were not adherent. Multivariate linear regression revealed that higher adherence was associated with faster recovery ($p = 0.046$). A linear regression indicated that adherence during week one was inversely

related to recovery time ($p = 0.046$) and to initial exercise tolerance ($p < 0.001$).

Conclusion: This prospective trial of adolescents with sport-related concussions found that those who adhered to an aerobic exercise program recovered faster than those with poor adherence.

Chizuk, H., Adolescents with Sport-Related Concussion Who Adhere to Aerobic Exercise Prescriptions Recover Faster. *Med Sci Sports Exerc.* 2022, September; 54(9):1410-1416.

VENTRAL NECK MUSCLES IN CHRONIC WHIPLASH PATIENTS

Whiplash, during a motor vehicle accident, exposes the cervical spine to rapid mechanical forces which can exceed the thresholds for cervical musculoskeletal strain injury. Roughly half of those affected may transition from acute to chronic whiplash-associated disorders (WAD), with symptoms such as neck pain, radiculopathy, headache, and dizziness. This study investigated the magnetic resonance imaging (MRI) findings of patients with chronic WAD.

This cross-sectional case-control study included patients with WAD, six to 36 months after a whiplash injury, and matched, uninjured controls. All underwent MRI to compare the muscle fat infiltration (MFI) and cross-sectional area (CSA) for the sternocleidomastoid (SCM), the longus capitis (LCA), and longus colli (LCO). The WAD group was divided by severity of scores on the Neck Disability Index (NDI); < 40 (moderate) and $40 \geq$ (severe).

For the 31 patients with WAD, a comparison of MRIs revealed no significant differences among the groups except for a significantly higher MFI in the SCM in the severe WAD group as compared to controls ($p = 0.02$). The median MFI in the right SCM of the severe WAD group was 550% higher ($p = 0.03$), while that in the moderate WAD group was 220% higher than that of the controls though this did not reach statistical significance.

Conclusion: This pilot study found that individuals with severe right-sided whiplash-associated disorder have elevated muscle fat infiltration, a condition associated with decreased muscle strength and function.

Peolsson, A., et al. Morphology and Composition of the Ventral Neck

Muscles in Individuals with Chronic Whiplash Related Disorders Compared to Matched Healthy Controls: A Cross-Sectional, Case-Control Study. **BMC Musculoskelet Dis.** 2022; 23: 867.

HYPERBARIC OXYGEN FOLLOWING TRAUMATIC BRAIN INJURY

Hyperbaric oxygen (HBO) has been found to suppress inflammation, inhibit apoptosis, and promote neurogenesis and angiogenesis. Prior studies of HBO for the treatment of traumatic brain injury (TBI) have been inconclusive. This study was designed to better understand the effects of HBO therapy for patients with TBI.

Subjects were patients, 18 to 80 years of age, each diagnosed with traumatic subarachnoid hemorrhage, epidural hematoma, subdural hematoma, intraventricular hemorrhage, diffuse axonal injury, or cerebral contusion, resulting in moderate or severe TBI. The patients were randomized to either a control group or an HBO group, the latter treated at two atmospheres of pressure for 60 minutes for 20 consecutive days. Cognition was measured using the Glasgow Coma Scale (GCS), the Coma Recovery Scale-Revised (CRS-R), the Rancho Los Amigos Scale-Revised (RLAS-R), and the Glasgow Outcome Score (GOS). The severity of the TBI was assessed with the Stockholm computed tomography (S-CT) score, quantitative electroencephalography (QEEG), and serum biomarkers.

At 20 days, the HBO group demonstrated greater improvement in scores on the CRS-R ($p=0.014$), the RLAS-R ($p<0.001$), and the S-CT ($p=0.008$). The HBO group also demonstrated better serum indicators of neuronal injury including neuron-specific enolase ($p=0.023$), S100 calcium-binding protein beta ($p=0.047$), glial fibrillary acidic protein ($p=0.001$), brain-derived neurotrophic factor ($p=0.009$), nerve growth factor ($p=0.002$), and vascular endothelial growth factor ($p=0.033$). At six months, as compared to the controls, the HBO group demonstrated better scores on the FIM ($p=0.046$), FIM-Cognition ($p=0.003$), and GOSE ($p=0.018$).

