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OPTIMAL CORTICOSTEROID DOSE FOR ADHESIVE CAPSULITIS

Early treatment of adhesive capsulitis with intra-articular corticosteroids is thought to reduce synovitis and shorten the course of the disease. However, little is known about the dose-dependent efficacy of corticosteroids. This study was designed to determine whether high-dose corticosteroid is more effective in treating pain and restoring function than is low dose steroid.

Fifty-three patients with adhesive capsulitis were randomized to receive either a single placebo injection, or a low dose (20 mg) or a high-dose (40 mg) of triamcinolone acetonide. The subjects were instructed to carry out a home exercise program for 12 weeks after the injections. All were assessed at baseline and at weeks one, three, six and 12 post-injection. Outcome measures included the SPADI, a self-report questionnaire for patients with shoulder pain, a visual analogue scale and a passive range of motion assessment.

Significantly greater improvements in pain and disability scores, as well as in passive range of motion, were found in both steroid groups as compared with placebo, with no significant difference noted between the low and high dose groups. No serious complications were seen in any of the treatment groups.

Conclusion: This study of patients with adhesive capsulitis found no significant difference in outcomes between those treated with high versus low-dose corticosteroid injections.

Yoon, S., et al. Optimal Dose of Intra-Articular Corticosteroids for Adhesive Capsulitis: A Randomized, Triple Blind, Placebo Controlled Trial. *Am J Sports Med.* 2013, May; 41(5): 1133-1139.

SUBACROMIAL INJECTION: CORTICOSTEROIDS VERSUS NSAIDS

The pain associated with external impingement syndrome is thought to be secondary to subacromial bursitis and tendinitis of the rotator cuff. Nonoperative treatment options for this syndrome include local corticosteroid injections and systemic nonsteroidal anti-inflammatory drugs (NSAIDs). As the effect of corticosteroids is thought to result from their anti-inflammatory properties, this study sought to determine whether subacromial injections with an NSAID would be as effective.

Patients were recruited from a sports medicine clinic, each diagnosed with subacromial bursitis. All subjects underwent standard radiographs to rule out glenohumeral arthritis. The participants were randomized to either an NSAID group (n=15), to receive 60 mg of ketorolac, or a steroid group (n=17), to receive 40 mg of triamcinolone. The primary outcome measures were the University of California at Los Angeles (UCLA) Shoulder Rating Scale and a visual analogue scale (VAS) for pain, both completed at baseline and at one month.

Compared with baseline, scores on the UCLA Shoulder Rating scale improved by 7.15 in the ketorolac group and by 2.13 and the steroid group (p=0.03). The mean improvements in VAS scores at four weeks were 1.83 for the ketorolac group and 0.9 for the steroid group (p=0.23). At four-week follow-up, active abduction decreased in the steroid group from 137° to 134°, while increasing in the ketorolac group from 129° to 151° (p=0.03).

Conclusion: This double-blind, randomized, controlled trial involving patients with subacromial bursitis found that a local injection with ketorolac resulted in greater improvement in UCLA Shoulder

Scores than did injection with triamcinolone.

Min, K., et al. A Double-Blind, Randomized, Controlled Trial Comparing the Effects of Subacromial Injection with Corticosteroid versus NSAID in Patients with Shoulder Impingement Syndrome. *J Should Elbow Surg.* 2013, May; 22(5): 595-601.

PARKINSONIAN APATHY AND PIRIBEDIL

Apathy is one of the most common symptoms encountered in Parkinson's disease (PD), with its prevalence estimated at 16% to 42%. Data suggest that apathy, depression and anxiety, observed after subthalamic nucleus deep brain stimulation, are part of a hypodopaminergic syndrome related to these thalamic lesions. Given the predominance of dopamine D3 receptors in the mesolimbic dopaminergic system, there is a clear rationale for targeting these receptors. This study reviewed the effects of piribedil, a non-ergot D2/D3 dopamine agonist, for the treatment of postoperative Parkinsonian apathy.

Consecutive patients with PD undergoing surgery for bilateral subthalamic nucleus deep brain stimulation were included in the study. Patients received domperidone (60 mg/day) and were randomly assigned to receive piribedil at up to 300 mg per day or a placebo for 12 weeks. The primary outcome measure was improvement in apathy, as measured with the Starkstein Apathy Scale. Secondary outcomes included depression, as measured primarily by the Beck Depression Inventory, anxiety, as measured by the Beck Anxiety Inventory, quality of life and anhedonia.

