

DeBruyne, J. Predicting Post-Concussive Syndrome Following Mild Traumatic Brain Injury in the Adult Population and Potential Methods of Prevention: A Clinical Review

Introduction

Mild traumatic brain injury (TBI) is recognized as one of the most common neurologic disorders. Most adults demonstrate resolution of symptoms in 7 to 10 days, however, persistent symptoms can be found in up to 10-20% of patients. Post-concussion syndrome (PCS) is associated with increased health care utilization and disability making it important for clinicians to predict who is at risk and employ evidence based methods of prevention.

Methods

A literature search was performed using MEDLINE, PubMed, Cochrane database, and ClinicalKey. Searches were limited to articles published within the last 5 years, and bibliographic searches were completed to include research outside of that timeline.

Results

Demographic and psychosocial factors were reviewed to determine their role in developing PCS. Advanced imaging and biomarkers have been studied within the context of mTBI, but there is little research regarding their use in predicting PCS. Increased levels of biomarker S100B may correlate to development of neuropsychological disorders following mTBI and may be a useful clinical tool in the future. Cognitive behavior therapy (CBT) is a possible preventative option for patients at risk for PCS.

Conclusions

Risk stratifying mTBI patients allows providers to better predict which patients are more likely to develop PCS. Those patients may benefit from early CBT.

Emmerich, EJ. Bariatric surgery in the adolescent population: [capstone paper]. La Crosse: University of Wisconsin Master of Physician Assistant Studies; 2018. (A. Baumgartner).

Introduction: Obesity is a public health concern in the United States, impacting 18.5% of adolescents and increasing risks for hypertension, diabetes, and hyperlipidemia. As conservative management of dietary and lifestyle modifications has produced limited success, interest and utilization of bariatric surgery in adolescents has increased in recent decades.

Methods: A literature review utilizing Cochrane, MEDLINE, and PubMed was completed for the terms bariatric surgery, obesity, Rou-en-Y gastric bypass, laparoscopic adjustable gastric band, laparoscopic sleeve gastrectomy, adolescent, BMI reduction, complications, and cost.

Results: There is low-quality evidence supporting bariatric procedures for the treatment of adolescent obesity. Data revealed bariatric surgery significantly reduced BMI in the short-term. Additionally, data supported the resolution of obesity related comorbidities in the years following bariatric procedures. Minimal surgical complications were reported within 30 days of the procedure. However, long-term effects of bariatric procedures in adolescents remain to be analyzed.

Conclusion: While there is some evidence that adolescent bariatric surgery improves weight loss and reduces comorbidities, studies are largely retrospective, observational, and include short-term follow-up. Additional research on the long-term morbidity and mortality of adolescent

bariatric surgery is necessary before it replaces standard obesity management with dietary and lifestyle modifications.

Fassbinder, JF. Hormone therapy for cardiovascular disease prevention in early postmenopausal women. MS in Physician Assistant Studies, May 2018, 46pp. (S, Sieck)

Introduction: Menopausal estrogen decline is a known cardiovascular risk factor. Hormone therapy (HT) is no longer indicated for preventing cardiovascular disease (CVD) as a result of three monumental randomized controlled trials (RCTs) showing increased CVD risk with HT use.¹⁻³ Age-stratified analyses of these studies, however, suggest that HT in early postmenopausal women could lower CVD risk.

Methods: A literature review concerning HT for preventing CVD in menopausal women was completed using MEDLINE, PubMed, and Cochrane Database of Systematic Reviews. Systematic reviews, RCTs, and observational studies were evaluated.

Results: Moderate-quality evidence suggests that HT in early postmenopausal women yields reduced all-cause mortality and coronary heart disease (CHD) risk, no change in stroke risk, and increased venous thromboembolism risk. HT studies of surrogate endpoints for CVD have found conflicting results. There is no robust evidence identifying the optimal dose, formulation, route, or duration of HT that maximizes the benefit to risk profile.

Conclusion: HT reduces mortality and CVD in early postmenopausal women. Given the uncertainty regarding optimal administration, HT should not be prescribed for CVD prevention but considered in the decision to use HT for approved reasons.

