–Minneapolis VA Health Care System–

VA Research Day 2021

Christopher Erbes, PhD, ABPP 1972–2021

Outstanding VA clinician-investigator,
mentor, colleague, and research leader

Program and Abstract List

(alphabetically, by author)

June 8-10, 2021

U.S. Department of Veterans Affairs

Veterans Health Administration

Office of Research and Development

☆Dedication☆

Christopher Russell Erbes, PhD, husband, father, clinical psychologist, researcher, and author passed away unexpectedly on May 30, 2021. Dr. Erbes was a valued mentor and role model for students and colleagues. He will be remembered for his intelligence, generous counsel, quick wit and the love he had for his wife Lisa, two children Erin (age 19) and Maia (17), his parents, and 6 siblings. Despite his demanding professional schedule, Dr. Erbes priority was always his family. He was a devoted and caring father who took great pride in the accomplishments of his children and always looked forward to weekly date nights and annual trips he took with his family. Through his professional as well as his personal relationships, he touched the lives of many people. Dr. Erbes was an extraordinarily well-rounded person who completed half a dozen marathons. He had wide ranging interests that encompassed an encyclopedic first-hand knowledge of craft beers, a keen interest in fantasy/scifi, and a zeal for heavy metal music.

After graduating from the University of New Mexico with a bachelor's degree in psychology in 1995, Dr. Erbes completed his graduate training in clinical psychology receiving his PhD from Texas Tech University in 2000. He completed his clinical internship at the Memphis VA Medical Center (Memphis, TN), and a postdoctoral fellowship in serious and persistent mental illness and Posttraumatic Stress Disorder at the Minneapolis VA Medical Center. From 2001 to 2003, he was a staff psychologist for the Douglas County Hospital Mental Health Unit in Alexandria, MN.

Dr. Erbes returned to the Minneapolis VA Medical Center in 2003, where he served for a decade on the Posttraumatic Stress Recovery Team as a staff psychologist and later as program manager. In 2013, he began serving as a Psychology Supervisor and heading the newly established Clinician Investigator Team. Throughout his career, he wore many hats. He was a talented researcher and statistician, and enjoyed sharing his craft with students. At the time of his death he was an Associate Professor in the Department of Psychiatry and Behavioral Sciences at the University of Minnesota as well as adjunct faculty member in the Graduate School of Professional Psychology at the University of St. Thomas and the Program of Counseling and Psychological Services at Saint Mary's University of Minnesota. He was certified by the American Board of Professional Psychology – Clinical Psychology Specialty and served as an Associate Editor for the Journal of Traumatic Stress and was a consulting editor for the Journal of Consulting and Clinical Psychology. Additionally, Dr. Erbes was a talented clinician in his own right and a sought after clinical supervisor who provided top quality empirically supported treatment for trauma related conditions during his career at the Minneapolis VA Medical Center.

Chris was dedicated to making the world a better place and he did this through his profession as a clinical scientist and through his relationships. He was widely respected as a professional due to his expertise in assessment, treatment, and research in PTSD and resilience processes for mental health problems related to trauma. He led numerous research studies, serving as a principal investigator or co-investigator on multiple grants and was a valued collaborator on many more. For more than 15 years, he co-directed the Readiness and Resilience in National Guard Soldiers (RINGS) Project, one of the first studies to collect pre-deployment data from a large group of service members deploying for combat. Dr. Erbes had recently participated in an invited inaugural webinar hosted by National Institute of Health entitled, "Designing Resilience Research in the Context of Military Stress." There he discussed the Advancing Research on Mechanism of Resilience (ARMOR) Study, his most recent work involving a large multilevel, prospective longitudinal study investigating resilience processes that promote adjustment among National Guard service members. An innovative thinker, Chris was a pioneer in rigorously studying narrative therapy as an approach for the treatment of PTSD. He collaborated widely, forging relationships with a group of biomedical engineers to study outcomes and reintegration following amputation, studying the use of mobile phone apps in mental health treatment, and exploring novel treatments for integrating families in care for PTSD. He also served as co-Director of the Family Therapy Training Clinic and the Narrative Therapy Training Clinic. His scholarly work includes more than 100 original scientific and professional papers, and he is cited as an authoritative source by top PTSD researchers and therapists.

Dr. Erbes will be missed by his students, colleagues, and most deeply by his wife Lisa, daughters Erin and Maia and his extended family. A celebration of life for Dr. Erbes life is being planned for late this summer.

–Melissa Polusny, PhD

☆Program☆

1. Opening Session (Tuesday, June 8, 12:00 - 1:30 pm)

☆**Introductions and Welcome**..... Hanna E. Bloomfield, MD, MPH
Associate Chief of Staff, Research Service

☆**2021 Lederle Award Presentation**..... Aasma Shaukat, MD, MPH

Recipient:
Orly Vardeny, PharmD, MS
"Effect of High-Dose Trivalent vs Standard-Dose Quadrivalent Influenza Vaccine on Mortality or Cardiopulmonary Hospitalization in Patients With High-risk Cardiovascular Disease: A Randomized Clinical Trial"

JAMA. 2021 Jan 5;325(1):39-49.

☆**Keynote Address**.....Karen Ashe, MD, PhD
Professor, Department of Neurology, University of Minnesota Medical School

2. Oral Presentation Session 1 (Wednesday, June 9, 12:00 - 1:30 pm)

12:00 ***The role of posttraumatic stress on memory complaints and performance in active-duty service members***
Seth Disner, Elsa Mattson, Nathaniel Nelson, Patrick Armistead-Jehle

12:15 ***Chlorhexidine oral rinses for symptomatic COPD: a randomized, blind, placebo-controlled preliminary study***
Alexa Pragman, Ann Fieberg, Cavan Reilly, Christine Wendt

12:30 ***Implementing cognitive behavioral therapy for insomnia (CBT-I) in VA primary care***
Erin Koffel, Hildi Hagedorn

12:45 ***Increasing Addiction Recovery Services Referrals for Alcohol Use Disorder in the Inpatient Setting: A Quality Improvement Project***
Baila Elkin, Kayla Murphy, Elizabeth Aby

1:00 ***Population and Community-Based Interventions to Prevent Suicide: A Systematic Review***
Noah Venables, Eric Linskens, Allison Gustavson, Nina Sayer, Maureen Murdoch, Roderick MacDonald, Kristen Ullman, Lauren McKenzie, Timothy Wilt, Shahnaz Sultan

1:15 ***Aortic Endograft Infections Are Associated with Secondary Interventions***
Daniel Ihnat, Jing Li, Paul Orecchia, Derrick Green, Lisa Smith, Christopher Creedon

3. Oral Presentation Session 2 (Thursday, June 10, 12:00 - 1:30 pm)

12:00 ***The Effect of Biopsychosocial Factors on Chronic Pain Functioning***
Cara Wienkes, Erin Koffel, Melissa Polusny, Erin Krebs

12:15 ***High fat diet effect on brain immune response and lipid metabolism***
David Roe, Rui Kuang, Joshua Nixon, Kendra Fleming, Simon So, David Bernlohr, Michael Lee, Tammy Butterick

12:30 ***High Satisfaction with Telehealth for Arthroplasty Post-operative Care at the Minneapolis VAMC***
Nathan Graden, Kelsey Wise, Kelly Edwards, Melissa Albersheim, Benjamin Williams, Amy Gravely, Vernon Franklin Sechriest

12:45 ***Protein kinase CK2 correlation with clinical outcomes in HPV(+) and HPV(-) oropharyngeal squamous cell carcinoma***
Janeen Trembley, Bin Li, Betsy Kren, Justin Peltola, Juan Manivel, Devi Meyyappan, Amy Gravely, Mark Klein, Khalil Ahmed, Emiro Caicedo-Granados

1:00 ***Are Clinicians Being Left Behind in the Age of Enlightenment for Exoskeleton Technology?***
Alec Basten, Nicole Walker, John Looft

1:15 ***Impact of Childhood Trauma on Post-Concussive Neurobehavioral Symptoms***
Alison Gammons, Seth Disner

4. Virtual Poster Session

Posters for this year's Research Week activities are saved to VA network at
W:\Research\Research Week 2021

Oral Presentations: Author Index *(first author only)*

Poster Presentations: Author Index *(first author only)*

Oral Presentations

1. Are Clinicians Being Left Behind in the Age of Enlightenment for Exoskeleton Technology?

Basten, Alec [1]; Walker, Nicole [1-2]; Looft, John [2]

1. University of Minnesota
2. Minneapolis VA Health Care System

Abstract: Background: We are living in the age of enlightenment for exoskeleton technology. A quick search using the term 'exoskeleton' in PubMed reveals less than 100 related articles were published in 2010. Since then, the number of related articles has increased exponentially, totaling over 500 articles in 2020. Exoskeleton technology has natural applications within a rehabilitation setting. The rehabilitation benefits of upright ambulation in exoskeletons for persons with SCI are immense; notably, improvements in spasticity level, mobility, walking speed, step length and electrical activity at the muscular level. As exoskeletons are becoming more prevalent in rehabilitation settings, it is increasingly important for clinicians to understand how best to apply them in evidence-based practice. This includes conducting studies using age- and sex-matched healthy controls and looking at clinically relevant measurements such as kinematic, spatiotemporal, and neuromuscular gait parameters. Direct comparisons between available exoskeletons are also necessary to provide the scientific basis clinicians need to make confident decisions about when to use one exoskeleton over another. Purpose: The goal of this review is to examine the current breadth of the literature regarding these ambulation parameters for persons with SCI using rehabilitation exoskeletons. Methods: A literature search was conducted across multiple databases (Ovid Medline, PsychInfo, Scopus, Web of Science, and CINAHL). Included literature directly compared exoskeleton gait of patients with SCI and age-matched, healthy controls. Direct comparisons between kinematic and/or temporospatial parameters were also necessary for literature inclusion. Excluded literature: included only healthy participants, included only patients with SCI, did not meet this study's definition of a rehabilitation exoskeleton, and/or, was not reproducible. Conclusion: Only two out of 38,963 works identified in the search met our inclusion criteria for clinical relevance. No article directly compared two exoskeletons. In the enlightenment age of exoskeletons, much is being done for research and development of the technology, but the specific needs of clinicians who apply it are not being met. The future of exoskeletons for rehabilitation is exciting ñ we must direct the enthusiasm for this technology towards boosting the clinically relevant evidence base in order to best improve patient outcomes.

Research Topic: Spinal Cord Injury
Funding agencies: UMN
Grant support: Undergraduate Research Opportunities Program

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2. The role of posttraumatic stress on memory complaints and performance in active-duty service members

Disner, Seth [1-2]; Mattson, Elsa [3]; Nelson, Nathaniel [4]; Armistead-Jehle, Patrick [5]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Case Western Reserve University
4. University of St Thomas
5. Munson Army Health Center

Abstract: Memory complaints are the most common form of cognitive dysfunction reported by military service members, but prior research suggests that mental health symptoms common in the military (such as posttraumatic stress symptoms [PTSS]) may account for the link between cognitive complaints and cognitive performance. However, the mechanisms underlying this relationship are largely unknown. Questions persist as to whether the general finding applies to memory symptoms, which clinical dimensions may account for the findings, and how the association varies when memory complaints are non-credible. Using a sample of 196 US military service members, the present study aims to address these gaps by modeling the relationship between memory performance and plausible/implausible memory complaints, then evaluating how the association is influenced by PTSS and clinical traits commonly found within PTSS (e.g. depression, anxiety, and somatic concerns). Overall memory complaints were associated with immediate and delayed recall, but both associations were fully mediated by PTSS severity (95% CI -0.14, -0.01; 95% CI -0.14, -0.02, respectively). Implausible memory complaints, however, were inconsistently linked to memory performance, and no mediation by PTSS was observed. Of the clinical traits, only depression moderated the impact of PTSS, specifically by influencing the link between PTSS and overall memory complaints (beta= -0.02, SE= 0.004, p< .001). These results corroborate the importance of assessment for PTSS and depression symptoms in service members who report subjective memory complaints and highlight how targeted intervention for these conditions may play a key role in the management of memory symptoms.

Research Topic: Neuropsychology
Funding agencies: RR&D
Grant support: IK2RX002922

3. Increasing Addiction Recovery Services Referrals for Alcohol Use Disorder in the Inpatient Setting: A Quality Improvement Project

Elkin, Baila [1-2]; Murphy, Kayla [1-2]; Aby, Elizabeth [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Alcohol use disorder (AUD) affects more than 40% of Veterans throughout their lifetime. In January 2021, the VA released a new nursing admissions risk assessment protocol which changed the way that patients are screened for AUD and referred to addiction recovery services (ARS). This protocol uses the AUD Identification Test - Concise (AUDIT-C) score to screen for AUD. Our goal was to gain a better understanding of AUD screening and ARS referrals at the Minneapolis VA. Data for all admissions to the Minneapolis VA from 1/1/21-3/25/21 were abstracted, including nursing admissions risk assessment completion, AUDIT-C assessment, AUDIT-C score, and ARS consultation. This data was stratified by admission type and admitting service. Of 1480 patients admitted from 1/1/21-3/25/21, 1142 (77.2%) had a nursing admissions risk assessment completed on admission, and 1013 (68.4%) had an AUDIT-C assessment completed. Of those patients who underwent AUDIT-C assessment, 161 (15.9%) had an AUDIT-C = 4, suggestive of alcohol misuse. Of these, only 39 (24.2%) were referred to ARS for AUD evaluation and treatment, leaving over 75% of Veterans with alcohol misuse without referral to ARS. We found that those with a higher AUDIT-C score were more likely to be referred to ARS (R2 = 0.94). Admissions to inpatient psychiatry, medical observation, and surgical observation were also associated with lower rates of nursing admissions risk assessment completion (p= 0.0007). Our data shows several gaps in the process of screening Veterans for AUD on admission and referring to ARS. Of admitted patients, only 68.4% underwent screening with an AUDIT-C. This represents an opportunity for improved screening on admission in order to better identify Veterans with AUD. Further, more than 75% of Veterans who had alcohol misuse based on screening were not referred to ARS, suggesting that many Veterans are not being appropriately linked to addiction services. Based on this data, we plan to focus our quality improvement interventions on increasing nursing completion of the AUDIT-C assessment and, if positive, Veteran referrals to ARS. Currently, the ARS referral system is 'opt in' while data suggests that 'opt out' systems are more effective. At the Minneapolis VA, an opt-out system is currently in use for opiate use disorder treatment referrals, which we will use as a model for ARS referrals for Veterans screening positive for alcohol misuse.

Research Topic: Alcoholism
Funding agencies: None
Grant support: N/A

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4. Impact Of Childhood Trauma on Post-Concussive Neurobehavioral Symptoms

Gammons, Alison [1]; Disner, Seth [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Adverse childhood experiences (ACEs) have been associated with a variety of adverse outcomes in adulthood including impaired stress response, changes in the immune and nervous systems, and poor physical and mental health. ACEs are relatively common among the general public, although higher rates are found among military veterans. The present analysis aimed to evaluate how childhood abuse and neglect might be associated with post-concussive neurobehavioral symptoms among veterans who have experienced mild traumatic brain injury (mTBI). The present study included 135 veterans (14.1% female, mean age=46 years (SD=13.9, 23-92)) who sought care for mTBI at the Minneapolis VA. ACEs were retrospectively assessed using the Childhood Trauma Questionnaire (CTQ). Five CTQ subscales were calculated measuring childhood physical abuse, emotional abuse, sexual abuse, physical neglect, and emotional neglect. Post-concussive symptoms were assessed using the Neurobehavioral Symptom Inventory (NSI). Four NSI subscales were calculated measuring emotional, vestibular, somatic/sensory, and cognitive symptoms. Using multivariate regression controlling for age and sex and correcting for multiple comparisons among predictors, childhood physical abuse was significantly associated with overall NSI severity following mTBI (p=0.006). For NSI subscales, childhood physical and emotional abuse were significantly associated with emotional symptoms following mTBI, (physical abuse: p=0.001; emotional abuse: p=0.004). There were also associations between childhood physical abuse and vestibular (p=0.034), somatic/sensory (p=0.026), and cognitive symptoms (p=0.037) and between childhood physical neglect and emotional symptoms (p=0.039) that were significant but did not withstand correction for multiple comparisons. The results demonstrate that childhood trauma, particularly childhood physical and emotional abuse, may be a key risk factor for persistent post-concussive symptoms. Providers would likely benefit from assessment of childhood trauma when evaluating and treating veterans seeking care for persistent mTBI symptoms.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: RR&D
Grant support: IK2RX002922

5. High Satisfaction with Telehealth for Arthroplasty Post-operative Care at the Minneapolis VAMC

Graden, Nathan [1]; Wise, Kelsey [1]; Edwards, Kelly [1]; Albersheim, Melissa [1]; Williams, Benjamin [1]; Gravely, Amy [2]; Sechriest, Vernon [2]

1. University of Minnesota
2. Minneapolis VA Health Care System

Abstract: Background: During the COVID-19 pandemic, the Minneapolis VA Medical Center (VAMC) Orthopedic Section substituted postoperative clinic visits with phone-calls at 6 to 12 months post shoulder, hip and knee arthroplasty. The purpose of this study was: 1) To evaluate patient satisfaction with telehealth follow-up after total joint replacement; and 2) To identify risk factors for low satisfaction with telehealth follow-up. We hypothesized that most patients would be satisfied with telehealth in lieu of in-person visits. We also hypothesized that lower satisfaction with telehealth would correlate with increased number of mental and physical health co-morbidities, patient proximity to the VAMC, and dissatisfaction with surgical outcome. Methods: All postoperative patients who received telephone follow-up with an orthopedic provider from April to June 2020 were identified. Patients were called and administered a standardized survey to assess satisfaction with surgery and the telehealth experience using the Likert scale. Personal preference for type of postoperative appointments was recorded. Demographics, medical history, and surgical information were collected from the medical record. Statistical analysis was performed using Fisher's exact test for categorical comparisons and independent t-tests for continuous comparisons. Results: A total of 140 patients were identified and contacted. Three patients declined participation and one could not be reached. Most patients (92.7%) were satisfied (n=67) or very satisfied (n=48) with postoperative phone visits. Forty-four patients (32.4%) preferred in-person visits, while 96 patients (67.6%) felt telehealth was sufficient. The most common reason for keeping in-person visits was a desire to have physical concerns evaluated. Decreased satisfaction with telehealth follow-up was significantly correlated with higher Charlson Comorbidity Index. Discussion and Conclusion: This is the first study to evaluate patient satisfaction with telehealth follow-up after total joint replacement within a VA system. Our findings support use of telehealth as an alternative to in-person follow-up at 6 to 12 months post total joint arthroplasty. Our findings also suggest patients with certain health profiles and physical concerns may be better served with in-person visits. Overall, telehealth provided most patients who were 6 to 12 months post total joint arthroplasty with a favorable experience based on greater convenience and access to care.

Research Topic: Orthopedic Surgery
Funding agencies: None
Grant support: N/A

6. Aortic Endograft Infections Are Associated with Secondary Interventions

Ihnat, Daniel [1]; Li, Jing [2]; Orecchia, Paul [1]; Green, Derrick [1]; Smith, Lisa [1]; Creedon, Christopher [3]

1. Minneapolis VA Health Care System,
2. Stony Brook Medical Center
3. San Antonio Uniformed Services Health Education Consortium

Abstract: Objective: Secondary interventions (SI) after endovascular aortic aneurysm repair (EVAR) are common for the treatment of endoleaks or occlusions. These procedures can lead to aortic graft infection (AGI). This study describes our experience with AGI and the relationship to SI. Methods: This is a single institution, retrospective analysis of patients who underwent elective EVAR from January 2001 to December 2015 for abdominal aortic or iliac artery aneurysm. Data collected includes patient demographics, graft characteristics, presence of endoleak, SI, and presence of AGI. Results: A total of 601 patients underwent EVAR with a mean follow up of 6.5 years. One hundred patients (17%) underwent 211 SI for endoleaks/limb occlusions. Eight patients (1.3%) developed AGI, 2 (25%) of whom had aortoenteric fistula (AEF). Presenting symptoms of AGI included: pain (88%), malaise (88%), fevers (75%), and anorexia/weight loss (50%). Blood cultures were positive in 4 (50%) patients. Six AGI presented shortly after a SI, 1 after a leg abscess, and 1 occurred 6 months after EVAR from AEF (Table 1). Infection rates in patients who underwent 0 SI, 1 SI, and >1 SI were 0.4%, 2.7% and 7.7% respectively. AGI was associated with SI (p=0.0028), and multiple SI (p=0.0007), but not diabetes, smoking, immunosuppression, graft material or type of endoleak. Thirty patients had concomitant femoral artery prosthetic grafts placed at the time of EVAR: 3 required an iliofemoral bypass, 7 a common femoral interposition graft for aneurysm, and 22 a femoral to femoral bypass. Three (10%) of these patients developed early, femoral prosthetic graft infections requiring explantation of the infected femoral graft, 1 femoral to femoral bypass and 2 femoral interposition grafts. None of these 3 developed AGI. Two of these patients survived 5 and 9 years after graft removal, the third died 11 days post-operatively. In this cohort, 4 patients (0.7%) developed ruptured abdominal aortic aneurysm (rAAA), 2 were treated with open repair, and 2 with limb extensions. Another 7 patients underwent removal of aortic endograft for aneurysm enlargement. Explantation for infection trended towards a larger physiologic insult (Table 2). Conclusions: Our data demonstrate a low incidence of AGI after EVAR. SI are common, and AGI is associated with SI. rAAA is rare following EVAR.