At follow-up, apathy was reduced by 34% in the study group and 3.2% in the placebo group (p=0.015). Beck

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Depression Inventory scores were reduced by 19.8% in the treatment group and increased by 1.4% in the placebo group. Depression, as measured by the Hamilton Depression Scale, also improved significantly in the treatment group ($p=0.05$). Anxiety scores were reduced by 22.8% in the treatment group and 8.3% in the placebo group. Quality of life scores improved by 16.2% in the treatment group, and worsened by 6.7% in the placebo group ($p=0.08$). Frequency of side effects observed during the protocol did not differ between groups

Conclusion: This randomized, controlled study of patients with Parkinsonian apathy found significant improvements in apathy scores through treatment with piribedil, a D2/D2 agonist.

Thobois, S., et al. Parkinsonian Apathy Response to Dopaminergic Stimulation of D2/D2 Receptors with Piribedil. **Brain**. 2013, May; 136(5): 1568-1577.

CHRONIC PAIN AFTER ISCHEMIC STROKE

Chronic pain syndromes are commonly reported among patients after ischemic stroke, with estimates ranging from eight to 55%. However, the clinical consequences of chronic pain syndromes are not well understood, although they are thought to have a negative effect on quality of life. This study was designed to better understand the prevalence, determinants and consequences of post-stroke pain syndromes.

Subjects comprised a subset of patients in the Prevention Regimen for Effectively Avoiding Second Stroke (PROFESS) trial. From this study, patients were identified with no pre-stroke history of pain, discomfort or unpleasant sensations for 15 days or more. These patients were then screened for confounding variables, with data analyzed to distinguish those with chronic pain from those with no such pain.

Of the 1,665 patients in the trial, 10.6% were found to have post-stroke pain, with central pain being the most common (2.7%), followed by peripheral neuropathy (1.5%) and pain due to spasticity (1.3%). Factors most correlated with the development of post-stroke pain included NIHSS

severity, female gender, previous depression, statin use or hyperlipidemia, diabetes mellitus, alcohol intake, peripheral vascular disease and antithrombotic medications. All chronic pain syndromes were associated with increased disability/dependence upon follow-up.

Conclusion: This study of patients with ischemic stroke found that over 10% develop chronic pain, with such pain associated with a significantly increased risk of disability and dependence.

O'Donnell, M., et al. Chronic Pain Syndromes after Ischemic Stroke. PROFESS Trial. **Stroke** 2013, May; 44(5): 1238-1243.

RECURRENT TRANSIENT ISCHEMIC ATTACK AND STROKE RISK

Data have shown that transient ischemic attacks (TIAs) precede stroke in almost 20% of cases. This study sought to better clarify the risk of stroke recurrence among patients with multiple TIAs

This study included consecutive patients diagnosed with TIA from 30 Spanish stroke centers. All were seen between January of 2008 and December of 2009. A TIA was defined as a reversible episode of neurological deficit of ischemic origin that resolves completely within 24 hours. Multiple TIAs were defined as the occurrence of at least two TIAs, the index TIA and one other, in the seven days before the index event. The primary outcome measure was the occurrence of a subsequent stroke at seven and 90 days follow-up.

A total of 1,137 patients with TIAs were included in the study, with a mean age of 68.6 years. Of these, 52.7% reported symptoms lasting for less than an hour. Multiple TIAs were seen in 24.1% of the patients. Large artery atherosclerosis was detected in 16.7%. At 90-day follow-up, 3.9% of the patients had a subsequent stroke. The seven and ninety day risk of subsequent stroke was significantly higher among those with multiple TIAs than among those with a single TIA (5.9% versus 1.5%, and 6.8% versus 3%, respectively; $p<0.004$). Among the patients with multiple TIAs and subsequent stroke, the stroke

occurred within the first seven days in 88.9% and within 48 hours in 72.5%.

Conclusion: This study found that patients with multiple TIAs within seven days have a greater risk of stroke than do those with a single TIA.

Purroy, F., et al. Recurrent Transient Ischemic Attack and Early Risk of Stroke: Data from the PROMAPSA Study. *J Neurol Neurosurg Psychiatry*. 2013, June; 84(6): 596-603.

VASCULAR ENDOTHELIAL GROWTH FACTOR AND ISCHEMIC STROKE

Vascular endothelial growth factor (VEGF) is a key protein, inducing angiogenesis in health and disease. In the brain, this molecule is important in mediating neuronal survival and angiogenesis. It is known that the expression of VEGF is upregulated in response to hypoxia. This study examined the temporal profile of plasma VEGF after stroke and the association of this molecule with neurologic outcome.