MeSH Terms: Hormone therapy, cardiovascular disease, coronary disease, stroke, venous thromboembolism, estrogens, progestins, postmenopause.

Hansen, MF. Outpatient management of generalized anxiety disorder in adults in primary care. Master of Physician Assistant Studies, May 2018, 32 pp. (K Graham)

Generalized Anxiety Disorder is a common mental illness that presents frequently in primary care and is often under-diagnosed and undertreated. Current therapies are lacking in efficacy and accessibility. This clinical review will assess current and emerging therapies for the treatment of generalized anxiety disorder in the outpatient setting. Articles were identified using the Medline, Cochrane, and the Mayo Library databases. First line treatments of SSRIs and SNRIs have response rates at 60-70% with side effects including sexual dysfunction. Second line treatments including tricyclic antidepressants and atypical antipsychotics show efficacy but are associated with significant side effects. Benzodiazepines are effective and work quickly, but are associated with tolerance, abuse, and withdrawal symptoms. Newer medications have shown inconsistent and unimpressive results. Internet cognitive behavioral therapy appears to be effective, but is not yet widely available. Complementary medicine, including herbal supplements and yoga, has shown some promise with minimal side effects, but strong evidence is lacking. Additional research is needed in all types of treatment to further support evidence for, or against, their use in the treatment of anxiety.

MeSH terms: generalized anxiety, anxiety, adults, treatment, pharmacotherapy, primary care, emerging therapies, complementary medicine, alternative medicine, herbal therapies

Janczak, AF. Treatment of Latent Autoimmune Diabetes of the Adult: A Case Report and Clinical Review. La Crosse: University of Wisconsin Master of Physician Assistant Studies; 2018. (S, Sieck)

Introduction: Latent autoimmune diabetes of the adult accounts for around 10% of all patients with diabetes but currently lacks guidelines for proper management.¹ In an effort to try to control these patients, researchers are studying which medications are safe for LADA and which might be harmful.

Methods: A literature search utilizing Cochrane Databases, MEDLINE, PubMed, Clinical Key, and the American Diabetes Association was completed.

Results: Multiple studies have found that sulfonylureas can be harmful in LADA treatment. Progression to insulin therapy is associated with GADA titer and BMI. DPP-4 activity is higher in patients with LADA and might confer some protective value against the loss of beta cells. SGLT-2 inhibitors have not shown an increased risk of hypoglycemia or diabetic ketoacidosis. Antigen immunotherapy has not proven to be a viable option for treatment.

Discussion: Current research shows that sulfonylureas can be harmful and that DPP-4 inhibitors might decrease the need for early or life-long use of insulin. Long-term studies are lacking. More research is needed in order to create safe guidelines for monitoring and treatment especially related to initiation of insulin.

MeSH terms: LADA, Latent Autoimmune Diabetes of the Adult, Diagnosis, Screening, Treatment, Complications, Guidelines, SGLT-2 inhibitors, DPP-4 inhibitors, Immunotherapy.

Johnson, EK. Emerging Therapies in Multiple Sclerosis. Master of Physician Assistant Studies, May 2018. (K. Graham).

Introduction/Objective: Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system. While there are disease-modifying therapies available, they are mostly used to reduce relapse events in patients with relapsing remitting multiple sclerosis (RRMS). This clinical review analyzes emerging therapies for MS including biotin, vitamin D, stem cell transplant, ocrelizumab, and leukemia inhibiting factor.

Methods: Articles were identified using the PubMed and Cochrane databases and the Neurology and Multiple Sclerosis journals, using the key terms listed below.

Results: High-dose biotin has uncertain benefit for patients with primary progressive MS (PPMS). The therapeutic benefit of vitamin D supplementation remains uncertain. Stem cell transplant is a promising option for young patients with RRMS and highly active disease. Ocrelizumab has shown mild benefit for delaying disease progression in patients with both RRMS and PPMS.

Conclusion: While the treatment of all forms of MS is improving, further research is necessary in order to better manage what can be a very debilitating disease. Future therapies need to focus on the different physiologic processes occurring in the various forms of MS in order to develop targeted treatments.