Research Topic: Vascular Surgery
Funding agencies: None
Grant support: N/A

7. Implementing cognitive behavioral therapy for insomnia (CBT-I) in VA primary care

Koffel, Erin [1]; Hagedorn, Hildi [1]

1. Minneapolis VA Health Care System

Abstract: Insomnia is a highly prevalent, debilitating condition that affects up to one-third of the general population and up to 50% of veterans. Poor sleep greatly increases the risk for mental and physical health comorbidities, including chronic pain and inflammation, depression and suicide, and cognitive decline. Cognitive behavioral therapy for insomnia (CBT-I) is a highly effective behavioral intervention that is widely considered the first-line treatment for insomnia. The Veterans Health Administration (VHA) evidence-based psychotherapy training program has trained nearly 1,000 providers to deliver CBT-I in hospitals and clinics nationwide. Despite increased access, most patients with insomnia receive sleeping medications instead of CBT-I. Unfortunately, insomnia medications can have adverse cognitive and behavioral effects, especially in combination with opioids, and are specifically contraindicated in older adults due to increased fall risk. The goal of this study was to explore provider perspectives on CBT-I implementation within VA over the last ten years, including barriers and successful strategies used to overcome these barriers. Semi-structured interviews, using the Consolidated Framework for Implementation Research (CFIR) as a guide, were conducted with 17 providers from five VHA facilities (8 primary care physicians, 4 primary care psychologists, and 5 CBT-I coordinators). Findings suggested implementation barriers and facilitators related to the CFIR constructs of intervention characteristic (e.g., limited knowledge of CBT-I evidence strength and quality among providers), inner setting (e.g., insomnia screening and treatment was low priority among primary care physicians) and outer setting (e.g., perceived reluctance of patients to see mental health provider), as well as several successful strategies, including enlisting champions, informing opinion leaders, and promoting network weaving.

Research Topic: Mental Health
Funding agencies: HSR&D
Grant support: CDA 15-063; PPO 19-084

8. Chlorhexidine oral rinses for symptomatic COPD: a randomized, blind, placebo-controlled preliminary study

Pragman, Alexa [1-1]; Fieberg, Ann [2]; Reilly, Cavan [2]; Wendt, Christine [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Objectives: Determine the effect of twice-daily chlorhexidine oral rinses on oral and lung microbiota biomass and respiratory symptoms. Setting: Single center. Participants: Participants were aged 40-85 with COPD and chronic productive cough or COPD exacerbation within the last year. Exclusions included antibiotics in the previous 2 months and/or those with less than four teeth. Forty-four participants were recruited and 40 completed the study. Intervention: Participants were randomized 1:1 to twice-daily 0.12% chlorhexidine oral rinses vs. placebo for two months along with daily diaries. SGRQ, blood tests, oral rinse and induced sputum were collected at randomization and the final visit. Primary and Secondary Outcomes: Primary outcome was a change in oral and sputum microbiota biomass. Secondary outcomes included: sputum and oral microbiota Shannon and Simpson diversity and taxonomy; inflammatory markers; BCSS and SGRQ scores. Results: Neither the oral microbiota nor the sputum microbiota biomass decreased significantly in those using chlorhexidine compared with placebo (oral microbiota mean log10 difference [SE] = -0.103 [0.23], 95% CI: -0.59, 0.38, p=0.665; sputum microbiota 0.80 [0.46], 95% CI: -0.15, 1.75, p=0.096). Chlorhexidine decreased both oral and sputum microbiota alpha (Shannon) diversity (linear regression estimate [SE] oral: -0.349 [0.091], p=0.001; sputum -0.622 [0.169], p=0.001). Chlorhexidine use did not decrease systemic inflammatory markers compared to placebo (CRP [chlorhexidine 1.8 ± 7.5 vs. placebo 0.4 ± 6.8, p=0.467], fibrinogen [22.5 ± 77.8 vs. 10.0 ± 77.0, p=0.406], or leukocytes [0.2 ± 1.8 vs. 0.5 ± 1.8, p=0.560]). Chlorhexidine use decreased St. George's Respiratory Questionnaire scores compared to placebo (chlorhexidine -4.7 ± 8.0 vs. placebo 1.7 ± 8.9, p=0.032). Conclusions: We did not detect a significant difference in microbiota biomass due to chlorhexidine use. Chlorhexidine decreased oral and sputum microbiota alpha diversity and improved respiratory health-related quality of life compared to placebo.

Research Topic: Respiration & Pulmonary Disease
Funding agencies: CVRE
Grant support: Flight Attendant Medical Research Institute (FAMRI) Clinical Innovator Award, (#150014 to CHW)

9. High fat diet effect on brain immune response and lipid metabolism

Roe, David [1-2]; Kuang, Rui [2]; Nixon, Joshua [1-2]; Fleming, Kendra [1,3]; So, Simon [1,3]; Bernlohr, David [2]; Lee, Michael [2]; Butterick, Tammy [1-3]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Center for Veterans Research & Education

Abstract: Obesity and associated comorbidities such as metabolic syndrome and diabetes affect up to 48% of Veterans, and are known risk factors for cognitive impairment and development of Alzheimer's disease. The incidence of these neurodegenerative diseases may be higher in Veterans than in the general population. Preclinical and clinical research supports the onset of brain immune response (neuroinflammation) supports a link between obesity and cognitive impairment. Dietary fatty acids directly affect lipid metabolism in brain immune cells (microglia) and can trigger chronic neuroinflammation. We hypothesize that obesogenic diets can alter microglial metabolism by directly dysregulating brain immune responses, resulting in impaired cognition and altered brain circuitry. To test this we used a mouse model of obesity and immunometabolism that lacks a fatty acid binding protein (FABP4) in microglia. FABP4 regulates the onset of inflammation, and mice lacking FABP4 are resistant to diet-induced chronic inflammation and metabolic syndrome. Mice were fed a high fat diet for 12 weeks and brain regions that regulate memory (hippocampus) or metabolism (hypothalamus) were used to identify genetic changes relevant to immune function and fatty acid metabolism. RNAseq transcriptomic and Reactome molecular pathway analysis demonstrated that mice lacking FABP4 presented with differences in gene expression in protective metabolic cellular signaling pathways that included downregulation of genes that increase insulin resistance and oxidative stress (Wnt signaling) and upregulation of genes related to protective lipid metabolism (PPARγ targets) or decreased fatty acyl-CoA biosynthesis. These data support that diet-induced neuroinflammation is an unexplored link between brain immune response and metabolic processes to dietary fat within the context of cognitive decline, and may represent a novel clinical therapeutic target. Our short-term goal is to characterize microglial metabolic state changes that promote neuroinflammation and subsequent cognitive decline. Our long-term goal is to leverage this knowledge to develop targeted therapies to treat cognitive impairment and neurodegenerative disease.

Research Topic: Basic Sciences
Funding agencies: BLR&D; CVRE
Grant support: I01BX004146, AARGD-17-505409, UMN HFHL

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10. Protein kinase CK2 correlation with clinical outcomes in HPV(+) and HPV(-) oropharyngeal squamous cell carcinoma

Trembley, Janeen [1-2]; Li, Bin [1,3]; Kren, Betsy [1]; Peltola, Justin [1-2]; Manivel, Juan [1-2]; Meyyappan , Devi [1,4]; Gravely, Amy [1]; Klein, Mark [1-2]; Ahmed, Khalil [1-2]; Caicedo-Granados, Emiro [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Kaiser Permanente
4. University of Texas Medical Branch

Abstract: Background: Protein kinase CK2 has an overarching role in cancer, especially in promoting tumor cell survival. In previous studies, high levels of CK2 have been associated with poor outcome in head and neck squamous cell carcinoma (HNSCC) patients. Human papillomavirus (HPV)-associated HNSCC, especially oropharyngeal squamous cell carcinoma (OPSCC), has rising incidence worldwide. In related work, we determined that inhibition of CK2 in HPV(+) and HPV(-) HNSCC cell lines induced cell death and improved response to cisplatin treatment. As the prognostic value of CK2 in HPV-related HNSCC is unknown, this retrospective study examined whether CK2-related clinical outcomes vary by HPV status in MVAHCS OPSCC patients. Methods: OPSCC patient tumors (n = 119) were stained for CK2, p16 and Ki-67 proteins and HPV E6/E7 RNA. This cohort comprised 84 HPV(+) and 35 HPV(-) tumors The relationships between CK2 protein levels in tumors and patient characteristics, HPV status, and Ki-67 index were assessed. Overall survival (OS) and progression-free survival (PFS) were analyzed using data from our cohort and using HNSCC mRNA data from The Cancer Genome Atlas. Results: The patients in the study population were all male and had a predominant history of tobacco and alcohol use. CK2 levels were higher in HPV(+) tumors compared to HPV(-) tumors. Increasing CK2 scores positively correlated with higher Ki-67 index. OS at 3 years improved with increasing CK2 score. In HPV(-) HNSCC, high CSNK2A1 mRNA levels associated with worse disease-specific survival, PFS, and OS. Conclusions: High CK2 protein levels are detected in HPV(+) OPSCC tumors, and demonstrate an unexpected association with improved survival in HPV(+) OPSCC. Worse survival outcomes for high CSNK2A1 mRNA levels in HPV(-) HNSCC accord with historical data. Given these surprising findings, further study is needed to understand the biological roles of CK2 in HPV(+) and HPV(-) HNSCC and the potential for therapeutic targeting of CK2 in these two classes of disease.

Research Topic: Cancer
Funding agencies: BLR&D
Grant support: I01BX003282; I01BX005091; Lion's award

11. Population and Community-Based Interventions to Prevent Suicide: A systematic Review

Venables, Noah [1]; Linskens, Eric [1]; Gustavson, Allison [1]; Sayer, Nina [1]; Murdoch, Maureen [1]; MacDonald, Roderick [1]; Ullman, Kristen [1]; McKenzie, Lauren [1]; Wilt, Timothy [1]; Sultan, Shahnaz [1]

1. Minneapolis VA Health Care System

Abstract: Background: Suicide is estimated to account for 1.4% of deaths worldwide making it among the leading causes of premature death. There are efforts to further advance community and pullulation-based intervention to prevent suicide. The current study provides a systematic review of the evidence for their effectiveness. Methods: We conducted a systematic review of the published literature to evaluate the effectiveness of community- and population-level interventions. The U.S. Center for Disease Control framework was used for grouping studies by strategy, setting and design. Results: Interventions that reduced access to lethal means, implemented organizational policies and culture in police workplace settings, and community screening for depression may reduce suicide deaths. It is unclear if other interventions such as public awareness and education campaigns, crisis hotlines, and gatekeeper training prevent suicide. Evidence was inconsistent for community-based, multi-strategy interventions. The most promising multi-strategy intervention was the European Alliance Against Depression. Conclusions: Community-based interventions that may reduce suicide deaths include reducing access to lethal means, implementing organizational policies in workplace settings, and screening for depression. The multi-strategy European Alliance Against Depression Program may also reduce death by suicide. Evidence was unclear, inconsistent, or lacking regarding many other single or multi-strategy interventions on suicide deaths.

Research Topic: Suicide Prevention
Funding agencies: HSR&D
Grant support: VHA HSR&D Evidence Synthesis Program (#09-009); VHA Advanced Fellowship in Clinical and Health Services Research (AMG; TPH 67-000)

12. The Effect of Biopsychosocial Factors on Chronic Pain Functioning

Wienkes, Cara [1]; Koffel, Erin [1]; Polusny, Melissa [1]; Krebs, Erin [1]

1. Minneapolis VA Health Care System

Abstract: Chronic pain is a highly prevalent, complex and debilitating health condition and is the leading cause of decreased quality of life. Biopsychosocial treatment shows promising effects on clinical outcomes, but chronic pain remains a worldwide health problem. This may be due to a failure of fully implementing the biopsychosocial model in treatment settings rather than a failure of the biopsychosocial model. The goal of this study is to examine effects of variables from the biological, psychological, and social domains on pain functioning and intensity. This study utilizes a cohort study of 3,035 U.S. service members originally recruited from four National Guard units deployed in support of Operation Iraqi Freedom (OIF), Operation Enduring Freedom (OEF), or Operation New Dawn (OND) between 2006 and 2011. Data were analyzed from participants who endorsed clinically significant chronic pain and had complete data (n=409) at Time 3 (36-96 months post-deployment). Final analyses examined a subset of participants with complete data (n=200). Independent variables included biological/physical functioning (Veteran's Rand Health Survey-12, PROMIS - Sleep), psychological functioning (Pain Catastrophizing Scale, Patient Health Questionnaire-8, PTSD Checklist ñ 5, Alcohol Use Disorders Identification Test), and social functioning (Endicott Work Productivity Scale, Dyadic Adjustment Scale). Dependent variables included chronic pain functioning (PROMIS ñ Pain Interference) and chronic pain intensity (PEG item referring to pain severity). Hierarchical linear regressions indicated that the biological and psychological domains were significantly associated with chronic pain interference and to a lesser extent, chronic pain intensity. Findings provide support for the importance of biopsychosocial factors in U.S. Veterans' chronic pain experiences. The results suggest continued assessment and intervention of biopsychosocial factors for chronic pain treatment.

Research Topic: Afghanistan & Iraq Veterans
Funding agencies: NIH
Grant support: NCCIH R01AT008387

Poster Presentations

1. VA Cooperative Studies Program (VA CSP) Network of Dedicated Enrollment Sites (NODES)

Adabag, Selcuk [1]; Condon, Debra [1]; Donaire, Marti [1]; Kantorowicz, Alexandra [1]; Johnson, Debra [1]

1. Minneapolis VA Health Care System

Abstract: The VA Cooperative Studies Program (VA CSP) Network of Dedicated Enrollment Sites (NODES) is a consortium of VA Health Care Systems that have facility-based teams dedicated to conducting VA CSP Research. The specific aims include; enhancing study performance and enrollment rates; provide a more consistent and comprehensive approach to CSP study management, quality and regulatory compliance at the VA Medical Centers; obtain center-level perspectives in the design and execution of studies; and provide opportunities for research personnel interested in supporting the VA CSP research mission. A Director, Co-Director, Operations Manager (Minneapolis & Salt Lake City Only), Administrator, and Research Nurse support these efforts at each individual NODES location. NODES shares facility-derived best practices and provides local insights to VA CSP partners for efficient management and conduct of all study activities. The following achievements reflect cumulative data of the NODES sites from October 2012–Present: Established cross-coverage on all open CSP studies; NODES staffing incorporated as part of local CSP study teams; Created Mentorship Program for new local study investigators and coordinators; Created procedures for mobile recruiting at CBOCs; Work stream meetings on improving study design & procedures; Creation of Work groups to develop and beta test case report forms; Enhanced recruitment through Mobile Recruiting Equipment; Reduced logistical and staffing barriers; Development of Partnership between NODES and Non-NODES facilities to assist in study teams with low recruitment; Creation of VA CSP-NODES Executive Board; Creation of CSP Studies Toolbox to facilitate NODES and Non-NODES VA sites in study implementation; Facilitated remote working for our local CSP study coordinators and research assistants in response to pandemic; Contributed to numerous manuscripts in peer-reviewed journals; Contributed, participated, and won national CSP Shark Tank competition for NODES Mobile Recruiting Units; Attended national Own The Moment training and facilitated TMS course creation and training for local study coordinators and research associates; Implemented a Hub-and-Spoke model to facilitate VA CSP research at other facilities within VISN23; and Members of a VA CSP-NODES Work group (ACCESS) in order to provide rural Veterans the opportunity to participate in VA CSP research studies.

Research Topic: Health Care Delivery
Funding agencies: CSR&D
Grant support: VA CSP

2. Lessons Learned in Shared Decision-Making

Adams, Natasia [1]; Bemmels, Heather [1]; Candy, Amy [1]; Carlstrom, Alyssa [1]; Thuras, Paul [1]

1. Minneapolis VA Health Care System

Abstract: Background: Shared Decision-Making (SDM) is a key component of patient-centered care, incorporated in multiple medical specialties (i.e., oncology, surgery, and primary care) and endorsed in the Patient Protection and Affordable Care Act. With an emphasis on collaborative effort to make medical decisions, combining available evidence with patient's preference, extant literature has supported SDM as a way to better health outcomes for commonly diagnosed chronic diseases. Members of the Academic Primary Aligned-Care Team (APACT) at the Minneapolis VA Health Care System engaged in program development and evaluation to improve General Internal Medical residents' SDM skills for discussing hypertension (HTN) treatment options with Veterans and their caregivers in primary care. We hypothesized that a training would increase APACT residents' confidence in their knowledge and skills using SDM. Methods: APACT developed a HTN decision aid, and delivered a 1-hour, interactive SDM training including information on how to use the decisional aid. 31 residents attended the SDM training. They completed a pre- & post- evaluation survey to evaluate confidence of their knowledge and skillset using SDM. Results: SDM training along with a HTN decisional aid was provided. Pre- evaluation survey demonstrated that residents varied widely on their knowledge and skill regarding SDM. Post-evaluation survey demonstrated an increase in residents' knowledge and ability. This increase was not clinically significant, or predicted by residency year or primary care experience. Currently, we are exploring whether hypertension outcomes within our Academic Patient Aligned Care Team (APACT) improved based following the SDM training and provision of the HTN decision aid. We hope to have pulled data (i.e., use of SDM language and return to clinic orders based on HTN decisional aid) through CPRS. This data will also be reported, if available at the time poster presentation.

Research Topic: Medical Education
Funding agencies: None
Grant support: N/A

3. COVID-19 Disease Outcomes in Veterans with Age-Related Macular Degeneration

Armbrust, Karen [1]; Westanmo, Anders [1]; Gravely, Amy [1]; Chew, Emily [2]; van Kuijk, Erik [3]

1. Minneapolis VA Health Care System
2. National Eye Institute
3. University of Minnesota

Abstract: Immune system dysregulation, including complement pathway abnormalities associated with age-related macular degeneration (AMD) pathogenesis, has been implicated in severe COVID-19. A prior study evaluating disease outcomes in patients at a single non-VA medical center early in the COVID-19 pandemic suggested that patients with a diagnosis of AMD have poorer COVID-19 outcomes (N = 11,116; 88 (0.8%) with a diagnosis of AMD). In this study, we test the hypothesis that patients with a diagnosis of AMD have poorer COVID-19 outcomes with a much larger study population. All US veterans = 50 years of age with positive COVID-19 testing prior to August 23, 2020 recorded in the United States Veterans Health Administration (VHA) Corporate Data Warehouse (CDW) were included in this study. Data were extracted as of January 20, 2021. The primary outcome measure was hospitalization within 60 days of positive COVID-19 testing, and secondary outcome measures were death within 60 days of positive COVID-19 testing, intensive care unit admission within 60 days of positive COVID-19 testing, and ventilation within 60 days of positive COVID-19 testing. Risk factors assessed were age at time of positive COVID-19 testing, gender, race, ethnicity, Charlson Comorbidity Index, AMD diagnosis based on International Classification of Diseases 10th Revision (ICD-10) coding, and severe AMD diagnosis based on ICD-10 coding or intravitreal anti-vascular endothelial growth factor injection. A total of 31,296 subjects met study criteria, of which 1355 (4%) had a diagnosis of AMD and 380 (1%) fulfilled study criteria for severe AMD. Multivariate regression analysis showed that AMD diagnosis and severe AMD diagnosis are not statistically significant risk factors for the study outcomes after adjusting for other risk factors. In conclusion, AMD diagnosis is not associated with poorer COVID-19 disease outcomes in the national Veteran population.

Research Topic: Clinical Epidemiology
Funding agencies: None
Grant support: N/A

4. Drivers of Health Disparities among Veterans with COPD: Rurality vs. Drive Time

Baldomero, Arianne [1-2]; Kunisaki, Ken [1-2]; Hammett, Patrick [1]; Bangerter, Ann [1]; Nelson, David [1]; Henning-Smith, Carrie [2]; Wendt, Chris H. [1-2]; Dudley, R. Adams [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: INTRODUCTION: Rural residents experience worse processes of care and health outcomes compared to urban residents in a wide range of conditions, including chronic obstructive pulmonary disease (COPD), but the mechanisms that lead to these poor outcomes are unknown. Therefore, we evaluated the impact of rurality and drive time on processes of care in COPD. METHODS: Retrospective analysis of veterans with newly-diagnosed COPD (=2 ICD-10 codes for COPD in 2016-2019) using national Veterans Affairs data. Using geocoded addresses, we assessed the: 1) rurality of residential address, 2) drive time to the closest primary care, and 3) drive time to the closest specialty care. The dependent variables were binary process measures of: 1) spirometry to confirm the diagnosis of COPD and 2) pulmonary clinic encounter. Designation of addresses as urban, rural, or highly rural was based on Rural Urban Commuting Area codes. Drive times, obtained from the VHA's Planning System Support Group Geocoded Enrollee Files, were calculated based on expected driving routes using Environmental System Research Institute mapping software. Multivariable logistics regression analysis was used to determine the strongest predictor of having a spirometry and pulmonary encounter. RESULTS: Of the 281,281 veterans with newly-diagnosed COPD, 106,913 (38%) resided in rural and 4,358 (1.5%) in highly rural areas. Highly rural residents drive 4- and 3-times longer than urban residents to the closest primary care and specialty care facilities, respectively. Compared to rurality and drive time to the closest primary care, drive time to specialty care was the strongest predictor of having a spirometry and pulmonary encounter. CONCLUSION: Drive times to care impacted health care services delivery among COPD patients, independent of rurality. Geographic measure of health care delivery based on drive times to care, in particular, drive time to the closest specialty care, generated more evidence of disparities than the most-commonly used 'rurality' which is based solely on the patient's residential address.