One hundred seventy one patients with ischemic stroke were matched with healthy subjects by age and gender. The patients with stroke were classified into four subtypes, including atherothrombotic infarction, lacunar infarction, cardioembolic infarction and other (OT). Plasma VEGF levels were measured, and clinical information was obtained on day zero, three, seven, 14 and 90 following ischemic stroke.

Plasma VEGF levels were significantly higher at day zero in the stroke patients as compared with controls, and were independently associated with brain infarction ($p < 0.001$ and $p = 0.003$, respectively). No significant association was seen between the plasma VEGF values and stroke related risk factors or pretreatment therapies. Plasma VEGF levels were higher in all stroke subtypes for up to 90 days following stroke. After adjusting for confounding factors, plasma VEGF values were independently predictive of worse outcomes in patients with cardioembolic infarction.

Conclusion: This study demonstrates that plasma vascular endothelial growth factor levels rise immediately after stroke onset,

although its clinical significance may differ among stroke subtypes.

Matsuo, R., et al. Clinical Significance of Plasma VEGF Levels in the Ischemic Stroke – Research for Biomarkers in Ischemic Stroke (REBIOS) Study. *BMC Neurol*. 2013; 13: 32.

PHANTOM LIMB PAIN IN DIABETICS

Phantom limb pain (PLP) affects approximately 80% of lower limb amputees. Traditionally, amputees with diabetes have been thought to experience less PLP, although there are little data to support this conclusion. This study was designed to better understand the effect of diabetes on the development of PLP.

All subjects had undergone one or more lower limb amputations in the previous three years, excluding those with amputations occurring less than three months from the start of the study. Questionnaires were sent, with queries regarding pain, including intensity, as well as medical history, including diabetes. The respondents were divided into diabetic and nondiabetic cohorts for analysis.

Among the 102 patients, the overall prevalence of PLP was 85.6%. The diagnosis of PLP occurred in 82% of those with diabetes and in 89.4% of those without diabetes ($p = 0.39$). Those with a diagnosis of diabetes of less than 10 years' duration had an average PLP score of 4.18, while those with diabetes for longer than 10 years had an average PLP score of 3.65, ($p = 0.57$).

Conclusion: This study of patients with amputations found no significant difference in the prevalence or intensity of phantom limb pain between those with and those without diabetes at the time of amputation.

Clark's, R., et al. Phantom Limb Pain after Amputation in Diabetic Patients Does Not Differ from that after Amputation in Nondiabetic Patients. *Pain*. 2013, May; 154(5): 729-732.

MANUAL THERAPY FOR CARPAL TUNNEL SYNDROME

Carpal tunnel syndrome (CTS) is estimated to affect nine percent of

women and six percent of men. Conservative treatments for CTS include local corticosteroid injection, systemic treatment with corticosteroids, ultrasound, electrotherapy, vitamin B6, vitamin B12 or nonsteroidal anti-inflammatory drugs. Several small studies have suggested that manual therapy interventions can improve symptoms by reducing tissue adhesions and increasing wrist mobility. This study was designed to better understand the efficacy of manual therapy for the treatment of CTS.

Subjects comprised 22 patients, including 19 with bilateral disease and electrodiagnostic evidence of CTS. All subjects were evaluated at baseline and at 12 weeks in order to review the natural progression of the disease. The participants were then treated for three weeks with manual therapy, two sessions per week for 15 minutes per session. The patients were evaluated at enrollment, at the end of treatment and 24 weeks' follow-up for signs and symptoms, and with the Boston Carpal Tunnel Questionnaire (BCTQ), and nerve conduction studies.

At the end of treatment, significant reductions were noted in the number of night awakenings, paresthesias, hypoesthesia, hand weakness and sensitivity, with improved Phalen test results. These improvements were maintained at 24 weeks. No significant changes were noted in electrophysiologic data or BCTQ scores.

Conclusion: This study of patients with carpal tunnel syndrome found that six sessions of manual therapy can improve some signs and symptoms, with benefits maintained at 24 weeks.

Bongi, S., et al. A Manual Therapy Intervention Improves Symptoms in Patients with Carpal Tunnel Syndrome: A Pilot Study. *Rheum Intern*. 2013; 33: 1233–1241.

