Minneapolis VA Health Care System

VA Research Week 2023

"Cutting Edge Care Through Research"

Program and Abstract List

(alphabetically, by author)

June 6-8, 2023

U.S. Department of Veterans Affairs

Veterans Health Administration

Office of Research and Development

Program

1. Research Coordinator Competency Fair (Tuesday, June 6, 8:00 am – 12:00 pm)

2. Oral Presentation Session (Wednesday, June 7, 1:00 – 3:00 pm)

1:00 ***Bringing research to the Veteran: home based and virtual enrollment for a VA Cooperative Studies Program trial of fecal microbiota therapy vs. placebo to prevent recurrent C. difficile infection***
Dimitri Drekonja*, Aasma Shaukat, Jane Zhang, Andrew Reinink, Sean Nugent, Jason Dominitz, Anne Davis-Karim, Dale Gerding, Tassos Kyriakides

1:15 ***Do mindfulness interventions cause harm? Findings from the Learning to Apply Mindfulness to Pain (LAMP) study***
Diana Burgess*, Collin Calvert, Ann Bangerter, Mariah Branson, Lee Cross, Roni Evans, John Ferguson, Jessica Friedman, Emily Campbell Hagel, Alexander C Haley, Sierra Hennessy, Colleen Kraft, Mallory Mahaffey, Marianne Matthias, Laura Meis, Greg Serpa, Stephanie Taylor, Brent Taylor

1:30 ***The pursuit of innovation for Veterans with phantom limb pain: Leveraging a Veteran- and clinician-informed research agenda***
Tonya Rich*, Erin Krebs, Kelvin Lim, Kierra Falbo, Andrew Hansen

1:45 ***Protein-Based Risk Scores Improve Hip Fracture Prediction More than Available Genetic Risk Scores***
Thomas Austin, Howard Fink*, Anna Törnqvist, Diana Jalal, Petra Buzkova, Joshua Barzilay, Laura Carbone, Maiken Gabrielsen, Louise Grahnemo, Kristian Hveem, Christian Jonasson, Jorge Kizer, Arnulf Langhammer, Kenneth Mukamal, Maria Nethander, Bruce Psaty, John Robbins, Yan Sun, Anne Heidi Skogholt, Bjørn Olav Åsvold, Rodrigo Valderrabano, Jie Zheng, Eivind Coward, Claes Ohlsson

2:00 ***Retrospective Analysis of Patients with Hidradenitis Suppurativa and Adalimumab/Infliximab Use in the Veterans Affairs Health Care System***
Zachary Wendland*, Katelyn Rypka, Lindsey Greenlund, Claire Herzog, Fatai Agiri, Amy Gravely, Lauren Orenstein, Amit Garg, Julie Lynch, Noah Goldfarb

2:15 ***Adverse Childhood Experiences Account for Post-Concussive Symptoms More Strongly than Injury History in Veterans with Mild TBI***
Colette Mahr*, Seth Disner

2:30 ***Characterizing Trauma-related Nightmares in Veterans Using Ambulatory Sleep Measurement***
Katherine Miller*, Steve Woodward, Phil Gehrman

3. Keynote Session (Thursday, June 8, 12:00 - 1:00 pm)

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

2022 Lederle Award Presentation.....Dimitri Drekonja, MD, MS

Recipient:
Areef Ishani, MD, MS
"Chlorthalidone vs. Hydrochlorothiazide for Hypertension-Cardiovascular Events"

N Engl J Med. 2022 Dec 29; 387(26):2401-2410.

Basic Science Paper of the Year Award..... Khalil Ahmed, PhD

Recipient:
Thomas Griffith, PhD
"Reduced T Cell Priming in Microbially Experienced 'Dirty' Mice Results from Limited IL-27 Production by XCR1+ Dendritic Cells"

J Immunol. 2022 Dec 1;209(11):2149-2159

Early Stage Investigator Project Award..... Seth Disner, PhD

Recipient:
Anne Melzer, MD, MS

Study Coordinator Leadership Award.....Aimee Hamel, RN, PhD

Recipient:
Miranda Hassler, BA

Keynote Address .....**Kelly D. Brownell, PhD**
Robert L. Flowers Distinguished Professor of Public Policy,
Professor of Psychology and Neuroscience, Duke University

"Harnessing Research for Social and Policy Change: Thinking About Impact"

4. Poster Session (Thursday, June 8, 2:00-4:00 pm)

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

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

Oral Presentations

1. Do mindfulness interventions cause harm? Findings from the Learning to Apply Mindfulness to Pain (LAMP) study

Burgess, Diana [1]; Calvert, Collin [1]; Bangerter, Ann [1]; Branson, Mariah [1]; Cross, Lee [1]; Evans, Roni [2]; Ferguson, John [2]; Friedman, Jessica [1]; Campbell Hagel, Emily [1]; C Haley, Alexander [2]; Hennessy, Sierra [1]; Kraft, Colleen [1]; Mahaffey, Mallory [1]; Matthias, Marianne [2]; Meis, Laura [1]; Serpa, Greg [2]; Taylor, Stephanie [2]; Taylor, Brent [1]

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

Abstract: Although mindfulness-based interventions (MBIs) have been established as evidence-based nonpharmacological treatments for chronic pain, there has been little systematic study of its potential risks, although concerns about harms have been raised. To address this gap, we examined differences in psychological and physical worsening among participants in the usual care and intervention conditions of a three-group, randomized pragmatic trial (Learning to Apply Mindfulness to Pain; LAMP) that tested the effectiveness of two approaches to delivering MBIs for chronic pain. The sample consisted of 368 male and 336 female Veterans with chronic pain who completed a 10-week follow-up survey (86% response rate), 63% of whom had a mental health diagnosis. Psychological and physical worsening was assessed by a checklist asking participants if they experienced specific symptoms since beginning the study. Participants in usual care were more likely than those in the MBIs to report experiencing symptoms (53% versus 25%) including: disturbing memories (13% versus 6%); feeling more upset than usual when something reminded them of the past (16% versus 7%); feelings of sadness (19% versus 6%); feelings of anxiousness (27% versus 11%); feeling more tired or fatigued than usual (42% versus 14%); feeling more isolated or lonely (23% versus 8%); and a worsening of their physical or mental symptoms (13% versus 4%). We conclude that the LAMP MBIs did not cause harm and instead appeared to result in fewer side effects for this population of patients with chronic pain and high levels of mental health comorbidities.

Research Topic: Pain
Funding agencies: DOD
Grant support: W81XWH-18-2-0003

2. Bringing research to the Veteran: home based and virtual enrollment for a VA Cooperative Studies Program trial of fecal microbiota therapy vs. placebo to prevent recurrent C. difficile infection

Drekonja, Dimitri [1-2]; Shaukat, Aasma [1]; Zhang, Jane [3]; Reinink, Andrew [1]; Nugent, Sean [1]; Dominitz, Jason [4]; Davis-Karim, Anne [5]; Gerding, Dale [6]; Kyriakides, Tassos [3]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. West Haven Cooperative Studies Program Coordinating Center
4. VA Puget Sound Health Care System
5. CSP Clinical Research Pharmacy Coordinating Center
6. Edward Hines, Jr. VA Hospital

Abstract: Introduction: Clinical trials are often centered at large academic centers, or in the VA, 1A facilities. The VA Cooperative Studies Program (CSP) has a history of designing and conducting clinical trials, typically using the model of a site investigator and study coordinator located at multiple large VA medical centers, coordinated by the study chair's office and an affiliated CSP coordnating center. This results in substantial personnel costs, and also limits participation in these studies to Veterans at these large facilities, or those willing/able to travel. We proposed and conducted a VA CSP trial whereby case identification was done centrally, with enrollment and study intervention conducted either at the Veteran's home, or later, by video visit. Methods: This is a randomized comparison of capsule-delivered fecal microbiota transplant for the prevention of recurrent C. difficile infection, administered after successful initial treatment of recurrent C. difficile infection with standard therapy. The primary endpoint is the incidence of recurrent C. difficile infection or death. Cases are identified in the VA Corporate Data Warehouse, with study coordinators then reaching out to potential participants. Interested individuals meeting inclusion criteria are scheduled for in-home consent, randomization, and capsule administration, followed by telephone follow-up for 6 months. To mitigate risks of COVID-19, enrollment via video visits was implemented to continue enrollment during the pandemic. Results: A total of 153 patients were enrolled, 67 via video visit. Participants were enrolled from 40 states, with 37% residing in a rural or highly-rural area. There were no participants lost to follow-up over the 6 months of study participation. Enrollment was halted by the data monitoring committee, with results pending publication. Discussion: Home enrollment, either in-person or virtually, is a feasible way to conduct clinical trials in the VA. Benefits include expanding participation in clinical trials to Veterans in rural areas, reduced staffing needs, and reduced costs.