Research Topic: Health Equity
Funding agencies: NIH; University of Minnesota
Grant support: NIH NCAT grants KL2TR002492 and UL1TR002494

5. Effectiveness and Harms of High-Flow Nasal Oxygen for Acute Respiratory Failure: An Evidence Report for a Clinical Guideline from the American College of Physicians

Baldomero, Arianne [1]; Melzer, Anne [1]; Greer, Nancy [1]; Majeski, Brittany [1]; MacDonald, Roderick [1]; Linskens, Eric [1]; Wilt, Timothy [1]

1. Minneapolis VA Health Care System

Abstract: Background: Use of high-flow nasal oxygen (HFNO) for treatment of adults with acute respiratory failure (ARF) has increased. Purpose: To assess HFNO versus noninvasive ventilation (NIV) or conventional oxygen therapy (COT) for ARF in hospitalized adults. Data Sources: English-language searches of MEDLINE, Embase, CINAHL, and Cochrane Library from January 2000 to July 2020; systematic review reference lists. Study Selection: Twenty-nine randomized controlled trials evaluated HFNO versus NIV (k = 11) or COT (k = 21). Data Extraction: Data extraction by a single investigator was verified by a second, 2 investigators assessed risk of bias, and evidence certainty was determined by consensus. Data Synthesis: Results are reported separately for HFNO versus NIV, for HFNO versus COT, and by initial or postextubation management. Compared with NIV, HFNO may reduce all-cause mortality, intubation, and hospital-acquired pneumonia and improve patient comfort in initial ARF management (low-certainty evidence) but not in postextubation management. Compared with COT, HFNO may reduce reintubation and improve patient comfort in postextubation ARF management (low-certainty evidence). Limitations: Trials varied in populations enrolled, ARF causes, and treatment protocols. Trial design, sample size, duration of treatment and follow-up, and results reporting were often insufficient to adequately assess many outcomes. Protocols, clinician and health system training, cost, and resource use were poorly characterized. Conclusion: Compared with NIV, HFNO as initial ARF management may improve several clinical outcomes. Compared with COT, HFNO as postextubation management may reduce reintubations and improve patient comfort; HFNO resulted in fewer harms than NIV or COT. Broad applicability, including required clinician and health system experience and resource use, is not well known.

Research Topic: Respiration & Pulmonary Disease
Funding agencies: None
Grant support: American College of Physicians

6. Program Evaluation of a Therapeutically Applied Role Playing Game Group Therapy with Veterans

Battles, Allison [1]; Erbes, Chris [1]

1. Minneapolis VA Health Care System

Abstract: Tabletop role-playing games are interactive, cooperative, rule-based storytelling experiences that have been applied to therapeutic environments. Utilizing vicarious scenarios, TA-RPGs prompt participants to develop and practice interpersonal effectiveness, problem solving skills, and emotion regulation. This presentation will discuss the findings of a program evaluation of the feasibility and acceptability of a novel therapeutically applied role-playing game (TA-RGP) group that utilizes Dungeons & Dragons with veterans. The group is being administered across three cohorts of six veterans of various diagnoses with identified social deficits who were referred from across the service line. The group meets for 12-session that run for 2-hours. Each session consists of 90-minutes of experiential narrative development in game play and 30-minutes of post-game processing. Evidence-based approaches are integrated across group experiences utilizing principles from Cognitive-Behavioral Social Skills Training, Interpersonal Process Therapy, and ACT. Participants completed the Liebowitz Social Anxiety Scale, Adult Self-Perception Profile, Strengths & Difficulties Questionnaire (SDQ), PHQ-9, GAD-7, and an adapted Client Satisfaction Questionnaire (CSQ) before and after group participation. Semi-structured pre-post group interviews were also used. Of the initial two cohorts, 58% of those enrolled successfully completed the group (cohort 1 n = [3]; cohort 2 n = 4) with participants completing an average of 11 sessions. The most common reasons for discontinuing early were lack of perceived fit (n = 2) and need to more intensive services (n = 2). Of those in the who completed group, 86% (n = 6) completed the post-group questionnaire. The mean CSQ score was 53.7 of a possible maximum of 63. Participants identified the most helpful parts of group to be the post-game processing and sense of connection. Preliminary results revealed a significant mean reduction in total GAD scores from pretreatment M = 14.63 to posttreatment M = 10, representing a 31.6% reduction, $t(5) = 6.22$, $p = .001$, $d = 0.88$, and a large effect size. Results also revealed a significant mean reduction in conduct problems (e.g., anger; measured by SDQ) from pretreatment M = 6.83 to posttreatment M = 6.17, representing a 9.7% reduction, $t(5) = 4.09$, $p = .001$, $d = 0.58$, and a medium effect size. The most reported improvements were in social skills, personal awareness, and trust.

Research Topic: Mental Health
Funding agencies: None
Grant support: N/A

7. Digital Interface Design and Development of a Pressure Monitoring System for Wheelchair Users and Clinicians

Bornstein, A. Soleil [1]; Truty, Timothy [1]; Vos-Draper, Tamara [2]; Fairhurst, Stuart [1]; Kemmer, Sara [1]; Eddy, Byron [1]; Goldish, Gary [1]; Gravely, Amy [1]; Hansen, Andrew [1]; Barrett, Benjamin [1]; Morrow, Melissa [3]; Olney, Christine [1]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Mayo Clinic

Abstract: Veterans with spinal cord injury or disorder (SCI/D) are at risk for pressure injuries if they do not shift their weight throughout the day while sitting in a wheelchair. To help prevent these injuries, our team developed a mobile application (app), known as AW-Shift, that provides real-time views of pressure distribution, funded by a previous DoD award. The system can give reminders for pressure reliefs and alerts to unexpected pressure changes. Data are transmitted from a pressure map placed on top of the wheelchair seat which is connected to a small hardware interface. Data uploads to the user's smart device to view and interact. During the first two years of this current VA merit award (RX003222) we aim to expand functionality of AW-Shift app system by creating smart watch capability (Android and iOS) for the Veterans use. The team also aims to create a clinical dashboard which will allow the VA seating specialists to monitor seating behavior and target their pressure injury prevention education. To expand the software for this system, we set up separate iterative virtual focus groups with Veterans (for the smartwatch) from across the VISN and clinicians (for the clinical dashboard) from across the nation. Further, data from user experience and usability surveys were completed by participants to gauge how they felt about the AW- Shift and improvements discussed. Data from the first focus groups were analyzed using Hamilton method. These analyzed data were then pushed to our design engineers. Based on the first focus group data analyses, the design engineers were able to build mockups, or wireframes, of what the smart watch for Veterans (n=7) and the clinical dashboard for clinicians (n = 6) might look like. This poster presents these wireframes and survey results. Both first virtual focus groups (Veteran and Clinician) occurred late summer 2020. Design engineers were able to successfully create wireframes for the smart watch and clinical dashboard, to present to the second iterative virtual focus groups (both Veteran and Clinicians). The second focus groups occurred late winter and earlier this spring and data from these focus groups are being analyzed. We will be conducting one last round of focus groups with each group in late summer 2021. Our design team has begun preliminary software development to create the actual framework in which the clinical dashboard can be used, and work in concert with the patient-facing smartwatch app.

Research Topic: Preventive Medicine
Funding agencies: RR&D
Grant support: I01RX003222

8. Preclinical model of military related burn pit inhalation exposure

Butterick, Tammy [1-3]; Trembley, Janeen [1-3]; Nixon, Joshua [1-2]; Fleming, Kendra [1,3]; So, Simon [1,3]; Nurkiewicz, Timothy [4]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Center for Veterans Research & Education
4. West Virginia University School of Medicine

Abstract: Chronic multisymptom illness (CMI) is an idiopathic disease characterized by chronic fatigue, musculoskeletal pain, impaired cognition, gastrointestinal disorders, respiratory problems, and skin rash. Many U.S. military Veterans who served in Operations Enduring Freedom and Iraqi Freedom suffer daily from CMI. These Veterans were exposed to toxic open-air burn pits that included medical waste, plastics, DEET, human excrement, and vehicles. Burn pit smoke contains a mixture of carcinogens, neurotoxins and endocrine toxins that are linked to chronic illness. Separate studies have demonstrated that exposures to complex mixtures of gases and particles present in burn pits can result in profound biologic consequences such as cancer, pulmonary, cardiovascular, and brain disease. Burn pit smoke has been characterized to include fine particulate matter ($PM_{2.5}$) and volatile organic compounds such as napthalene (NA). These substances are known to induce cardiovascular, pulmonary and inflammatory responses. We established an initial preclinical model of military burn pit exposure using whole-body inhalation of carbon black (CB) particulate matter, a key component of burn pit emissions. Preliminary data demonstrate that CB inhalation induces multiple inflammatory markers in rats that are linked to CMI. Male Sprague Dawley rats were exposed to CB aerosols by whole body inhalation at 3 doses. A panel of 9 pro-inflammatory biomarkers were measured in arterioles, brain, heart, kidney, liver, lung, plasma, and spleen. Biomarkers of cardiovascular injury were also assayed in plasma and arterioles. CB inhalation increased CMI-related proinflammatory biomarkers in tissues such as interferon gamma (IFNγ) and keratinocyte chemoattractant/growth-regulated oncogenes (KC/GRO). CB exposure also induced markers of cardiovascular injury that included soluble cell adhesion molecules (sE-selectin and sI-selectin). We are currently incorporating a more complex toxicant exposure strategy using CB and NA to further our studies on the pathological effects following military burn pit exposure.

Research Topic: Basic Sciences
Funding agencies: BLR&D; CVRE
Grant support: I01BX004146, CVRE

9. Implementation Of An Order Set at The VAHCS For Medical Optimization Of Fragility Fractures

Cespedes-Gomez, Omar [1]; Sechriest, Vernon [2]; Diem, Susan [2]; Diesburg-Stamwood, Amy [2]; Shumate, Kaitlen [2]; Timm, Lindsey [2]; Mueller, Amand [2]

1. University of Minnesota
2. Minneapolis VA Health Care System

Abstract: Osteoporosis is a risk factor for fragility hip fractures. In the Veterans Affairs Health Care System, 1 in 3 men die within 12 months after a hip fracture. The purpose of our study was to implement a system to facilitate pharmacologic treatment after discharge in patients who suffered a fragility hip fracture by analyzing osteoporosis pharmacologic treatment at 3 months and at 6 months after hospital admission. Methods: Pre-op and post-op fracture order sets were implemented and all patients admitted after implementation were retrospectively chart reviewed. The preop order set involved co-management of the patient between orthopaedics and internal medicine, fall risk assessment, interprofessional consults, and pertinent labs. The postop order set involved provider selection of patient within the hospital, nursing orders to assess fall risk assessment, and pertinent labs as well. The number of patients who received osteoporosis treatment with zoledronic acid, denosumab, or alendronate at 3 months and 6 months was tracked. Medication prescriptions upon discharge were compared to data gathered before implementation of the order sets. Results: A total of 35 patients were evaluated for osteoporosis during their hospital admission. The average age was 82 years (range 59-99 years). 40% of patients received osteoporosis treatment with zoledronic acid or denosumab within 3 months of hospital discharge. 51% of patients received osteoporosis treatment within 6 months of hospital discharge. Conclusion: Prior to implementation, only 5.1% of patients were treated for osteoporosis within 3 months and 4.4% within 6 months. After implementation, there was a significant improvement in treatment to 40% at 3 months and 51% at 6 months. Despite the increase in patient access, barriers to treatment persisted. Contraindications to osteoporosis treatment such as poor dentition, limited insurance coverage to see a VA dentist. Patients enrolled in palliative care services also did not get postoperative osteoporosis treatment.

Research Topic: Orthopedic Surgery
Funding agencies: None
Grant support: N/A

10. Stressful Life Events Do Not Consistently Interact with Clinical Personality Dimensions to Predict State Psychological Distress

Cruitt, Patrick [1-2]; Finn, Jacob [1,3]; Arbisi, Paul [1,3]

1. Minneapolis VA Health Care System,
2. Washington University in St. Louis
3. University of Minnesota

Abstract: Previous research offers mixed support for the hypothesis that stressful life events moderate the relationship between personality traits and health/well-being. The current study seeks to extend this literature by examining multiple different types of stressful life events (unemployment, the end of a romantic relationship, and combat-related trauma) and clinically relevant dimensions of personality, conceptualized in terms of the Personality Psychopathology Five model (PSY-5). We hypothesized that Negative Emotionality/Neuroticism would interact with all three stressful life events to predict residualized increases in psychological distress at follow-up. The current analyses represent secondary data analysis of two samples of National Guard Soldiers (RINGS-1 and RINGS-2) who provided longitudinal data pre- and post-deployment. For the purposes of the current analyses, we examined four of the five PSY-5 constructs: Psychoticism, Disconstraint, Negative Emotionality/Neuroticism, and Introversion. RINGS-1 used abbreviated versions of the MMPI-2 PSY-5 scales, whereas RINGS-2 used the full MMPI-2-RF PSY-5 scales, excluding Psychoticism. Psychological distress was assessed pre-deployment and at two to three waves of data collection during/post-deployment using measures traditionally used to screen for depression: Beck Depression Inventory-II in RINGS-1 and the Patient Health Quesitonnaire-8 in RINGS-2. Stressful life events that occurred during the intervening period between follow-ups were assessed using the Deployment Risk and Resilience Inventory. Multilevel linear models predicting residualized change in psychological distress from each of the personality dimensions, each stressful life event, and the interactions between them did not reveal consistent interaction effects across the two studies. No interaction effect remained significant after accounting for the number of significance tests conducted. Many theories from personality and clinical psychology predict broad interactions between environmental factors and personality traits in the prediction of health and well-being. Future work is needed to refine the specificity of these predictions, including the timing of effects after the event and which lower-order personality traits may be involved. Pursuing this line of research will help illuminate how the negative effects of stressful life events and clinical personality dimensions on health and well-being can be modified through intervention.

Research Topic: Mental Health
Funding agencies: HSR&D; DOD
Grant support: University of Minnesota Press; Minnesota Medical Foundation (3662-9227-06); DoD W81XWH-07-2-003; SDR 10-398

11. Perioperative Management for Patients Using Naltrexone: A Quality Improvement Project

Deviley, Sarah [1]

1. University of Minnesota

Abstract: Problem/background: Patients using naltrexone, an opioid antagonist, in the perioperative period present a special concern for anesthesia practitioners as they will have no response to opioid medications that are commonly given for pain control during surgery. Patients using naltrexone are often unaware of its implications and do not initiate proper planning prior to an elective procedure. Likewise, anesthesia personnel are unaware of proper perioperative management for patients using this medication. This quality improvement (QI) project was implemented to improve the perioperative management of patients using naltrexone through patient and provider education and improved interprofessional communication. Strategy: Patients at a Midwestern veterans hospital with an active prescription for naltrexone were mailed education letters and anesthesia staff completed an education session on the implications of naltrexone. Additionally, a standardized opioid antagonist note was added to the anesthesia record to improve communication. Methods: Pre and post-implementation data were collected through chart review with goals of improved preoperative planning, decreased inappropriate narcotic use intraoperatively, and improved post-operative pain scores. Results: Thirty-one cases total were reviewed: 23 pre-intervention and 8 post-intervention. Eight percent of pre-intervention cases had a note written in their chart, compared to 100% post-intervention, and inappropriate narcotic usage decreased from 71% pre-intervention to 0% post-intervention. Post anesthesia care unit pain scores were similar pre and post-intervention. Conclusion: Education and improved communication strategies were successful in improving the perioperative care of patients using naltrexone at this health care center.

Research Topic: Anesthesiology
Funding agencies: None
Grant support: N/A

12. Perioperative Change in Left Ventricular Systolic Function Predicts Long-Term Mortality After CABG

Downey, Michael [1-2]; Hooks, Matthew [1-2]; Gravely, Amy [1]; Naksuk, Niyada [3]; Buelt-Gebhardt, Melissa [1]; Carlson, Selma [1-2]; Tholakanahalli, Venkat [1-2]; Adabag, Selçuk [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. University of Nebraska

Abstract: Introduction: Substantial numbers of patients undergoing CABG have concurrent left ventricular systolic dysfunction (LVEF<50%). But how CABG affects the LVEF of these patients is not well understood. Hypothesis: We hypothesized that patients with preoperative LV systolic dysfunction would have an improvement in LVEF post-CABG. Methods: We studied 549 patients with LVEF<50% who underwent CABG as part of the Surgical Treatment for Ischemic Heart Failure (STICH) trial and had pre- and 4 month post-CABG LVEF assessments using the same cardiac imaging modality, evaluated at a core lab. An absolute change of >5% in LVEF was considered clinically significant. Patients were classified into 3 groups: improved LVEF, unchanged LVEF, and decreased LVEF. Results: Of the study patients (mean age 61.4±9.6 years and 13% women), 240 (43.7%) had an improvement in LVEF following the surgery, with their LVEF increased from 25.9±8.6% to 39.5±10.5% (p<0.001). However, 89 (16.2%) patients had a decrease in postoperative LVEF, with their LVEF reduced from 34.4±7.8% to 23.6±7.8% (p<0.001). A >5% improvement in LVEF was independently associated with age (OR 1.10, p=0.045), baseline LVEF (OR 0.74, p<0.0001), concurrent surgical ventricle restoration (SVR) (OR 1.93, p=0.0004), and prior myocardial infarction (OR 0.56, p=0.028). A >5% decrease in LVEF post-CABG was associated with higher long-term mortality (log-rank p=0.019). Conclusions: Nearly 44% of patients with LV systolic dysfunction experienced a significant improvement in LVEF post-CABG. On the other hand, 16% had worsened LVEF, which was associated with higher long-term mortality. These results provide guidance for physicians and their patients considering CABG, and identify a postoperative subset of CABG patients with elevated long-term mortality risk.

Research Topic: Cardiovascular Disease
Funding agencies: None
Grant support: Medtronic

13. Design and Development of a Hardware Mounting System for a Pressure Monitoring System for Wheelchair Users

Fairhurst, Stuart [1]; Bornstein, A. Soleil [1]; Vos-Draper, Tamara [2]; Truty, Timothy [1]; Kemmer, Sara [1]; Eddy, Byron [1]; Goldish, Gary [1]; Gravely, Amy [1]; Hansen, Andrew H. [1]; Barrett, Benjamin [1]; Morrow, Melissa [3]; Olney, Christine [1]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Mayo Clinic

Abstract: Veteran's with spinal cord injury or disorder (SCI/D) are at risk for pressure injuries if they do not shift their weight throughout the day while sitting in a wheelchair. To help prevent these injuries, our team developed a mobile application (app) that provides real-time views of pressure distribution (DoD award). It can give reminders for pressure reliefs and alerts to unexpected pressure changes. The app receives data transmitted from a pressure map placed on top of the wheelchair seat connected to a small hardware interface, allowing for inconspicuous and continuous use throughout one's day. One problem experienced by the participants in that study was the clumsiness of the wires and hardware. During the first two years of the current VA merit (RX003222) our team aims to improve the functionality of AW-Shift app system, to include the creation of a user driven hardware mounting system for wheelchair users. We set up virtual focus groups with Veterans on a web-based video platform to understand the important components for a hardware mounting system, where the users wanted the hardware to be located on their wheelchairs, and what the dealbreakers were for the hardware mounting. User experience and usability surveys were completed by participants following the study session to gauge how the Veterans felt about the pressure mapping system and hardware mounting system. Focus group data were analyzed using the Hamilton method. Based on feedback from the first Veteran focus group (n=7), our design engineering team developed a prototype mounting system that allows the pressure map's hardware interface to be placed in a variety of places on several different types of wheelchairs. Veterans with SCI/D provided initial feedback during a virtual focus group late summer 2020. Several prototypes were created to offer the Veteran with SCI/D several options for placement of the hardware mounting system, which will house the wires and hardware of the Aw-Shift. The options were shown to the second iteration of Veterans focus group in spring 2021. Though data are not completely analyzed from this second round, there was a consensus by the Veteran participants that the design met and exceeded their expectations

Research Topic: Preventive Medicine
Funding agencies: RR&D
Grant support: I01RX003222

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14. Doing more with less: Adapting an intensive evidence-based retention model to optimize follow-up in a highly mobile military population.