SPECIALIZED FOOTWEAR FOR KNEE OSTEOARTHRITIS

Osteoarthritis (OA) management is largely palliative, and generally focuses on oral analgesics. Lower limb OA is mediated in part by dynamic loads transmitted across the joints. Some have suggested biomechanical interventions targeted at decreasing joint loading, and have

included orthotic shoe inserts, knee braces, and footwear. This study evaluated the effects of mobility footwear (designed to mimic barefoot walking) on the knee loading in patients with medial compartment knee OA.

Inclusion criteria were symptomatic OA of the knee and pain while walking (defined as at least 30 mm of pain on a 100-mm scale). In addition, subjects were required to have a peak external knee adduction moment (KAM) of ≥ 2.00 %BW \times Ht (% body weight \times height), as measured by gait analyses. Mobility shoes, designed to mimic barefoot mechanics, were worn for at least six hours per day, six days per week. Gait evaluations were repeated at six, 12 and 24 weeks for changes in KAM and in the adduction angular impulse (AddImp).

Sixteen participants with medial compartment knee OA were evaluated. Overall, compared to knee loading while walking in one's own shoes at baseline, walking in the mobility shoes resulted in an 18% reduction in the KAM and a 19% reduction in the AddImp by 24 weeks. (each $p < 0.001$). At six months, a significant reduction in pain of 36% ($p < 0.05$) was observed by wearing the mobility shoes.

Conclusion: This study suggests that the use of mobility footwear, designed to mimic barefoot walking, can significantly reduce loading, as well as pain, among patients with knee osteoarthritis.

Shakoor, N., et al. Improvement in Knee Loading after Use of Specialized Footwear for Knee Osteoarthritis. *Arth Rheumat* 2013, May; 65(5): 1282 -1289 C.

WHOLE BODY VIBRATION THERAPY AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

Anterior cruciate ligament (ACL) injury is often treated with surgical reconstruction to improve the mechanical stability of the knee joint. Several studies have reported that patients with ACL reconstruction have deficits in postural control. At the early phase of rehabilitation, the exercise intensity is insufficient to increase neural drive and stimulate muscle hypertrophy in order to provide graft protection. As whole

body vibration therapy (WBVT) has been demonstrated to be effective in improving balance, postural control, muscle strength and functional performance, this study assessed the effect of WBVT on neuromuscular control after ACL reconstruction (ACLR).

Subjects included 48 patients who had undergone an ACLR using a single bundle hamstring method. The patients were randomized to a control group or a treatment group, with both groups undergoing the same conventional rehabilitation protocol. The treatment group began WBVT at one month post-surgery, using a standard neuromuscular rehabilitation protocol. This group received two sessions per week for 16 sessions. Outcome measures included joint position sense tests, a postural control test, isokinetic testing, clinical assessment and functional mobility testing.

By six months post-surgery, all patients had achieved full knee range of motion, with clinical assessments revealing stable knee joints. The treatment group demonstrated significantly better postural control, muscle performance, single-leg hop and shuttle run performances than did the control group ($p < 0.05$ for all comparisons). No significant difference was seen between the groups in knee joint position sense, triple hop or carioca test.

Conclusion: This prospective study found that whole body vibration therapy, started at one month after anterior cruciate ligament reconstruction, may improve performance without compromising knee range of motion and stability.

Fu, C., et al. Effect of Early Whole Body Vibration Therapy on Neuromuscular Control after Anterior Cruciate Ligament Reconstruction. A Randomized, Controlled Trial. *Am J Sport Med* 2013, April; 41(4): 804–814.

THE AGING BRAIN AND COGNITION

The two most common pathologic changes seen in the aging brain are beta amyloid deposition and vascular brain injury. While the presence of beta-amyloid is a diagnostic criterion for Alzheimer's disease, approximately 25% of clinically normal elderly individuals have beta-amyloid

deposition. This study was designed to examine the relationship between measures of vascular brain injury and the deposition of brain beta-amyloid and their association with cognition

Participants were recruited from the Aging Brain project, designed to study individuals with substantial vascular disease risk factors and vascular brain injury. Sixty participants were recruited across three groups, including clinically normal subjects, cognitively impaired subjects and patients with dementia. All underwent cognitive testing using a battery of standardized neuropsychological tests, as well as MRI. Infarctions were identified by using the T1-weighted and FLAIR MRIs, and categorized by size and location (cortical gray matter, white matter, subcortical gray matter and other). A β (Pittsburgh Compound B–positron emission tomographic (PiB-PET)) imaging was used to estimate areas of amyloid deposition

Of the 61 participants, 34 had imaging results consistent with infarction, and 29 with amyloid deposition. A trend was seen toward worse cognitive status among patients with infarctions ($p = 0.005$), particularly among those with cortical lesions. Vascular brain injury and A β deposit were independent in both cognitively normal and cognitively impaired participants. The presence of an infarction did not increase the likelihood that an individual was PiB positive.

