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TRANSGENDER ATHLETIC PERFORMANCE

With the rise of transgender athletes, questions have arisen as to which gender category in which these athletes should compete. This study examined the effect of sex hormones on body composition, and athletic performance among transgender individuals.

This retrospective review of medical records and fitness tests were obtained from self-identified military personnel who had filed a request to begin gender transition while serving in the United States Air Force. Trans-women (TW) were defined as genotypical males transitioning to phenotypical females. For physical performance, data collection included the annual required physical fitness assessment. These results were compared to those of all fitness tests performed by men (control men; CM) and women (CW) between 2004 and 2014.

Data were completed for 29 trans-men (TM), and 46 TW, with a mean age of 26.2 years. Prior to sex hormone therapy, the number of pushups performed in one minute was greatest among CM and fewest among CW. At two years after the initiation of hormone therapy the greatest number of pushups was performed by TM, with TW able to do fewer, but still more than CW. For the 1.5-mile run, the best times at baseline were among the CM and TW groups. After two years of hormone therapy, the times had significantly worsened in the TW group and significantly improved in the TM group, achieving statistical equivalence with the CM subjects. For sit ups, the most performed at baseline occurred in the TW group, with the least in the CW participants. After two years of hormone therapy, the greatest performance was found in the TM group and the worst in the TW subjects.

Conclusion: This study found that, among transgender athletes, the use of sex hormones associated with the transgender process resulted in significant changes in athletic performance.

Roberts, T. et al. Effect of Gender Affirming Hormones on Athletic Performance in Trans-Women and Trans-Men: Implications for Sporting Organizations and Legislators. **Br J Sport Med.** 2021, June; 55(11): 577-583.

VITAMIN D SUPPLEMENTATION AND RESPIRATORY INFECTION

Studies have shown that Vitamin D influences both innate and adaptive immunity. This study explored the influence of Vitamin D in upper respiratory tract infections (URTIs) in a physically active sample.

In study 1, 1644 military recruits were observed across basic military training. In study two, 250 British Army recruits, scheduled to undergo 12 weeks of military training, were randomized to one of four intervention groups, 1) oral vitamin D3 supplementation (ORAL), 2) oral placebo supplementation (ORAL-P), 3) solar simulated radiation (SSR) or 4) solar simulated radiation-placebo (SSR-P). Military records were used to identify a diagnosis of URTI and days lost due to the URTI. Vitamin D deficiency was defined as <50 nmol/L.

In study one, serum 25(OH)D levels were deficient in 21% of the participants. The recruits that were vitamin D-sufficient were 40% less likely to suffer URTI (odds ratio 0.06). In study 2, 110 URTI episodes were recorded with 7% of participants having at least one physician-diagnosed URTI. Vitamin D-sufficient participants were 40% less likely to have a physician-diagnosed URTI. The association between vitamin D status and URTI prevalence remained when controlling for sex and smoking ($p < 0.05$). Compared with placebo, vitamin D supplementation reduced the severity of peak URTI symptoms by 15%, and days with URTI by 36%. Supplementation with oral D3 and sunlight produced similar effects.

Conclusion: This study of active military recruits found that Vitamin D supplementation, to achieved sufficiency, was effective in reducing the severity of symptoms and days lost due to upper respiratory tract infections.

Harrison, S., et al. Influence of Vitamin D Supplementation by Simulated Sunlight or Oral D3 on Respiratory Infection during Military Training. **Med Sci Sport Exer.** 2021, Jul 1; 53(7): 1505-1516.

MISSING LINK BETWEEN AEROBIC FITNESS AND COGNITION

Previous studies have shown that spontaneous eye blink rate (sEBR) can be used as a noninvasive indicator of the brain dopaminergic system. Several studies have revealed that dopamine agonists increase sEBR, whereas dopamine antagonists decrease sEBR through the involvement of basal ganglia and the spinal trigeminal complex. This study assessed the association between aerobic fitness and executive function.

Thirty-five, healthy Japanese males underwent testing on three days. On the first day, the subjects completed a demographic health questionnaire and a graded exercise test to determine aerobic fitness. On the second day, the sEBR was recorded. On the third day, executive function was measured with the Color-Word Stroop Task (CWST). Cortical activation during the CWST was monitored using functional, near-infrared spectroscopy, focusing on the dorsolateral prefrontal cortex (DLPRC). Neural efficiency (NE) was estimated by the ratio of CWST performance/I-DLPRC activation.

After controlling for age and body mass index, VO_{2peak} was found to be related to higher sEBR ($p=0.03$) and better CWST performance ($p=0.007$). The sEBR was positively correlated to NE ($p=0.04$). Further analysis indicated that the relationship

between VO_{2peak} and CWST is mediated by sEBR.

Conclusion: This study demonstrates that the spontaneous blink rate mediates the association between aerobic fitness and executive function through prefrontal neural efficiency.