Research Topic: Infectious Diseases
Funding agencies: VA CSRD
Grant support: VA CSP

3. Protein-Based Risk Scores Improve Hip Fracture Prediction More than Available Genetic Risk Scores

Fink, Howard [1]; Austin, Thomas [2]; Törnqvist, Anna [3]; Jalal, Diana [4-5]; Buzkova, Petra [2]; Barzilay, Joshua [6]; Carbone, Laura [7-8]; Gabrielsen, Maiken [9]; Grahnemo, Louise [3]; Hveem, Kristian [9]; Jonasson, Christian [9]; Kizer, Jorge [10-11]; Langhammer, Arnulf [9,12]; Mukamal, Kenneth [13]; Nethander, Maria [3]; Psaty, Bruce [2]; Robbins, John [14]; Sun, Yan [15]; Skogholt, Anne Heidi [9]; Åsvold, Bjørn Olav [9,16]; Valderrabano, Rodrigo [17]; Zheng, Jie [18-19]; Coward, Eivind [9]; Ohlsson, Claes [3,20]

1. Minneapolis VA Health Care System
2. University of Washington
3. University of Gothenburg
4. VA Iowa City Healthcare System
5. Carver College of Medicine
6. Kaiser Permanente of Georgia
7. Charlie Norwood VA Medical Center
8. Augusta University
9. Norwegian University of Science and Technology
10. San Francisco VA Health Care System
11. University of California San Francisco
12. Nord-Trøndelag Hospital Trust
13. Beth Israel Deaconess Medical Center
14. University of California, Davis
15. Emory University
16. Trondheim University Hospital
17. Harvard Medical School
18. Shanghai Jiao Tong University School of Medicine
19. University of Bristol
20. Sahlgrenska University Hospital

Abstract: Hip fractures are associated with significant disability and mortality. Early identification of patients at high risk of hip fracture is important to inform efficient intervention strategies. Published genetic risk scores (GRS) improve hip fracture prediction modestly. The present study aimed to develop and validate a protein-based risk score (PrRS) for hip fracture prediction. In the Cardiovascular Health Study (CHS) and the HUNT study, we performed a comprehensive circulating protein association study on incident hip fractures using the aptamer-based 5K SomaScan assay, including 4,979 aptamers. A PrRS was developed in CHS (3,171 subjects, mean 74.4 yrs, 39% men, 456 hip fractures) using two different strategies. In the first strategy, univariate associations between protein levels and hip fractures were calculated using age and sex-adjusted Cox regression models. A weighted PrRS (W-PrRS) was developed, including the 18 proteins passing the significance level after adjustment for multiple testing. In the second strategy, using machine learning (ML), LASSO with repeated splits of training (70%) and testing data sets (30%) was carried out to develop a PrRS including 6 proteins (ML-PrRS) with optimal improvement of c-index. The performances of the two PrRSs to predict incident hip fractures were determined in the independent HUNT validation cohort (3,259 subjects, mean 64.5 yrs, 61% men, 187 hip fractures). Age and sex-adjusted Cox regression models revealed that both the W-PrRS (Hazard ratio (HR) 1.51, 95% confidence interval 1.25-1.81 per standard deviation increase in risk score) and the ML-PrRS (HR 1.42, 1.19-1.69) improved fracture prediction more than GRSs previously developed using 47 genome-wide significant markers for femoral-neck BMD (FN-BMD-GRS; HR 1.14, 0.98-1.32) or using ML (21,716 genetic markers) of ultrasound-derived speed of sound in the heel (gSOS-GRS; HR 1.09, 0.94-1.26). Hip fracture prediction for the two PrRSs were only marginally attenuated after adjustment for clinical risk factor based FRAX score (W-PrRS, HR 1.45, 1.19-1.75; ML-PrRS, HR 1.37, 1.14-1.64). Discriminative analyses revealed that both the W-PrRS and the ML-PrRS ($p<0.05$), but not the FN-BMD-GRS or the gSOS-GRS, improved the c-index for hip fractures compared with an age and sex-adjusted base model. In conclusion, our developed PrRSs improve hip fracture prediction more than available GRS and may add clinically useful information for hip fracture prediction.

Research Topic: Geriatrics
Funding agencies: NIH; Other
Grant support: Swedish Research Council 2020-01392; Swedish ALF-agreement ALFGBG-720331 and ALFGBG-965235; Lundberg Foundation LU2021-0096; Novo Nordisk Foundation NNF 190C0055250; Knut and Alice Wallenberg FoundationKAW 2015.0317; Contracts HHSN268201200036C, HHSN268200800007C, HHSN268201800001C, N01HC55222, N01HC85079, N01HC85080, N01HC85081, N01HC85082, N01HC85083, N01HC85086, and 75N92021D00006; NHLBI and NINDS U01 HL080295, U01 HL130114, and R01 HL144483; NIA R01 AG023629

4. Adverse Childhood Experiences Account for Post-Concussive Symptoms More Strongly than Injury History in Veterans with Mild TBI

Mahr, Colette [1]; Disner, Seth [1]

1. Minneapolis VA Health Care System

Abstract: Adverse childhood experiences (ACEs), including psychological and emotional abuse and neglect, can have a profound impact on health outcomes in adulthood. Prior research suggests that ACEs have life-long neuropsychological consequences, including elevated risk of mental illness, substance abuse, memory impairment, and stroke. However, it is less clear how ACEs influence long-term symptoms after traumatic brain injury (TBI). While full recovery after mild TBI (mTBI) is expected, persistent symptoms are common in a subset of cases, including an estimated 20-48% of Veterans. The current study sought to investigate the role of childhood trauma in persistent mTBI symptoms in the Veteran population. As part of the PROUD research study, 270 Veterans diagnosed with mTBI completed a battery of assessments (87% male; mean age: 45 years, SD: 12.6 years; mean time since injury 6.9 years, SD=7.7 years). Assessments completed included the Childhood Trauma Questionnaire (CTQ), which measures type and number ACEs, and the Neurobehavioral Symptom Index (NSI), which measures type and severity of persistent post-concussive symptoms. TBI clinical characteristics were accessed from VA medical records. Separate models evaluated the effect of number of mTBIs (divided into groups of 1, 2-3, and 4+) and CTQ score on overall NSI scores. When looking at the individual models, both CTQ (β=0.22, $p \leq 0.001$) and mTBI (β=0.12, p=0.045) were found to be significant positive predictors of NSI symptom severity. Multiple linear regression was then used to directly compare these effects, correcting for multiple comparisons using false discovery rate. The multiple regression model showed that CTQ scores were significantly positively associated with NSI symptom severity (β=0.21, p=0.0009), while the number of mTBIs experienced was only marginally associated with NSI symptom severity (β=0.11,p=0.07). Furthermore, CTQ scores were positively associated with all NSI subscales, including vestibular and cognitive symptoms. The specific ACE types most strongly associated with NSI symptoms were emotional abuse (β=0.149, p=0.002) and physical abuse (β=0.174, p=0.005). These findings suggest that ACEs are strongly linked to both neurological and affective symptoms experienced by Veterans following mTBI and are important to measure to better understand contributors to post-concussive symptomatology.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: VA RRD
Grant support: IK2 RX002922

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5. Characterizing Trauma-related Nightmares in Veterans Using Ambulatory Sleep Measurement

Miller, Katherine [1-2]; Woodward, Steve [3-4]; Gehrman, Phil [5-6]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. National Center for PTSD Dissemination & Training Division
4. VA Palo Alto Health Care System
5. Corporal Michael J. Crescenz VA Medical Center
6. University of Pennsylvania

Abstract: Trauma-related nightmares in Veterans are associated with poor clinical outcomes and increased risk of suicide. In spite of an urgent need to reduce the burden of trauma-related nightmares, the underlying physiological changes accompanying their occurrence are poorly understood, and there are no clear evidence-based recommendations for their treatment. Limitations of current assessment procedures represent a barrier to improved care. In-laboratory sleep studies infrequently capture nightmares, limiting our knowledge of phenotypic markers and their response to treatment. The present study aims to address these limitations by using extended, in-home sleep monitoring to capture physiological parameters associated with nightmare reports in Veterans, and assessing how these physiological features are altered throughout a cognitive-behavioral nightmare treatment. This presentation will review the current state of the ongoing VA-funded study, including descriptive data from 39 randomized Veterans and approximately 1,500 nights of in-home mattress actigraphy systems. Additionally, results from a preliminary analysis of these data examining the association of baseline sleep reports and neighborhood disadvantage will be presented. This examination found that those residing in neighborhoods with greater disadvantage reported elevated fear of sleep and had reduced sleep period respiratory sinus arrhythmia compared to those living in advantaged neighborhoods. These initial data suggest that sleep context may serve as an additional mechanism by which trauma-induced sleep disruptions are maintained.