MeSH Terms: biotin, multiple sclerosis, nanotherapy, natalizumab, ocrelizumab, stem cell transplant, primary progressive, leukoencephalopathy, vitamin D

Komarek, CV. Emerging non-dietary therapies for celiac disease. La Crosse: University of Wisconsin Master of Physician Assistant Studies; 2018, 34 pp. (A. Baumgartner)

Introduction/Objectives: Celiac disease causes distressing symptoms and requires lifelong gluten avoidance, to which it is difficult for patients to adhere. A gluten-free diet is not always effective at alleviating symptoms and preventing long-term consequences of celiac disease. Alternative treatments are needed, and multiple potential therapies are currently in development.

Methods: A literature search using MEDLINE, PubMed, Clinical Key, and Cochrane databases was completed for celiac or coeliac disease, celiac or coeliac sprue, non-dietary, treatment, larazotide acetate, probiotics, AN-PEP or *Aspergillus niger* prolyl-endopeptidase, Nexvax2, hookworm, and latiglutenase or ALV003. Systematic reviews and randomized controlled trials were identified and utilized.

Results: Currently, there is insufficient evidence from clinical trials to suggest efficacy in these emerging therapies. Larazotide acetate does not show a dose-dependent significant difference in intestinal permeability compared to placebo. Probiotic *B. breve* does significantly decrease TNF- α production, but *B. longum* does not. Glutenases AN-PEP and latiglutenase do not have a significant benefit over placebo. Nexvax2 appears to be well-tolerated. Hookworm infections do not induce significant positive histological or symptomatic changes from placebo.

Conclusion: There remains a need for further development of alternative or adjunct therapies for CD. All developing therapies must be compared with the safe gold standard GFD treatment.

Lange, MM. Non-Opioid Analgesics and Alternative Therapies for Chronic Non-Cancer Pain [capstone paper]. La Crosse: University of Wisconsin Master of Physician Assistant Studies; May 2018. (M. Devine)

Introduction/Objective: Chronic pain and opioid overuse are prevalent and widespread problems affecting both patients and providers in multiple specialties. There is a great need for effective, non-opioid therapies to treat chronic pain. Patients often inquire about alternative treatments, and primary care providers should be comfortable discussing and prescribing appropriate regimens for chronic pain.

Methods: MEDLINE, PubMed, CINAHL, and Cochrane were searched using the terms listed below.

Results: There is moderate evidence to show that NSAIDs are effective, especially for

musculoskeletal pain. Topical NSAIDs have fewer long term adverse effects and are more effective than placebo. There is sparse evidence for acetaminophen but what is available concludes that it is generally a poor choice for chronic pain. Anticonvulsants and topical capsaicin are appropriate choices for neuropathic pain. Essential oils may be beneficial, but studies tend to be flawed. CBT may be effective, especially in older, more educated patients.

Conclusion: There are many therapies other than opiates available for the treatment of chronic pain, and each case should be approached in an individualized and multifactorial manner. A strong patient-provider relationship is also paramount to successful treatment.

MeSH terms: chronic pain, ibuprofen, NSAIDs, acetaminophen, anticonvulsants, essential oils, capsaicin, essential oils, cognitive behavioral therapy

Leisen, EL. A Review of Patient Care for Traumatic Spleen Injury. Master of Physician Assistant Studies, May 2018, 34 pp. (M. Devine)

Introduction: Our understanding of the spleen continues to evolve, and with it, the need for further understanding of how we treat patients with splenic trauma. This review compares patient outcomes for splenectomy to conservative therapies and their impact on the immune system.

Methods: Literature search was completed using PubMed, Cochrane, ClinicalKey, and Midline, followed by bibliographic reviews for other relevant articles. Search terms included: splenectomy, splenic artery embolization (SAE), conservative management, non-operative management (NOM), observation, and trauma.