Kuwamizu, R., et al. Spontaneous Eye Blink Rate Connects Missing Link between Aerobic Fitness and Cognition. **Med Sci Sport Exer**. 2021, July; 53(7):: 1425-1433.

HEALTHY LIFE-YEARS LOST WITH DELAY OF ENDOVASCULAR THROMBECTOMY

Endovascular thrombectomy (EVT) has produced substantial changes in the outcomes associated with acute ischemic stroke due to large vessel occlusion. Most analyses of EVT time-benefit associations have emphasized the time interval from symptom onset/last known well (LKW) to thrombectomy. This study investigated lifetime outcomes associated with the speed to EVT.

Data were analyzed from the Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke (HERMES) trials collaboration of randomized clinical trials investigating stent retriever thrombectomy for anterior circulation large vessel occlusion. Time metrics were collected including last known well–to-door (LKWTD) time; last known well/onset-to-puncture (LKWTP) time; last known well–to-reperfusion (LKWR) time; door-to-puncture (DTP) time; and door-to-reperfusion (DTR) time. The primary outcome variable was gain or loss of healthy life, quantified using the disability-adjusted life-years (DALYs) metric.

Among the 781 EVT-treated patients, 406 (52.0%) were treated within four hours of LKW (LKWTP ≤4 hours) and 375 (48.0%) were treated between four and twelve hours (LKWTP >4-12 hours). In the LKWTP ≤4 group, each one hour of delay in LKW-to-puncture time was associated with a loss of 0.81 healthy life-years. In the late treated population, no significant association was found between LKW-to-puncture time and DALYs, although substantial reperfusion was achieved more often in early than in late patients (78.4% vs 68.4%).

Conclusion: This study found that, for patients with acute ischemic stroke, treated by thrombectomy within four hours, each hour of delay was associated with 0.81 years of healthy life lost.

Almekhlafi, M. et al. Healthy Life-Year Costs of Treatment Speed from Arrival to Endovascular Thrombectomy in Patients with Ischemic Stroke. A Meta-analysis of Individual Patient Data from Seven, Randomized, Clinical Trials. **JAMA Neurol.** 2021, June; 78(6): 709-717.

TRANSCRANIAL DIRECT CURRENT STIMULATION FOR ACUTE STROKE

Cathodal manual direct current stimulation (C-tDCS) is a noninvasive neuro stimulation method involving the application of a weak current to the scalp that modulates the excitability of underlying cortical neurons. This study was designed to determine whether C-tDCS, applied during the hyperacute phase of ischemic stroke, can reduce ischemic core growth.

Subjects were adults, 18 years of age or older, with acute ischemic stroke in the middle cerebral artery territory. Eligible participants had National Institutes of Health Stroke Scale (NIHSS) scores of between four and 25 and were eligible for intravenous thrombolysis (IVT). In the case of proximal disease, mechanical thrombectomy was used. The patients were randomized to receive either C-tDCS, using 1.5 mA delivered for 20 minutes, or a sham C -tDCS. The primary outcome variable was the change in DWI lesion volume between MRI_1 and MRI_2.

The median growth in infarct volume between MRI_1 and MRI_2 was 5.4 ml in the C-tDCS group and 8.3 ml in the sham group (p=0.28). No major adverse events occurred in either group. The percent of cases with modified Rankin Scale scores of 0-2 at three months was 63.3% in the C-tDCS group and 43.5% in the control group (p=0.18). A significant potential benefit was found among the pre-specified subgroups of those with moderate to severe stroke, among those with NIHSS scores of greater than 10 and among those with large vessel occlusion.

Conclusion: This study of patients with acute ischemic stroke found that cathodal transcranial direct current stimulation may be effective in reducing the infarct volume, particularly among those with moderate to severe strokes or with NIHSS scores of greater than ten.

Pruvost-Robieux, E. et al. Cathodal Transcranial Direct Current

Stimulation in Acute Ischemic Stroke: Pilot. Randomized, Controlled Trial. **Stroke.** 2021, June: 52 (6): 1951-1960.

INTRACRANIAL STENOSIS AND COGNITIVE DECLINE

Intracranial stenosis (ICS) is considered significant when narrowing is more than 50%. As ICS is a known risk factor for ischemic stroke and transient ischemic attack, this study assessed the effect of ICS on the risk of cognitive decline.

This prospective study included patients recruited from a memory clinic at the National University Hospital in Singapore. The inclusion criteria were no cognitive impairment (NCI), cognitive impairment with no dementia (CIND) and dementia. All underwent neuroimaging, assessment of ICS using MRA, and determination of MRI markers based on the STRIVE (Standards for Reporting Vascular Changes on Neuroimaging). Assessment of cognition was completed using the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MOCA), and a formal detailed neuropsychological test battery (National Institute of Neurological Disorders and Stroke–Canadian Stroke Network battery).