Research Topic: Posttraumatic Stress Disorder (PTSD)
Funding agencies: VA CSRD
Grant support: IK2 CX001874

6. The pursuit of innovation for Veterans with phantom limb pain: Leveraging a Veteran- and clinician-informed research agenda

Rich, Tonya [1-2]; Krebs, Erin [1-2]; Lim, Kelvin [1-2]; Falbo, Kierra [1-2]; Hansen, Andrew [1-2]

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

Abstract: Veterans with amputations experience multiple types of amputation-related pain. Phantom limb pain (PLP), one type of amputation pain, affects up to 90% of individuals with amputation. Although well acknowledged, PLP is poorly understood with few non-drug treatment options. The Minneapolis Adaptive Design & Engineering research program is pursing the development and testing of non-drug treatments for PLP. To inform our path forward, we are using a Veteran-and clinician-informed research agenda with a series of projects. In our interviews with 50 Veterans, we learned PLP was distinct from other types of persistent pain experienced and Veterans perceived few effective non-drug treatment options. In our national VA amputation clinician online survey, we learned there is little agreement on measurement of PLP and a desire for innovation in non-drug treatment. In our innovation work, we are using a human centered design approach that involves Veterans and clinicians early in the development process to ensure their priorities are incorporated into the design of technologies. We are evaluating the feasibility and acceptability of our innovations in our pursuit of real world solutions. To augment the evaluation of our technologies, we are exploring relevant assessment measures to evaluate Veteran-specific goals for tracking meaningful outcomes. Taken together, this research agenda will guide us to valuable solutions for non-drug treatment options for pain in this population.

Research Topic: Pain
Funding agencies: None
Grant support: IK1 RX003216; 2023 CVRE New Investigator Award

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7. Retrospective Analysis of Patients with Hidradenitis Suppurativa and Adalimumab/Infliximab Use in the Veterans Affairs Health Care System

Wendland, Zachary [1-2]; Rypka, Katelyn [1]; Greenlund, Lindsey [2]; Herzog, Claire [2]; Agiri, Fatai [3]; Gravely, Amy [1]; Orenstein, Lauren [4]; Garg, Amit [5]; Lynch, Julie [3]; Goldfarb, Noah [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. VA Salt Lake City Healthcare System
4. Emory University
5. Donald and Barbara Zucker School of Medicine at Hofstra/Northwell

Abstract: Background: Hidradenitis suppurativa (HS) disproportionately affects young Black women. Adalimumab (ADA) is the only FDA-approved biologic for HS. Alternative management with tumor necrosis factor (TNF)-α inhibitors, such as infliximab (IFX), is common. A previous study, utilizing the Explorys database, found significant differences in ADA/IFX based on age, gender, and race. Objective: To evaluate the prevalence of HS in the VAHCS and assess biologic use prescription patterns in the Veteran Affairs health care system (VAHCS). Methods: Retrospective cross-sectional analysis using Veterans Affairs Informatics and Computing Infrastructure system data. Results: 35,589 individuals were identified via diagnosis of HS (ICD-9:705.83; ICD-10:L73.2). Prevalence of HS in the VAHCS is 0.29%. Overall prevalence of biologic use amongst patients with HS was 7.0%. Our study cohort was largely white (59.5%), obese (59.0%), men (75.8%) with a history of current/previous tobacco use (74.2%). Increased age decreased the likelihood of being prescribed a biologic for HS (aOR=0.45 [0.36-0.55]; $p<0.001$). BMI>30 increased the odds of biologic prescription compared to non-obese patients (aOR=1.19;[1.06-1.34]; $p<0.001$) Discussion: The prevalence of ADA/IFX prescriptions for patients with HS in the VAHCS was notably higher (7.0%) than the civilian population previously analyzed (1.8%). This may be because the VAHCS is a single-payer healthcare system, which potentially also allows for more efficient, coordinated care. Although biologic use was more common in our study than among civilians, HS patients at VAHCS could still benefit from greater medication access.

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

Poster Presentations

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

Adabag, Selcuk [1-2]; Diem, Susan [1]; Hill, Debra [1]; Donaire, Marti [1]; Johnson, Debra [1]; Muschler, Katherine [1]; Yang, Gloria [1]

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

Abstract: The VA Cooperative Studies Program (VA CSP) Network of Dedicated Enrollment Sites (NODES) is a consortium of VA Health Care Systems that have teams dedicated to conducting VA CSP Research. NODES goals include enhancing study performance and enrollment rates; providing a consistent and comprehensive approach to CSP study management, maintaining quality and regulatory compliance, obtaining center-level perspectives in the design and execution of studies, and providing opportunities for research personnel interested in supporting the VA CSP research mission. A Director, Co-Director, Associate Director-Operations, Operations Manager, Quality Assurance Manager/Clinical Research Nurse, Administrator, and Research Assistant support these efforts at the Minneapolis VA NODES site. NODES shares 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 CSP studies; Incorporated NODES staff in local CSP study teams; Created Mentorship Program for new local study investigators and coordinators; Created procedures for mobile recruiting at CBOCs; Hosted meetings on improving study design & procedures; Created work groups to develop and beta test case report forms; Enhanced recruitment through Mobile Recruiting Equipment; Reduced logistical and staffing barriers; Developed partnership between NODES and Non-NODES facilities to assist study teams with low recruitment; Created VA CSP-NODES Executive Board; Created CSP Studies Toolbox to facilitate study implementation; Facilitated virtual study visits and remote work for local CSP study coordinators and research assistants in response to the pandemic; Authored manuscripts in peer-reviewed journals; Won national 2020 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 In line with national initiatives to expand VA healthcare services to Veterans in rural areas, participated in VA CSP-NODES ACCESS work group to provide rural Veterans opportunities to participate in VA CSP research studies.

Research Topic: Health Care Delivery
Funding agencies: VA CSRD
Grant support: VA CSP

2. Stem Cell-Derived Exosome Patch with CABG Restores Systolic and Diastolic Function in Hibernating Myocardium

Aggarwal, Rishav [1]; Shao, Annie [1]; Potel, Koray [2]; So, Simon [3]; Swingen, Cory [1]; Rose, Rebecca [1]; Wright, Chris [1]; Hocum Stone, Laura [1]; McFalls, Edward [4]; Butterick, Tammy [1,3]; Kelly, Rosemary [1]

1. University of Minnesota
2. Queen's University Belfast
3. Minneapolis VA Health Care System
4. Richmond VA Medical Center