Results and Discussion: Splenectomy remains the gold standard treatment for hemodynamically unstable splenic trauma patients. It is, however, associated with overwhelming post-splenectomy infection (OPSI) and requires increased monitoring with vaccinations and on-hand antibiotic prescriptions. It is not uncommon for asplenic patients to be under-vaccinated or lack on-hand antibiotic prescription. For hemodynamically stable patients, SAE or observational management are preferred approaches that preserve the hematological and immunological functions of the spleen. Current vaccination trends support the practice of not vaccinating SAE or NOM patients.

Conclusion: All splenic trauma patients may benefit from close follow-up by a primary care provider aware of standard vaccination schedules and methods for OPSI prevention. Further research is needed to develop a standard measurement of splenic function.

Lewis, E. Hyperbaric oxygen therapy for diabetic foot ulcers.

Introduction Hyperbaric oxygen therapy (HBOT) is a treatment option that can be successful for conditions with poor prognoses refractory to first-line treatments. Despite its clear parameters for which it is covered by Medicare, the role of adjunctive HBOT for the treatment of diabetic foot ulcers (DFU) has not been widely accepted or implemented.

Methods A literature search using MEDLINE, PubMed, and Cochrane databases was completed for HBOT indications, side effects, diabetic foot ulcers epidemiology and treatment options, and

the efficacy of HBOT for diabetic foot ulcers. Recent systematic reviews with rigorous methodology and randomized control trials that focused on cost-efficacy were identified and reviewed.

Results There is moderate quality evidence that HBOT is an effective treatment option for Wagner grade III, IV, and V DFUs when used as adjunctive treatment when standard treatment alone has failed. Two cohort studies with over 15,900 total patients have demonstrated a significant cost advantage in utilizing HBOT as an adjunctive treatment by decreasing rates of lower extremity amputations and hospitalization costs. HBOT is not an effective treatment for Wagner grade I and II DFUs.

Conclusion Current research demonstrates HBOT has a role in the treatment of severe diabetic foot ulcers that have failed standard therapy. Given the significant cost and mortality associated with DFUs and lower extremity amputations, HBOT must be utilized as an adjunctive treatment within the algorithm of comprehensive limb salvage protocols. Further randomized control trials and systematic reviews that are limited to Wagner grade III, IV, and V wounds are necessary to clarify the efficacy of HBOT when used prudently under the accepted indications.

Lyng, T.E. Pharmacotherapy in Pediatric Depression. Masters of Physician Assistant Studies, May 2018, 27 pp. (M. Rathgaber)

Introduction Major depression in the pediatric population is a prevalent disease which is often under-diagnosed and undertreated. MDD in the pediatric patient can be diagnosed and managed by primary care providers, however, controversy over the safety and efficacy of antidepressants in this population may make providers wary of treatment. Therefore, a better understanding of antidepressant use in pediatric patients is required to encourage sufficient diagnosis and treatment.

Methods A literature search using EBSCO Host, PubMed, Cochrane Database of Systematic Reviews, and the Cochrane Central Register of Controlled Trials was completed for pediatric/adolescent depression, child/adolescent psychiatry, antidepressant, SSRI, TCA, atypical antipsychotic, CBT, prescribing practices, and diagnosis. Retrospective cohort studies, systematic reviews and meta-analyses, and relevant historical documents were included.

Results There is good quality evidence that the FDA black box warning for antidepressants lead to a decrease in diagnosis and treatment of pediatric MDD. There is moderate quality evidence that antidepressants increase suicidality in pediatric patients. Fluoxetine is the only antidepressant not shown to increase this risk and it does have the best efficacy of the antidepressants studied.

Conclusions Fluoxetine is a good first-line pharmacotherapy treatment option for unipolar pediatric MDD under the close management of a primary care provider.

McLimans, AJ. The decision to screen for prostate cancer: a clinical review of the factors and process. Master of Physician Assistant Studies, May 2018, 40 pp. (P. Campbell)

Introduction: It is estimated that 180,890 new cases of prostate cancer were diagnosed in 2016 making it the most commonly diagnosed non-skin cancer in men¹. Screening using Prostate Specific Antigen (PSA) is frequently performed in the primary care setting; however, a significant cancer-specific decrease in mortality has not been well established². Harms associated with the overdiagnosis of prostate cancer, are early, frequent, and potentially deadly³.