Conclusion: This study of patients with traumatic brain injury found that 20 consecutive days of hyperbaric oxygen improved consciousness, cognitive function,

and prognosis in patients with severe or moderate injury.

Chen, Y., et al. Hyperbaric Oxygen Therapy Promotes Consciousness, Cognitive Function, and Prognosis Recovery in Patients following Traumatic Brain Injury through Various Pathways. **Front Neurol.** 2022. DOI 10.3389/fneur.2022.929386.

ACUTE SERUM BIOMARKERS AND OUTCOME AFTER TRAUMATIC BRAIN INJURY

Long-term disability and residual symptoms are common among patients who experienced a traumatic brain injury (TBI), even among some with a mild TBI. Recently, blood-based protein biomarkers have received attention for their role in diagnosing mild TBI. Some have suggested a role for these biomarkers for prognostication. This study assessed the incremental prognostic value of serum biomarkers alone or in combination with other recognized assessment tools.

Participants were drawn from the collaborative European Neurotrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) core study. This prospective multicenter longitudinal observational study included patients presenting within 24 hours of a TBI, with acute evaluations including blood serum and brain CT, with the six-month functional assessment using the Glasgow Outcome Extended (GOSE). Serum assays included S100 calcium-binding protein B (S100B), neuron-specific enolase (NSE), glial fibrillary acidic protein (GFAP), ubiquitin C-terminal hydrolase L1 [UCH-L1], neurofilament protein-light (NFL), and total tau (t-tau).

Data were available for 2,283 patients with a median age of 51 years. At six months 270 had died, 593 had an unfavorable outcome and 1,443 had an incomplete recovery. High levels of serum biomarkers were associated with a worse outcome with the strongest association for UCH-L1, NFL, S100B, t-tau, and GFAP compared with NSE. Adding the biomarkers to the prognostic models improved the accuracy of predicting the six-month GOSE, with UCH-L1 found to have the greatest prognostic value. Adding biomarkers to established prognostic models resulted in a relative increase in R^2 of 48–65% for IMPACT and 30–34% for CRASH prognostic models

Conclusion: This study found the

serum biomarkers have incremental prognostic value for a functional outcome after a traumatic brain injury with UCH-L1 found to be the best of these.

Helmrich, I., et al. Incremental Prognostic Value of Acute Serum Biomarkers for Functional Outcome After Traumatic Brain Injury (CENTER-TBI): An Observational Cohort Study. **Lancet Neurol.** 2022, September; 21(9): 792-802.

HIP ABDUCTOR STRENGTHENING FOR KNEE OSTEOARTHRITIS

It has been estimated that osteoarthritis of the knee (KOA) affects 867 million adults worldwide. Studies have shown that subjects with KOA have weak hip abductors, increasing the medial joint compressive forces. This literature review was designed to assess the efficacy of hip abductor muscle strengthening in patients with KOA.

A literature search was completed for articles involving hip abductor strength training for subjects with KOA. A meta-analysis was then performed, focusing on changes in pain (VAS) and functional outcomes (WOMAC).

The literature review identified seven randomized controlled trials, and three studies of good methodological quality, involving a total of 388 subjects with KOA. The meta-analysis of the articles found that hip abductor strengthening significantly reduced the VAS pain scores ($p<0.001$) and improved WOMAC function scores ($p<0.001$). Both low- and high-resistance exercise programs were found to improve knee pain and function.

Conclusion: This literature review and meta-analysis of studies involving patients with osteoarthritis of the knee found that strengthening of the hip abductors can result in an improvement in pain and function.

Thomas, D., et al. Hip Abductor Strengthening in Patients Diagnosed with Knee Osteoarthritis- A Systematic Review and Meta-Analysis. **BMC Musculoskelet Dis.** 2022; 23: 622.

ROTATOR CUFF REPAIR AND RETURN TO DRIVING

Patients who undergo rotator cuff repair (RCR) often have surgeon-imposed driving restrictions. However, the U.S. National Highway

Traffic Safety Administration has no return to driving recommendations following these surgeries. This study was designed to better understand the safety of returning to driving after an RCR.