Conclusion: This study found that vascular brain injury had more influence than did amyloid deposit in determining cognitive function in the aging brain, with no evidence that vascular brain injury increases the likelihood of amyloid deposition.

Marchant, N., et al. The Aging Brain and Cognition. Contribution of Vascular Injury and A β to Mild Cognitive Dysfunction. *JAMA Neuro*. 2013, April; 70(4): 488–495.

SUBCLINICAL ISCHEMIA DURING CAROTID ENDARTERECTOMY

Previous studies have demonstrated that some patients undergoing carotid endarterectomy (CEA) experience a subtle cognitive decline. While the mechanisms underlying post-CEA neurocognitive changes are poorly understood, some have suspected hypoperfusion during

the procedure. This study further evaluated the etiology of post CEA cognitive decline.

This study included 81 consecutive patients who underwent unilateral CEA between September of 2007 and December of 2011. All subjects underwent preoperative and postoperative neuropsychological evaluations at six months post-CEA. None had experienced any other events which might have affected cognitive function. During the operative procedures, somatosensory evoked potentials (SSEPs) were recorded, with an SSEP amplitude reduction of more than 50%, for more than five minutes at N20-P25, defined as moderate to severe hypoperfusion. Pre-and post-operative neuropsychological evaluation results were compared with multiple variables, including hypoperfusion.

A total of 81 patients were studied. A significantly greater worsening in neuropsychological evaluation results was noted among patients with SSEP of less than 50% for more than five minutes, as compared to those without ($p=0.012$). Multiple regression analysis demonstrated that this finding was independently related to cognitive decline ($p=0.002$).

Conclusion: This study of patients undergoing carotid endarterectomy found that hypoperfusion, as verified by SSEP, seems to play a significant role in cognitive decline following this procedure.

Inque, T., et al. Subclinical Ischemia Verified by Somatosensory Evoked Potential Amplitude Reduction during Carotid Endarterectomy: Negative Effects on Cognitive Performance. *J Neurosurg.* 2013, May; 118: 1023-1029.

SIMVASTATIN AND VASOSPASMS AFTER SUBARACHNOID HEMORRHAGE

Vasospasm after aneurysmal subarachnoid hemorrhage (aSAH) plays a major role in both mortality and morbidity. Previous studies have suggested that statins may reduce the incidence of vasospasm. This prospective, double-blind study was designed to determine the effect of simvastatin on patients with aSAH.

Consecutive patients admitted for treatment of aSAH within 96 hours of

symptom onset were included in this study. The subjects were randomized to receive either simvastatin at 80 mg per day or placebo for 14 days. All patients subsequently underwent surgical clipping of the aneurysm, and were then followed for six months. The primary outcome measure was the development of clinical cerebral vasospasm, with secondary outcomes including Glasgow Outcome Scores (GOS), modified Rankin Scale scores, and Barthel Index scores, measured at one, three and six months.

At follow-up, on one or more days during the study, 16% of the patients in the treatment group and 26% of those in the placebo group were found to have vasospasms. However, this finding did not reach statistical significance ($p=0.70$). Neurologic deterioration occurred in 26% of the treatment group and 42% of the placebo group, again not reaching statistical significance.

Conclusion: This pilot study of patients undergoing surgical clipping of an aneurysmal subarachnoid hemorrhage found that treatment with a statin may reduce vasospasms and neurologic deterioration, although this finding did not reach statistical significance.

Garg, K., et al. Role of Simvastatin in Prevention of Vasospasm and Improving Functional Outcome after Aneurysmal Subarachnoid Hemorrhage: A Prospective, Randomized, Double-Blind, Placebo-Controlled Pilot Trial. *Br J Neurosurg.* 2013, April; 27(2): 181-186.

ADDING CHIROPRACTIC MANIPULATION FOR ACUTE BACK PAIN

The lifetime prevalence of low back pain (LBP) has been estimated to be as high as 84%. At least 7.5% of United States adults seek care from chiropractors annually. This study assessed whether the addition of chiropractic manipulative therapy (CMT) to standard medical care (SMC) accelerates the treatment of LBP.