Methods: A literature search using PubMed, MEDLINE, and Cochrane databases was completed for the MeSH terms listed below.

Results: There is low quality evidence that PSA screening reduces the risk of prostate cancer mortality and moderate quality evidence that screening with appropriate treatment reduces the risk of bone metastases. There is moderate quality evidence that men with localized prostate cancer can safely undergo active surveillance without additional prostate cancer mortality risk.

Conclusion: Further research is necessary for more definitive conclusions regarding PSA screening efficacy. The harms of overtreatment are well-documented; however, when screening is targeted to the correct population with the appropriate follow-up, these risks can be mitigated while maximizing the potential for benefit.

MeSH terms: prostate specific antigen (PSA), prostate cancer screening, shared decision making, decision aids, benign prostatic hypertrophy, active surveillance, watchful waiting, prostate cancer biomarkers, tumor, mortality, kallikrein markers, 4-kallikrein (4K) score, prostate health index (PHI), prostate cancer antigen 3 (PCA3), cost analysis

Mitchell, CL. What is the cost?: The many implications of the clinician-pharmaceutical representative relationship. Master of Physician Assistant Studies, May 2018, 41 pp. (P. Campbell)

Introduction/Objective: The role of pharmaceutical representatives (PRs) in a clinician's practice is a hotly debated and intensely contested topic. This clinical review analyzes the available research regarding the clinician-PR relationship and aims to assess what the advantages, disadvantages, and ultimate cost to the healthcare system are. Articles were identified using MEDLINE, CINAHL, and PubMed databases. Current available data primarily examines physician-prescribing patterns, but there is some data that supports physician assistants prescribe similarly to physicians. There is a large amount of evidence supporting the claim that meeting with PRs alters physician-prescribing behavior. Identified advantages of the clinician- PR relationship are easy access to information and free drug samples. However, easy access to information does not lead to increased quality of prescribing, and the free drug samples are not going to the patients with the greatest need. Disadvantages are increased off-label prescribing of medications and increased cost of prescribing. More research is needed regarding how the clinician-PR relationship impacts patient outcomes.

MeSH Terms: pharmaceutical spending, pharmaceutical representative, drug representative, clinician, physician, prescription drug cost, cost of prescription drugs, cost of prescribing,

pharmaceutical industry ethics, physician prescribing, detailing, regulations, laws, drug samples, advanced practice provider, physician assistant, nurse practitioner, advanced practice registered nurse, and free samples

Moore, K. The use of endoscopic retrograde cholangiopancreatography in gallstone pancreatitis: A review. La Crosse: University of Wisconsin Master of Physician Assistant Studies; 2018. (Amie Baumgartner).

Introduction/Objective: Endoscopic retrograde cholangiopancreatography's utility in gallstone pancreatitis was first researched in 1988. A multitude of studies including 8 meta-analyses on the topic have been published since then. When this intervention is best utilized and with what severity of the disease process has been an ongoing debate within the literature.

Methods: MEDLINE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and PubMed were searched using the MeSH terms listed below.

Results: Although the first three meta-analyses found a utility for ERCP in severe gallstone pancreatitis without cholangitis when it comes to morbidity and mortality, the five most recent have not. Even so, similar studies have been used throughout all of the different meta-analyses, but the studies included within them have uncertain quality.

Discussion/Conclusion: The most recent data does not support ERCP as a treatment for gallstone pancreatitis without cholangitis. Because of the questionable quality of the studies involved, further research with improved study parameters is needed.

MeSH terms: biliary pancreatitis, gallstone pancreatitis, endoscopic retrograde cholangiopancreatography, ERCP, endoscopic ultrasound, EUS, timing, conservative treatment, acute pancreatitis

Spindler, IL. Advanced Care Planning: What are the current completion rates in the United States and how can medical education increase planning for end-of-life. Master of Physician Assistant Studies, May 2018, 30 pp (P. Campbell)

Advance Care Planning (ACP) is a process to help patients discuss preferences for medical care in the event that they are unable to communicate their wishes. Although the Patient Self-Determination Act (PSDA) was passed in the United States nearly 30 years ago, the reported current completion rates of ACP including Advance Directives (ADs) varies widely. Some of the best evidence currently available shows that only approximately one-third of Americans have any form of ACP. In addition, numerous studies provide evidence that black and Hispanic Americans have lower completion rates than white Americans. One factor that contributes to the overall low completion rate of ACP is provider comfort with introducing and discussing end-of-life (EoL) care. Current literature suggests that provider education along with focused targeting of minority groups may lead to increased overall completion rates of ACP and EoL care consistent with patients' wishes.