Subjects were 364 patients with a mean age of 71.9 years. Of these, 25% had NCI, 42.6% had CIND and 32.4% were diagnosed with dementia. Of the total cohort, 18.1% had ICS. A regression analysis found that ICS was associated with worse performance on executive function at all times measured. This association was independent of patient demographics, baseline diagnosis or vascular risk factors.

Conclusion: This study found that patients with intracranial stenosis had poorer executive function across all times measured.

Lim, M. et al. Effect of Intracranial Stenosis on Cognitive Decline in a Memory Clinic Cohort. **Eur J Neurol.** 2021; 28(6): 1829-1839.

INTERLEUKIN-6 INHIBITION AND ATHEROSCLEROSIS

Inflammation inhibition, targeting the central NLRP3 inflammasome to the IL-1 to IL-6 pathway of innate immunity is an emerging method for atherosclerosis treatment and prevention. This study tested whether ziltivekimab, a fully human monoclonal antibody directed against the IL-6 ligand, could reduce biomarkers of inflammation and thrombosis among patients with high cardiovascular risk.

RESCUE is a parallel-group, double-blind, randomized, placebo-controlled, phase 2 trial, that recruited patients 18 years of age or older who had stage III to V chronic kidney disease, with residual inflammatory risk defined as a high-sensitivity CRP (hsCRP) level of 2 mg/L. The patients were randomized in a 1:1:1:1 ratio to receive placebo or ziltivekimab 7.5 mg, 15 mg or 30 mg every four weeks for up to 24 weeks. The primary outcome measure was the change in high-sensitivity CRP.

Data were completed for 215 trial participants with a median age of 68 years. The median reductions in hsCRP were 4% in the placebo group, 77% for the 7.5 mg group, 88% for the 15 mg group, and 92% for the 30 mg group (all $p<0.0001$). Reductions of at least 50% of hsCRP were found at 12 weeks. A similar pattern of improvement was found for the reduction in hsCRP of at least 50% at 12 weeks ($p<0.0001$).

Conclusion: This study of patients at high risk for atherosclerosis found that ziltivekimab, a monoclonal antibody targeting the IL-6 ligand, markedly reduced multiple biomarkers of systemic inflammation, associated with the atherothrombotic process.

Ridker, P. et al. IL-6 Inhibition with Ziltivekimab in Patients at High Atherosclerotic Risk (RESCUE): A Double-Blind, Randomised, Placebo-Controlled, Phase 2 Trial. **Lancet.** 2021, May 4; 397(10289): 2060-2069.

ULTRASOUND-GUIDED CARPAL TUNNEL RELEASE

Carpal tunnel syndrome (CTS) is the most common peripheral entrapment neuropathy. For patients requiring surgical intervention, ultrasound (US) guided release has been introduced as a technique that is less invasive than endoscopic release techniques. This study evaluated the long-term success of this procedure.

This retrospective review included 51 patients with CTS which was refractory to conservative interventions. All underwent US guided release, with follow-up at two weeks and then up to one year. Assessments included three questionnaires, the Quick Disabilities of the Arm, Shoulder and Hand (QDASH) and two parts of the Boston Carpal Tunnel Syndrome Questionnaire, the Symptom Severity (BCTSQ-SS) and Functional Status [BCTSQ-FS] scales, to assess function and discomfort.

Subjects were 40 patients with a mean age of 60.7 years. At two-week follow-up evaluations, 83% (38 of 46) of the surveyed patients reported feeling satisfied or very satisfied with the procedure. This rate rose to 93% at one year.

Conclusion: This retrospective study of patients with carpal tunnel syndrome, resistant to conservative intervention, found that ultrasound guided carpal tunnel release improved hand function and reduced hand discomfort within two weeks.

Kamel, S. et al. Minimally Invasive Ultrasound Guided Carpal Tunnel Release Improves Long-Term Clinical Outcomes in Carpal Tunnel Syndrome. **Am J Roen.** 2021, August; 217: 1-9.

COMPLICATIONS AND REOPERATIONS AFTER CARPAL TUNNEL SURGERY

Carpal Tunnel Syndrome (CTS) is the most common of entrapment neuropathies, with an estimated prevalence of between five and ten percent. While the initial management is conservative, many undergo surgical release. This study explored the complications associated with CTS surgery.

This British study used data from the National Health Service in England, reviewing data from all carpal tunnel decompression surgeries in adults between April 1998, and March 31, 2017. The primary outcome variables were the number of infections, dehiscence and neurovascular or tendon injuries that required rehospitalization or reoperation within 90 days of hospitalization.

During the study, 855,832 primary carpal tunnel surgeries were completed, involving individuals with an average age of 57 years and a median follow-up of 7.53 years. Local, serious complications occurred in 620 (0.07%) within 30 days and 698 within 90 days (0.082%). Reoperation occurred in 29,288 cases at a median time to the second surgery of 351 days.

Conclusion: This British study of patients with carpal tunnel syndrome who underwent surgical release found that the rate of serious complications was less than 0.1%.