Abstract: Significance to VA Healthcare: Coronary artery disease (CAD) is a leading cause of death globally and predominantly affects Veterans. Its incidence, effect on patient quality of life and cost to the health care system remain high. CAD is one of the leading causes of hospitalization within the VA healthcare system and there is a critical need to improve treatment options for this highly prevalent disease. Objective: Hibernating myocardium (HM) is an adaptive response to chronic ischemia, resulting in reduced cardiac function and mitochondrial bioenergetics but preserved viability. Revascularization with coronary artery bypass grafting (CABG) does not fully recover cardiac function. Our porcine model of HM has shown that a mesenchymal stem cell (MSC) patch placed during CABG improves recovery of cardiac function. We identified MSC-derived exosomes as a potential signaling mechanism. Our work investigates the impact of exosomes as an adjuvant therapy with CABG on cardiac and mitochondrial function. Methods: In our in vitro model of HM and CABG, hypoxic H9C2 myocytes were reoxygenated and co-cultured with porcine MSCs via a transwell. The SeaHorse assay was used to measure mitochondrial function. The MSC exosome patch (EXP) was created using $3x10^8$ exosomes/patch. HM was created by placing a c-shaped constrictor on the proximal LAD, causing significant stenosis without infarction by 12 weeks. We performed CABG with or without EXP compared to HM. CABG animals recovered for 4 weeks and were sacrificed. Animals underwent MRI at rest and under stress prior to sacrifice to assess systolic and diastolic cardiac function. Histology and electron microscopy imaging were performed. Results: Reoxygenation+MSC increased ATP production, basal and maximal mitochondrial respiration in hypoxic cardiomyocytes, which was blunted with the inhibition of exosome release. MRI showed significant improvement in diastolic and systolic function in CABG+EXP compared to the HM and CABG groups. CABG+EXP had decreased interstitial fibrosis compared to the HM and CABG groups. Mitochondrial number, size, and circularity increased in CABG+EXP compared to the HM and CABG groups. Conclusion: CABG+EXP improved systolic function, diastolic relaxation and fibrosis. Exosomes enhance mitochondrial bioenergetics in HM in vitro and improves mitochondrial morphology and number in vivo. EXP may improve recovery of HM through increased mitochondrial recovery and decreased fibrosis.

Research Topic: Basic Sciences
Funding agencies: VA BLRD; UMN
Grant support: I01 BX004146

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3. Interstate Collaboration in Fat Emboli Stroke Secondary to Sickle Cell Disease: Case Report

Al Lawati, Zainab [1]

1. Minneapolis VA Health Care System

Abstract: The differential diagnosis for ischemic stroke in young patients involves different etiologies including: blood disorders, vasculopathy, cardiac defects, recent pregnancy, other hypercoagulable states, smoking, illicit drug use, premature atherosclerosis, hypertension, metabolic disorders, and possibly migraine. We report a young woman who developed a multifocal infarct with fat emboli secondary to sickle cell disease while vacationing in Florida. Magnetic resonance imaging revealed multiple punctate foci of restricted diffusion involving the periventricular, deep, and subcortical white matter; cortex; deep gray nuclei and corpus callosum. The patient was admitted to the acute hospital in Miami to manage her active medical issue. Patient was later transferred to the rehabilitation hospital to optimize recovery. Collaborations were established between the physiatrist in Miami and her actual physiatrist in Minnesota to continue the patient's care in her home town and optimize recovery. The patient was seen in the follow up evaluation. She had significant improvements in her strength and sensation. She was making progress with her cognition. Certain recommendations were advised to resume her studies back in college. Significance: This report illustrates the value of interstate collaboration in optimizing stroke rehabilitation and the role of physiatrists in optimizing the stroke recovery. Funding for project (if any): None Keywords: Sickle Cell Disease (SCD), Stroke, Magnetic resonance imaging (MRI).

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

4. Feasibility of Brief Behavioral Therapy for Insomnia (BBTI) Group in Veteran Populations

Batool, Hina [1]; Saxby, Dyani [1]; Urosevic, Snezana [1]

1. Minneapolis VA Health Care System

Abstract: Approximately 40% of Veterans in primary care report sleep concerns (Mustafa et al., 2005). Brief Behavioral Therapy for Insomnia (BBTI) is an evidence-based treatment and delivered in a group format in the Primary Care Mental Health Integration setting helps to minimize barriers associated with accessing individual Cognitive Behavioral Therapy for Insomnia (Bramoweth et al., 2020). This program evaluation is among the first to examine BBTI delivered in a group format. Participants included 28 Veterans with sleep concerns at the Minneapolis VA. Using the inclusion/exclusion criteria, Veterans were screened to determine fit for participation in the group. Group consisted of 5 sessions with the first session introducing BBTI and gauging Veterans readiness to participate. Veterans were encouraged to complete sleep logs to track sleep data on a weekly basis. Following completion of group, Veterans were contacted for a brief phone interview. Sleep log data was gathered from 12 of the 28 Veterans and Insomnia Severity Index (ISI) and Epworth data was gathered from all Veterans. Results revealed significant improvement in pre-post group ISI scores (Cohens d=1.3) which is a large effect size and consistent with effects found for CBT-I (Hedges g=0.98; van Straten et al., 2018). Paired t-test analyses revealed significant improvement in ISI scores ($t(24)=5.29$, $p=0.000$) and wakefulness after sleep onset (WASO) scores ($t(11)=2.30$, $p=0.042$). Total sleep time (TST), sleep efficiency (SE), and sleep latency (SL) changes pre-post were not significant. Rapid qualitative analysis revealed 6 themes: BBTI provided Veterans with information regarding sleep behaviors they previously did not know; Veterans felt that BBTI helped improve their sleep; Veterans found it helpful knowing that others have similar sleep concerns; they did not like reviewing individual sleep data; they preferred sleep log to be digital; and when added, the Annie application had some issues. These findings demonstrate the effectiveness and utility of a brief group intervention for insomnia.

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

5. Can we detect pressure injury earlier? Piloting the sub epidermal moisture (SEM) scanner use for early detection to prevent of pressure injuries

Belew, John [1]; Wacek, Amber [1]; Abebe, Fetlework [1]; Alebachew, Banchi [1]; Nwanokwale, Merja [1]; Smeltzer, Ashley [1]; Eddy, Byron [1]; Olney, Christine [1]

1. Minneapolis VA Health Care System

Abstract: Background: The SEM Scanner is used for detecting differences in sub-epidermal moisture (SEM) to show pressure-induced tissue damage which can become a pressure ulcer. Tissue inflammation is the first response to damage and causes increased dilation and permeability of surrounding blood vessels. This leads to leakage of plasma and fluid, creating a layer of sub-epidermal moisture. A literature review found 3 prospective studies, 1 pilot study and 3 abstracts involving 1,870 adults, which included scanning of only two anatomical sites: the sacrum and the heels. Purpose: This pilot project was part of a larger research study "Refinement of the Comprehensive Mobile Assessment of Pressure (CMAP) system for prevention of pressure injuries". The purpose was to understand if the SEM scanner might be an early detection method for pressure injury while conducting the larger study. Methods: Inpatient RNs from Minneapolis VAHCS Spinal Cord Injury/Disability unit participated. They were trained by the study staff on SEM. Training included several hands-on sessions in which a specific area of the body was scanned (sacral), the correct and consistent patient position during the scan, when to scan and how to report and share the data to the study team. Findings: Nurses conducted 16 SEM sacral scans on three different study participants, who were in-patients at the MVA SCI/D Center. Two participants had SEM readings indicating they were at risk for pressure injury. One participant had high SEM reading after extended time in shower chair. In each of the cases, per the study protocol, the study provider was notified, and resulted determined that the patient was cleared to continue to participate in the larger study for testing the mobile pressure mapping system, although extra monitoring of their sacral areas did occur to ensure intact skin. The nurses reported that the SEM scanner was easy to use and usually took less than 5 minutes. Discussion: While readings from the SEM scans were elevated indicating possible early pressure injury; the clinical opinion, after examination, was that there wasn't other supporting evidence of an evolving pressure injury. Conclusions: The SEM Scanner should not replace current methods of identifying pressure ulcers for our study. Per the literature review, for our study we will continue use known methods to ensure skin is intact in the sacral area. Further evidence comparing SEM Scanner and other non-invasive tests is needed.