Subjects were patients, 40 to 69 years of age scheduled for RCR surgery. All driving and parking tests were completed with a safety monitor in the rear seat of a car equipped with an emergency steering wheel and brake, as well as electronic data capture tools. At baseline, the participants performed 45 to 55 minutes of driving on a combination of suburban, urban, and highway public roads. After surgery, the subjects repeated the test at two, four, six, and 12 weeks, with subjective and objective results recorded.

Twenty-seven patients completed all driving tests, with these data included in the final analysis. All subjects were able to drive without injury to the operatively treated shoulder. Kinematic data analysis demonstrated that driving fitness at postoperative weeks two through 12 was non-inferior to baseline for all metrics. The subjective rating of performance was inferior to that of the in-car monitor until week 12.

Conclusion: This study of patients who underwent rotator cuff repair found that driving fitness returned to baseline as early as post-operative week two, although the driver's confidence did not return to baseline until week 12.

Badger, A., et al. Patients Who Undergo Rotator Cuff Repair Can Safely Return to Driving at Two Weeks Postoperatively. *J Bone Joint Surg Am.* 2022 Sep 21; 104(18): 1639-1648.

ANKLE PROPRIOCEPTION IN STROKE SURVIVORS

A recent study found that deficits in ankle proprioception are a strong predictor of balance after a stroke. This study explored the efficacy of the active movement extent discrimination apparatus (AMEDA) for the assessment of ankle proprioception acuity among stroke survivors.

The subjects were 20 adults who had experienced their first unilateral stroke and 20 healthy controls. Each was assessed for proprioceptive acuity using the AMEDA. During testing, the subject was asked to actively tilt the movable platform until it reached one of the four

predetermined angles and then return the platform to the original flat position. All subjects were tested on both ankles.

Data were completed for 20 controls with a mean age of 60.85 years and 20 stroke patients with a mean age of 61.2 years. The AMEDA scores demonstrated significant deficits in stroke survivors compared with healthy controls ($p=0.045$). An analysis of variance found that there were no differences however in proprioceptive acuity between the affected and the uninfected side of patients after their stroke.

Conclusion: This study found that patients with a recent ischemic stroke had bilateral deficits in ankle proprioceptive acuity compared with age-matched healthy controls.

Pan, L., et al. Assessing Bilateral Ankle Proprioceptive Acuity in Stroke Survivors: An Exploratory Study. *Front Neurol.* 2022, August 11; 13: 929310.

FATIGUE FOLLOWING ANEURYSMAL SUBARACHNOID HEMORRHAGE AND EMPLOYMENT

Among survivors of aneurysmal subarachnoid hemorrhage (aSAH), approximately 50% report fatigue continuing beyond one year. This study assessed the frequency and effect of fatigue on survivors of an aSAH.

Using data from the United Kingdom Biobank, the authors identified 869 cases of aSAH, and 3,316 matched controls. Fatigue was assessed using a seven-point scale, with significant fatigue defined as tiredness or little energy more than half of the time. The primary outcome variable was the frequency of fatigue.

Fatigue was reported by 13.7% of the control group and 18.7% of the aSAH group ($p<0.001$). The frequency of significant fatigue decreased by half from 19.6% in the first year following aSAH to 11.1% in the eleventh year ($p=0.04$). Of the respondents, 24.0% noted that fatigue negatively impacted their ability to sustain employment.

Conclusion: This study of patients with aneurysmal subarachnoid hemorrhage found that almost 20% complained of significant fatigue, with fatigue contributing to an inability to maintain employment.

Gaastra, B., et al. Long-Term Fatigue following Aneurysmal Subarachnoid Hemorrhage and the Impact on

Employment. *Euro J Neurol.* 2022, Aug 30. DOI: 10.1111/ene.15533. Epub ahead of print. PMID: 36039524.

DISEASE-MODIFYING, ANTI-RHEUMATIC DRUGS FOR OSTEOARTHRITIS

Patients with osteoarthritis (OA) frequently exhibit clinical synovitis, which has been clinically correlated with levels of inflammatory cytokines, interleukin one, and interleukin 6 which also mediate rheumatoid arthritis (RA). This meta-analysis was designed to better understand the effects of disease-modifying anti-rheumatic drugs (DMARDs) including on the symptoms of patients with OA.