Lane, J. et al. Serious Postoperative Complications and Reoperation after

Carpal Tunnel Decompression Surgery in England: A Nationwide, Cohort Analysis. **Lancet Rheum**. 2021, January 30; 3(1): e49.

SHOCKWAVE THERAPY FOR CHRONIC PLANTAR FASCIITIS

Plantar fasciitis (PF) is the most common painful foot syndrome. Extracorporeal shockwave therapy (ESWT) has been trialed for the treatment of PF, though the results of those studies have been inconclusive. This literature review was designed to better understand the efficacy of ESWT for patients with PF.

A literature review was completed of studies published between January of 2016 and May of 2020. Eligible papers were randomized, controlled trials (RCTs) including adults with chronic PF who received either ESWT or conventional therapy.

Of the articles reviewed, 11 RCTs were chosen, involving 650 participants. The intervention duration ranged from 15 to 30 minutes per session, one to five times per week for three to twelve weeks. Of the 11 trials, nine found significantly greater improvement in pain in the ESWT group than in the control group. Improvements on measures of foot function were significant greater in the ESWT group in nine of 11 studies. Of the four studies which included information about plantar fascia thickness, three found a greater positive effect in the ESWT group as compared to the control group.

Conclusion: This literature review of adults with chronic plantar fasciitis found extracorporeal shockwave therapy to be effective in reducing pain and improving function.

Melese, H. et al. Extracorporeal Shock Wave Therapy on Pain and Foot Functions in Subjects with Chronic Plantar Fasciitis: Systematic Review of Randomized, Controlled Trials. **Disability Rehab.** 2021, May 26:1-8.

STEM CELLS FOR KNEE OSTEOARTHRITIS

For patients with knee osteoarthritis (OA), there are several options for reducing pain and disability. Among the more recent is the intraarticular injection (IA) of mesenchymal stem cells (MSC). This literature review and meta-analysis was designed to better understand the efficacy of this treatment option.

A literature review was completed for randomized controlled trials (RCTs) involving patients with OA of the knee. From these, 14 were chosen, with a total of 408 patients in the MSC arm and 300 in the control arm.

In the trials comparing MSC with hyaluronic acid, the MSC group demonstrated greater gains after 24 months in International Knee Documentation Committee (IKDC) scores (p=0.001). Compared to platelet-rich plasma (PRP), similar efficacy was found in visual analog scale (VAS) pain scores, as well as scores on the IKDC and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Compared to exercise, the MSC group had better Lower Extremity Activity Scale scores and Knee Society Scores (KSS). Among those receiving autologous-derived stem cells, at one-year follow-up, 63% demonstrated better pain scores than did controls. In studies using autologous peripheral blood-derived stem cells, compared to hyaluronic acid, the stem cell group had better WOMAC scores, with fewer undergoing total knee arthroplasty.

Conclusion: This literature review of randomized, controlled trials of patients with osteoarthritis of the knee found that mesenchymal stem cells are effective in improving clinical outcomes, comparing favorably to other non-surgical options.

Wiggers, T. et al. Autologous Stem Cell Therapy in Knee Osteoarthritis: A Systemic Review of Randomized, Controlled Trials. **Br J Sport Med.** 2021; 0:1–10. doi: 10.1136/bjsports-2020-103671.

HYDRODILATION FOR ADHESIVE CAPSULITIS OF THE HIP

Adhesive capsulitis of the hip (ACH) is characterized by a painful decrease in active and passive range of motion. This prospective study evaluated the efficacy of ultrasound (US) guided hydrodilation for the treatment of this disorder.

This prospective study included adults diagnosed with ACH, with data collection comprising patient demographics, baseline symptoms and magnetic resonance angiography (MRA). Using ultrasound guidance, the subjects were injected with 0.5% lidocaine (25 mL) with triamcinolone (40 mg; 1 mL). The injections were repeated in two weeks. Outcome measures included a visual analog scale (VAS) for pain, passive range of motion of the hip, distance from the floor to knee when sitting in a cross-legged position and the Hip Disability and Osteoarthritis Outcome Score (HOOS).

Data were analyzed for 84 patients with a mean age of 55.5 years. The average 10-point VAS score improved from 7.1 at baseline to 0.8 at final follow-up ($p<0.001$). All subsets of the patient-reported HOOS demonstrated improvement ($p < 0.001$).

Conclusion: This study of patients with adhesive capsulitis of the hip found that ultrasound-guided hydrodilation is a safe and effective intervention for symptom relief.

Yoon, B. et al. Ultrasound-Guided Hydrodilation for Adhesive Capsulitis of the Hip is a Safe and Effective Treatment. **Int Ortho.** 2021, June; 45: 1455-1461.