Research Topic: Spinal Cord Injury
Funding agencies: VA RRD
Grant support: I01 RX003222

6. Algorithmic CT Scan Analysis for Prognosticating Brain Injury: A Preliminary Effort

Broadbent, Charles [1]; Kadaba Sridhar, Sharada [2]; Gupta, Rishabh [1]; Sterk, Brett [1]; Koller, Michael [1]; Kuang, Rui [1]; Samadani, Uzma [2]

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

Abstract: Background: Predicting which trauma patients will progress to brain death is currently based on history, physical examination and radiographic findings. Objective: The present study investigates the ability of computed tomography (CT) scans to predict brain death. Methods: 38 trauma subjects, 18 which progressed to brain death (BD), who suffered from high-velocity trauma with presumed diffuse axonal injury, cardiopulmonary/respiratory arrest, and/or found down were included. BLAST-CT was used to identify four lesion types: intraparenchymal hemorrhage, extra-axial hemorrhage, perilesional oedema, and intraventricular hemorrhage. Cerebrospinal fluid volumes were extracted using SimpleITK. These two sets of features were obtained from whole head CT scans and within 117 standardized brain atlas regions. Five ROC curves for classifying BD versus non-BD were generated using a support vector machine trained on (1) BLAST-CT (4 features), (2) Regional BLAST-CT (468 features), (3) Regional CSF volumes (117), (4) BLAST-CT + Regional CSF volumes (121 features), and (5) Regional BLAST-CT + Regional CSF volumes (585 features). Results: For BLAST-CT alone, area under the curve (AUC), sensitivity, specificity, and accuracy in classifying BD were 0.7806, 0.6111, 0.9500, and 0.7895 respectively. For regional BLAST CT, they were 0.7611, 0.5556, 1.000, and 0.7895 respectively. For regional CSF volume, they were 0.7056, 0.9444, 0.5000, and 0.7105. For BLAST-CT + regional CSF volumes, they were 0.8389, 0.9444, 0.6500, and 0.7985. For regional BLAST-CT + regional CSF volumes, they were 0.9083, 0.8333, 1.000, 0.9211. Conclusions: Results indicate that the present model using regional BLAST-CT + regional CSF volumes is able to classify brain death with a large specificity, sensitivity, and accuracy above 90%. Given the clinical value of a tool to assist physicians in predicting progression to BD, additional prospective trials with larger samples and testing cohorts should be conducted.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: Other
Grant support: Minnesota State Office of Higher Education

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7. Supine Pedaling Device for Peripheral Artery Disease Diagnosis

Brown, Rebecca [1-2]; Durre, Meghan [2]; Kuffel, Zach [2]; Miller, Moira [2]; Zehr, Carter [2]; Thew, Olivia [2]; Salisbury, Dereck [2]; Olney, Christine [1]; Voss, Gregory [1]; Hansen, Andrew [1-2]; Treat-Jacobson, Diane [2]; Ihnat, Daniel [1]; Morin, Steve [1]; Davis, Drew [1]

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

Abstract: Background: Peripheral artery disease (PAD) is a debilitating atherosclerotic disease caused by blockages in the arteries of the lower extremities resulting in limited blood flow to the working muscles during exertion. PAD affects over 8.5 million Americans and those with PAD have a 4-5-fold increase in risk of cardiovascular-related mortality. PAD detection is poor, with as many as half of patients with PAD undiagnosed. Most individuals with PAD have atypical symptoms or are reportedly asymptomatic, though many asymptomatic patients manage symptoms through activity avoidance. The hallmark symptom of PAD, claudication, is experienced by just 10-20% of the population with PAD. Similar to women's cardiovascular symptoms, women's vascular symptoms are more likely to be atypical, and thus women are at disproportionate risk of living with undiagnosed PAD. Furthermore, the guideline-recommended diagnostic test (the ankle brachial index or ABI) has a false negative rate of nearly 40%. Comprehensive vascular tests are available in vascular laboratories to accurately detect PAD, however, a recent study found that women are referred for more comprehensive evaluations at a lower rate compared to men. Thus, there is a need to improve the first line diagnostic test to mitigate bias in PAD detection and to improve access to care for Veterans who do not live near vascular laboratories. Methods: Five University of Minnesota mechanical engineer students partnered with the Minneapolis MADE group to create a light-weight, fast, accurate device to improve detection of PAD. Results: The supine pedaling device for peripheral artery disease (PAD) diagnosis prototype is an exercise device designed to increase the accuracy of current PAD diagnosis tests. Muscle engagement, joint movement, and resistance capability of the device were evaluated. It was found that the device successfully activates multiple muscle groups. The range of motion of the hip, knee, and ankle joints indicate adequate joint movement. Additionally, the resistance was found to provide variable resistance up to a maximum moment of 135 lb-in in opposing the start of motion. These results suggest that the device will successfully induce blood flow and improve the accuracy of PAD detection compared to the current resting ABI. Discussion: It is feasible to design a pedal device to engage necessary muscle groups to theoretically increase the sensitivity of the resting ABI. Additional testing is required.

Research Topic: Women's Health
Funding agencies: Other
Grant support: Minneapolis Adaptive Design and Engineering Program

8. Development of a Predictive Screening Tool for Improved Detection of Peripheral Artery Disease (PAD): The PREDICT PAD Study

Brown, Rebecca [1-2]; Schorr, Erica [2]; Treat-Jacobson, Diane [2]

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

Abstract: Description of Background: Of all the major manifestations of atherosclerosis, peripheral artery disease (PAD) is one of the most underdiagnosed and undertreated vascular diseases, due, in part, to the large number of individuals who experience atypical symptoms, yet our current screening tools are designed to detect those with classic symptoms. The purpose of this study was to determine which, if any, symptom descriptors accurately discriminate peripheral artery disease (PAD) from non-PAD in a community-based sample of individuals with self-reported persistent lower extremity symptoms of any kind. Methods: Using a prospective cross-sectional design, symptom descriptors were linked to PAD disease status using diagnostic testing in individuals who report lower extremity symptoms (n=25). Consecutive sampling was used to identify those with atypical symptoms in the population. Symptom descriptors were obtained via questionnaires and structured interviews. Symptoms were assessed pre and post physical function tests. Calf muscle tissue oxygenation level was measured using near infrared spectroscopy to further differentiate ischemic vs. non-ischemic symptoms during exercise. The primary outcome was the diagnostic accuracy of patient-reported symptoms that discriminate between PAD and non-PAD conditions. Results: Four questions discriminated between groups. These were: "Does the pain/discomfort every disappear while you are walking?" "Do you have trouble keeping up with your friends or family?", "Do you have pain or discomfort while sitting", and "Where is the pain?". Pain or discomfort while sitting occurred more frequently in the PAD group compared to the non-PAD group as well as pain or discomfort outside of the calf or thigh. Questionnaires had low sensitivity and specificity and were not more accurate following a bout of exercise. Conclusion: Low diagnostic accuracy of the questionnaires may be attributed to the high prevalence of participants in the PAD group who experience pain while sitting and pain outside of the calf and thigh. Furthermore, inclusion of more women than men may have better represented the breadth of atypical symptoms experienced by those with PAD.

Research Topic: Women's Health
Funding agencies: NIH; UMN
Grant support: TL1 R002493; UL1 TR002494

9. Test Re-test Reliability of the Peripheral Artery Disease Quality of Life Questionnaire (PADQOL)™

Brown, Rebecca [1]; Schorr, Mary [2]; Treat-Jacobson, Diane [2]

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

Abstract: Description of Background: The Peripheral Artery Disease Quality of Life Questionnaire (PADQOL) is a validated disease-specific questionnaire developed to assess the impact of PAD on patients' perceptions of health-related quality of life, specifically the physical, psychosocial, and emotional impact PAD has on one's life. The purpose of this study was to establish test re-test reliability of the PADQOL. Methods: Eligible participants (n=52) completed five questionnaires at two time points: the PADQOL, Short-form 36 (SF-36), Profile of Mood States (POMS), Walking Impairment Questionnaire (WIQ), and a demographic form. Participants were recruited from prior studies and through targeted recruitment mailings. The time between timepoints was 2-4 weeks. Intraclass correlation coefficients were conducted to measure reproducibility (reliability). Results: Intraclass Correlations were as follows: Factor 1: Social Relationships and Interactions 0.97 (CI 0.94-0.98), Factor 2: Self-concept and Feelings 0.95 (0.92-0.973), Factor 3: Symptoms and Limitations in Physical Functioning 0.93 (0.88-0.96), Factor 4: Fears and Uncertainty 0.93 (0.88-0.96), Factor 5: Positive Adaptation 0.84 (0.72-0.91), Job Interference 0.79 (0.62-0.88), Sexual Function 0.86 (0.75-0.93) and Intimate Relationships 0.77 (0.59-0.87). This study is limited by the small sample size and non-diverse sample. Conclusion: These results indicate that the PADQOL is highly reliable. Overall, scores showed "high" (0.61-0.80) (Job Interference and Intimate Relationships) or "almost perfect" (0.81-1.00) reliability (Factors 1-5 and Sexual Function) (Cronbach α>0.8). The PADQOL provides a meaningful measure of disease impact and is a useful tool to assess the effectiveness of treatments based on patient-centered outcomes.