A literature review was completed for studies assessing the effects of DMARDs (hydroxychloroquine, methotrexate, Interleukin-1 inhibitors, TNF inhibitors, and tocilizumab) on OA disease activity compared with controls. From the studies reviewed, 23 were chosen for the meta-analysis, including 2,298 patients. Of the 23 studies, 13 involved OA of the hand and the knee.

The pooled effect of DMARDs on OA outcomes (symptoms, quality of life, and sed rate) over time was not significantly different from that of the control. The exception was in the use of MTX used for patients with knee OA, which found statistically significant improvement of all tested parameters, except the quality of life.

Conclusion: This meta-analysis comparing the effects of DMARDs to those of a placebo found that these medications have little effect on the symptoms of osteoarthritis, except for methotrexate for OA of the knee.

Mathieu, S., et al. Effect of Disease Modifying Anti-Rheumatic Drugs in Osteoarthritis: A Meta-Analysis. *Joint Bone Spine.* 2022; 89(6):105444.

STROKE UNIT CARE AND SURVIVAL AMONG THE ELDERLY

Specialized stroke units have been associated with better outcomes including survival, the likelihood of being independent, and living at home one year after the stroke. This study assessed whether the benefit of a stroke unit can be found in a cohort of older patients with ischemic stroke.

This retrospective cohort study included patients insured by Germany's largest health insurer (30% of the population). This

database was reviewed for all hospitalized patients with a primary diagnosis of ischemic stroke between 2007 and 2017. Patient data were followed to determine mortality at 10, 30, and 90 days, and up to five years after the initial event. The primary outcome was a combination of death and stroke recurrence and any hospitalization within one year. Those treated in a specialized stroke unit were compared to those treated in other units (controls).

Data were analyzed for 232,246 patients including 29,885 patients aged ≥ 90 years. Of the total, 131,026 received treatment in a stroke unit, and 101,220 were not and served as controls. In a multivariate analysis, compared to the controls the odds ratio (OR) of mortality among those treated in a stroke unit was significantly less in all age groups, and at all times up to five years follow up. Compared to the controls, the risk of death in ≥ 90 -year-old stroke patients was OR 0.72 at 30 days after the primary event and OR of 0.70 at five years.

Conclusion: This German study of patients hospitalized with an acute stroke found that those treated in a stroke specialty unit had significantly improved mortality and morbidity as measured from 10 days to five years.

Geraedts, M., et al. Long-term Outcomes of Stroke Unit Care in Older Stroke Patients: a Retrospective Cohort Study. *Age and Aging*. 2022, September; 51(9): 1-7. DOI: 10.1093/ageing/afac197.

ONLINE YOGA FOR KNEE OSTEOARTHRITIS

As exercise can improve pain, function, and muscle strength in people with osteoarthritis of the knee (KOA), it is universally recommended by clinical guidelines. Yoga, using a combination of static and dynamic postures, has been shown to improve strength and balance. This study assessed the effectiveness of an unsupervised, 12-week, online yoga program for patients with KOA.

Subjects were 212 patients 45 years of age or older with painful KOA. Those randomized to a yoga group were given website access to a 12-week progressive yoga program. Each program included 30-minute videos, to be performed three times per week. A control group was given access to a website containing educational material concerning treatment options, exercise, physical activity, weight loss, and symptom

management. The primary outcome variables were the change in pain on an 11-point Numeric Rating Scale and the change in physical function as measured with the Western Ontario and the McMaster Universities Osteoarthritis Index (WOMAC) function subscale.

At the 12-week follow-up, compared to controls, the yoga group demonstrated greater improvement in WOMAC function scores of knee stiffness, quality of life, and arthritis self-efficacy than the control group. Only small between-group differences were noted in knee pain during walking.

Conclusion: This study of adults with osteoarthritis of the knee found that an unsupervised, online yoga program improved function but not pain.