Filetti, Clarissa [1-2]; Noel, Valentin [1-2]; Jensen, Alex [1-2]; Leverton, Dylan [1-2]; Erbes, Christopher [1-2]; Polusny, Melissa [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Retention efforts in longitudinal cohort studies can be resource-heavy and time consuming, especially when conducted with highly mobile populations. The Advancing Research on Mechanisms of Resilience (ARMOR) Project implemented the intensive Engagement, Verification, Maintenance, and Confirmation (EVMC) follow-up model to maintain adequate retention and response rates with limited staff resources. In the present study, we examined the extent to which components of the EVMC follow-up model are associated with participant retention and response rates. Data from ARMOR's participant tracking app, a SQL database used to systematically track, collect, and record participant outreach, was merged with participant survey response and demographic data. Data were analyzed from the initial follow-up survey time-point. Overall, the response rate at the initial follow-up survey time-point was 73%. Results indicated post-recruitment outreach to verify participant contact information and text reminders the day before and day of survey is emailed to participants were associated with survey response. Confirmation calls, made six weeks prior to each follow-up survey window to confirm the date, time, and email address of the upcoming follow-up survey, was not associated with survey response. There was no significant difference in response rate between race, ethnicity, or gender. After four reminder call attempts response rates decreased, from 60% to 22% at five attempts, suggesting diminishing utility given limited resources. Although the original EVMC model calls for an unlimited number of outreach attempts to increase response rates, it may be more efficient for longitudinal studies with limited resources to make a maximum of four reminder call attempts. The adapted-ARMOR EVMC model effectively maintained adequate retention and response rates while utilizing limited resources. Results suggest additional adaptions could be made to the EVMC model to further minimize resource costs while maintaining adequate retention and response rates.

Research Topic: Psychiatry
Funding agencies: NIH
Grant support: 5UH3AT009651

15. Association of Cardiovascular Autonomic Nervous System Function with Incident Hip Fracture Risk: The Cardiovascular Health Study

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1. Minneapolis VA Health Care System
2. Washington University School of Medicine
3. University of Washington School of Public Health
4. University of California Davis School of Medicine
5. Beth Israel Deaconess Medical Center
6. University of Pittsburgh School of Public Health
7. Medical College of Georgia at Augusta University
8. University of Miami Miller School of Medicine
9. Kaiser Permanente of Georgia

Abstract: Autonomic nervous system (ANS) function modulates bone remodeling in rodent models but its relevance to human bone health is uncertain. We tested whether cardiovascular autonomic function is associated with hip fractures in humans. Participants were 1299 community-dwelling men and women aged >=65 years from the Cardiovascular Health Study who completed 24-hour Holter ECG monitoring at the 1989-90 study visit. Eight Holter heart rate variability (HRV) measures (time and frequency domains, detrended fluctuation analysis in the non-linear domain, and heart rate turbulence [HRT]) were derived in participants in sinus rhythm. Frequency domain variables were ln transformed and HRT variables were categorized based on previously established cut points. Incident hip fractures were confirmed from hospital records and Medicare claims. Cox models were used to estimate the hazard ratio (HR) of incident hip fracture per standard deviation (SD) for continuous HRV variables and for abnormal versus normal for categorical HRV variables. Models were adjusted for demographics, anthropometrics, medical history, medication use, smoking and alcohol use, difficulties with ADLs and IADLs, and log transformed C-reactive protein. HRV variables also were examined adjusting for the relationship of all other HRV variables with hip fracture risk. Median follow up for incident hip fracture was 14.7 years. There were 144 incident hip fractures in 714 women (1.31; 95%CI, 1.06-1.61] per 100 patient years) and 46 incident hip fractures in 585 men (0.62; 95%CI, 0.43-0.90] per 100 patient years). Among the HRV variables examined, in women, after multivariable adjustment, a 1 SD increase in variation between normal heart beats (the SD of NN intervals [SDNN]), possibly reflecting better global ANS function, was associated with reduced hip fracture risk (HR, 0.80; 95%CI, 0.65-0.98) while the association between ln(very low frequency power) and hip fracture was borderline statistically significant (HR, 0.82; 95%CI, 0.67-1.00). When adjusting for all 8 HRV variables plus covariates, a 1 SD higher SDNN remained significantly associated with reduced hip fracture in women (HR, 0.71; 95%CI, 0.50-0.99). No HRV variable was significantly associated with hip fracture in men. Among older women, better 24-hour ANS function as measured by HRV may reduce incident hip fracture risk. Possible explanatory mechanisms linking ANS function and hip fracture risk are under investigation.

Research Topic: Clinical Epidemiology

Funding agencies: NIH

Grant support: This research was supported by contracts HHSN268201200036C, HHSN268200800007C, HHSN268201800001C, N01HC55222, N01HC85079, N01HC85080, N01HC85081, N01HC85082, N01HC85083, N01HC85086, 75N92021D00006, and grants U01HL080295 and U01HL130114 from the National Heart, Lung, and Blood Institute (NHLBI), with additional contribution from the National Institute of Neurological Disorders and Stroke (NINDS). Additional support was provided by R01AG023629 from the National Institute on Aging (NIA).

16. Development and Evaluation of a Measure of Mild TBI Misconceptions

Finn, Jacob [1]; Lamberty, Greg [1]; Nelson, Nathaniel [2]

1. Minneapolis VA Health Care System
2. University of St. Thomas

Abstract: Although misconceptions about mild traumatic brain injury (mTBI; concussion) have been identified among military veterans, their families, and their healthcare providers, relatively few studies have examined how misconceptions relate to post-concussion symptoms and recovery. To better understand mTBI misconceptions, we developed the Common Misconceptions about TBI (CM-TBI) scale. Pilot CM-TBI items were identified from previous TBI misconception measures, evaluated for clarity by the current authors and a group of neuropsychologists, organized by content area, and selected based on clarity and content (i.e., mTBI recovery). Ten previous test items were used verbatim, 10 previous test items were modified for clarity, and one original item was written. The CM-TBI was administered to 64 veterans (81% male, 88% White, mean age = 45.1 years) who were admitted to a VA outpatient rehabilitation clinic and had a reported history of mTBI. The CM-TBI items ranged from 25.8% to 96.8% correct in this sample (mean = 64.2% correct); and the CM-TBI scores ranged from 1 to 15 (mean = 7.5, SD = 2.88), with higher scores indicating more misconceptions. The CM-TBI's internal consistency was estimated in this sample (a = .55). The CM-TBI scores were associated with negative mTBI beliefs (r = .36), attribution of current symptoms to mTBI (r = .29), reporting atypical symptoms (r = .26), and less interest in rehabilitation (r = -.31). The current results indicate mTBI misconceptions can be measured and are associated with injury- and treatment-related beliefs. Clinical implications and future directions will be discussed.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: CVRE
Grant support: Investigator grant

17. Quality Improvement Study of a Hybrid Model of Neuropsychological Assessment during COVID-19

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2. Georgia State University
3. University of Minnesota

Abstract: In efforts to maximize both patient safety and testing validity during the COVID-19 pandemic, the MVAHCS NPAC has utilized a hybrid model of care since July 2020. Veterans present in person to the Clinic and complete neuropsychological testing partially face-to-face with personal protective equipment and partially via room-to-room video conferencing. Veterans and providers complete questionnaires at the conclusion of the visit. The present study aimed to evaluate patient satisfaction and the effects of technology use on satisfaction and test performance in the context of this hybrid model. Data were available for 108 Veteran participants (7 female; age range 25-89 years, M=69.60, SD=13.39). Frequency of technology use (FTU; computer/tablet/smartphone) varied (18.8% never, 25.9% occasionally, 55.3% frequently). 100% of Veteran participants reported experiencing good care. 99% of Veteran participants reported being satisfied with their care. Preferred visit type varied (15.7% telemedicine, 46.1% face-to-face, 38.2% hybrid). Providers reported 86.4% satisfaction and indicated that the hybrid model met the needs of the patient 'very well' 83.5% of the time. Technology trouble occurred during 10.6% of visits. An ordinal logistic regression model indicated that age, education, technology use, and technology problems combined predicted the degree to which the hybrid model met patients' needs. Model was significant (.2=59.15, p=.041) but interpreted with caution due to a high count of empty cells. Analyses of variance indicated no effect of FTU on verbal fluency, confrontation naming, or verbal learning and memory tasks conducted via video. A main effect of FTU was observed on Digit Span total raw score, controlling for age and education. Contrasts indicated a significant difference between Veterans who never and frequently used technology. Veterans and providers appear overwhelmingly satisfied with the hybrid neuropsychological testing model instituted at MVAHCS. It is generally able to meet Veterans' needs very well, though multiple factors may impact this. Veterans' FTU does not generally predict performance on video-based assessment measures. Differences in performance on an attention/working memory task could be due to familiarity with listening closely to others via video or may reflect skills needed to effectively navigate new technologies. Overall, results suggest that this is a broadly viable method of assessment for most Veterans.

Research Topic: Health Care Delivery
Funding agencies: None
Grant support: N/A

18. Does interest in psychotherapy or pharmacotherapy differ depending on race/ethnicity among Veterans with PTSD?

Gebregiorgis, Desta [1]; Spoont, Michele [1]

1. Minneapolis VA Health Care System

Abstract: Post-traumatic stress disorder (PTSD) is a prevalent mental health disorder in Veteran populations, with higher rates in racial/ethnic minority Veterans. Treatments are the most effective when they are targeted to address patient's needs and treatment preferences; treatment preference is associated with better treatment adherence, engagement, and outcomes. Unfortunately, after initiating treatment, racial/ethnic minority Veterans have higher PTSD treatment dropout rates and less symptom improvement compared to white Veterans. Expanding and increasing access to Veterans' preferred treatment can help providers better personalize treatment recommendations to alleviate the health disparities associated with PTSD. Therefore, we examined whether Veterans who were recently diagnosed with PTSD were interested in receiving psychotherapy or pharmacotherapy and whether this differed depending on Veterans' race/ethnicity. White, African American, and Latino Veterans (n = 6,196) participated in a national study of Veterans who were newly diagnosed with PTSD and were at the beginning of a possible episode of care. Veterans' interest in receiving psychotherapy or pharmacotherapy were modeled separately using backward elimination logistic regression. Demographics, treatment need, treatment-related beliefs, and social determinants of health were considered as predictors. Understanding the factors that contribute to differences in pursuing mental health treatment can help to inform whether we are meeting patient's needs and treatment preferences. Future directions and policy implications for VA service users will also be discussed.

Research Topic: Health Services
Funding agencies: HSR&D
Grant support: IAC 06-266

19. Automatic 2D Segmentation of Chronic Subdural Hematoma from Head CT Scan

Ghosh, Atishya [1-2]; Samadani, Uzma [1-2]; Sham, Yuk [2]

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Traumatic Brain Injury (TBI) can cause bleeding and clotting of blood on the surface of the brain resulting in subdural hematoma (SDH). Untreated, SDH can become chronic within days. Excess bleeding and expansion of clot can compress and damage adjacent brain which can lead to seizures, stroke, neurological damage and death. Enzymatic breakdown of clot releases iron that is cytotoxic to brain tissue. The one-year mortality rate for chronic subdural hematoma (CSDH) patients is 32% with survivors vulnerable to long-term incapacitating dementia and Alzheimer's diseases. The standard treatment involves surgical drainage using craniotomy or burr hole craniostomy with a recurrence rate greater than 10%. A newer, minimally invasive approach, called Twist-Drill Craniostomy (TDC), can be performed bedside under local anesthesia with decreased length of hospital stay. However, TDC also suffers from 18% recurrence risk due to imperfect drill placement that often results in residual hemorrhage. The objective of the study is to apply supervised learning to automate CSDH detection from a head CT scan and optimize TDC drill site placement to enable better diagnosis and treatment. An algorithm created for automatic 2D segmentation by supervised learning of CT scans from 35 TBI patients with CSDH is presented.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: None
Grant support: Minnesota Office of Higher Education. Award Number# 165646

20. Global and Local Network Efficiency Changes in Veterans with Chronic Mild Traumatic Brain Injury

Gilmore, Casey [1]; Boroda, Elias [2]; Armstrong, Michael [1]; Gentz, Carolyn [1]; Fenske, Alicia [1]; Hendrickson, Timothy [2]; Roediger, Donovan [2]; Mueller, Bryon [2]; Kardon, Randy [3]; Lim, Kelvin [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Iowa City VA Health Care System

Abstract: Background: In mild traumatic brain injury (mTBI), diffuse axonal injury results in disruption of functional networks in the brain and is thought to be a major contributor to cognitive dysfunction even years after trauma. Objective: Few studies have assessed longitudinal changes in network topology in chronic mTBI. We utilized a graph theoretical approach to investigate alterations in global network topology based on resting-state functional connectivity in veterans with chronic mTBI. Methods: 50 veterans with chronic mTBI (mean of 20.7 yrs. from trauma) and 40 age-matched controls underwent two functional magnetic resonance imaging scans 18 months apart. Graph theory analysis was used to quantify network topology measures (density, clustering coefficient, global efficiency, and modularity). Hierarchical linear mixed models were used to examine longitudinal change in network topology. Results: With all network measures, we found a significant group ◊ time interaction. At baseline, brain networks of individuals with mTBI were less clustered ($p = 0.03$) and more modular ($p = 0.02$) than those of HC. Over time, the mTBI networks became more densely connected ($p = 0.002$), with increased clustering ($p = 0.001$) and reduced modularity ($p < 0.001$). Network topology did not change across time in HC. Conclusion: These findings demonstrate that brain networks of individuals with mTBI remain plastic decades after injury and undergo significant changes in network topology even at the later phase of the disease.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: RR&D; DOD
Grant support: DoD, Chronic Effects of Neurotrauma Consortium (CENC) Award W81XWH-13-2-0095; Dept of Veterans Affairs CENC Award I01CX001135

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21. Opioid-Related Mortality in the U.S.: A Physician-Elicited Bias Analysis

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1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Background: Opioid-related mortality remains high in the U.S., with over 47,600 documented opioid-related deaths in 2017. U.S. mortality data rely on cause-of-death information from death certificates completed by health care providers and medical examiners. Opioid misuse and abuse among older adults are thought to be underestimated. We conducted physician expert elicitation and quantitative bias analysis to assess the potential influence of age-related misclassification on U.S. opioid-related mortality estimates. Methods: We obtained de-identified cause-of-death data from the U.S. National Center for Health Statistics. We estimated crude opioid-related mortality rates by age category (under 55, 55-64, 65+). We developed and piloted a physician elicitation method, then conducted elicitations with 10 internal medicine physicians to quantify beliefs on sensitivity of opioid-related cause-of-death data from U.S. death certificates. We combined distributions, calculated specificity values at preset percentiles, and applied resulting parameters in simulation studies. Results: Physicians perceived the elicitation method as feasible and conceptually valid. Physicians estimated lower sensitivity of U.S. death certificate data as an indicator of opioid-related mortality among people older at death. Bias analyses adjusting for physician-estimated misclassification yielded increased U.S. opioid-related mortality rates in all age groups. At maximum specificity, for people aged 65 and older, adjusting for physician-elicited misclassification yielded an estimate of opioid-related deaths 3.07 times the observed number (95% uncertainty interval 1.24-23.53); for people aged 55-64, the adjusted/observed ratio was 2.52 (1.14-12.95), and for people aged 25-54, 1.63 (1.10-4.33). Opioid-related mortality rate estimates in the older age groups were more responsive to specificity value changes, consistent with more limited admissible specificity ranges. Conclusions: We developed a feasible method of quantitatively eliciting physician expert opinion and applied findings in bias analyses adjusting for differential misclassification. The elicitation method can inform bias analysis of medical record-based research by quantifying physician opinion on physician-produced data quality. Opioid-related mortality rates may be underestimated in the U.S., particularly among people aged 65 and older, due to age-related misclassification in cause-of-death data from death certificates.

Research Topic: Epidemiology
Funding agencies: None
Grant support: N/A

22. Covid-19 Post Acute Care Major Organ Damage: A Living Rapid Review

Greer, Nancy [1]; Bart, Bradley [1]; Billington, Charles [1]; Diem, Susan [1-2]; Ensrud, Kristine [1-2]; Kaka, Anjum [1]; Klein, Mark [1]; Melzer, Anne [1]; Reule, Scott [1]; Shaukat, Aasma [1-2]; Sheets, Kerry [1]; Starks, Jamie [1]; Vardeny, Orly [1]; McKenzie, Lauren [1]; Stroebel, Benjamin [1]; Duan-Porter, Wei [1]; Wilt, Timothy [1]

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Coronavirus disease-2019 (COVID-19) is a viral illness caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) and was declared a pandemic in March, 2020. As of 4/28/21, there have been over 32 million cases and over 570,000 deaths in the US. This systematic review examined post-acute prevalence of major organ damage and healthcare/service use needs among adults hospitalized with or for COVID-19. For the current version of the review, we searched MEDLINE, Embase, and the Cochrane Library through January 12, 2021. We included studies of adults discharged (or ready for discharge) from hospitalization following admission with or for proven COVID-19. We excluded studies reporting only mean or median values for "surrogate measures" (eg, radiologic or laboratory measures) as means or medians do not provide a reliable measure of organ damage prevalence or healthcare/service use. We also excluded studies reporting only general symptoms (eg, fatigue, pain), because symptoms are not specific to a disease or organ damage. We identified 90 reports of post-acute major organ damage or healthcare/service use outcomes in adults hospitalized with or for COVID-19. Frequently reported outcomes included pulmonary fibrosis (present in 7%-61% of patients), pericardial effusions (present in 0%-20%), need for renal replacement (present in 4%-31%), readmission (0%-15% of patients), and discharge disposition other than home (3%-47% of patients). Interpretation of findings is difficult due to study limitations. Available data are largely from studies of convenience samples with poorly described study populations and primarily physiologic outcomes; few included control groups for comparison of COVID-19 and non-COVID-19 patients. Most studies had short follow-up post-discharge; long-term outcomes are unknown. Applicability of findings to sub-groups (eg, age, gender, COVID severity) and non-hospitalized patients is unknown. Future updates are likely to identify additional relevant data.

Research Topic: Health Systems
Funding agencies: HSR&D
Grant support: VA HSR&D

23. Role of the ApoE Gene on Verbal Learning and Memory Following a Mild Traumatic Brain Injury

Grund, Peter [1-2]; Disner, Seth [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Mild traumatic brain injuries (mTBIs) are common among the U.S. veteran population, and chronic symptoms of mTBI can impact verbal memory performance. While many benefit from cognitive rehabilitation approaches following mTBI, there are others for whom treatment does not result in significant recovery. Identifying genetic biomarkers that influence the biological processes underpinning verbal learning and memory may provide additional explanations for discrepancies in mTBI recovery. One possible biomarker is apolipoprotein E (ApoE), a protein associated with neuronal repair and neuroinflammation. ApoE is encoded by the APOE gene. APOE has three common variants designated APOE-e2, -e3, and -e4. The functional mechanisms that these alleles influence differ, with e4 being associated with the pathogenesis of several neurological conditions and poorer recovery following neurotrauma. The current study's aim is to understand the association between the e4 allele and verbal memory after the occurrence of mTBI. The present analysis was composed of 275 participants (95.7% male, mean age = 24.9 years (SD = 8.43, 22-62)) from two previously completed research projects done through the Minneapolis VA Medical Center for which genetic data is available; the Study of the Aftereffects of Trauma: Understanding Response in National Guard (n = 145) and the Essential Features of Neural Damage in Mild Traumatic Brain Injury (n = 130). Verbal learning and memory were measured via the California Verbal Learning Test-II, a neurocognitive test subdivided into four factors: Attention Span, Learning Efficiency, Delayed Memory, and Inaccurate Memory. Each factor measures a specific domain of the verbal learning and memory construct. It is hypothesized that the presence of at least one copy of the e4 allele will be associated with poorer verbal learning and memory performance.† Using univariate linear regression of APOE-e4 carrier status, a preliminary analysis on 138 veterans did not indicate a significant association with any of the four CVLT-II factors (all $p > 0.180$). Additional analyses on the entire dataset are planned in advance of VA Research Day. The findings of this research will help determine if APOE could serve as a genetic biomarker to better explain the link between mTBI and cognitive changes. It may also help identify factors that confer risk for negative cognitive outcomes, directing clinicians towards prescribing the most effective forms of treatment for patients.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: RR&D
Grant support: W81XWH-08-2-0038, I01RX000622, IK2RX002922

24. Patients' attitudes towards active surveillance for basal cell carcinoma

Han, Joohee [1]; O'Neal, Sydney [2]; Gravely, Amy [1]; Goldfarb, Noah [1]

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Basal cell carcinoma (BCC) is the most common cancer in the US. 30-50% of BCCs may remain stable or shrink in size. Most BCCs are managed surgically regardless of life-expectancy. More than 40% of patients with limited life-expectancy die within 5-years of their BCC treatment, rarely from skin cancer, and likely do not live long enough to benefit from their treatment. Active surveillance has been proposed for some of these patients. The objectives of this study were to determine patients' attitudes and concerns regarding active surveillance, and to evaluate the effect of an educational video on patients' attitudes and concerns. We conducted a pre/post survey study of 201 patients in the dermatology clinic at the Minneapolis VA Medical Center from August 2019 to October 2020. An educational video on BCC was created, and reviewed/accepted by the Minneapolis VA IRB to ensure educational rather than coercive content. The primary study outcomes were change in the number of patients with concerns regarding BCC active surveillance, change in specific concerns, and the percent of patients comfortable in participating in a study for BCC active surveillance pre- and post-video. Significantly less respondents were concerned with their doctor monitoring their BCC post- versus pre-video (61% vs 48%; p= 0.0065). Respondents were most concerned with tumor growth (41%) and metastases (38%). Post-video, significantly more patients were concerned with making the wrong decision (15% vs 26%; p = 0.0070). Almost half of respondents felt comfortable or very comfortable in participating in a study for active surveillance of BCCs, with no significant differences found between pre- and post-video (49.5% vs 56%; p = 0.3706). We did find that older participants (=75 years of age) and those without a prior history of BCC were more likely to be comfortable or very comfortable with active surveillance both pre- and post-video compared with younger patients and those with a prior history of BCC, respectively. Providing education on BCCs may alleviate patients' concerns regarding active surveillance.