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

10. Inclusion of Women Veterans in VA Research

Buelt-Gebhardt, Melissa [1]; Hill, Debra [1]; Danan, Elisheva [1]; Adabag, Selcuk [1]

1. Minneapolis VA Health Care System

Abstract: Women Veterans are the fastest growing subpopulation using the Veterans Health Administration. Over half a million women Veterans received health care in the VA in FY19, more than tripling in number from the year 2000. Women Veterans' rapid growth among VA users has escalated demand for a stronger evidence base to provide high-quality care tailored to women Veterans' needs. To provide patient-centered, evidence-based care, attention to sex and gender in scientific research is needed; findings from research done solely on men cannot necessarily be safely generalized to women. Equitable inclusion of women in VA research is required but recruiting sufficient women Veteran participants in VA clinical trials can be challenging. Despite their growing numbers, women remain a numerical minority, accounting for less than 10% of VA patients. Underrepresentation of women Veterans in research can also be attributed to factors such as mistrust in VA, women's unique healthcare needs, VA eligibility, and sociodemographic differences from men. For example, today's women Veterans are an increasingly diverse population, and are on average younger, have more caregiving responsibilities, and have less social support than male Veterans. To address these factors, key strategies aimed at engaging more women and gender-diverse Veterans in research studies are being explored. Inclusion of women in VA clinical trials in sufficient numbers to enable sex and/or gender-based analyses of treatment outcomes will improve the real-world care of women Veterans.

Research Topic: Women's Health
Funding agencies: VA CSRD
Grant support: VA CSP

11. How mindfulness predicts pain and comorbidities: a cross-sectional study of Veterans with chronic pain

Calvert, Collin [1-2]; Taylor, Brent [1]; Bangerter, Ann [1]; Branson, Mariah [1]; Cross, Lee [1]; Evans, Roni [2]; Allen, Kelli [2]; Haley, Alexander [2]; Ferguson, John [2]; Friedman, Jessica [1-2]; Hagel Campbell, Emily [1]; Meis, Laura [1]; Burgess, Diana [1]

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

Abstract: Prior studies have shown that mindfulness practice can improve pain and pain-related comorbidities. Few have examined how mindfulness and pain are related among Veterans with chronic pain, and those that do have limited generalizability due to small sample sizes and few female Veterans. We used baseline data from a three-site, three-arm randomized controlled trial of two mindfulness-based interventions to improve chronic pain (n=1,737). The sample consisted of 947 male and 790 female Veterans with diagnosed chronic pain. We used multivariable generalized linear models to estimate the relationship between self-reported use of mindfulness in everyday life (assessed using the Applied Mindfulness Process Scale) and several pain outcomes (pain interference, pain intensity, pain catastrophizing, and pain-related comorbidities). Greater mindfulness was associated with lower levels of pain interference (standardized effect: -0.06; confidence interval [CI]: -0.12, -0.01) and pain catastrophizing (-0.11; CI: -0.16, -0.06), but not pain intensity. Greater mindfulness was also associated with lower levels of anxiety (-0.15; CI: -0.21, -0.10), fatigue (-0.16; CI: -0.21, -0.10), sleep disturbance (-0.14; CI: -0.20, -0.09), depression (-0.21; CI: -0.26, -0.15), and PTSD (-0.17; -0.22, -0.12), and higher levels of physical function (0.10; CI: 0.05, 0.14) and ability to fulfill social roles and activities (0.08; CI: 0.02, 0.14). Among Veterans with chronic pain, application of mindfulness to daily life was associated with improved pain, better pain coping and fewer pain-related comorbidities. Increasing the reach of mindfulness programs has the potential to help the many Veterans with chronic pain.

Research Topic: Pain
Funding agencies: DOD
Grant support: W81XWH-18-2-0003

12. ProTECT III Trial Revisited: Algorithmic Classification of Injury Does Not Identify a Subset of Responders

Cheong, Scarlett [1]; Samadani, Uzma [2]; Sham, Yuk [1]

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

Abstract: ProTECT III has reported that progesterone does not improve the outcome of TBI subjects six-months post-injury, based on GOS-E score. Progesterone also does not decrease serum biomarker levels of glial and neuronal cell injury in TBI subjects at baseline, 24 and 48-hour post-injury. The objective of this research is to identify whether a subset of ProTECT patients benefited from progesterone treatment by classifying brain injury according to total brain lesion volume and basal biomarker expression. BLAST-CT is an open-source deep-learning image analysis algorithm for quantifying brain lesion volume. Herein, we determined the brain lesion volume in each subject and classified their injury into no brain lesion ≤0.1mL), low (>0.1–10mL), medium (>10-50mL), and high volume (>50mL). The biomarker expressions in each group were further divided into placebo and progesterone treatment groups. Statistical analyses were conducted to compare the treatment group within each timepoint. Progesterone-treated subjects' biomarker levels showed no difference from placebo subjects across all total brain lesion volume groups and timepoints. There was also no difference when the groups were further divided into their respective gender across all timepoints, treatment, and total brain lesion groups. Baseline biomarkers for placebo and progesterone treatment groups were established by identifying a subset of subjects whose radiology assessment result reported no visible trauma in its CT scan, and BLAST-CT output total brain lesion volume using is <0.1mL. Biomarker levels of both GFAP and S100B have significantly increased across three timepoints and total brain lesion volume groups (except high volume), regardless of the treatment groups. This suggested that GFAP and S100B biomarker levels correlate with the total volume of brain lesion output from BLAST-CT. In conclusion, Progesterone treatment does not decrease biomarkers levels of GFAP, UCH-L1, S100B, and SBDP150, despite incorporating BLAST-CT as an objective measure to categorize brain injury according to its brain lesion volume. The result of this post hoc analysis is consistent with the results reported from its previous research. However, we were able to identify TBI-positive patients with detectable brain lesion volume with elevated levels of GFAP and S100B to improve future TBI diagnosis using quantifiable measures.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: Other
Grant support: MN OHE

13. 3D Printing Capability at the Minneapolis VA

Davis, Drew [1]

1. Minneapolis VA Health Care System

Abstract: 3D printing has emerged as a valuable tool for patient education, pre-surgical planning, patient-matched interventions, and assistive technology. With the addition of segmentation software, we can create patient specific models with CT and MRI data to help communicate complex ideas and procedures. 3D printing and 3D VR visualization can reduce time under anesthesia, improve communication between clinicians and patients, and support training/education. Other applications include functional prototypes and assistive devices. We have a robust fleet of 3D printers and more importantly, a stable of experts available now to help realize identify and execute appropriate applications. These experts can operate the software and hardware so that you can focus on the most important tasks.