This prospective, randomized trial included 91 active-duty military personnel between the ages of 18 and 35 years. All subjects were diagnosed with acute LBP of less than four weeks' duration. The study

did not restrict access to SMC, with participants randomized to receive SMC alone or SMC plus CMT. CMT included high velocity, low amplitude manipulation twice per week for four weeks. The primary outcome measures at two and four weeks included pain and function, assessed with a numerical rating scale (NRS), the Roland-Morris Disability Questionnaire (RMQ) and the Back Pain Functional Scale (BPFS). Secondary outcomes included satisfaction and overall improvement.

At both two and four weeks, the CMT group obtained better NRS scores ($p<0.001$ and $p=0.02$, respectively), as well as higher RMQ scores ($p<0.001$ and $p=0.004$, respectively) as compared to the SMC only group. In addition, more patients in the CMT group than in the SMC only group reported an overall improvement rating of pain being completely gone, much better or moderately better, (73% versus 17%) and higher satisfaction on a 10 point scale (8.9 versus 5.4) at four weeks.

Conclusion: This study of patients with acute low back pain found that the addition of chiropractic manipulative therapy to standard medical treatment can improve pain and functional outcomes more than does standard medical care alone.

Goertz, C., et al. Adding Chiropractic Manipulative Therapy to Standard Medical Care for Patients with Acute Low Back Pain. *Spine.* 2013, April 15; 38(8):627- 634

EFFECTS OF GLUCOSAMINE AND EXERCISE ON LEPTIN LEVELS

Osteoarthritis (OA) is a common, chronic disease characterized by a deterioration of articular cartilage. Leptin, synthesized almost exclusively by adipose, has recently been found to have actions including modulation of the immune response and effects on bone and cartilage metabolism. This study assessed the effects of glucosamine sulfate and exercise on leptin levels and clinical outcomes of knee OA.

Subjects included 37 women with knee OA, randomized to an exercise only group or an exercise plus glucosamine group. Exercise consisted of 12 weeks of flexibility and strengthening training. The study group received 1,500 mg of glucosamine sulfate daily, in addition

to performing the exercises. Outcome measures included serum concentrations of leptin, functional performance, muscle strength and WOMAC pain and disability scores.

At baseline, plasma leptin levels were significantly related to body mass index ($p=0.0001$) and duration of symptoms ($p=0.038$), but not to age, pain, disability, functional performance, muscle strength or severity of disease based on imaging. After 12 weeks, both groups showed significant reductions in leptin levels ($p=0.001$ and $p=0.003$, respectively), pain ($p=0.001$) and disability ($p=0.001$). Both muscle strength and functional performance improved ($p=0.001$). No significant difference occurred between the groups on post-treatment clinical parameters.

Conclusion: This study found that, among patients with OA of the knee, exercise is associated with improved function, reduced pain symptoms and decreased leptin serum levels. Glucosamine did not influence the outcome of any of these variables.

Durmus, D., et al. Effects of Glucosamine Sulfate and Exercise Therapy on Leptin Levels in Patients with Knee Osteoarthritis: Preliminary Results of a Randomized, Controlled Trial. *Rheum Internat.* 2013, March; 33(3): 593–599.

EMPLOYER SPONSORED FINANCIAL INCENTIVES FOR WEIGHT LOSS

Increasing obesity in the United States poses a public health challenge, with increased mortality rates and higher healthcare costs. Recent studies have begun to explore the use of financial incentives to promote weight loss in the face of this looming crisis. This study investigated the effectiveness of financial incentive designs in promoting weight loss among obese employees.

This randomized controlled trial included 105 employees with a body mass index (BMI) between 30 kg/m² and 40 kg/m². The employees were assigned one of three groups including: a monthly weigh-in control group, a group provided with an individual incentive of \$100 per person per month for meeting or exceeding weight loss goals, or a group incentive of \$500 per month split between participants within

groups of five who met or exceeded weight loss goals. All groups were provided a link to the weight control information network of the National Institute of Diabetes and Digestive and Kidney Diseases. The primary outcome was weight loss at 24 weeks. Secondary outcomes included weight loss at 36 weeks, 12 weeks after incentives had ended.

At 24 weeks, the group incentive participants lost 4.4 kg more than did the control group ($p<0.001$), and 3.2 kg more than did the individual-incentive participants ($p=0.008$). At 12 weeks after the incentives had ended, group-incentive participants maintained greater weight loss than did control group participants ($p=0.016$), but not significantly greater than individual-incentive participants ($p=0.024$).

Conclusion: This study of financial incentives for weight loss suggests that group-based financial incentives may be more effective than individual incentives for promoting weight loss.