Research Topic: Dermatology
Funding agencies: None
Grant support: N/A

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25. Physicians' attitudes towards active surveillance for basal cell carcinoma

Han, Joohee [1]; O'Neal, Sydney [2]; Gravely, Amy [1]; Goldfarb, Noah [1]

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Most BCCs are treated surgically regardless of life-expectancy. This has resulted in over 100,000 BCCs being treated annually in patients' final year of life with presumed minimal value gained from these treatments. Active surveillance has been proposed as a method for managing patients with limited life-expectancy. Limited data is available on physician comfort and practice in regard to active surveillance of BCCs. The objectives of this study were to determine physicians' comfort level with active surveillance of BCC, and understand which factors and concerns influence their decisions. We conducted a cross-sectional survey study of physician members of the Association of Professors of Dermatology in August/September 2019 to evaluate physicians' attitudes regarding active surveillance of BCC. The main outcomes were percent of physicians comfortable with active surveillance of BCC, factors influencing their decision to monitor BCC, and feared complications. Seventy out of 528 members (16%) responded to the survey. Eighty-three percent of respondents felt comfortable monitoring nodular and/or superficial BCCs. Factors such as medical comorbidities (90%), functional status (84%), age (83%), anatomic location (77%), size (71%), and histologic subtype (66%) determined the level of comfort with monitoring BCC. Over 70% of physicians would feel comfortable monitoring BCC in patients with grade 4 functional ECOG status and age older than 85. The top feared complications were larger surgical site defects (84%), bleeding (83%), ulceration (80%), local destruction to adjacent vital organs (64%), and pain (51%). Metastasis (6%) and death (6%) were uncommon concerns. There were no significant differences in responses between general dermatologists and Mohs micrographic surgeons. Majority of physicians were comfortable with active surveillance of BCCs in elderly adults with low functional status, taking into consideration, size, anatomic location and histologic subtype.

Research Topic: Dermatology
Funding agencies: None
Grant support: N/A

26. Patterns of Endorsed Dementia Care Among VISN 23 Providers

Hemmy, Laura [1-2]; McCarten, J Riley [1-2]; Miller, Margaret [1]; Ueckert, Nicole [3]; Parsons, Jana [3]; Simone, Amanda [3]; Ross, Debra [3]; Starks, Jamie [1-2]; Fink, Howard [1-2]; Meiches, Robert [3]; Ratner, Edward [1]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. VA VISN 23

Abstract: Background: Alzheimer's Disease (AD) or related dementias are present in 10% of Veterans over age 65 and are associated with increased morbidity, mortality and health care utilization (Zhu 2021). Quality measures for dementia care have been defined by professional societies. VHA has a variety of initiatives to address challenges from dementia for Veterans and caregivers. Information about patterns of care could help prioritize quality improvement interventions in VHA dementia care. Methods: An anonymous on-line survey designed by the VISN 23 Dementia Committee was circulated via email within VISN 23 facilities in Fall 2020. Respondents were asked for observations related to scenarios of dementia care in their primary setting over the past year. Results were captured using Qualtrics and analyzed using SPSS 27. Results: 453 surveys were received, although not all included every item. Surveys were submitted from 28% inpatient, 25% outpatient primary care, 25% specialty clinics, 4% emergency, and 20% other settings. Clinical disciplines included 22% physicians, 15% advance practice providers, 32% nurses, 6% psychologists, 8% social workers, 4% physical and occupational therapists, and 13% others. Responses indicated variable use of cognitive screening tools (MoCA most common, 59%). Best practices were not routinely used in the documentation or delivery of a new dementia diagnosis: just 37% of respondents reported holding family meetings to deliver diagnosis, 53% indicated telling patients of an AD diagnosis, and 29% always recorded a new dementia diagnosis in the EHR. Only 28% of respondents said they usually found advance directives documented. Ancillary services and referrals for support appear underutilized: <33% of providers reported using social work, pharmacy, occupational therapy, etc. in the initial diagnosis and management of dementia. Reported use of referrals increased when the scenario described a dependent veteran (several services by >50% of respondents) but use of community resources remained low (e.g. 36% non-VA support groups, 31% Alzheimer's Assoc). Discussion: A large and diverse group of VISN 23 dementia providers surveyed reported patterns of care that suggest opportunities for improvement in the care of Veterans with dementia. These include improving delivery and documentation of a new diagnosis, consistency in tools used to assess cognition, promoting advance care planning, and increasing referrals for patient and caregiver support.

Research Topic: Alzheimer's Disease
Funding agencies: None
Grant support: N/A

27. Cognitive Function Among a Veteran COPD Case Management Population

Henkle, Benjamin [1]; Freese, Rebecca [2]; Dahlheimer, Mary [1]; Kane, Catherine [1]; Kunisaki, Ken [1]

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Introduction/rationale: Cognitive impairment in chronic obstructive pulmonary disease (COPD) is more common in advanced disease, in those requiring supplemental oxygen, and during an acute exacerbation. However, cognitive function is not currently assessed in the routine management of COPD. Cognitive function may have significant impact on health outcomes in COPD. Methods: We enrolled individuals in the Minneapolis VA COPD Case Management program which identifies all patients hospitalized or in the emergency department for acute exacerbations of COPD and assists in their clinical management. Case management participants were enrolled during their first post-exacerbation clinic visit. Participants were screened for cognitive impairment with the Montreal Cognitive Assessment (MoCA). Inhaler technique was assessed with logistic regression. Home action plan (HAP) use, emergency department (ED) visits and hospitalizations were monitored prospectively for 6 months from the time of enrollment. Results: Among 47 veterans, 29 (62%) were found to have a MoCA concerning for mild cognitive impairment. A MoCA score <26 was seen more often in participants with black race, lower educational attainment, prescription of supplemental oxygen, and home health services. Participant MoCA subscores were commonly abnormal for delayed recall (92%), visuo-constructional skills & executive function (77%), language (62%), and attention (60%); less common abnormalities included abstraction (19%), naming (17%), and orientation (4%). The odds of having poor inhaler technique in those with abnormal MoCA was 5.5 (95% CI 1.5 to 24.2). There was no difference in rates of home action plan use, emergency room visits, or hospitalizations at 6 months in those with and without abnormal MoCA scores. Conclusions: Among this veteran COPD Case Management population, cognitive impairment was present in over half of participants and associated with poor inhaler technique. We found no difference in healthcare utilization (HAP use, ED visits, or hospitalizations). Further investigation into the impact of cognition on COPD clinical outcomes is merited.

Research Topic: Clinical Epidemiology
Funding agencies: None
Grant support: N/A

28. Psychological Predictors of Treatment Outcomes in a VA Chronic Pain Rehabilitation Program

Heyrman, Katelyn [1]; Finn, Jacob [1]; Heideman, Paul [1]; Hachiya, Kiki [1]

1. Minneapolis VA Health Care System

Abstract: Chronic pain is one of the most expensive and common reasons adults seek medical care in the United States, and approximately 50 million people have a diagnosis of chronic pain. Within the Veteran population, chronic pain symptoms are more severe and chronic when compared to the general population. Chronic pain has been associated with anxiety, depression, sleep disturbances, unemployment, substance abuse, poor health, and reduced quality of life. Previous research has suggested that identifying psychological predictors early is essential in optimizing treatment and recovery in individuals with chronic pain. The current study aimed to identify psychological constructs at the Minneapolis VA's Chronic Pain Rehab Program (CPRP) admission that contribute to the prediction of pain interference at program discharge, as well as 6-months and 12-months post-discharge. Three hierarchical regression models were conducted. PEG scores at discharge, 6-months, and 12-months were the dependent variables for the three models. Within each model, age, gender, and PEG score at admission were included as control variables. Five psychological constructs were also included: PTSD symptoms, depression symptoms, pain catastrophizing, pain-related self-efficacy, and pain-related acceptance. Results from the three analyses indicated that pain-related self-efficacy significantly predicted pain interference scores at discharge, 6-months, and 12-months. Additionally, at 6-months post-discharge, pain catastrophizing and gender also significantly predicted pain interference scores. Clinical implications are discussed.

Research Topic: Pain
Funding agencies: None
Grant support: N/A

29. Trait Absorption and Enhanced Discrimination of Facial Emotions

Hitz, Andrea [1]; Marquardt, Craig [2]; Erbes, Christopher [2]; Polusny, Melissa [2]

1. St. Catherine University
2. Minneapolis VA Health Care System

Abstract: The personality trait of absorption is related to sentience, propensity to episodes of imaginative involvement and altered awareness, as well as susceptibility to hypnosis. In the present study, we examined associations between trait absorption and accuracy as well as speed when discriminating facial emotions. Emotion differentiation was measured using the UPenn Cognitive Battery Emotion Differentiation Test among a cohort of new military recruits from the Minnesota National Guard (n = 571). Absorption was measured using the Multidimensional Personality Questionnaire-Brief Form (MPQ-BF) self-report inventory. Participants viewed one of four emotional faces along with a neutral expression face and attempted to identify which face displayed the emotional content. Emotional faces were difficult to discern because perceptual differences compared with the neutral faces were small (10%, 20%, 30%, and 40% differences depending on the task condition). We employed two sets of generalized linear models with missing REML data imputation: models with each emotional face condition as single outcome variables (either happy, sad, fearful, or angry) and models using a within-subject factor for the percent difference manipulation (4 levels). Within-subject effects were estimated using an auto-regressive covariance structure. Participants with higher absorption scores demonstrated better emotion differentiation for sad, anger, and fear conditions, but not happy conditions. Moreover, higher levels of absorption were associated with greater ability to recognize emotion in others particularly when the cues were subtle (10%, 20% and 30% differences). Finally, participants with higher absorption scores had longer correct response times during the 10% difference condition, which was consistent with more elaborative processing of the faces. The associations with absorption were significant even when covarying for other broad domains of personality such as negative and positive emotionality. These findings suggest that other aspects of personality may play a role in predicting cognitive outcomes over and above that which can be explained by other trait domains related to emotional experience.

Research Topic: Mental Health
Funding agencies: None
Grant support: N/A

30. Diuretic Comparison Project: Odds of Provider Declining Consented Patient for Randomization

Ikeri, Eustacia [1]; Taylor, Olivia [1]

1. Minneapolis VA Health Care System

Abstract: Patients who consent to participate in the Diuretic Comparison Project (DCP) must be approved for randomization by their providers prior to enrollment. We examined the odds of a consented patient being declined by their PCP based on VA site and VISN. Furthermore, we determined whether these odds changed after adjusting for VA site complexity rating and the number of days a site has been active. Raw data was pulled from the DCP's ProjectFlow and modified so that the outcome variable was coded as binomial. A logistic regression was run in SAS University and the beta estimates of each logistic regression model were used to calculate the odds of interest. Our outcome is defined as a provider declining a patient's participation in the DCP after the patient has consented. The percent odds of the outcome based on the study site were calculated for each of the 60 sites in our dataset. Of these odds values, the values for 22 sites were statistically significant. The percent odds of the outcome based on VISN were calculated for the 18 VISNs. None of the calculated odds were statistically significant. The adjusted odds of the outcome based on study site after adjusting for site complexity and days active resulted in no statistically significant odds values for any site. The same was found for the odds of the outcome based on VISN after adjusting for complexity and days active. The DCP study is a point-of-care trial, which is a novel study design within the VA health care system. Therefore, it is worthwhile to measure engagement among providers who consented to participate in this point-of-care format. One strength of this analysis was that the data included 12,077 observations. The site complexity rating assigned to each study site does not always correspond to all clinics or hospitals within that site. This may have affected the p-values of some of the odds found within the adjusted models. As our analysis was quantitative, it would be beneficial to better understand why a provider chooses to decline a patient's participation in the DCP. An avenue to explore this would be through a qualitative analysis. Study site only seems to be a statistically significant predictor of the outcome for certain sites. After adjusting for site complexity and days active, study site is no longer a significant predictor of the outcome. VISN does not appear to be a statistically significant predictor of the outcome, even after adjusting for site complexity and days active.

Research Topic: Clinical Epidemiology
Funding agencies: CSR&D
Grant support: CSP 597

31. Semi-Automated Evaluation of Callosal Angle (CA) and Evan's Index (EI) for Identification of NPH on CT scans

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Abstract: Normal pressure hydrocephalus (NPH) is a neurodegenerative condition caused by an accumulation of cerebrospinal fluid (CSF) in the brain. The etiology is not fully understood however it is possibly due to conditions as varied as traumatic brain injury (TBI), hemorrhage, tumor, meningitis or other inflammatory trigger. 80% of cases are misdiagnosed, with most cases falsely attributed to Alzheimer's disease (AD) due to common clinical features like incontinence, dementia, and gait disturbance. Given that NPH is also the only dementia subtype which has shown complete reversibility of symptoms after treatment with ventricular shunting in some cases, timely and accurate diagnosis is highly valuable. Current diagnostic methods involve clinical examination, trial of cerebrospinal fluid drainage, and radiographic evaluation for ventricular enlargement unattributable to cerebral atrophy. Among the prominent radiographic features are Callosal angle (CA) between 40 and 90 degrees, and Evan's index (EI) greater than 0.3, which are generally assessed by manual evaluation primarily of magnetic resonance images (MRI). Removing inter-observer variability in measurements is crucial for reproducibility, high accuracy, and precision. Here, we present a semi-automated methodology to evaluate CA and EI from head computed tomography (CT) images using image processing pipelines developed in Python. We show that our method can address the segmentation of lateral ventricles under varying anatomical conditions and output the radiographic features for further evaluation. This can eliminate time spent on manual evaluation and utilize CT images which are faster, less expensive, and more frequently obtained.

Research Topic: Neurology & Neurobiology
Funding agencies: None
Grant support: Minnesota State Office Of Higher Education

32. Assessing Noise Generated from Surgical Suction Devices While Using Upper Endoscope: A Quality Improvement Project

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1. University of Minnesota
2. Minneapolis VA Health Care System

Abstract: Introduction: There is paucity of data regarding noise levels generated within endoscopy suite during gastrointestinal endoscopic procedures. Occupational noise exposure can lead to noise-induced hearing loss with significant health and economic consequences. The CDC and Prevention and National Institute for occupational safety and health (NIOSH) have published a recommended exposure limit of 85-decibels for workplace exposure. A recent study by our group measured sound levels using a colonoscope where the threshold was not exceeded. We aimed to replicate the study with an upper endoscope. Methods: The noise generated from an adult upper endoscope at various levels of suction were measured using the 'NIOSH Sound Level Meter' smartphone application. Neptune 3 (Stryker, Kalamazoo, MI) mobile surgical suction device (SSD) allows a wide range of suction pressure levels compared to traditional wall suction (WS). Noise measurements were obtained as average levels over a 30-second interval in outpatient ambulatory endoscopy room without a patient. Measurements were obtained at various positions within the room (endoscopist, nurse, technician) as well as next to the endoscope suction button. The measurements were obtained with the endoscopist applying no suction, partial suction and complete suction. To further validate the measurements, sample noise measurements using an industrial grade sound level meter (3M/Quest SoundPro SP DL-2) were taken. Results: The highest sound levels were generated when partial suction was applied on the scope, compared to no suction or full suction. The sound levels increased proportionally to the level of the suction. None of the measurements exceeded recommended exposure limits. The measurements using industrial grade sound meter were within 5 dB range compared to the sounds measurements by smartphone based app. Discussion: There is variability in level of noise produced by an upper endoscope based on the pressure level of suction, as well as various modes of endoscope suction. In this study, the level of noise did not exceed the threshold limit set by NIOHS. However, high level of noise could impact communication between team members in the endoscopy suite and potentially impact patient care. Smartphone based apps are validated tools for sound measurement and are readily available for use. Moreover, noise levels during equipment operation, and not at baseline alone, should be a consideration when acquiring new equipment.

Research Topic: Gastroenterology
Funding agencies: None
Grant support: N/A

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33. User Experience and Satisfaction with the Habit Camera - A Skin Screening Camera

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1. Minneapolis VA Health Care System

Abstract: In 2020 our SkinSyte camera, invented by engineers with the Minneapolis Adaptive Design & Engineering (MADE) Program, went through a successful technology transfer and licensure to an industry partner, a Veteran-owned business. Now called Habit Camera, it is a tool used by individuals to check their skin for hard-to-see areas of concern, such as those with spinal cord injury (SCI) to check their backside to prevent pressure injuries and individuals with diabetes mellitus (DM) to check their feet to prevent foot ulcers. The current method of performing these skin checks is to use a long-handled mirror, but this can be difficult for those with limited mobility or flexibility and/or eyesight concerns. The goal is that this camera system (a camera device and a mobile app) will improve the lives of Veterans who wish to screen their skin for early stage skin issues such as pressure injuries. We aim to iteratively test and refine a beta version of the Habit camera system provided by the industry partner for usability and communication capabilities between Veteran users in their home environment and a VA wound specialist. Pre-post structured interviews (beginning and end of the test month) were conducted with Veterans (six with SCI, six with DM). After an introduction to the Habit camera, initial impressions were collected, about the camera as a whole, the size, the usability, the app, etc. User experience and usability of the system were assessed with three surveys at both time points. Veterans also sent in weekly photos through MyHealtheVet for image quality assessment by a wound specialist. The study team has completed the first of two beta test periods. At the beginning of the month, physical safety/security and effectiveness of the camera system were rated as the highest average satisfaction scores by our participants. By the end of the month, satisfaction with durability, safety/security and weight had the highest average scores from our participants. Ease of use, adjustments and effectiveness were ranked as highest importance at both timepoints. Other outcomes will be presented in the poster. Twelve Veterans are currently enrolled and used the first iteration of the camera for one month. All are awaiting trialing the next iteration. We will begin testing of the second iteration of the Habit Camera in early summer 2021.

Research Topic: Preventive Medicine
Funding agencies: RR&D
Grant support: I21RX002533

34. Cyclin-Dependent Kinase Inhibition in Mesothelioma

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1. Minneapolis VA Health Care System

Abstract: Mesothelioma is a cancer that arises out of the pleura or the peritoneum and is considered incurable in the majority of patients afflicted. Abnormalities of the cell cycle pathway are among the most common molecular alterations in mesothelioma. Previously, we have demonstrated that inhibition of CDK4/6 by abemaciclib or palbociclib is effective against mesothelioma in vitro. Increased expression of Cyclin E has been demonstrated to be one mechanism of resistance to CDK4/6 inhibition in other cancers. We hypothesized that select cell cycle-related proteins may compensate for inhibition of one part of the cell cycle machinery and that the CDK2 inhibitor dinaciclib may act synergistically in combination with abemaciclib. Methods. Dinaciclib was evaluated for activity against mesothelioma cells in vitro with regard to cell proliferation and colony formation. In addition, dinaciclib was evaluated in combination with abemaciclib at several concentration combinations in a cell proliferation assay to determine if the combination may be additive or synergistic. Combination indices (CI) were calculated via the Chou-Talalay method. Immunoblotting was used to evaluate for expression of key survival proteins after treatment with abemaciclib. Results. The IC50 of dinaciclib was determined to be 18 nM, 23 nM, 32 nM, and 33 nM in mesothelioma cell lines H2373, H2052, H2452, and H2461, respectively. Colony formation was decreased significantly after 72 hours incubation with 50 nM or 100 nM dinaciclib in Bap1-expressing (35.1 ± 2%; 22.8 ± 2%) and Bap1-null cell lines (14.5 ± 3%; 8.1 ± 2%) versus untreated controls. CI < 1 (denoting synergism) was identified for several combinations of varied concentrations of abemaciclib and dinaciclib for both cell lines evaluated. Further, treatment with abemaciclib for 72 hrs in both Bap1-expressing and Bap 1-null cells at 1x the IC50 resulted in complete loss of FoxM1 expression and pro-survival survivin and significantly decreased the expression of Mcl-1 and XIAP. Conclusions. Dinaciclib is a potent inhibitor of mesothelioma cell growth. The combination of abemaciclib and dinaciclib is synergistic across a spectrum of concentrations in vitro. Further experiments are currently underway to determine which CDKs and related proteins may be more effectively targeted in mesothelioma. As the cell cycle is altered in the vast majority of mesothelioma tumors, select combinations of CDK inhibition may be a feasible future therapeutic strategy.