Bennell, K., et al. Effectiveness of an Unsupervised, Online Yoga Program on Pain and Function in People with Knee Osteoarthritis. *Ann Intern Med*. 2022 Sep 20. DOI: 10.7326/M22-1761. Online ahead of print.

SEMAGLUTIDE AND WEIGHT LOSS

Semaglutide is a glucagon-like peptide receptor agonist initially used to treat diabetes. This study assessed weight loss outcomes associated with semaglutide treatment for patients with type II diabetes.

This retrospective review included medical records of patients in the Mayo health system with a diagnosis of Type 2 diabetes and a body mass index (BMI) of ≥ 27 kg/m². Eligible patients had been prescribed semaglutide between January 1, 2021, and March 15, 2022. The primary endpoint was the percentage of weight loss at three and six months after treatment onset.

Data were available for 175 patients, of whom 102 had available BMI data at six months. Of those 175 patients, 89 (50.9%) had a mean BMI of ≥ 41.3 kg/m². The mean BMI loss at three months was 6.7 kg, or 5.9% ($p=0.01$). At three months, those who received the highest doses achieved a mean weight loss of 6.9%, compared to 5.1% for patients receiving lower doses. At six months, those receiving the highest doses achieved a mean loss of 12.1%, compared to 9.2% for patients receiving lower doses.

Conclusion: This retrospective study of patients treated with the highest doses of subcutaneous semaglutide found the mean

percentage of weight loss to be 6.9% at three months and 12.1% at six months.

Ghusn, W., et al. Weight-Loss Outcomes Associated with Semaglutide Treatment for Patients with Overweight or Obesity. *JAMA Network Open*. 2022; Sep; 5(9): e2231982.

MICROVASCULAR AND CARDIOVASCULAR OUTCOMES WITH GLYCEMIC REDUCTION FOR DIABETES

Among the long-term complications of type II Diabetes Mellitus (DM-II) are microvascular and cardiovascular disease. This study of patients with DM-II compared the efficacy of four commonly used classes of glucose-lowering medications when added to metformin.

This parallel-group, comparative, effectiveness, clinical trial included patients diagnosed with DM-II and treated with metformin, ≥ 500 mg/d. The participants were randomized to receive one of four additional medications (glargine, glimepiride, liraglutide, or sitagliptin). The primary endpoint was the maintenance of a HgA1C level of below seven percent. Secondary outcomes included hypertension, dyslipidemia, peripheral neuropathy, renal function, cardiovascular events, hospitalization for heart failure, or an aggregate of any cardiovascular event and death.

Over the mean five-year follow-up, 71% of the 5,047 subjects had a primary metabolic outcome event, including 77% of the sitagliptin group, 72% of the glimepiride group, 68% of the liraglutide group, and 67% of the glargine group. The risk of a primary outcome event was significantly lower (better) with glargine than with sitagliptin (a 29% risk reduction) and with glimepiride (an 11% risk reduction). The difference between the glargine and liraglutide groups was not significant. The rates of secondary-outcome events followed a pattern similar to that of the primary outcome event, with lower rates in the glargine and liraglutide groups.

Conclusion: This study of patients with type 2 diabetes, treated with metformin, found that adding glargine, glimepiride, liraglutide, or sitagliptin could significantly reduce the number of patients with a glycated hemoglobin level of seven percent or more.

GRADE Study Research Group. Glycemia Reduction in Type II Diabetes: Microvascular and Cardiovascular Outcomes. **N Engl J Med.** 2022, Sep 22; 387(12): 1075-1088.

THROMBECTOMY IN PATIENTS WITH PRE-STROKE DISABILITY

Approximately 20% of patients with stroke, seen in a clinical practice setting, have impaired functional status before the presenting stroke. This study investigated the association between thrombectomy, mortality, and morbidity in patients presenting with pre-stroke disability.

Subjects were consecutive patients with an acute ischemic stroke (AIS) due to large vessel occlusion, admitted to the University Hospital of Erlangen. All had a pre-stroke disability, as defined by a modified Rankin Scale (mRS) score of three or four. The primary outcome variable was functional recovery at 90 days, defined as clinical recovery to pre-stroke functional status.