FOOD SUPPLEMENTATION AND COGNITION IN YOUNG CHILDREN

While undernutrition remains prevalent among young children worldwide, supplementary feeding programs and single nutrient trials in low-income countries have not produced clear improvements in cognition. This study compared a new multi-component supplementary food (NEWSUP) with the fortified blended food (FBF) widely used in international food assistance programs.

This randomized, controlled trial included rural villages in West Africa. Members of all families received 1300 kJ, five mornings per week, for 23 weeks. The families were randomized to receive NEWSUP, high in plant polyphenols and omega 3 fatty acids, with a wide variety of micronutrients and a high protein content or FBF used in nutrition programs, or a traditional rice breakfast (control). The primary outcome was working memory, with secondary outcomes including hemoglobin concentration, growth, body composition and index of cerebral blood flow (iCBF) measured non-invasively using a combination NIRS-DCS instrument.

Compared with the control group, the NEWSUP group demonstrated improved working memory among children younger than four years of age, both in the intention to treat and per protocol cohorts ($p=0.03$ and $p=0.007$). Also, the NEWSUP group had greater increases in iCBF compared to both the control group and the FBF group ($p=0.04$ for both).

Conclusion: This nutrition study found that a new nutritional supplement, five days per week for

23 weeks could improve executive function and cerebral blood flow among those four years of age or younger.

Roberts, S. et al. Effects of Food Supplementation on Cognitive Function, Cerebral Blood Flow and Nutritional Status in Young Children at Risk of Undernutrition: Randomized, Controlled Trial. **BMJ.** 220; 370: M2397.

ANTICOAGULATION AND ELECTIVE SPINE SURGERY

Venous thromboembolism (VTE) is one of the major complications of surgery. However, in spine surgery, the risk of hematoma is also of great concern. This study evaluated the effect of pharmacologic anticoagulation to protect against VTE, as well as hematoma, resulting from spine surgery.

This retrospective review included patients undergoing elective spine surgery at a single institution between 2015 and 2017. Symptomatic VTEs were recorded, with symptoms including shortness of breath, lower extremity pain or swelling. All events were confirmed using venous duplex ultrasound or a computed tomography angiogram. In addition, episodes of hematoma that required further surgery were recorded.

Data were analyzed for 1,776 patients, with control cases matched using propensity scoring. Demographic, operative, postoperative and comorbidity factors were characterized. The primary outcome variables were unplanned reoperation for hematoma, and VTE or PE within 30 days of surgery. Of those undergoing elective spine surgery, 888 received pharmacologic anticoagulation and 888 received no such medication. The rates of VTE, PE and unplanned reoperation for hematoma in this cohort were 0.96%, 0.34% and 1.13%, respectively. VTE occurred in 0.9% of those receiving anticoagulation and in 1.01% of those without anticoagulation. Pulmonary embolism occurred in 0.34% of each group. Hematomas requiring repeat surgeries occurred in 2.03% of those receiving anticoagulation and in 0.23% in those not receiving anticoagulation (p=0.002).

Conclusion: This study of patients undergoing elective spine surgery found that pharmacologic anticoagulation does not significantly decrease the risk of symptomatic venous thromboembolism after surgery, but significantly increases the risk of repeat surgery for symptomatic hematoma.

Thota, D. et al. Anticoagulation in Elective Spine Cases. Rates of Hematomas versus Thromboembolic Disease. **Spine.** 2021, July; 46 (13): 901-906.

ASPIRIN DOSING AND CARDIOVASCULAR DISEASE

The European Society of Cardiology has published clinical guidelines which provide recommendations for low-dose aspirin in patients with stable cardiac disease. However, the American College of Cardiology-American Heart Association clinical guidelines do not provide definitive recommendations. This study, Aspirin Dosing: A Patient-Centric Trial Assessing Benefits and Long-Term Effectiveness (ADAPTABLE) was designed to assess whether aspirin, 325 mg per day, can lower the risk of death among patients with established atherosclerotic cardiovascular disease more than a dose of 81 mg per day.

This multicenter trial included patients with established atherosclerotic cardiovascular disease, randomly assigned to receive 81 mg or 325 mg per day of aspirin. Routine follow-up occurred every three or six months. The primary efficacy outcome was any event in the composite of death from any cause, hospitalization for myocardial infarction or hospitalization for a stroke.

At the time of randomization, 13,172 patients with a mean age of 67.6 years were enrolled. The primary outcome occurred in 7.51% of the 325 mg group and in 7.28% in the 81 mg group [Hazard Ratio (HR) 1.02]. Death from any cause occurred in 3.8% of the 81 mg group and in 4.43% of the 325 mg group (HR 0.87). Hospitalization for major bleeding requiring a blood product transfusion occurred in 0.63% of the 81 mg group and in 0.6% of the 325 mg group. Discontinuation of aspirin use was reported by seven percent of the 81 mg group and by 11.1% of the 325 mg group.

Conclusion: This large, open label, pragmatic, multicenter trial found no statistically significant differences in efficacy or safety between those receiving 81 mg of aspirin per day and those receiving 325 mg.