Research Topic: Cancer
Funding agencies: BLR&D
Grant support: I01BX004655

35. Gulf war illness inflammation reduction trial: effects of low-dose prednisone chronotherapy on health-related quality of life

Krug, Hollis [1-2]; Bach, Ronald [2]; Rudquist, Rebecca [1]; Erbes, Christopher [1-2]; Trembley, Janeen [1-2]; Gravely, Amy [1]; DeCarolis, Douglas [1]; Johnson, Gerhard [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Aims: Gulf War illness is an unexplained deployment-related chronic multi-symptom illness affecting many US military Veterans of the 1990-91 Gulf War. A proinflammatory blood biomarker fingerprint was discovered in our previous observational study of Gulf War illness. Thus, inflammation was identified as a potential therapeutic target for this illness. By measuring the effects of an anti-inflammatory drug on quality of life, symptoms (results not reported here) and biomarkers (results not reported here), this study tests the hypothesis that QOL as measured by the Veterans Short Form 36-Item Health Survey (VSF-36) Physical Component Summary (PCS) will be significantly improved at week 8 in those randomized to prednisone compared to placebo. Methods: A total of 83 Gulf War Veterans meeting the Kansas case definition for Gulf War illness were randomized to receive either 5 mg modified-release prednisone (N=42) or placebo (N=41). The intervention phase of 8 weeks was followed by a washout phase of 8 weeks. The primary outcome measure was defined as a 7-point improvement from baseline to 8 weeks of Veterans Short Form 36-Item Health Survey Physical Component Summary (PCS) scores. Results: A significantly increased proportion of participants with a 7-point improvement in PCS score in response to medication versus placebo was not observed at 8 weeks. When PCS was analyzed as a continuous variable, there was no significant difference observed between medication vs. placebo groups. The groups did follow the same trends however improving at 8 weeks and back to baseline at 16 weeks. Conclusions: Response to treatment, measured continuously and as proportion of those with clinical responses, did not differ between the two conditions. Effect sizes suggest that this is unlikely to be the result of inadequate power. Therefore, prednisone, in the low-dose, short duration regimen utilized, did not significantly improve health related quality of life as defined by the VSF-36 PCS compared to placebo. Analyses comparing the specific markers of inflammation that have been implicated in GWS in our prior work are ongoing, as are analyses of self-reported symptom outcomes. Findings from these key analyses will inform our future work in this area.

Research Topic: Gulf War Veterans
Funding agencies: DOD
Grant support: W81XWH-14-1-0477 /CDMRP

36. Effect of IA OnabotulinumtoxinA and Vanilloids on Substance P and Neurokinin 1 Receptor Expression in the Dorsal Root Ganglia of Mice with Monoarthritis

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1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Purpose: Neurotoxins are increasingly being proposed as analgesics for arthritis pain. Phase II and III clinical trials have shown efficacy but with potential toxicities. We have shown efficacy of intra-articular (IA) onabotulinumtoxinA (BTX) and the vanilloids capsaicin (CAP) and resiniferatoxin (RTX) in murine monoarthritis. To better understand the effect of these toxins on the sensory nervous system we examined their effect on substance P (SP) and neurokinin 1 receptor (NK1) expression in the dorsal root ganglion (DRG). Methods: C57/Bl6 male mice received IA Complete Freund's Adjuvant (CFA) to produce chronic inflammatory monoarthritis. IA therapies were given at appropriate intervals before examination and DRG harvest. DRGs were obtained 3 weeks after CFA induction when mice were aged 12 weeks. Tissue was subjected to immunohistochemistry and real-time RT-PCR. Neurotransmitter SP protein expression was measured as percent of DRG neurons expressing SP. Both SP and NK1 gene expression were quantified using real-time RT-PCR and expressed as a fold change relative to GAPDH values. Results: CFA induction resulted in a significant increase in % SP protein expressing cells in DRG's but gene expression of SP and NK1 were not significantly changed from naïve. Neither vanilloids nor BTX had any effect on SP protein expression in nonarthritic animals. 0.001% RTX significantly increased SP gene expression in nonarthritic animals but had no effect on NK1 gene expression. 0.003% RTX, CAP, and BTX all normalized % SP protein expressing cells in arthritic animals' DRGs but NK1 and SP gene expression was not significantly different from naïve. SP gene expression was more variable in all treated arthritic animals and in nonarthritic animals treated with BTX and CAP. NK1 gene expression in low dose RTX and CAP treated non arthritic animals was also more variable than other groups. Conclusions: Alterations in SP protein expression in the DRG of mice with chronic monoarthritis does not appear to be related to increased gene expression of either SP or NK1. Although the mechanism of action of BTX and vanilloids is hypothesized to be quite different, there does not appear to be a consistent effect of impaired neurotransmitter release (BTX) or enhanced release (vanilloids) on SP or NK1 gene expression. Although numbers were small in this experiment, variability may be due to inherent differences in the animals' pain perception, pain behavior, and response to therapy.

Research Topic: Pain
Funding agencies: RR&D
Grant support: I01RX000379

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37. Cognitive Diversity and Personal Experience of the COVID-19 Pandemic

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1. Minneapolis VA Health Care System
2. Oregon Health & Science University
3. University of Minnesota

Abstract: Emotional and behavioral reaction to the COVID-19 pandemic, as well as adherence to COVID-related safety measures, likely vary greatly depending on individual, demographic, and clinical characteristics. Literature supports that cognitive ability can impact how an individual interprets and reacts to stressful events. This study explored differences in how typical aging (TA) older adults (OA) and OA classified with mild cognitive impairment (MCI) differentially experienced the COVID-19 pandemic. The sample contained 242 OA from five cohort studies across three states, age range 57 to 97 (M = 75.54; SD = 8.13). They were 50% male, mostly White (n = 223; 91.7%), non-Hispanic (n = 238; 97.9%), well-educated (M = 15.43 years; SD = 2.37 years), and classified as TA (n = 178; 73.6%). All participants completed the Oregon Center for Aging and Technology COVID-19 Experience Survey and a validated neuropsychological test battery. Comparisons between TA and MCI OA were calculated with ANOVAs, Kruskal-Wallis, or Chi-squares. Relationships between items and cognitive domains were examined via Pearson or Spearman correlations. In the entire sample, 94.6% OA worried about the impact the pandemic would have, changing their behavior accordingly. Most OA practiced good safety protocol adherence. Compared to those with MCI, TA OA endorsed taking on more responsibility ($t(167.87) = 2.48$, $p = .014$) and less frequently avoiding significant other's homes ($K = -1.97$, $p = .049$). In the entire sample, better attention was related to more perceived behavior change ($r = .167$, $p = .016$), more public space avoidance ($r = .140$, $p = .045$), and shorter bouts of time spent in the house ($r = -.142$, $p = .042$). Better verbal fluency and confrontation naming were related to more COVID-related worry ($r = .162$, $p = .015$; $r = .360$, $p = .021$) and perceived behavior change ($r = .166$, $p = .013$; $r = .345$, $p = .031$). Better verbal memory was correlated with taking on more responsibility ($r = .178$, $p = .016$) and visiting more with others ($r = .176$, $p = .017$). Better executive functioning was associated with less optimism about managing the pandemic ($r = .152$, $p = .030$). Overall, OA with better cognitive functioning were more worried and less optimistic about the pandemic, undertook more behavioral change, and maintained better contact with others. Understanding these differences may help tailor where to intervene to reduce negative experiences of the pandemic for cognitively diverse older adults.

Research Topic: Neuropsychology
Funding agencies: CSR&D; NIH
Grant support: R01AG058687; I01CX001669; P30AG008017; P30AG066518; P30AG024978; 1 U3C AG05439701; IIR 17144; UL1 TR002369; RF1AG22018; R01 AG17917; P30 AG10161

38. All of Us Research Program

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2. University of Minnesota

Abstract: Background: The main goal of the All of Us Research Program is to build on the Precision Medicine Initiative which aims to consider how genes, the environment, and a person's lifestyle might impact their health. The program is an ambitious effort to collect and study data (including clinical data and "panomics") from 1 million or more people living in the United States. The program will be open to people both healthy and sick, from all communities. Unlike a single research study focused on a specific disease or population, All of Us will serve as a national research resource to inform thousands of studies, covering a wide variety of health conditions affecting many different people. Participants will have opportunities over many years to provide data about themselves that will help researchers learn more about how individual differences in lifestyle, environment, and biological make-up can influence health and disease. By taking part, participants will contribute to an effort to advance the health of generations to come. Methods: To achieve the goal of creating a research cohort of 1 million or more U.S. participants, the NIH has engaged a number of organizations to establish the infrastructure of the All of Us Research Program. The key program components include a Data and Research Center, a Participant Technology Systems Center, Participant Center, a Biobank, and a number of Health Care Provider Organizations (HPO). The VA is a core HPO, and the Minneapolis VA Healthcare System is one of the first wave of VA sites to open for enrollment. NIH and VA have a goal to have approximately 100,000 Veterans enroll in the All of Us and MVP studies simultaneously for comparison. Enrollment Activities: Once a participant indicates interest, participants are scheduled for an appointment. At the study visit, participants learn about the program (including data security), provide consent, answer surveys electronically, and have 8 tubes of blood plus one urine sample collected. Samples are sent to the Biobank (run by Mayo Medical Laboratories). As of May 17th, 2021, the All of Us Research Program has enrolled 280,807 total core participants nationally and 886 core participants at the Minneapolis VA. Participants also have the opportunity to view some of their genomic testing in addition to the overall study activities. Conclusion: The All of Us Research Program will provide a national panomics resource and lay a scientific foundation for Precision Medicine.

Research Topic: Genomics
Funding agencies: NIH
Grant support: NIH - no number and no Institute due to special funding arrangement

39. Computer Use Moderates the Relationship Between Sleep and Cognitive Performance in Older Adults

Maple, Kristin [1]; Mattek, Nora [2]; Gothard, Sarah [2]; Beattie, Zachary [2]; Lee, Samuel [1,3]; Kaye, Jeffrey [2]; Hughes, Adriana [1,3]

1. Minneapolis VA Health Care System
2. Oregon Health & Science University
3. University of Minnesota

Abstract: Older adults with cognitive disorders are less likely to use computers, although regular electronic device training may improve aspects of cognition. Additionally, poorer sleep is related to greater daily screen time and poorer cognitive performances. There is a need to comprehensively investigate the relationships between computer use, sleep, and cognition with objective measures. The present study investigated: (1) the relationship between daily computer use and cognition, (2) the relationship between daily computer use and objective and self-reported sleep, and (3) whether sleep and computer use interact in relationship with cognition. Participants included 97 older adults (62.9% male), classified as healthy controls or meeting research criteria for Mild Cognitive Impairment (MCI) (M age = 72.0, SD = 6.3). Individuals underwent baseline and 1-year follow-up assessments and year-long in-home daily activity tracking. Participants also completed questionnaires and validated neuropsychological tests at baseline. The current analysis used baseline clinical assessments and in-home activity tracking for the first 30 days, including wrist-watch activity monitors that quantified aspects of sleep, as well as computer monitoring software that tracked daily home computer use activity. T-tests and Pearson correlations were used to address Aims 1 & 2. Multiple regressions were used to investigate Sleep*Computer Use relationships with cognitive performance. Individuals with MCI had fewer daily computer use sessions ($p= 0.019$) and spent less time using computers daily ($p= 0.065$) relative to controls. Daily computer use time moderated the relationship between total self-reported nightly sleep and psychomotor speed ($p < 0.001$), such that among those with greater computer use, those with less sleep had slower psychomotor speed. Number of daily computer use sessions moderated the relationship between total self-reported nightly sleep and psychomotor set-shifting ($p < 0.000001$), such that among those with more daily sessions, those with less sleep performed more poorly. With objective measures of computer use, results suggest that those with MCI use computers less often. Shorter sleep duration was related to poorer processing speed and mental flexibility, only in those participants who use computers more frequently. Although results are correlational, it is possible that computer use confers benefits for cognitive efficiency that are eliminated without adequate sleep.

Research Topic: Neuropsychology
Funding agencies: CSR&D; NIH
Grant support: NIH (R01AG058687, U2C AG0543701, P30AG008017, P30AG066518, P30AG024978), VA (I01CX001669, IIR 17-144), OCTRICTSA (NCATS UL1 TR002369)

40. Examining Change in Neuropsychological Test Performance After External Lumbar Drain in Normal Pressure Hydrochephalus

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Abstract: The overall aim of this longitudinal study sought to examine the effect of both temporary (lumbar drain, LD) and permanent (ventriculoperitoneal shunt placement, VPS) cerebrospinal fluid diversion on neuropsychological functioning in a group of Veterans with suspected normal pressure hydrocephalus. As the initial phase in data analysis, we present data characterizing cohort demographics, shunt placement status, and neuropsychological test performance across several time points, including pre-LD, post-LD (3 days later), and at first follow-up (approximately 6 months post-LD). To date, 20 patients have completed pre-LD evaluations. This sample was predominantly older (average age = 73), male (95%) and all had completed at least high school or GED-equivalent (average years of education = 13.3, SD = 2.2). Nineteen patients had complete data for post-LD evaluation (testing discontinued for n = 1 patient). Regarding neuropsychological test performances, pre-LD performances (n = 20) were notable for at least moderate reduction (<5th percentile) in processing speed (45% of sample), basic auditory attention (45%)/working memory (45%), new learning (60%), memory (immediate, 75%; delayed, 75%; recognition, 60%), language (35%), executive functioning (70%) and fine motor speed (dominant hand, DH, 16.6%; non-dominant hand, NDH, 50%). Regarding mental health (MH) symptoms, less than half of the sample had elevated symptoms of anxiety (30%) or depression (30%). At post-lumbar evaluation (n = 19), moderately-reduced performances were found in processing speed (42%), basic auditory attention (36%)/working memory (36%), new learning (63%), memory (immediate, 68%; delayed, 63%; recognition, 63%), language (37%), executive functioning (47%), and fine motor speed (DH, 47%; NDH, 37%). On MH screen measures, elevations in anxiety (11%) and depression (21%) were again observed. Follow-up (approximately 6-month) data has been collected for 14 patients. More than half (55%) of the initial 20 patients had received VPS placement at the time of first follow up, which included 10 of 14 patients seen.

Research Topic: Neuropsychology
Funding agencies: None
Grant support: N/A

41. Evaluating Resilience Capacity in Response to COVID-19 Pandemic-related Stressors Among Mental Health Outpatients

Marquardt, Craig [1]; Venables, Noah [2]; Erbes, Christopher [2]; Davenport, Nicholas [2]; Disner, Seth [2]; Finn, Jacob [2]; Gilmore, Casey [2]; Kuzenski, Laci [2]; Hill, Jessica [2]; Chu, Carol [2]; Urošević, Snežana [1]

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Abstract: The COVID-19 pandemic has caused widespread psychosocial disruptions. There is public health interest in understanding which individuals with preexisting psychiatric conditions have heightened vulnerabilities to pandemic-related stressors or exhibit protective effects against worsening symptomatology. As part of ongoing quality improvement efforts at the Minneapolis VAHCS, 669 veterans receiving outpatient mental healthcare responded to surveys using Patient-Reported Outcomes Measurement Information System (PROMIS) symptom measures and measures of pandemic-related stressors and positive behavioral adaptations (Epidemic Pandemic Impact Inventory [EPII]). A subset of patients (n = 396) completed both pre-pandemic (Time 1) and during-pandemic (Time 2) assessments. Hierarchical linear regression with bootstrap confidence intervals was applied to distinguish between individual promotive/risk (i.e., main effect) and protective/vulnerability (i.e., moderation) factors in the context of stressor loading. As expected, stressor loading predicted both cross-sectional levels (β = .36, β = .46) and longitudinal increases (β = .19, β = .27) in depression and anxiety symptoms. Pre-existing internalizing psychopathology was a risk factor and predicted longitudinal increases in anxiety (β = .11; b = .35, 95% CI [.119 .580]) irrespective of individual stressor exposure. Percentage of positive behavioral adaptations enacted during the pandemic moderated stressor effects on changes in depression (β = -.23; b = -14.79, 95% CI [-25.46 -3.64]). Stressor effects were attenuated when greater percentages of positive change behaviors were endorsed, which was consistent with a protective effect. Higher pandemic stressor exposure poses a risk for increased depression and anxiety among individuals with common forms of internalizing and externalizing psychopathology. Nevertheless, behavioral activation and purposeful maintenance of social connections appear important for reducing the longitudinal impact of adverse life events.

Research Topic: Mental Health
Funding agencies: None
Grant support: N/A

42. Orexin in Dorsal Raphe Nucleus enhances Physical Activity and Energy Expenditure

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Abstract: Lateral hypothalamic (LH) orexin (OX) neurons modulate spontaneous physical activity (SPA), and energy expenditure (EE). Orexin deficiency results in weight gain, whereas heightened LH OX sensitivity results in obesity resistance. Orexins act on multiple brain sites, including the serotonergic dorsal raphe nucleus (DRN), which receives excitatory projections from the OX neurons. Our earlier studies show presence of both orexin-1 (OX1R) and orexin-2 receptors (OX2R) in DRN, and higher expression of OX1R and OX2R in DRN of obesity resistant (OR) rats. We hypothesized that OX in DRN enhances SPA and EE. Secondarily, we hypothesized that DRN GABA (gamma-aminobutyric acid) signaling mediates the effect of OX on SPA and EE. We manipulated OX tone in DRN either by direct injections of orexin A (OXA) into DRN or by chemogenetic activation of LH OX neurons in aged (~15 mo) orexin-cre mice. Mice were implanted with a guide cannula targeting DRN, and simultaneously prepared with the stimulatory (hM3Dq floxed) designer receptors exclusively activated by designer drugs (DREADD) virus in LH (N = 16). All mice recovered for 3 weeks to allow transfection of the DREADD virus, and randomly assigned to saline or clozapine N-oxide (CNO, DREADD activator) treatment. Mice were transferred to Promethion indirect calorimetry cages (Sable Systems International) to continuously monitor SPA and EE. Body weight and food intake were measured daily. After acclimation, mice received either IP vehicle or CNO (1 mg/kg) in a repeated measure design. Fifteen minutes prior to IP CNO or saline, animals were infused with either the GABA agonist muscimol (32.5 pmol/0.2 µl), GABA antagonist bicuculline (32.5 pmol/0.2 µl) or vehicle into DRN. In a separate experiment, either OXA (250 pmol/0.2 µl) or saline was injected into DRN without IP CNO injection, to study the direct effect of DRN OX on SPA and EE for 24h post-injection. We found that DREADD activation of LH OX neurons increases SPA and EE. Manipulation of GABA receptors (by muscimol or bicuculline) in DRN did not affect OX neuron activation induced enhancement of SPA. On the other hand, intra-DRN OXA enhanced SPA and EE in these mice up to 4h post-injection, without affecting food intake. These results show that OXA in DRN facilitates negative energy balance by increasing SPA induced EE. Thus, modulation of DRN OXA is a potential strategy to treat age-induced reductions in SPA and EE.

Research Topic: Endocrinology & Metabolism
Funding agencies: BLR&D
Grant support: 1I01BX003004, 1I01BX003687

43. Small Molecule Orexin Agonists Enhance Physical Activity, Cognition and Sleep Quality in Aged Mice

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Abstract: Aging affects physical activity, the sleep-wake cycle, and cognition, processes regulated in part by lateral hypothalamic orexin neurons and which influence obesity. We hypothesized that newly developed small molecule orexin agonists will mitigate age-related declines in these outcomes, which may reduce the propensity for obesity. Orexin tone was manipulated with peripheral injections of small molecule orexin receptor agonists (RTIOXA-47, RTIOXA-43, and RTIOXA-133) in middle aged (12-mo) mice. Cognition was measured using two-way active avoidance (TWAA) and contextual object recognition task (CORT) (after RTIOXA-47 and RTIOXA-133). An indirect calorimetry system was used to measure spontaneous physical activity (RTIOXA-47), and sleep-wake variables (after RTIOXA-47 and RTIOXA-43) were measured by telemetry. In adult (12 mo) mice, peripheral injection of RTIOXA-47 enhanced physical activity up to 4h post-injection. Peripheral injection of RTIOXA-47 or RTIOXA-133 increased discrimination index in the CORT, while decreasing latency and increasing total responses in the TWAA, indicating improved cognition. Similarly, RTIOXA-47 or RTIOXA-43 improved wake time, reduced sleep time (NREM and REM) and sleep/wake fragmentation. In addition, both RTIOXA-47 and RTIOXA-43 improved sleep/wake quality by decreasing the number of episodes and increasing the duration of these episodes. These results suggest that novel orexin agonists may have therapeutic potential for age-related obesity, sleep problems and cognition changes. Despite that orexin tone decreases with age, orexin receptors remain intact, which improves the therapeutic potential of their stimulation. Future studies of orexin neuromodulation during aging will focus on approaches to target orexin pathways with small molecule agonists.