Kullgren, J., et al. Individual versus Group-Based Financial Incentives for Weight Loss. *Ann Intern Med.* 2013, April 2; 158(7): 505–514.

TETRAHYDROCANNABINOL/ CANNABIDIOL ORAL MUCOSA SPRAY FOR CENTRAL NEUROPATHIC PAIN

Many patients with multiple sclerosis (MS) report central neuropathic pain, which is often resistant to treatment. Cannabinoid receptors are found at nerve terminals, inhibiting neurotransmitter release. This study assessed the efficacy of a delta-9-tetrahydrocannabinol (THC)/cannabidiol (CBD) spray for the treatment of MS-related neuropathic pain.

Subjects were patients with at least three months of MS-related, central neuropathic pain. Phase A of the study looked at 339 patients who added either THC/CBD or placebo spray for 14 weeks to their current medications. Each subject was allowed a maximum of 12 doses per day for 14 weeks. This phase ended with a double-blind, four-week withdrawal phase, assessing the presence or absence of withdrawal symptoms. The primary efficacy endpoint for phase A was the

response to treatment, defined as an improvement of 30% or more in the patient's mean pain Numerical Rating Scale (NRS) score from baseline to the last week of treatment. In phase B, the primary endpoint was time to treatment failure during the withdrawal period.

The primary endpoint at week 14 of phase A of the study was not met ($p=0.234$). During phase B, the primary endpoint of time to treatment failure was significant, with 57% of the placebo group failing treatment, as opposed to 24% of the study group ($p=0.04$). Secondary endpoints of pain reduction and sleep improvement showed superiority in the active group over the placebo group.

Conclusion: This study of a THC/CBD oromucosal spray for central neuropathic pain in patients with multiple sclerosis found a positive result of the study drug for reducing pain, with results complicated by a high placebo response.

Langford, R., et al. A Double-Blind, Randomized, Placebo-Controlled, Parallel Group Study of THC/CBD Oral Mucosa Spray in Combination with Existing Treatment Regimen in the Relief of Central Neuropathic Pain in Patients with Multiple Sclerosis. *J Neurol.* 2013, April; 260: 984–997.

NEUROPATHIC PAIN IN THE COMMUNITY

Chronic pain with neuropathic features is thought to affect seven to eight percent of the general population. The proportion of these cases meeting the International Association for the Study of Pain (IASP) classification of neuropathic pain not responding to standard treatment is unknown. This study was designed to estimate the percentage of neuropathic pain in this population that is refractory to treatment.

This United Kingdom study surveyed 10,000 individuals at five locations, using a questionnaire that contained information concerning chronic pain with neuropathic characteristics (NC), including severity, number and duration of medications used, healthcare use, quality-of-life and pain self-efficacy. These data were combined to determine the presence and characteristics of "refractory" neuropathic pain.

The sample available for analysis included 4,306 individuals who returned the questionnaire with complete data. Of those, 2,296 respondents reported no chronic pain and 2,010 reported chronic pain, including 1,611 individuals with chronic pain without NC, and 399 with chronic pain with NC. The 399 respondents who reported chronic pain with NC represented 8.9% of the study sample, and 18.1% of those reporting any chronic pain.

Those with chronic pain with NC were more likely to be women, unmarried and living in public housing. They were also more likely to be unable to work due to illness or disability, to have no educational qualifications and to be smokers than were those with chronic pain without NC. Of those with possible neuropathic pain, 117 were not treated and 98 were treated. Comparing those who had been treated with at least one neuropathic pain medication with those with no such treatment, significant differences were found on SF-12 PCS and MCS scores, EQ-5D and PSEQ scores.

Conclusion: This study found a significant number of people with persistent neuropathic type pain that is untreated or undertreated.

Torrance, N., et al. Neuropathic Pain in the Community: More Undertreated than Refractory? *Pain*. 2013, May; 154(5): 690–699.

MEMANTINE FOR AXIAL SIGNS IN PARKINSON'S DISEASE

In late stage Parkinson's disease (PD), axial signs, abnormal posture, falls and poor balance reduce individual independence. Previous studies have demonstrated that N-methyl-D- aspartic acid (NMDA) related receptor antagonists can facilitate locomotion in animal models. Memantine is a noncompetitive, partial antagonist to the NMDA receptor which has been shown to decrease akinesia and rigidity in a rat model. This study assessed the effect of this medication in humans.