Data were completed for 205 patients with a median age of 82 years. Thrombectomy was performed in 102 of 205 patients. Treatment with intravenous alteplase was performed in 61 of 102 patients (59.8%) in the thrombectomy group versus none in the control group. At 90 days, recovery of functional status was achieved in 19.6% of the thrombectomy group and 7.8% of the control group ($p=0.005$). Mortality at 90 days occurred in 52.9% of the thrombectomy group and 73.8% of the control group ($p<0.001$). On day two, the mean infarct volumes were 40.5 ml in the treatment group and 133 ml in the control group ($p<0.001$).

Conclusion: This study of patients with large vessel ischemic strokes with a pre-stroke disability found that thrombectomy could improve functional status at 90 days.

Sprügel, M., et al. Evaluation of Functional Recovery following Thrombectomy in Patients with Large Vessel Occlusion and Pre-Stroke Disability. **JAMA Netw Open.** 2022; 5 (8): e2227139. doi: 10.1001/jamanetworkopen.2022.27139.

ECG GATED CARDIAC CT AND ISCHEMIC STROKE

For patients presenting with an acute ischemic stroke, guidelines recommend an echocardiography to

screen for structural sources. This study compared the diagnostic efficacy of transthoracic echocardiography (TTE) with that of an EEG-gated cardiac computed tomography (gCT).

This prospective, observational, cohort study included consecutive adult patients with acute ischemic stroke who were eligible for reperfusion therapy (intravenous thrombolysis [IVT]) or endovascular treatment [EVT] at the time of admission. Eligible participants underwent gCT and TTE during the initial stroke workup. All subjects were interviewed at three and 24 months to determine the functional outcome, measured by the modified Rankin Scale (mRS). The primary outcome variable was the proportion of patients with a predefined high-risk cardio-aortic source of embolism identified by gCT as compared to TTE.

Data were completed for 350 patients. High risk was identified in 11.4% with gCT and in 4.9% with TTE. The most common high-risk abnormalities were cardiac thrombi, found in 7.1% of gCT and 0.6% of TTE, and endocarditis found in 1.7% of gCT and in 0.9% of TTE. Cardiac gCT detected each high-risk source of an embolism at an equal or higher frequency than did TTE.

Conclusion: This study found that integrated cardiac CT, as a part of the diagnostic workup of patients with acute ischemic stroke, is feasible and provides better sensitivity than does transthoracic echocardiogram.

Rinkel, L., et al. Diagnostic Yield of ECG Gated Cardiac CT in the Acute Phase of Ischemic Stroke versus Transthoracic Echocardiography. **Neurol.** 2022. published ahead of print. 10.1212/WNL.0000000000200995.

CAROTID ENDARTERECTOMY OR STENTING FOR MODERATE TO SEVERE ASYMPTOMATIC CAROTID ARTERY STENOSIS

The optimal treatment for patients with asymptomatic carotid stenosis is still under debate. Randomized controlled studies comparing best medical treatment (BMT) alone or combined with carotid endarterectomy (CEA) or carotid artery stenosis (CAS) are lacking. This study was designed to better understand the relative efficacy of these interventions.

The Stent-Protected Angioplasty versus Carotid Endarterectomy

(SPACE) study is a randomized, multicenter, open-label, phase-three trial involving adults, 50 to 85 years of age, with asymptomatic carotid stenosis of at least 70%. The patients were randomized to receive either BMT, CEA plus BMT (CEAS+), or CAS plus BMT (CAS+). The primary efficacy endpoint was the cumulative incidence of any stroke or death from any cause within 30 days of randomization or any ipsilateral ischemic stroke within five years of follow-up.

Among the 513 patients, the incidence of the primary efficacy endpoint was 2.5% in the CEA + group, 4.4% in the CAS + group, and 3.1% in the BMT group. The differences among groups were not found to be significant ($p=0.62$). Among the secondary outcomes, an ipsilateral transient ischemic attack was noted in 1% of the CEA+ group, 4.3% of the CAS+ group, and 8.2% of the BMT group ($p=0.017$).