Research Topic: Aging
Funding agencies: BLR&D
Grant support: 1I01BX003004, 1I01BX003687

44. Development of Moisture Management Liner and Active Cooling System for Improving Residual Limb Skin Care

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1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Socket comfort is a primary driver of satisfaction among individuals who use lower-limb prostheses. Studies show that shortly after the prosthetic socket is donned, socket temperatures can increase by 0.8 deg C. After 30 minutes of walking, socket temperatures can increase even further (2.5 deg C) and remain elevated long after activity cessation. To address this problem, Liberating Technologies, Inc. (LTI) and Vivonics, Inc. have developed a thermo-electric cooling-based module called the Intrasocket Cooling Element (ICE), which is embedded into the prosthetic socket to cool the residual limb. This study investigated the potential for the ICE system to cool the residual limb in a controlled laboratory environment and at home. Human-subject testing was conducted on ten experienced transtibial prosthesis users at the Minneapolis VA Health Care System and LTI. A certified prosthetist integrated the ICE system into a custom socket. Subjects wore a standard liner and if needed, thermally conductive gel socks. Residual-limb temperatures were measured before and after a 15-minute bout of treadmill exercise using a prospective, double-blinded, block-randomized, crossover study design. Two versions of the cooling system were evaluated in the same session: an active ICE cooling system (condition: ICE) and a placebo ICE system with a fan turned on but no cooling functionality (condition: SHAM). Treadmill speed was controlled between conditions and pre- and post-exercise intrasocket temperatures were measured at six sites on the residual limb using thermocouples. Following exercise, subjects rested for 45 minutes with their socket on, then doffed their socket for approximately 15 minutes to allow the residual-limb to return to baseline temperature levels. Testing was then repeated for the second socket condition. Subjects also completed at least one week of at-home testing with both socket conditions. The average temperature across all thermocouple sites was calculated pre-exercise (after the socket was donned) and post-exercise (at the end of the 45-minute rest period). As expected, the ICE system considerably reduced residual-limb temperatures compared to the SHAM condition. A clinical trial of the ICE system is currently underway to understand the impact of this technology on long-term health outcomes. Improvements in thermal socket comfort are expected to improve residual-limb skin health and increase prothesis use, leading to psycho-social and physical benefits.

Research Topic: Prosthetics
Funding agencies: DOD
Grant support: U.S. Army under Contract No. W81XWH-17-C-0005

45. Examining Mental Health Engagement Among Veterans Diagnosed with Serious Mental Illness

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1. Minneapolis VA Health Care System

Abstract: Veterans diagnosed with serious mental illness (SMI) are among the costliest consumers in the VA healthcare system, primarily due to the fact that these Veterans are the highest utilizers of inpatient hospitalizations. Psychosocial mental health services (PSR) have been demonstrated to help decrease the frequency and duration of costly inpatient hospitalizations. In spite of the growing evidence regarding the effectiveness of psychosocial mental health services, as well as the VHA's commitment to providing these services, engaging Veterans diagnosed with SMI in mental health psychosocial services remains a challenging task. This study explored and identified the factors related to engagement in psychosocial mental health services (individual therapy, skills training groups, education groups) among Veterans diagnosed with serious mental illness. Semi-structured, qualitative interviews conceptually based on the Theory of Planned Behavior were conducted with 36 Veterans diagnosed with SMI who received care at the Minneapolis VAHCS. Veterans were stratified into three groups: engaged in PSR, engaged in psychiatric care only, and not engaged in mental health care. Transcripts were summarized in a matrix of key domains and evaluated for themes. Mental health care was perceived as being valuable across groups. However, differences existed between groups regarding when people should seek care, as well as the specific aspects of care that were valuable. Veterans engagement groups also varied with regard to perception and response to stigma. Potential barriers to care were noted by Veterans in all engagement groups. These findings can help to inform delivery of care for Veterans diagnosed with SMI. The findings provide a means of reflecting on successes, areas for improvement, and missed opportunities in the provision of PSR services. Furthermore, they highlight the need to attend to all aspects of an individual's identity in the provision of services, thus speaking to the benefit of a comprehensive, recovery-oriented approach to the care of Veterans diagnosed with SMI.

Research Topic: Mental Health
Funding agencies: RR&D
Grant support: D6981R

46. Research Staff Burnout in a Large Scale, Randomized, Controlled, Point of Care Trial

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1. Minneapolis VA Health Care System
2. VA Boston Healthcare System

Abstract: Burnout can have a negative impact on job satisfaction and productivity. Antecedents to burnout include workload, control, values, fairness, reward, community and job-person incongruency. To better understand the impact of burnout in research staff, these seven antecedents to burnout were analyzed within the Diuretic Comparison Project. Consent to participate in the DCP was obtained over the phone. Two call centers were analyzed with respect to these antecedents to burnout. Consent rates and employee turnover of the two call centers were compared as a means of comparing productivity and job satisfaction, respectively. An odds ratio of 0.13 indicates that an employee at the Minneapolis call center had lower odds of leaving than an employee at the Canandaigua call center. Minneapolis had a consent rate that was 5.4 times higher than that of Canandaigua. The higher consent rate and lower turnover rate of the call center in Minneapolis may be a result of lower levels of burnout among callers. The protocol of the Minneapolis call center appears to take into consideration the antecedents to burnout more so than that of the Canandaigua call center. Research staff could benefit from strategies to help reduce burnout. Organizations should provide proper protocols and training concerning stress and burnout to improve the wellbeing of employees and, in turn, their productivity.

Research Topic: Health Care
Funding agencies: None
Grant support: N/A

47. Comparison of Monitored Anesthesia Care vs. General Anesthesia in Patients who underwent Transcarotid Artery Revascularization

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2. University of Minnesota

Abstract: TransCarotid Artery Revascularization (TCAR) is a hybrid procedure, introduced in 2012, for patients not eligible for carotid endarterectomy (CEA) or are at high risk for neurological events from Stenting. This procedure is indicated for patients with high anatomic risk, which includes restenosis post-CEA, neck irradiation, radical neck dissection, and cervical spine immobility. A recent retrospective study using the ACS NSQIP demonstrated lower mortality and morbidity in patients with managed anesthesia care (MAC) vs. general anesthesia (GA). There are also no similar studies in the VA population. The objective of this study was to characterize the intraop- and post-operative hemodynamic profile of patients undergoing the TCAR procedure under MAC or GA. This was a retrospective study of veterans who received the TCAR procedure at the Minneapolis VA between 1/2015 and 1/2020 (n=47) after IRB submission. Patient EMRs were used to record preoperative, intraoperative and postoperative data. Patients were categorized by anesthetic type, GA or MAC. The primary outcomes were intraoperative hypotension (systolic BP<90 mmHg) and bradycardia (HR<50 bpm), as well as % change from baseline for both outcomes, pressor use and mortality directly related to the procedure. In addition, case duration and length of stay was compared. Continuous data were expressed as mean (SD) and categorical data as counts and percentages. Further exploratory analysis were conducted based on the primary descriptive data results. Results: There were 33 patients in the GA and 14 patients in the MAC group. There were no statistically significant differences with respect to demographic and preoperative clinical data and comorbidities between the 2 groups. MAC vs. GA groups data: age 73.8(6.5) and 72.7(7.1), baseline SBP was 149.4(23.7) and 144.5(18.4), baseline HR 67.7(6.6) and 68.6 (12). 36% of the MAC group vs. 58% of the GA had at least on hypotensive episode. (p=0.17). 14% of the MAC group vs. 24% of the GA group had a least one bradycardic episode (p=0.336). All patients received at least one dose of intraop vasopressor. There was a trend toward lower amounts of vasopressors (phenylephrine) use in the MAC group. There were no difference in PACU and hospital LOS This pilot study did not demonstrate major differences in preop and post op data among the GA vs. MAC groups except for a trend towards a lower incidence of intraop hypotension, bradycardia and vasopressors in the MAC group.

Research Topic: Anesthesiology
Funding agencies: None
Grant support: N/A

48. Community Reintegration for Service Members and Veterans with Traumatic Brain Injury: A Scoping Review

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2. Minneapolis VA Health Care System
3. HealthPartners Institute

Abstract: Objective: Since 2000, The Defense and Veterans Brain Injury Center reports that nearly 414,000 traumatic brain injuries have been diagnosed by among Service Members. Brain injury impacts multiple body systems resulting in the mood disorder, functional impairment, and pain, which often cause barriers to return to work. Although previous work has investigated return to work outcomes for patients with traumatic brain injury (TBI), little is known about how to improve outcomes for United States Service Members and Veterans who face unique psychosocial issues associated with military service. Our objective is to evaluate the current literature related to vocational outcomes among our Service Members and Veterans. Design: Ovid Medline, PsycINFO, Embase, CINAHL Plus, Cochrane Library, Scopus, SPORTDiscus databases were queried for human studies published in English between the database inception and January 15, 2020. We included studies that focused on United States Service Members and Veterans who sustained TBIs and their vocational outcomes. Conference abstracts, systematic reviews, literature reviews, editorials, consensus reports, commentaries, dissertations and qualitative studies were excluded. Two rounds of independent reviews were performed. Details of study design, intervention, and vocational outcomes were recorded. Results: The search yielded 5,667 articles; 54 articles met inclusion criteria. 49 studies were observational (91%), 5 were randomized control trials. Majority of interventions were in the outpatient setting (71%). Interventions related to return to work and school utilized Physical Therapy and Occupational Therapy to address cognitive skills, functional deficits, and provide supportive employment. Conclusion: Brain injuries among Veteran community reintegration research is underdeveloped. Due to heterogeneity of severity and smaller sample sizes, no consensus on interventions that with improve vocational outcomes. Evidence thus far suggest that future studies should incorporate an interdisciplinary team approach beyond Physical Therapy and Occupational Therapy.

Research Topic: Rehabilitative Medicine
Funding agencies: None
Grant support: N/A

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49. Examination of Poor Sleep Quality on Subjective Well-Being and Objective Functioning in Patients with Schizophrenia

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1. Minneapolis VA Health Care System

Abstract: Disturbed sleep is common among individuals with schizophrenia. The study aim was to investigate whether poor sleep quality contributed to subjective well-being and performance on measures of cognition and functional capacity independent of symptom severity. Data was collected from 67 outpatients with schizophrenia or schizoaffective disorder. Symptom severity and sleep quality were assessed with the BPRS and the PSQI. Well-being was measured with the BPNS and the MIC-SR. Community functioning was measured with the SFS. Cognition and functional capacity were assessed with the MCCB, SSPA, and UPSA. Poor sleep quality was reported by 67% of the sample. Sleep quality and mood symptom severity were related to each other, and both related negatively to psychological well-being, perceived cognitive problems, and self-reported interpersonal engagement. Regression analyses revealed that sleep quality made a significant independent contribution to two facets of psychological well-being as well as patient perception of interpersonal engagement and frequency of cognitive problems in daily life. Unexpectedly, sleep quality was not significantly related to performance on measures of cognition and functional capacity. Findings indicate that poor sleep quality is prevalent and compromises subjective well-being. Results suggest that treatment of schizophrenia might be improved through routine assessment and treatment of sleep quality.

Research Topic: Psychiatry
Funding agencies: RR&D
Grant support: D6981R

50. Geocoding Participant Addresses to Study Neighborhood Disadvantage within Survey Research

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1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Childhood and adolescent environments can have lasting effects on behavior and functioning into adulthood. In particular, the quality of our neighborhoods and ease of access to community socioeconomic resources may be an important contributor to later cognitive functioning and personality development. This project presents methods for 'geocoding' current addresses among a sample of new military recruits (n = 610) in the Minnesota National Guard. Environmental resource access was determined using the Area Deprivation Index (ADI), a composite score of 17 census variables that approximates disparities between census tracts in the United States. This HIPPA-compliant geocoding method was accomplished using the DeGAUSS software application, which runs on local computers and does not expose personally identifiable information to external internet services. For this sample of new recruits, we observed a wide range current neighborhood disadvantage. ADI was negatively associated with cognitive functioning at the time of entry into the National Guard, even when covarying for past education, age, and self-reported history of prior life stressors. Follow-up analyses revealed indirect effects of ADI on the personality domain of Constraint (i.e., trait-level control over behavior) by way of cognitive functioning. Specifically, this indirect effect was most relevant for predicting increased levels of the personality sub-domains of Harm Avoidance and Traditionalism. Similar indirect effects were not observed for other personality domains of positive and negative emotionality. These findings demonstrate the potential utility of considering neighborhood quality within large-scale surveys focused on mental health and functioning outcomes. Access to community resources may play a unique role in shaping cognitive functioning and personality during emerging adulthood.

Research Topic: Behavioral Sciences
Funding agencies: None
Grant support: N/A

51. Reopening Clinics in the COVID-19 Era: an approach to risk stratification

Okamoto, Casey [1]; Macedo, Franz [1]; Paidin, Mark [1]; Branson, Richard [1]; Knuff, Stephen [1]; Lauck, James [1]; Kesha, Ranjit [1]; Gravely, Amy [1]

1. Minneapolis VA Health Care System

Abstract: This article describes the development of a risk-stratification tool for identifying veterans at elevated risk of mortality following infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Quantifying a patient's risk informs clinical decisions about when and for what purposes a patient may need to be seen in-person or via telehealth. This tool was developed in the early stages of the pandemic when limited data was available and without the use of sophisticated computer modeling. We began by conducting a review of comorbid conditions commonly associated with SARS-CoV-2-related critical illness or death. Odds ratios, relative risks, hazard ratios, and comparative prevalence data were used to estimate the contribution of each comorbid condition to the outcome of mortality. Based on these estimates a tool was developed and subsequently validated using early (March 2, 2020 - May 27, 2020, n=12,206) and late (June 1, 2020 to October 1, 2020, n=40,952) validation cohorts representing all positive cases within the Veterans Health Administration (VHA) over their respective time periods. The areas under the receiver operator characteristic curve were 0.76 and 0.80 for the first and second data sets, respectively. The process by which this tool was developed and implemented in the early stages of the pandemic may serve as an example of how to risk-stratify at the outset of a future pandemic when choosing to deliver healthcare in-person versus via telehealth.

Research Topic: Health Care Delivery
Funding agencies: None
Grant support: N/A

52. Lateral Hypothalamus Orexin Displays Sex- and Age-Dependent Effect on Learning and Memory

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1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Lateral hypothalamus (LH) orexin neurons project onto the hippocampus. The underlying role of the LH in reward and reinforcement combined with the hippocampus's role in learning and memory suggests a dynamic effect on cognition. Our earlier studies support a relationship between orexin and cognitive performance by showing a reduced number of orexin neurons and impaired memory in orexin-ataxin mice, as well as loss of orexin neurons and impaired memory in older mice. We hypothesized stimulation of orexin neurons restores memory in older mice and the extent of this effect would vary between sexes of the same age group. We manipulated orexin tone by chemogenic activation of LH orexin neurons in two groups of aged (~15 mo, ~18 mo) orexin-cre mice (N=12). Mice were prepared with the stimulatory (hM3Dq-floxed) designer receptors exclusively activated by designer drugs (DREADD) virus in LH, recovered for 3 weeks to allow virus transfection, and randomly assigned to saline or clozapine N-oxide (CNO, DREADD activator) treatment. Mice completed three tests for hippocampus-dependent learning and memory (Barnes maze, contextual object recognition (CORT), two-way active avoidance (TWAA)), and received their assigned treatment at the end of training and tested after 24 hours. Activation of LH orexin neurons increases CORT discrimination index in aged female mice, reduces TWAA latency in aged male mice, and increases number of escapes in aged male mice in TWAA. These results support sex being an influential factor in the role of LH orexin on learning and cognition. Orexin's role in cognition may vary between sexes during stages of aging and type of learning (aversive vs. non-aversive), and could be a target in geriatric care.

Research Topic: Aging
Funding agencies: None
Grant support: N/A

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53. Engaging Veteran stakeholders in early-stage research: The key to developing novel self-management approaches.

Rich, Tonya [1-2]; Phelan, Hannah [1,3]; Matsumoto, Mary [1-2]; Gravely, Amy [1]; Hansen, Andrew [1-2]; Goldish, Gary [1-2]; Voss, Greg [1]; Fairhurst, Stuart [1]; Egginton, Jason [4]; Looft, John [1]; Olney, Christine [1]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Medical College of Wisconsin
4. Mayo Clinic

Abstract: Sustained behavior change is a core component of many rehabilitation interventions and when accomplished, long term improvement in function and participation in daily life can result. However, facilitating successful behavior change is enigmatic, posing unique research challenges. In the Minneapolis Design & Engineering (MADE) Program, we study medical devices and intervention development to support improved functioning in Veterans' daily life. The MADE group engages with stakeholders at all phases of research (e.g., preliminary to research, during iteration, during or after testing, during industry collaboration). By incorporating stakeholder feedback, through multiple approaches, we can design, identify, and test solutions to everyday problems that prevent full engagement in daily life and embracing change. METHODS: Our group has recently completed two studies using Veteran-informed approaches by utilizing focus groups and interviews with Veterans with spinal cord injury (SCI) at risk for pressure injuries and individual interviews in Veterans with amputations who experience phantom limb pain. RESULTS: 1) Iterative focus groups with Veterans with SCI (n=7) informed engineers regarding problems encountered with trunk control, the need for a trunk control device, and identified key features required in a successful, usable trunk control device. A prototype was developed based on the focus group feedback. 2) Individual interviews with Veterans experiencing phantom limb pain (PLP) (n=50) were conducted to inform future intervention design. We first needed to investigate the effect of PLP on daily life and how standardized clinical measures capture this unique type of pain. We learned that PLP is a heterogeneous experience and limitations exist in pain outcome measures. CONCLUSIONS: Including the voice of the Veteran in early-stage research and throughout the research process is a necessary component to achieving sustained behavior change. Our experiences suggest that by gathering informant feedback early in the research process, we can develop practical solutions to improve the care and self-management of chronic conditions and enhance sustained behavior change.

Research Topic: Rehabilitative Medicine
Funding agencies: RR&D
Grant support: 1IK1RX003216, MN Spinal Cord Injury and Traumatic Brain Injury Research Grant Program through the MN Office of Higher Education

54. Accuracy of Self-Reported Risk Factors for Hydroxychloroquine Retinopathy

Santilli, Christopher [1]; Garbo Maxey, Amy [2]; Lattery, Christine [2]; Carpel, Emmett [1-2]; Armbrust, Karen [1-2]

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2. Minneapolis VA Health Care System

Abstract: Purpose: Hydroxychloroquine (HCQ) is an effective and typically well-tolerated anti-inflammatory medication, but retinal toxicity is a potential side effect. Current screening guidelines specify retinal examination within the first year of treatment and then yearly examination with visual field and optical coherence tomography after 5 years of HCQ use. The presence of HCQ retinopathy risk factors such as HCQ duration > 5 years, HCQ daily dose > 5 mg/kg real body weight, tamoxifen use, or renal disease should increase suspicion for retinopathy and may modify the retinopathy screening timeline. Identifying these risk factors requires taking a patient history or reviewing the electronic health record (EHR). The primary goal of this study is to evaluate whether the patient interview accurately identifies HCQ retinopathy risk factors, and the secondary goal is to evaluate whether eye care providers accurately identify these risk factors. Methods: After informed consent, all 93 study subjects completed an in-person interview survey regarding HCQ retinopathy risk factors. We reviewed the eye care provider note at the study visit and queried the EHR for HCQ retinopathy risk factors, cognitive diagnoses, and psychiatric diagnoses. After identifying subjects with HCQ retinopathy risk factors by EHR review, we determined whether the subject interview and eye care provider note identified these risk factors. Results: The patient interview identified HCQ duration > 5 years in 75% of cases but was less successful at identifying HCQ daily dose > 5 mg/kg and renal disease. Similarly, the eye care provider note identified HCQ duration > 5 years but not HCQ daily dose > 5 mg/kg or renal disease in most cases. The presence of a cognitive or psychiatric diagnosis did not reduce self-reporting accuracy: 4/9 (44%) subjects with a cognitive disorder, 8/28 (29%) subjects with a psychiatric diagnosis, and 19/42 (45%) subjects with neither cognitive nor psychiatric diagnoses did not correctly report all HCQ risk factors. Conclusion: Solely using the patient interview or prior eye care provider notes may not consistently identify HCQ retinopathy risk factors. Optimizing EHR use, with either manual review carried forward or automated templates, would improve quality of care in HCQ retinopathy screening.