Jones, W. et al. Comparative Effectiveness of Aspirin Dosing in Cardiovascular Disease. **N Eng J Med.** 2021, May 27(21); 384: 1981-1990.

ABOBOTULINUMTOXIN A FOR UPPER LIMB SPASTICITY IN CEREBRAL PALSY

Upper limb impairment is common among individuals with cerebral palsy (CP). While botulinum neurotoxin A (BoNT-A) has become an established treatment for these patients, available evidence for this treatment was insufficient for regulatory approval in pediatric patients. This study assessed the safety and efficacy of repeated BoNT-A in the pediatric population.

The participants were children weighing 10 kg or more, two to 17 years of age with a diagnosis of CP. After baseline assessments, the children randomized to receive 2 U/kg, 8 U/kg or 16 U/kg of BoNT-A, injected into target muscle groups of the wrist and elbow flexors. These injections were combined with occupational therapy. For the second cycle of injections, children initially allocated to the 2U/kg low-dose control group were randomized to receive either 8U/kg or 16U/kg BoNT-A. The primary outcome variable was the change in modified Ashworth Scale (MAS) scores of spasticity.

Data were completed for 210 children. At week six, those in the 8 U/kg group (p=0.012) and the 16 U/kg (p<0.001) group had significantly lower MAS scores than did the 2 U/kg group. Statistical superiority was maintained at week 16. Improvements were similar between the 8U/kg and 16U/kg doses.

Conclusion: This study of children with cerebral palsy found that botulinum neurotoxin A injections can significantly improve upper extremity spasticity.

Delgado, M. et al. Efficacy and Safety of AbobotulinumtoxinA for Upper Limb Spasticity in Children with Cerebral Palsy: A Randomized, Repeat-Treatment Study. **Dev Med Child Neurol.** 2021, May; 63(5): 592-600.

AUTONOMIC IMBALANCE AND STROKE

The autonomic nervous system regulates multiple involuntary functions, including cardiovascular function. Studies have suggested a link between autonomic imbalance and cognitive performance among dementia-free individuals. This study

examined whether autonomic imbalance may be a predictor of acute stroke and/or dementia.

Data were obtained from the Framingham offspring cohort, including participants who were recruited in 1971. Autonomic function was assessed at the third examination. Heart rate variability (HRV) was evaluated by two different indices; 1) the standard deviation (SD) of normal-to-normal RR intervals (SDNN), which represents total variability and, thus, joint sympathetic and parasympathetic modulation of HRV. 2) The root mean square of successive differences (RMSSD) between normal heartbeats, which more narrowly represents parasympathetic activity. Outcome measures were the incidence of all-cause dementia and acute stroke by the time of the seventh examination cycle.

Of the cohort, resting heart rate data were obtained for 3,491 and HRV data for 1,831 participants. Overall, autonomic imbalance was not associated with the risk of dementia. However, among older individuals, SDNN and RMSSD were associated with the risk of dementia. Also, a high resting heart rate was associated with an increased risk of stroke. In men, a high SDNN was associated with a lower risk of stroke (HR 1.18).

Conclusion: This study, reporting on data from the Framingham study, found that a high resting heart rate may be a risk factor for stroke, and that some indicators of cardiac heart rate variability precede the diagnosis of stroke and dementia in specific subpopulations.

Weinstein, G. et al. Autonomic Imbalance and Risk of Dementia and Stroke: The Framingham Study. **Stroke**. 2021, June; 52(6): 2068-2076.

SURGERY VERSUS BOTOX FOR SIALORRHEA

Drooling (sialorrhea) is a prevalent problem among children with nonprogressive neurodevelopmental disabilities. Treatments have included botulinum toxin injections as well as bilateral submandibular duct ligation. This study compared the efficacy of these two treatment strategies.

This randomized, controlled trial was conducted between April of 2012 and August of 2017. Subjects were children, eight years of age or older and diagnosed with a nonprogressive neurodevelopmental disorder who reported moderate or severe drooling. The participants were randomized to receive either bilateral submandibular duct ligation or botulinum toxin injections under general anesthesia with 25 units delivered to each submandibular gland. Drooling severity was determined by questionnaires completed by caregivers at baseline and eight- and 32-weeks post-treatment. Drooling was rated as none, mild, moderate, severe, or very severe.

Data were completed for 57 children and adolescents. In the botulinum group the mean excessive drooling dropped from 74% to 46% at eight weeks ($p<0001$), rising to 66% at 32 weeks. In the surgical group, the mean percentage declined from 71% at baseline to 15% at eight weeks and increased to 34% at 32 weeks ($p<0001$).

Conclusion: This study of children and adolescents with cerebral palsy or other nonprogressive neurodevelopmental disorders found that surgical ligation of the submandibular gland was superior to botulinum toxin injections for the reduction of sialorrhea.