Research Topic: Medical Education
Funding agencies: Other
Grant support: N/A

14. An innovative technique for measuring phantom limb pain to identify patient-specific interventions

Falbo, Kierra [1-2]; Hansen, Andrew [1]; Rich, Tonya [1]

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

Abstract: Phantom limb pain (PLP) after amputation has widely different effects on individuals with amputation in its intensity, frequency, duration, and impact on function. Although managed clinically, success rates with PLP treatments vary. There is little evidence to understand how pain reduction occurs for some individuals and not for others. The inconsistency in clinical presentation between individuals and the variability in treatment success suggest that different factors contribute to PLP for different individuals. There remains a critical need to accurately assess these patient-specific PLP factors (e.g., activity level, mood, prosthesis use) for clinicians to identify appropriate targets in recommending effective treatments. Without this understanding, clinicians are dependent on patient report of symptoms and their understanding of what might contribute to their pain. Existing patient-reported outcome measures are limited by recall bias, and no real-time assessments exist. The purpose of this research is to establish ecological momentary assessment (EMA) as a feasible and acceptable method for measuring patient-specific factors of PLP to identify personalized treatment targets. In this demonstration poster, we highlight our process and study design. We have developed a list of potential PLP contributors through a literature review, and we will refine this list through focus groups with individuals with amputation (planned n=15). We will then develop EMA surveys, which will systematically measure these real-time personal and environmental factors in a participant's natural environment over 40 days (planned n=15). Through repeated surveys on a mobile device, EMA collects data on predictive factors and an outcome of interest (e.g., pain). We will utilize causal discovery analysis to examine for relationships between contributing factors and the onset of PLP episodes to identify evidence-based targets for clinical treatments. Through this research, we expect to establish feasibility and acceptability of an innovative, systematic assessment tool to examine patient-specific factors contributing to a person's unique experience of PLP. This is the first step in leveraging the power of real-time assessment using EMA, which in the future could create a paradigm shift in PLP management techniques. Future applications of EMA could drive outcome measurement and intervention design.

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

15. Perceived Environmental Barriers Among Service Members and Veterans in the First Five Years After a Traumatic Brain Injury: A VA TBI Model Systems Study

Finn, Jacob [1-2]; Klocksieben, Farina [3]; Cristan, Katharyn [1]

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

Abstract: Traumatic brain injury (TBI) can result in long-term changes to a person's physical, cognitive, and emotional health. After a TBI, Service Members and Veterans (SMVs) may encounter novel environmental barriers in their home and community. These barriers negatively impact community re-integration and health service access, which is critical for physical health and well-being post-injury. Additionally, environmental barriers are associated with having more unmet family needs post-injury. The current study described the environmental barriers reported by SMVs after a TBI using the VA Polytrauma Rehabilitation Centers (PRCs) TBI Model Systems (TBIMS) national database. SMVs are enrolled in VA PRC TBIMS during their inpatient rehabilitation stay and participate in follow-up assessments at 1, 2, 5, and every 5 years post-TBI. In the current study, we analyzed data from 427 SMVs who completed at least one follow-up assessment within their first five years post-injury. Perceived environmental barriers were assessed using the Craig Hospital Inventory of Environmental Barriers Short Form (CHIEF-SF), a 12-item survey constructed for use with individuals with a disability. Respondents are asked to rate the frequency (i.e., daily, weekly, monthly, less than monthly, or never) and the impact (i.e., big problem or little problem) of the barrier in the past year. The current analyses examined the CHIEF-SF total score, domain scores, and the item level scores. Overall, approximately 16% of participants reported no barriers, 51% reported one to four barriers, 21% reported five to seven barriers, and 12% reported eight to twelve barriers. The most often reported environmental barriers were surroundings (e.g., lighting, noise, crowds; 57.4%), natural environment (e.g., temperature, terrain, climate; 47.4%), and attitudes of others at home (36.9%). Among those who experienced a particular barrier, the barriers most often experienced daily were transportation (29.4%), discrimination (19.3%), and surroundings (19.3%). Among those who experienced a particular barrier, the barriers most often described as a "big problem" were healthcare (51.3%), government policies (49.6%), and transportation (42.1%). Addressing these environmental barriers will likely improve post-injury outcomes in SMVs and their families. Increasing awareness may also lead to policy changes and resource implementation. Future research should identify factors associated with these barriers to target resources.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: Other

Grant support: HT0014-21-C-0012; Defense Health Agency TBI CoE

16. Gender differences in post-traumatic stress disorder severity, pain catastrophizing, interference, and intensity in Veterans: baseline findings from the Learning to Apply Mindfulness to Pain study

Friedman, Jessica [1-2]; Taylor, Brent [1]; Hagel Campbell, Emily [1]; Allen, Kelli [2]; Bangerter, Ann [1]; Branson, Mariah [1]; Bronfort, Gert [2]; Calvert, Collin [1]; Cross, Lee [1]; Evans, Roni [2]; Ferguson, John [2]; Haley, Alexander [2]; Meis, Laura [1]; Burgess, Diana [1]

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

Abstract: Chronic pain and PTSD are thought to share several mutually reinforcing mechanisms. While prior studies have examined differences in pain outcomes and PTSD severity, few have disaggregated these differences by gender. To address this need, we examined gender differences in PTSD, pain catastrophizing, interference, and intensity among participants enrolled in a three-site, three-arm randomized pragmatic trial (Learning to Apply Mindfulness to Pain; LAMP). The analytic sample consisted of 421 male and 386 women Veterans with chronic pain who provided complete data on PTSD symptoms (assessed using PCL5≥ 31 indicating more severe vs. PCL5<31 less severe symptoms) and pain catastrophizing (high PCS≥30 vs. low PCS<30), pain interference, and pain intensity (using BPI subscales). We used x^2 and t-tests to examine differences between gender and self-reported PTSD and pain outcomes. No differences were observed between proportions of women and men Veterans with severe PTSD (42% vs. 38%; p=0.22) or high pain catastrophizing (28% vs. 23%; p=0.08). Despite no overall gender differences in pain catastrophizing, analysis of subscales including threshold levels of: rumination (34% vs. 26%; p=0.01), magnification (58% vs. 51%; p=0.05), and helplessness (31% vs. 24%; p=0.04) revealed differences between women and men, respectively. Women Veterans also reported higher mean pain interference (5.8 vs. 5.4; p<0.05) and intensity scores (5.7 vs. 5.4; p<0.05) compared to men. In conclusion, despite no gender difference in the proportion reporting severe PTSD symptoms, several pain related outcomes were more prevalent or more severe among women compared to men.

Research Topic: Pain
Funding agencies: DOD
Grant support: W81XWH-18-2-0003

17. Brain signatures during the course of emergence from the unresponsive wakeful/vegetative state after severe brain injury

Gilmore, Casey S. [1]; Peterson, Michelle D. [1]; Mortimer, Diane J. [1]; Pellizzer, Giuseppe [1]

1. Minneapolis VA Health Care System

Abstract: Disorders of consciousness (DOC) result from severe brain injuries. The assessment of DOC patients relies primarily on observed motor output. However, this assessment is often challenging due to the sensory, motor, and cognitive impairments resulting from the brain injury. This issue is particularly critical since diagnosis and prognosis have important ethical and medical consequences for the selection of care and treatment decisions. Consequently, families of DOC participants often struggle in making long-term decisions. An alternative, objective methodology could help them in this process. We are currently investigating the use of electroencephalography (EEG) in assisting with the assessment of DOC patients. We have recorded 2 to 25 EEG sessions from 5 DOC patients who had been admitted to the Emerging Consciousness Program of the Polytrauma Rehabilitation Center. The recordings were done at rest and during an auditory oddball paradigm. The Coma Recovery Scale-revised (CRS-r) was used to rate the state of consciousness of the patients. Also, the EEG of 10 control participants was recorded during resting state and the auditory oddball paradigm. The control participants had a history of severe brain injury and loss of consciousness for at least 24 hours following the injury before emerging. We found that the characteristics of the EEG power spectrum changed with the patients' level of consciousness. More importantly, we found that there was a transient increase in beta (13-30 Hz) and gamma (>30 Hz) frequency activity during the period of transition from unresponsive to emerged state (n=3 DOC patients). In contrast, no such change in EEG power spectrum was observed in the patients who did not emerge (n=2 DOC patients). Furthermore, we found that the auditory oddball paradigm could show improvement in the differentiation of the P300 event-related potential, an indicator of conscious perception, even in cases where the CRS-r score did not improve. These results suggest that the auditory oddball paradigm may provide evidence of cognitive processing even when the patients are otherwise unresponsive. We showed that EEG has the potential to provide objective information that can assist with the assessment of DOC patients. In particular, the development of a prominent beta-frequency peak and increase in gamma activity may be biomarkers indicating a positive prognosis for the emergence to consciousness.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: VA RRD
Grant support: I21 RX003007

18. COVID-19 Pandemic Disruptions and Chronic Pain among US Military Veterans on Long-Term Opioid Therapy

Goldsmith, Elizabeth [1-2]; Hammett, Patrick [1]; Martinson, Brian [1]; Noorbaloochi, Siamak [1]; Clothier, Barbara [1]; Krebs, Erin [1-2]