Theil, L. Risk communication value and strategies in general medicine.

Objective: This analysis aims to compile the risk communication strategies highlighted in research of this century which are pertinent to the daily efforts of a physician assistant working in general medical practice. *Methods:* Literature review was performed using MEDLINE, Cochrane Central Register of Controlled Trials, CINAHL, ClinicalKey, PubMed, PsychInfo, and review of reference article citations. Preliminary search was limited to 2014 and later inclusive of study samples of medical decision-makers. *Results:* Effective methods of communicating risk included presentation of probabilistic information, visual aids, and simplified ideas, while qualitative risk descriptors, relative risk reduction, and number needed to treat were identified to poorly communicate risk information.

Key words: Risk communication, risk information, risk magnitudes, strategic risk communication, patient education, informed decision making, shared decision making, visual communication, graphical displays, graph perception, statistical risk information, numeracy, risk comprehension, risk perception, intention, adherence

Wawrzaszek, KL. Ketamine use in treatment resistant major depressive disorder. Master of Physician Assistant Studies, May 2018, 30 pp (P. Campbell)

Depression is one of the leading causes of morbidity and mortality worldwide. The treatment of depression typically includes some form of therapy, cognitive or dialectic behavioral being the most common, and pharmacologic therapy with selective serotonin reuptake inhibitors. Patients refractory to those options are often switched to serotonin and norepinephrine reuptake inhibitors, tricyclic antidepressants, monoamine oxidase inhibitors or atypical antidepressants like bupropion or mirtazapine. In the field of treatment resistant depression, commonly defined as those failing standard therapy (both pharmacologic and psychosomatic), ketamine shows some early promise. Ketamine is a CNS depressant and dissociate, that has been shown in small trials with short follow up to be safe and effective in treating depression. At this time, the use of ketamine for depression is controversial and not recommended by the American Psychiatric Association given the paucity of data as well as its potential for abuse.

MeSH terms: depression, intentional harm, suicidal ideation, ketamine, emergency department, urgent care, abuse and dependency, repeat infusion trials, treatment resistant depression

Zinnel, B. Care considerations for anti-tumor necrosis factor-a biologic therapy in inflammatory bowel disease. University of Wisconsin-La Crosse Master of Physician Assistant Studies; 2018. K. Graham.

Introduction Biologics are becoming widely utilized drugs, especially for chronic inflammatory conditions like Inflammatory Bowel Disease (IBD), thus increasing the complexity of disease management. Currently, anti-tumor necrosis factor-a agents are among the most popular agents.

Methods A literature review was performed using MEDLINE, Pubmed, and Cochrane databases using MeSH terms listed below and references were cross-referenced for further inclusion.

Results Evidence suggests that biologics increase the risk of opportunistic infections and reactivation of latent infection. Additionally, research demonstrates increased risk of malignancy of gut, cervix, and skin. Therapeutic drug monitoring is important in preventing anti-drug antibodies and loss of response, which leads to maintenance of remission and improved longterm outcomes. Biologics are cost-effective for remission induction, but not maintenance treatment of IBD despite their efficacy and superior long-term disease outcomes.

Conclusion Primary care providers play a pivotal role in closing the gap in maintenance and preventative care for patients with IBD, including those on biologics. Further research is needed to evaluate emerging biologic therapies and biosimilars, as well as cost-effectiveness and efficacy on long-term disease outcomes for current therapies.

MeSH terms Inflammatory bowel disease, biologic therapy, biologics, biologic treatment, monitoring, health maintenance, disease outcomes, long-term outcomes, cost-effectiveness, efficacy, adverse effects.