Bekkers, S. et al. Surgery versus Botulinum Neurotoxin A to Reduce Drooling and Improve Daily Life for Children with Neurodevelopmental Disabilities: A Randomized, Controlled Trial. **Dev Med Child Neurol.** 2021. May 16. doi: 10.1111/dmcn.14924
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VESTIBULAR OCULAR MOTOR SCREENING FOR CONCUSSIONS

Sport related concussions (SRC) often involve a clinical profile including vestibular symptoms, with dizziness, nausea and vertigo, as well as ocular changes, with convergence insufficiency, blurred vision, diplopia, and eye strain. This study investigated the discriminative utility of the Vestibular/Ocular Motor Screening (VOMS) for the evaluation of patients with concussion.

This study was a secondary analysis of data collected from the National Collegiate Athletic Association-Department of Defense (NCAA-DoD) CARE Consortium, comprising collegiate athletes and military cadets from eight institutions. All were diagnosed with a concussion and had completed a VOMS. Those in a control group were drawn from the same cohort and were without current concussion. Before the initiation of testing, the participants were asked to rate their current levels of headache, dizziness, nausea and fall units on a scale of 0-10. All then underwent vestibular and ocular function testing, with measurements including smooth pursuits, horizontal and vertical saccades, near point of convergence (NPC), vestibular/ocular reflex (VOR) in the horizontal and vertical directions (H-VOR and V-VOR), and visual motion sensitivity, as well as NPC distance.

The concussion group obtained significantly higher VOMS scores for each item, as well as higher total scores. The total VOMS score had the highest discriminative utility for singling out concussion in this population, with a 91% accuracy, with the optimal cutoff score ≥8. In a regression analysis, vertical saccades ≥1 ($p = 0.01$) and horizontal-VOR ≥2 ($p = 0.01$) were the only discriminators of concussion.

Conclusion: This study of collegiate athletes found that the Vestibular/Ocular Motor Screening assessment may be a valuable tool for identifying concussion within three days of injury.

Kontos, A. et al. Discriminative Validity of Vestibular Ocular Motor Screening in Identifying Concussion among Collegiate Athletes. A National Collegiate Athletic Association-Department of Defense Concussion Assessment, Research and Education Consortium Study. **Am J Sport Med.** 2021, July: 49(8): 2211 –2217.

LUMBAR SPINAL STENOSIS, DISABILITY AND MORTALITY IN OLDER ADULTS

Lumbar spinal stenosis (LSS) is caused by gradual narrowing of the spaces around the neurovascular elements, such as the spinal canal, lateral recesses or intravertebral foramen. This study investigated the association between LSS and future disability and mortality.

This prospective, observational study analyzed data from the Locomotive Syndrome and Health Outcomes in the Aizu Cohort Study (LOHAS). Subjects were independent adults 65 years of age or older. All were tested for LSS with a diagnostic support tool. At baseline, data were gathered included age, gender, body mass index, tobacco abuse, diabetes, affective disorders, osteoarthritis of the lower extremities, hand grip strength and walking habits. The primary outcome of interest was the occurrence of severe disability or mortality.

Data were completed for 1,560 subjects, of whom 17% were

diagnosed with LSS. The subjects' mean age was 72.3 years. At a median follow-up of 5.8 years, those with LSS had a higher cumulative occurrence of severe disability or mortality, at 11.9%, than did those without LSS, at 6.9% (p=0006). The adjusted hazard ratio for the primary endpoint among those with LSS was 1.55.

Conclusion: This study found a significant association between lumbar spine stenosis and future severe disability or mortality.

Hijikata, Y. et al. Association of Lumbar Spine Stenosis with Severe Disability and Mortality among Community Dwelling Older Adults: The Locomotive Syndrome and Health Outcomes in the Aizu Cohort Study. **Spine**. 2021 Jul 15; 46(14): E784-E790.

BLOOD FLOW RESTRICTION TO FAILURE VERSUS NOT TO FAILURE

Traditional blood flow restriction (BFR) exercise involves training at 20 to 50% of the 1RM during blood flow restriction, with repetitions until volitional failure. Evidence suggests that satellite cell (SC) activation, proliferation, and the subsequent addition of new myonuclei have been implicated in the hypertrophic response. This study compared the effects of short-term high-frequency failure versus non-failure blood flow-restricted resistance exercise (BFRRE) on changes in SCs, myonuclei, muscle size and strength.

Subjects were 18, healthy, untrained men who underwent stratified randomization between the right and left leg. One leg was assigned to train with a failure protocol (FP), and the other to a non-failure protocol (NF). Fourteen sessions were distributed over two, five-day blocks, separated by a 10-day rest interval. All received 20g of whey protein after each session. Strength was measured at baseline, with muscle biopsies competed before and two hours after the training session at five days after the 7^{th} session and 10 days after the second training block.