Research Topic: Ophthalmology
Funding agencies: None
Grant support: N/A

55. Change in Hemoglobin A1c After Cataract Surgery

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2. Minneapolis VA Health Care System

Abstract: Purpose: To determine if hemoglobin A1c (HbA1c) levels change after cataract surgery. Design: Retrospective observational single-site study. Subjects: There were 436 total subjects recruited from the Minneapolis Veterans Affairs Health Center with 424 males and 12 females. The mean age of the subjects was 71 years. Methods: Post-operative HbA1c levels 3-6 months after and 2 years after cataract surgery were compared to pre-operative HbA1c. Subgroup analysis was based upon age and elevated (>8) pre-operative HbA1c. The change in best corrected visual acuity (VA) before and after cataract surgery was compared to the change in HbA1c. Main Outcome Measures: The main outcome measure was the difference in HbA1c prior to and 3-6 months after cataract surgery. Secondary outcome measures were (1) the difference in HbA1c prior to and 2 years after cataract surgery and (2) the correlation between the pre-operative and post-operative changes in HbA1c and VA. Results: Pairwise comparison of pre-operative versus post- operative HbA1c showed a trend towards reduction at 3-6 months in all subjects, with a statistically significant HbA1c reduction at 2 years for all subjects. There was also significant reduction in HbA1c at 3-6 months and 2 years in older subjects and those with higher pre-operative HbA1c levels. There was little to no correlation between the degree of improvement in HbA1c and visual acuity, however the higher pre-operative HbA1c subgroup had the largest improvement in VA and HbA1c 3-6 months after surgery. Conclusions: HbA1c levels improved after cataract surgery, especially in older subjects and those with higher pre-operative HbA1c values. While the exact reason for improved HbA1c after cataract surgery remains unknown, this study suggests that cataract surgery offers an opportunity for better glycemic control as well as visual function.

Research Topic: Ophthalmology
Funding agencies: None
Grant support: N/A

56. Implementation of Liposomal Bupivacaine for Pain Management in Patients Undergoing Total Shoulder Arthroplasty: A Quality Improvement Project

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2. University of Minnesota

Abstract: Problem/Background: Pain associated with Total Shoulder Arthroplasty (TSA) has traditionally been managed using a continuous interscalene nerve block (CISB) that remains in place for up to five days, but has known risks and limitations. Liposomal bupivacaine (LB) is a new long-acting local anesthetic that eliminates the need for a catheter and is FDA approved for single-shot interscalene nerve blocks. This project aimed to demonstrate comparable pain management of LB in patients undergoing TSA when compared to historical data of patients who received CISB. Overall narcotic use, pain scores through post-operative day three, and intraoperative vital sign variation and Propofol infusion rates were analyzed to identify efficacy of the block. Strategy: Patients scheduled for TSA were evaluated for block placement prior to surgery. Those deemed appropriate for a regional block received LB and underwent surgery with Monitored Anesthesia Care (MAC) with continuous sedation. Methods: A retrospective chart review for TSA patients receiving either CISB or LB during the specified date range was completed. Data pertaining to intraoperative vital signs, Propofol infusion rates, postoperative pain scores, and opioid narcotic use were recorded. Results: The LB group had a statistically significant reduction in heart rate (CISB: 77.50, LB: 70.41, p=0.029) and respiratory rate (CISB: 18.22, LB: 16.04, p=0.020) in the Post-Anesthesia Care Unit. No other statistically significant differences were found between patients receiving LB for TSA and those who had received CISB. Patients receiving LB and CISB had comparable vital sign variability at incision and had comparable rates of conversion to general anesthesia. Both patient groups also demonstrated comparable opioid consumption, measured via Morphine Equivalent Units (MEUs) through postoperative day three. LB recipients trended toward a slightly higher Propofol infusion dose than CISB catheter recipients, though it was not a statistically significant increase. Conclusion: Overall, the patients who received LB for TSA demonstrated comparable pain control to a historical cohort of patients who received CISB for TSA.

Research Topic: Anesthesiology
Funding agencies: None
Grant support: N/A

57. Association of covert brain infarcts and white matter hyperintensities with risk of incident hip fracture in older adults: The Cardiovascular Health Study

Sheets, Kerry [1-3]; Buzkova, Petra [4]; Chen, Zhao [5]; Carbone, Laura [6]; Cauley, Jane [7]; Barzilay, Joshua [8]; Starks, Jamie [1-2]; Miller, Lindsay [9]; Fink, Howard [1-2]

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2. University of Minnesota
3. Hennepin Healthcare
4. University of Washington
5. University of Arizona
6. Augusta University
7. University of Pittsburg
8. Kaiser Permanente of Georgia
9. University of California San Diego

Abstract: Incidental markers of cerebrovascular microvascular disease such as covert brain infarcts and white matter hyperintensities (WMHs) are common and associated with falls, gait and balance impairment, and lower bone mineral density. However, the association between covert brain infarcts, WMHs, and incident hip fracture, an outcome associated with significant functional disability for older adults, is not clear. We used data from the Cardiovascular Health Study (CHS), a longitudinal, multi-site cohort of community-dwelling men and women aged > 65 years, to evaluate the association of covert infarcts and WMHs with risk of incident hip fracture. The analytic cohort consisted of 3,373 adults (mean age 75 years) with a brain MRI in years 1992-1994 and without a confirmed history of stroke or transient ischemic attack prior to the MRI. Covert infarcts were categorized by number of infarcts and size of largest infarct (3 to <20 mm vs. >20 mm); WMH extent was assessed visually by radiologists and graded from zero to nine. Incident hip fractures were identified from review of hospital and Medicare records. Risk of incident hip fracture was estimated using Cox hazards regression. There were 465 incident hip fractures during a mean follow-up of 12.8 years. The unadjusted incidence rate was 1.03 per 100 person-years (95% confidence interval [CI], 0.89-1.20) among participants without covert infarct and 1.41 (95%CI, 1.08-1.83) among participants with > 1 covert infarct(s). The hazard of incident hip fracture after adjustment for demographics, medications, medical history, functional status, and falls was 25% higher among participants with any covert infarct compared to those without infarcts (hazard ratio [HR] 1.25; 95%CI, 0.99-1.57). Incident hip fracture risk per increase in infarct number was 1.10 (95%CI, 0.98-1.23); risk in individuals whose largest infarct was 3 to <20mm versus >20mm appeared similar. Among participants with WMH grades 0-1, 2-3 and 4-9, the unadjusted incidence rate per 100 person-years was 0.83 (95%CI, 0.66-1.03), 1.23 (95%CI, 1.02-1.50) and 1.81 (95%CI, 1.35-2.42), respectively. Compared with WMH grade 0-1, the multivariable-adjusted hazard of incident hip fracture was 1.24 (95%CI, 0.98-1.56) for grade 2-3 and 1.34 (95%CI, 0.95-1.90) for grade 4-9, respectively. Our results show older, community-dwelling adults with covert infarcts and/or WMHs may be at increased risk of future hip fracture.

Research Topic: Geriatrics
Funding agencies: NIH
Grant support: HHSN268201200036C, HHSN268200800007C, HHSN268201800001C, N01HC55222, N01HC85079, N01HC85080, N01HC85081, N01HC85082, N01HC85083, N01HC85086, 75N92021D

58. COVID-19 Telehealth Engagement among Community-Dwelling Older Adults

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Abstract: The COVID-19 pandemic has exacerbated pre-existing physical and mental health disparities among older adults (Morley & Vellas, 2020). Pre-COVID literature promotes telehealth as innovative, feasible, and acceptable among older health consumers (Kruse et al. 2020), including those with health burden (Guo & Albright, 2017), pain (Bhattarai & Phillips, 2017), and mild cognitive impairment (MCI; LaMonica et al., 2017). The present study investigated telehealth engagement among community-dwelling adults (n = 84, 52.8% male) aged 65-90 years (M = 73.87, SD = 6.00) during the COVID-19 pandemic. Participants were enrolled in an NIH R01 longitudinal study and completed a self-report Telehealth Use Survey (Kurlander et al., 2019). Exploratory analyses found few significant differences in telehealth engagement between MCI (n = 38, 45.2%) and cognitively intact (n = 46, 54.8%) older adults. Cognitively intact older adults were more likely to be offered telehealth visits with specialists, .2 (3, n = 58) = 9.42, p = .02, but among older adults not offered such visits, those with MCI endorsed higher interest, .2 (1, n = 43) = 7389, p = .01. Exploratory correlations across the subsample (n = 84) revealed that older age was related to less social video calling, r(70) = -.28, p = .04, less concern with physical exam unavailability, r(70) = -.28, p = .03, and higher confidence in telehealth efficacy, r(70) = .29, p = .03. Older adults with higher health burden, r(70) = .36, p = .01 and lower energy-related quality of life, r(70) = -.28, p = .03 attended more telehealth visits in the past year. In contrast, higher energy-related quality of life was associated with more frequent social video calling, r(70) = .30, p = .03. Older adults with lower pain-related quality of life were less likely to attend primary care telehealth visits in the past year, r(70) = .49, p = .001, and were more likely to identify physical exam unavailability as a telehealth concern, r(70) = -.33, p = .01. Results suggest that telehealth may be acceptable and feasible among older adults, including those with MCI. Characteristics such as age, health burden, pain, and fatigue contributed to telehealth engagement and may inform health care delivery during and after the COVID-19 pandemic crisis.

Research Topic: Geriatrics
Funding agencies: NIH
Grant support: R01AG058687

59. The Role of Microglial Fatty Acid Signaling in Alzheimer's Disease

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Abstract: Obesity and associated comorbidities such as metabolic syndrome and diabetes affect up to 48% of Veterans, and are known risk factors for cognitive impairment and development of Alzheimer's disease. The incidence of these neurodegenerative diseases may be higher in Veterans than in the general population. Our ongoing preclinical research supports that the onset of brain immune response (neuroinflammation) represents a link between obesity and cognitive impairment. This may represent a common link between altered fatty acid metabolism and lipid transport in AD. Fatty acid stimulation of immune cell activation links the fatty acid binding protein uncoupling protein-2 (FABP4-UCP2) axis as a potential mechanism by which HFD exacerbates neuroinflammation and AD pathology. Our overall hypothesis is that obesogenic diets impair metabolic adaptation in microglia and exacerbate ongoing AD neuropathology. In microglia, we have demonstrated that the loss of FABP4 results in increased UCP2 expression. UCP2 upregulation opposes the onset of proinflammatory cytokines and oxidative stress. Conversely, loss of UCP2 in microglia potentiates NFκB pro-inflammatory pathways via the FABP4-UCP2 axis. The onset of inflammation is driven by metabolic shifts in the tricarboxylic (TCA) cycle. Polarization of microglia is regulated by shifts in glycolysis and β-oxidation. Our preliminary data demonstrate that inhibition of FABP4 drives shifts in TCA cycle utilization and in gene expression of immune responsive gene-1 protein, a key mitochondrial TCA enzyme. Further, our preliminary data show a decrease in UCP2 expression in hippocampal tissue from an AD rodent model (APPswe/PS1.E9 transgenic mice). Collectively, our work supports that the FABP4-UCP2 axis represents a strategic therapeutic target in preventing diet-induced cognitive decline. Our proposed studies will establish whether FABP4 mediates pro-inflammatory effects of Aβ, and characterize the FABP4-UCP2 axis as a novel therapeutic target for AD.

Research Topic: Basic Sciences
Funding agencies: BLR&D; UMN; CVRE
Grant support: 1I01BX004146, CVRE, AARGD-17-505409, UMN HFHL

60. Investigation of Postoperative Delirium in the Setting of Ambulatory Surgery in a US Veteran Population

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Abstract: Background: Postoperative delirium is a common complication in older patients hospitalized after major orthopedic surgery. However, little is known about postoperative delirium in patients undergoing ambulatory orthopedic surgery. The aim of this study was to quantify patient-specific risk factors for postoperative delirium in a U.S. Veteran population undergoing shoulder arthroscopy in an outpatient setting. Methods: A single-center retrospective review of electronic medical records for 100 patients who underwent ambulatory shoulder arthroscopy in 2019 was conducted at a single VA facility. Patient-specific risk factors were recorded, including demographics, medical comorbidities, neuropsychiatric conditions, and medications. Descriptive analysis was performed to summarize data sets. Results: U.S. Veterans undergoing ambulatory shoulder surgery had an average age of 56 years (+/-14.5, range: 28-78), 90% were male, and the average Charlson Co-morbidity index was 1.5 points (+/-1.5, range: 0-6). The most common health risk factors for postoperative delirium included depression (36%), antidepressants (35%), sleep deprivation/disturbance (28%), antihistamine use (17%), and hearing impairment (13%). For 73% of patients, 1 or more risk factors were present, 51% had 2 or more, and 38% had 3 or more. Conclusions: Most U.S. Veterans undergoing ambulatory shoulder surgery had 2 or more health risk factors for postoperative delirium. Our findings led to the creation of preoperative educational material, 'Is your loved one confused after surgery?' which is now provided to all patients' caretakers to improve their awareness of this potential postoperative complication. Further prospective study is needed to determine if patient-specific risk factors and/or other factors (i.e. anesthesia type) correlate with postoperative delirium after ambulatory orthopedic surgery in a U.S. Veteran population.

Research Topic: Orthopedic Surgery
Funding agencies: None
Grant support: N/A

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61. CSP 2014: Comparative Effectiveness of Two Formulations of Buprenorphine for Treating Opioid Use Disorder in Veterans (VA BRAVE)

Swanson, Heather [1]; Dickmann, Patricia [1]; Steen, Katie [1]; Westermeyer, Joseph [1]

1. Minneapolis VA Health Care System

Abstract: CSP 2014 (Comparative Effectiveness of Two Formulations of Buprenorphine for Treating Opioid Use Disorder in Veterans (VA-BRAVE)) is part of VA's initiative to improve healthcare, and specifically improve treatment for veterans with opioid use disorder (OUD). The purpose of this study is to understand whether buprenorphine given in a monthly injection form works similarly to or better than buprenorphine taken daily in an oral form (the standard of care) and determine if one of the two forms is better at helping Veterans stay in treatment for OUD and limit their drug use behaviors. This is a large, open-label and randomized nation-wide trial that will include ~900 male and female veteran patients from ~20 VA medical centers across the country. Secondary goals of the study are to examine comorbid substance use, fatal and non-fatal overdose, HIV and HCV testing results and risk behaviors, incarceration, quality of life, psychiatric symptoms of depression and posttraumatic stress disorder, housing status, and cost-effectiveness. Participants have a 50:50 chance of receiving one of the two forms of buprenorphine. All participants start receiving oral buprenorphine, then are randomized and will receive either a 28 day supply of sublingual buprenorphine or come in and receive an injection every 28 days at study visits. Active participation will last for 1 year and involves weekly study visits for the first 4 weeks then study visits every two weeks until the end of 52 weeks. Study visit activities include periodic blood draws (e.g. hepatitis panel, HIV, liver function tests, blood buprenorphine levels), EKG, a physical exam, and each study visit will involve a urine sample to test for opioids, pregnancy test, medication management, and questionnaires and clinical interviews.

Research Topic: Drug Dependence
Funding agencies: None
Grant support: N/A

62. β-blocker dialyzability and adverse cardiovascular outcomes in hemodialysis patients: A meta-analysis

Tella, Abhinav [1]; Vang, William [1]; Ikeri, Eustacia [1]; Taylor, Olivia [1]; Zhang, Alicia [1]; Mazanec, Megan [1]; Raju, SriHari [1]; Ishani, Areef [1]

1. Minneapolis VA Health Care System

Abstract: There is conflicting evidence regarding the type of beta blocker to use in dialysis patients. This meta-analysis seeks to determine whether highly dialyzable β-blockers are associated with higher rates of cardiovascular events and mortality in hemodialysis patients compared to poorly dialyzable β-blockers. A systematic review of existing literature was conducted. Selected studies were evaluated for quality using the ROBINS-I tool. A meta-analysis was performed using data from selected studies. This meta-analysis examined a total of 75,165 adult hemodialysis patients taking beta-blockers: 40,289 on highly dialyzable β-blockers and 34,876 on poorly dialyzable β-blockers. The studies involved patients in the U.S., Canada, and Taiwan. We developed a search string and searched OVID MEDLINE from 1990 through September 2020. Exclusion criteria eliminated articles without adult hemodialysis participants and without comparisons of at least two β-blockers of different dialyzability. Baseline and outcomes data were extracted from each study and pooled by cohort. In RevMan5, random effects models were used to calculate pooled risk ratios. For the adjusted hazard ratio analysis, Highly Dialyzable Beta Blockers had a hazard ratio of 0.94 [CI: 0.81-1.08] compared to Poorly Dialyzable Beta Blockers for All Cause Mortality and a hazard ratio of 0.88 [CI: 0.83-0.93] in comparison to Poorly Dialyzable Beta Blockers for Cardiovascular Events. Through OVID medline, 78 articles were discovered. An abstract screening resulted in an exclusion of 74 articles. Limitations include the misclassification of beta blockers in one study, pooling of data from cohort studies that used different analytic methods for comorbidity adjustment and the lack of randomized controlled trials. Pooling of the data suggests use of highly dialyzable beta blockers in hemodialysis patients reduces both cardiovascular events and all cause mortality compared to using poorly dialyzable beta blockers.

Research Topic: Cardiovascular Disease
Funding agencies: None
Grant support: N/A

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63. Timing of Brain Responses During Word Processing and Recognition: Associations with Posttraumatic Reexperiencing Symptomatology

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Abstract: Individuals with posttraumatic stress disorder (PTSD) commonly experience impairments in verbal learning and memory. In particular, reexperiencing symptoms of PTSD exhibit associations with verbal memory performance in terms of inefficient encoding and worse word recall. In this study, previously deployed veterans (n = 140) completed a laboratory task separately assessing facets of verbal memory such as encoding, implicit repetition priming, and recognition. We observed associations between the latency of event-related potentials (ERPs), behavioral response times, and reexperiencing symptoms of PTSD. The timing of the late positive component (LPC) from 475-1000 ms at the electrode site Pz was associated with recognition memory performance for word stimuli. In addition, there were associations between latency of LPC and response times during the encoding and implicit repetition priming phases of the task. Finally, LPC latency was associated with reexperiencing symptoms during implicit repetition priming and word recognition. These findings indicate that the timing of LPC has associations with multiple facets of verbal memory performance as well as reexperiencing symptoms of PTSD, thus revealing an important link between PTSD-related verbal memory impairments and brain responses.

Research Topic: Posttraumatic Stress Disorder (PTSD)
Funding agencies: DOD
Grant support: N/A

64. Gout Uric Acid Testing at Home

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1. Minneapolis VA Health Care System

Abstract: Uncontrolled gout is very painful, leads to frequent visits to the ER, and often ordering of unnecessary x-rays. This project is important as we have found an innovative approach to managing gout that we think has never been done before. Similarly, like patients who have diabetes and a glucose meter, we are going to issue uric acid meters so patients can monitor their uric acid at home. It is important as autonomy promotes self-care and medication compliance.

Research Topic: Rheumatology
Funding agencies: None
Grant support: N/A

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65. Impact of Repeated tDCS Administration on Psychiatric Symptoms in Veterans with Mild Traumatic Brain Injury

Wing, Erik [1]; Yamada, Torricia [1]; Gilmore, Casey [1]; Lamberty, Gregory [1]; Nelson, Nathaniel [2]; MacDonald, Angus [3]; Thuras, Paul [1]; Lim, Kelvin [1]; Rust, Andrew [1]; Schulte, Cody [1]; Nienow, Tasha [1]

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Abstract: An innovative treatment approach for mild Traumatic Brain Injury (mTBI) is transcranial direct current stimulation (tDCS), a non-invasive brain stimulation technique that utilizes low levels of electrical current to activate targeted brain regions (e.g., Dorsal Lateral Prefrontal Cortex – DLPFC). When paired with cognitive training, several studies have found a promising effect of tDCS, as compared to sham stimulation, on cognitive impairment in TBI populations (See Zaninotto et al 2019 for systematic review). Less is known about the impact of tDCS on psychiatric symptom severity among those with mTBI. The aims of the present study were to assess the relationship between psychiatric symptom severity at baseline and study dropout, as well as to assess reductions in psychiatric symptoms as a function of tDCS facilitated cognitive training. Forty-one veterans with mTBI were enrolled in a double-blind, sham-controlled trial providing 24 sessions of cognitive training supplemented with either concurrent anodal tDCS targeting the DLPFC or sham stimulation. Psychiatric symptom severity was assessed pre- and post-intervention with the Patient Health Questionnaire-9 (PHQ-9), Patient Health Questionnaire-15 (PHQ-15), PTSD Checklist for DSM-5 (PCL-5), and the Neurobehavioral Symptom Inventory (NSI). Study completion was defined as completing at least 80% of study training sessions. Only one difference in symptom severity at baseline was found between study completers and those who withdrew. Study completers ($n = 18$, $M = 12.5$, $SD = 5.78$) reported significantly higher levels of depressive symptoms at baseline than participants who withdrew ($n = 23$, $M = 8.04$, $SD = 4.89$), $F_{(1, 39)} = 7.14$, $p = .01$. Repeated measure ANOVAs assessing symptom change amongst completers found that those receiving sham stimulation ($n = 8$) reported a greater decrease in NSI-affective symptoms than those receiving tDCS ($n = 10$), $F_{(1, 16)} = 4.71$, $p = .045$, with no other statistically significant differences. In conclusion, moderate levels of psychiatric distress were not found to cause treatment dropout. In fact, increased depressive symptoms (i.e., to a moderate level of severity) might actually promote completion of tDCS treatment. However, tDCS facilitated cognitive training did not contribute to psychiatric symptom reduction beyond that found with a sham control. Results should be interpreted cautiously given the small sample size and low statistical power.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: None
Grant support: State of Minnesota Office of Higher Education