Consecutive patients with PD and severe gait disorder were invited to participate in this trial. The subjects were randomized to receive either a placebo or memantine. The study drug was titrated over 30 days to a study dose of 20 mg per day for 30

days. The primary efficacy criterion was the change in stride length under "on L-dopa" conditions, with secondary criteria including gait velocity and cadence, motor handicap, as assessed by the United Parkinson's Disease Rating Scale (UPDRS) motor score and its axial subscore, Dyskinesia Rating Scale (DRS) score and its axial subscore, hypertonia and trunk flexor and extensor strength.

Twenty-five patients were included in the final analysis. Three patients, including two in the placebo group and one in the memantine group, dropped out. No differences were noted between groups in stride length. However, the medication group demonstrated significantly better outcomes than did the placebo group in UPDRS scores, the UPDRS axial subscore, axial hypertonia, axial and overall DRS score and its axial subscore.

Conclusion: This study of patients with Parkinson's disease and gait disorders found that the addition of memantine can reduce axial motor symptoms and dyskinesia scores, but does not improve gait.

Moreau, C., et al. Memantine for Axial Signs in Parkinson's Disease: A Randomized, Double-Blind, Placebo-Controlled Pilot Study. *J of Neur Neurosurg Psych*. 2013, May; 84(5): 552–555.

BRAIN GAMES FOR BRAIN INJURY

After a traumatic brain injury (TBI), attention deficits are a common complaint. This study reviewed two, computer-based treatments for attention deficits after TBI.

This pilot trial included four adults diagnosed with severe TBI. All subjects underwent eight weeks of training using the attention process training-3 (APT-3) and Lumosity: Reclaim Your Brain™ brain games. Two participants were first treated with APT-3, while the other two received Lumosity treatment first. The researchers used an A-B-A-C-A (pre-testing, intervention phase 1, post-testing 1, intervention phase 2, and post-testing 2) design, recording the effects of each intervention. The Test of Everyday Attention (TEA) and a researcher-generated, repeatable probe were used to assess each participant's attention performance

(a) before the start of the first intervention, (b) after completing the first intervention and before initiating the second intervention and (c) after completing the second intervention.

All four participants demonstrated statistically significant progress in reaching new levels of difficulty on intervention tasks. One participant demonstrated significantly improved performance on one of five probe measures, and one other participant showed improved performance on some sub-tests of the TEA. No other significant generalization results emerged.

Conclusion: This study of two attention remediation tests found that patients with severe brain injury can improve, although the results did not generalize to other tests of attention.

Zickefoose, S., et al. Let the Games Begin: A Preliminary Study Using Attention Process Training-Three and Luminosity Brain Games to Remediate Attention Deficits following Traumatic Brain Injury. *Brain Inj*. 2013, June; 27(6): 707–716.

COST OF DEMENTIA IN THE UNITED STATES

Dementia affects a large number of older adults in the United States. Estimating the cost of this disease is difficult, as coexisting conditions are common among those afflicted. This study was designed to better understand the monetary costs associated with dementia related care.

Data were obtained from the Health and Retirement Study (HRS), a nationally representative, longitudinal survey of persons 51 years of age or older, beginning in 1992. From this study, 856 individuals underwent a detailed in-home clinical assessment for dementia. Based upon that assessment, the authors categorized the patient's cognitive status as reflecting dementia, cognitive impairment without dementia or normal aging.

Cost of care was estimated based upon out-of-pocket, Medicare, nursing home, and in-home expenses attributed to the dementia. Formal in-home care costs were estimated using home health agencies' 2010 average hourly rate. Values for informal (unpaid) care were determined as either as the cost of equivalent formal (paid) care or as

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the estimated wages forgone by informal caregivers.

The estimated prevalence of dementia among persons older than 70 years of age in the United States in 2010 was 14.7%. The annual population cost was estimated to be \$109 billion for care purchased in the market. When the value of informal care was included, the population cost estimate rose to \$159 billion to \$215. After adjustment for coexisting conditions and demographic characteristics, the attributable yearly cost per person, including both the cost of care purchased in the marketplace and the cost of informal care, was \$41,689 when the valuation of forgone wages was used. This estimate rose to \$56,290 when the valuation of replacement cost was used.

Conclusion: This study of the overall cost of dementia in the United States, based on 2010 data, found that the individual cost ranged from \$41,000 to \$56,000 per individual, with total costs ranging from \$157 to \$215 billion.

Hurd, M., et al. Monetary Cost of Dementia in the United States. **N Eng J Med.** 2013, April 4; 368(14): 1326 – 1333.

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