At follow up, compared to baseline, significant increases were found for both the FP and the NF groups in type I and type II muscle myonuclear fiber types, as well as in SC in type I and type II muscle fibers ($p<0.05$). Muscle size increased by five to ten percent in both legs. MVC and 1RM decreased by five to ten percent after block one but increased in both legs at 24 days after intervention (Post24) by six to eleven percent ($p<0.05$). While the gains in SC and myonuclear numbers as well as muscle size and strength were similar between the legs, perceptions of exertion, pain, and DOMS were lower in the non-failure leg.

Conclusion: This study of blood flow restricted exercise found that training at high frequency without failure can produce gains that are similar to those of traditional training to failure.

Bjornsen, T. et al. Frequent Blood Flow Restricted Training Not to Failure and to Failure Induces Similar Gains in Myonuclei and Muscle Mass. **Scan J Med Sci Sports.** 2021, July; 31(7): 1420-1439.

PRE-INJURY AND POST-INJURY FACTORS PREDICTING CONCUSSION RECOVERY

Among athletes with a sport related concussion (SRC), most experience symptomatic recovery within two weeks. This study explored preinjury risk factors to better understand the probability of clinical recovery or persistent symptoms.

This prospective cohort of male and female collegiate athletes utilized data collected before or after injury. Baseline studies included the SCAT-3, Generalized Anxiety Disorder 7–Item (GAD-7), Patient Health Questionnaire-9 (PHQ-9), ImPACT and self-reported history of concussion, learning disability (LD), attention-deficit hyperactivity disorder (AD/HD), headaches/migraines and depression.

Subjects were 1,152 athletes with a mean age of 19.42 years. The mean time between baseline evaluation and injury was 410 days. Among the sports followed, those playing men's ice hockey were more likely to experience concussion ($p<0.001$) compared to other sports. The mean time until symptom free was 9.84 days. The mean days until full return to play was 20.21. None of the pre-injury risk factors were correlated with recovery time. After injury, those reporting more total symptoms and higher symptom severity had longer days until symptom free ($p<0.001$ for both). Among those tested within two days of concussion, the Immediate Post-concussion Assessment and Cognitive Test (ImPACT) visual motor ($p=0.004$), reaction time ($p<0.001$) and symptoms score ($p=0.054$) were related to days until symptom free.

Conclusion: This prospective study of collegiate athletes found that post-concussion evaluations, including impact, reaction time and symptom scores, were useful in predicting clinical recovery.

Putukian, M. et al. Pre-Injury and Post-Injury Factors that Predict Sports Related Concussion and Clinical Recovery Time. **Clin J Sport Med**. 2021, January; 31(4): 15-22. doi.org/10.1097/JSM.0000000000000705.

PRINTED 3-D ARTHROPLASTY

After total knee arthroplasty (TKA), aseptic loosening can limit life expectancy of the device. Cementless TKA offers potential for strong biological fixation, with new cementless designs including 3-D printing. This retrospective review acquired data from 341 patients undergoing cementless TKA.

The participants were followed for postoperative outcome, comparing scores on the Knee Injury and Osteoarthritis Outcome Scale for joint replacement (KOOS JR), as well as on the 12-Item RAND/Short Form Survey (VR/SF-12). The primary outcome was aseptic loosening and revision for any reason.

At follow-up, 11 revisions had occurred, with an overall revision rate of 2.94%. These included five for infection, three for loosening, two for instability and one for pain. The twelve-year survivorship was 97.06%.

Conclusion: This study of patients undergoing total knee arthroplasties with 3-D printed joint components found that the five-year survivorship was 97.06%.

Restrepo, S. et al. Excellent Midterm follow-up for a New, 3-D Printed, Cementless Total Knee Arthroplasty. **Bone Joint J**. 2021, June; 103-B: 32-37.

SOCIAL DETERMINANTS OF PHYSICAL THERAPY USE

The World Health Organization (WHO) has recognized rehabilitation to be a key driver for health with the adoption of Rehabilitation 2030. Rehabilitation 2030 emphasizes rehabilitation needs, noting that effective action on combating health inequalities starts with monitoring inequalities through data sources and research. This literature review was designed to identify and summarize the social determinants of health, cited in the literature, and to evaluate

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their association with individuals using physical therapy services.

This literature review produced 36 papers involving 2,699,437 participants. The data were qualitatively synthesized in relation to the association between social determinants of health (SDH) and physical therapy use. The predisposing SDHs of PT use were gender, race, ethnicity, education, environment, and employment.

The groups more likely to use PT were females, Caucasians, those with higher levels of education, those living in more densely populated areas and those living in areas with transportation to health care facilities.

Conclusion: This literature review found that the social determinants of health associated with a higher likelihood of using physical therapy were female gender, non-Hispanic white race, living in densely populated areas, increased education, employment, and urban environment.

Braaten, A. et al. Social Determinants of Health are Associated with Physical Therapy Use: A Systematic Review. **Br J Sport Med.** 2021. doi: 10.1136/bjsports-2020-103475.

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