Conclusion: This randomized trial of patients with asymptomatic carotid artery stenosis, found no significant difference in the occurrence of stroke or death from any cause between patients receiving medical treatment alone and those treated with either carotid endarterectomy or a carotid artery stent.

Reiff, T., et al. Carotid Endarterectomy or Stenting or Best Medical Treatment Alone for Moderate to Severe Asymptomatic Carotid Artery Stenosis: Five-Year Results of a Multi-Center, Randomized, Controlled Trial. **Lancet Neurol.** 2022, October; 21 (10): 877-888.

CIRCULATING FOLATE AND RISK OF MILD COGNITIVE IMPAIRMENT

Mild cognitive impairment (MCI) is the transitional state between normal aging and dementia, with an annual conversion rate of 10 to 15%. The homozygous 677TT mutation of the 5,10-methylenetetrahydrofolate reductase (MTHFR) gene has been linked to reduced serum folate and elevated homocysteine (Hcy) concentrations. As this mutation is prevalent among the Chinese population, this study explored the association between circulating folate and incident MCI in a Chinese sample.

Data were collected from the Tianjin Elderly Nutrition and Cognition (TENC) cohort study of individuals ≥ 60 years of age. Serum was

collected to assess for C677T polymorphisms and APOE genotypes. Dietary intake was determined using a validated food frequency questionnaire. Incident MCI was assessed with a modified version of the Peterson criteria, with the diagnosis based on the expert consensus of a panel of physicians.

During 8,656 person-years of follow-up, 560 incident MCI cases were diagnosed. Compared to the lowest quintile of folate, the hazard ratios (HRs) for MCI across the three highest quintiles were 0.66, 0.57, and 0.66, respectively ($p < 0.001$). For homocysteine, compared to the lowest quintile, the HRs of MCI in the three highest quintiles were 1.39, 1.54, and 1.51, respectively ($p = 0.003$).

Conclusion: This Chinese prospective study found that low folate and high homocysteine concentrations in the serum are independently associated with the risk of incident mild cognitive impairment.

Fu, J., et al. Circulating Folate Concentrations and the Risk of Mild Cognitive Impairment: A Prospective Study on the Older Chinese Population without Folic Acid Fortification. *Europ J Neurol.* 2022, October; 29(10): 2913-2924.

PREDICTIVE FACTORS OF GALCANEZUMAB TREATMENT IN REAL-LIFE MIGRAINE PATIENTS

Studies evaluating monoclonal antibodies (mAbs) targeting the calcitonin gene-related peptide (CGRP) pathway (mAbs anti-CGRP) have added to available migraine prevention strategies. This trial investigated the effectiveness and tolerability of galcanezumab for the real-life treatment of episodic migraine (HFEM) and chronic migraine (CM).

Data were collected as part of the Galcanezumab in Real Life Migraine Patients in Italy (GARLIT) trial. This observational, prospective, multicenter study trial at 16 Italian headache centers. Subjects were consecutive patients 18 years of age or older with high-frequency, episodic migraine (HFEM) or chronic migraine (CM). All participants underwent a face-to-face interview addressing socio-demographic factors, medical conditions, and medical treatments. A daily headache diary was maintained, with pain rated on a 10-point numeric rating scale (NRS). The primary endpoint was the change

from baseline in monthly migraine days (MMDs) at one year.

Data were available for 191 patients. For patients with CM, relative to baseline, a 50% or greater reduction was noted in the treatment group for MMDs ($p < 0.00001$). This was also true for secondary outcomes of MAMI, NRS HIT-6 scores, and MIDAS scores ($p < 0.0001$). For those with a diagnosis of HFEMs, the same pattern of improvement was found, for both primary and secondary outcomes. In addition, for patients with CM, an MMD of 50% RR or more was found in 55.4% at one month and in 60.5% at one year. For those with HFEMs, an MMD of 50% RR or more was found in 65.1% of the patients at the end of one month and in 73.8% at one year.

Conclusion: This study of patients with chronic or episodic, recalcitrant migraine headaches found galcanezumab to be an effective and well-tolerated preventative treatment.

Vernieri, F., et al., Maintenance of Response and Predictive Factors of One-Year Galcanezumab Treatment in Real-Life Migraine Patients in Italy: The Multicenter, Prospective, Cohort GARLIT Study. *Euro J Neurol.* 2022 Sep 13. doi: 10.1111/ene.15563.

PSYCHOLOGY AND RETURN TO SPORT AFTER ACL RECONSTRUCTION

Over 200,000 anterior cruciate ligament (ACL) injuries occur each year in the United States. This literature review investigated the effects of psychological factors on patients' ability to return to sports after ACL reconstruction.

A literature search was conducted for studies of patients undergoing ACL repair that included psychological data. Data were also obtained from knee-specific patient-reported outcome scores (International Knee Documentation Committee (IKDC), Tegner Activity Level Scale, Knee injury and Osteoarthritis Outcome Score, and ACL-Quality of Life) as well as clinical measurements (limb symmetry index (LSI) and laxity). The scores on these outcome measures were compared between those who did and those who did not return to sports participation.

Data were analyzed from studies including 3,744 patients. The IKDC scores were not significantly different between patients who did and did not

return to sport. Compared to those who did not return to sports, patients who return to sports scored significantly higher on the Anterior Cruciate Ligament-Return to Sport after Injury (ACL-RSI) scale, a validated tool to quantify a patient's psychological readiness to return to sport ($p < 0.001$). Compared to those who did not return to sport, scores on the TSK/TSK-11 kinesiophobia scale were significantly lower for those who did return ($p = 0.004$). For measures of self-efficacy, those who returned to sports had significantly better scores on the K-SES than those who did not return to sports.

Conclusion: This systematic review of patients who had undergone ACL reconstruction, found that those who returned to sport had similar functional scores, but superior psychological readiness scores than did those who did not return.

Xiao, M., et al. Patients Who Return to Sport After Primary Anterior Cruciate Ligament Reconstruction Have Significantly Higher Psychological Readiness: A Systematic Review and Meta-Analysis of 3744 Patients. *Am J Sports Med.* 2022. doi:10.1177/03635465221102420.

AURICULAR VAGUS NERVE STIMULATION FOR MILD COGNITIVE IMPAIRMENT

The number of patients suffering from dementia in China is expected to reach 26 million by 2040. Recent studies have demonstrated that invasive vagus nerve stimulation can improve the cognitive function of patients with Alzheimer's disease (AD). As there is a unique vagus nerve distribution on the surface of the auricular concha I, some have speculated that stimulation at this site could benefit patients with MCI.

This double-blind, randomized controlled trial involved patients with mild cognitive impairment 55-75 years of age. Those randomized to receive active stimulation placed electrodes at a pair of auricular acupoints including the heart (concha, CO15) and kidney (CO10), in the distribution of the vagus nerve. The sham group delivered similar stimulation at the acupoints of the elbow (scaphoid fossa, SF3) and shoulder (SF4,5). Stimulation was delivered in 30-minute sessions twice per week, five days per week, for 24 weeks. The primary outcome was the Montreal Cognitive Assessment-basic (MOCA-B) assessed at

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baseline and at 24 weeks.

Data were obtained for 25 patients in the active and 27 patients in the sham treatment groups. Compared with baseline, scores on the MOCA-B increased significantly in the treatment group compared to those at baseline ($p < 0.001$) and were significantly better at follow-up than the sham group. In the secondary test, scores on the AVLT-H test of memory, the STTB of executive function, the BNT, PSQI, RBDSQ, ESS and FAQ improved after intervention ($p < 0.001$, $p < 0.001$, $p = 0.016$, $p < 0.001$, $p = 0.002$, $p = 0.025$, $p < 0.001$ and $p = 0.006$ respectively), though no significant differences were noted between the treatment and the sham group.

Conclusion: This randomized controlled study of patients with mild cognitive impairment found that vagus nerve stimulation at the surface of the ear may be effective in improving MOCA-B memory scores.

Wang, L., et al. The Efficacy and Safety of Transcutaneous Auricular Vagus Nerve Stimulation in Patients with Mild Cognitive Impairment: A Double-Blinded Randomized Clinical Trial. *Brain Stimul.* 2022. DOI: <https://doi.org/10.1016/j.brs.2022.09.003>.

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