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

Abstract: Background: The COVID-19 pandemic may influence chronic pain outcomes through pandemic effects on systems and communities as well as through COVID-19 illness. We evaluated associations of COVID-19 illness and pandemic disruptions with pain-related function within a cohort of US military Veterans prescribed long-term opioid therapy for chronic pain. Methods: The Effects of Prescription Opioid Changes in Veterans (EPOCH) study is a national cohort that enrolled 9082 Veterans in 2016. Participants have completed yearly surveys including Brief Pain Inventory Interference scale (BPI-I: 0-10 score, higher=worse; minimum clinically important change 1 point). Year 4 surveys (7/2020—2/2021) included NIH-VA-DOD Pain Management Collaboratory COVID-19 questions assessing pandemic disruptions. We estimated binomial logistic regressions with BPI-I change (worsened vs. stable/improved) as the dependent variable and pandemic experience indicators as independent variables, applying design weights and inverse probability weights to adjust for confounding. Results: Within the final analytic sample (n=3833), 75% (n=2876) of year 4 surveys were returned between July and November 2020, prior to the late 2020 US COVID-19 peak. Mean BPI-I was 6.3 (SD 2.2) at both year 3 and year 4. 5% of respondents reported COVID-19 illness before survey return. 59% reported pandemic-worsened ability to get healthcare. 53% reported pandemic-worsened mental and emotional health. Self-reported COVID-19 illness did not significantly associate with BPI-I change between year 3 and year 4 (OR 0.90, 95% CI 0.53-1.54). Self-reported pandemic-related worsening of ability to get healthcare was associated with higher odds of worsening BPI-I vs. remaining stable or improving (OR 1.32, 95% CI 1.04–1.69). Self-reported pandemic-related worsening of mental/emotional health was associated with higher odds of worsening BPI-I (OR 1.72, 95% CI 1.34–2.21). Other pandemic disruptions were also associated with worsening BPI-I (worsened finances OR 1.37, 95% CI 1.07–1.74; worsened ability to meet basic needs OR 1.38, 95% CI 1.08–1.77). Conclusions: In the first COVID-19 pandemic year, most Veterans with chronic pain reported pandemic-related disruptions to healthcare access or mental/emotional health. Disruptions, but not reported COVID-19 illness, were significantly associated with worse pain outcomes. Health care access and support for mental/emotional health should be maintained during health emergencies.

Research Topic: Pain
Funding agencies: VA HSRD
Grant support: IIR 19-083

19. Changes in meaningful non-drug therapy use among U.S. military Veterans within a comparative effectiveness trial augmenting primary care management of chronic pain

Goldsmith, Elizabeth [1-2]; Hammett, Patrick [1]; Nelson, David [1]; Kats, Allyson [2]; DeRonne, Beth [1]; Becker, Will [3-4]; Krebs, Erin [1]; Seal, Karen [5-6]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. VA Connecticut Healthcare System
4. Yale School of Medicine
5. San Francisco VA Health Care System
6. University of California-San Francisco

Abstract: Background: Non-drug therapies (NDTs) are first-line chronic pain treatments. The Veterans' Pain Care Organizational Improvement Comparative Effectiveness (VOICE) trial enrolled Veterans with chronic pain prescribed long-term opioid therapy. This secondary analysis assessed changes in participants' meaningful use of NDTs for pain. Methods: From October 2017—March 2021, 821 Veterans enrolled in VOICE, a pragmatic trial of integrated pain team vs. telecare collaborative management at 10 sites. Patients reported behavioral (relaxation, meditation, psychotherapy), exercise (stretching/strengthening, aerobic, yoga, and tai chi), and manual (acupuncture, chiropractic, and massage) NDT use. Investigator/clinician consensus defined cutoffs for meaningful use. As arms did not differ significantly in any meaningful NDT use at 12 months, descriptive statistics and logistic regressions evaluated meaningful NDT use at follow-up vs. baseline in the overall trial population. Results: Meaningful behavioral therapy use increased at 6 months (51%; OR=1.82, 95%CI 1.53-2.15) and 12 months (53%; OR=1.89, 95%CI 1.59-2.26) vs. baseline (37%), driven by relaxation and meditation. Meaningful exercise therapy use increased at 6 months (60%; OR=1.54, 95%CI 1.29-1.84) and 12 months (58%; OR=1.38, 95%CI 1.16-1.63) vs. baseline (49%), driven by stretching/strengthening. Meaningful manual therapy use did not differ significantly at 6 months (42%; OR=0.85, 95%CI 0.72-1.01) or 12 months (49%; OR=1.14, 95%CI 0.96-1.36) vs. baseline (46%). Meaningful use of 2+ NDT modalities increased at 6 months (53%; OR=1.53, 95%CI 1.29-1.81) and 12 months (53%; OR=1.50, 95%CI 1.26-1.78) vs. baseline (43%). Conclusions: Overall, meaningful NDT use (primarily behavioral and exercise therapies) increased over 12 months among participants in both integrated pain team and telecare collaborative management arms. Results suggest that interventions augmenting primary care management of chronic pain can effectively increase non-drug therapy use for pain, particularly self-management strategies.

Research Topic: Pain
Funding agencies: Other
Grant support: PCORI OPD-1511-33052

20. Examining the Role of Dietary Restriction, Cognitive Restraint, and Fasting in Loss of Control Eating Using Ecological Momentary Assessment

Guidinger, Claire [1]; Stevenson, Brittany [1]

1. Minneapolis VA Health Care System

Abstract: Loss of control eating (LOC) is characterized by the subjective experience of being unable to control what or how much is being eaten, regardless of the actual amount of food consumed. Restraint and restriction models of LOC eating theorize a cyclical relationship between dietary restriction and cognitive restraint. Few studies to date have validated these theories using naturalistic data collection methods. The purpose of this study was to identify if cognitive restraint, dietary restriction, and fasting in hours predicts LOC eating, and vice versa, using Ecological Momentary Assessment (EMA). It was hypothesized that restraint, restriction, and fasting above one's average would lead to a higher likelihood of LOC eating at the next EMA assessment, and that the presence of LOC eating would lead to greater restraint, restriction, and fasting at the next EMA assessment. 37 young adults (84% female, Mage=21.40, 81.58% White) completed a 10-day EMA protocol that entailed completing surveys assessing mood, restraint, restriction, and fasting at five semi-random points throughout each day and self-initiating eating episode assessments. Data were first de-identified, screened, and cleaned in Stata. Multilevel path analysis was conducted in MPlus. After adjusting for positive and negative affect, time-lagged analysis showed that as fasting hours increased since a participant's last eating episode, there was a reduced likelihood of LOC eating at the next eating episode (OR: 0.91, $p \leq 0.05$). Restraint and restriction levels relative to one's mean did not predict a greater likelihood of LOC eating during the next eating episode. The presence of LOC eating also predicted fewer fasting hours before the next eating episode (β=-0.48, $p \leq 0.001$). The presence of LOC eating did not predict subsequent restraint or restriction. Overall, the findings of the current study diverge from prior research and do not support the theory that there is a cyclical pattern between restraint, restriction, and fasting with LOC eating, and vice versa. Interestingly, longer fasting hours predicted a reduced likelihood of LOC eating, and LOC eating predicted fewer fasting hours at the next EMA assessment. Findings also suggest that the presence of LOC at an eating episode may be associated with eating again sooner, suggesting that LOC has a lingering disinhibiting effect. Future research with a larger and more diverse sample is needed to confirm this theory.

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

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21. Lymphatic Morphology, Growth and Apoptosis in Brain Slice Cultures

Hansen, Eric [1]; Lam, Cornelius [1]

1. Minneapolis VA Health Care System

Abstract: Brain slice culture (BSC) is a well-known three-dimensional model of the brain. We use organotypic slices for studying neuro-lymphatic physiology in a model mimicking the natural condition. It has been hypothesized that g-lymphatics are a brain-wide para-vascular pathway for cerebrospinal and interstitial fluid exchange that facilitate efficient clearance of solutes and waste from the brain. We directly test the longstanding assumption that the brain is not a hospitable milieu for typical lymphatic vessels. Immortalized lymphatic rat cell lines were used to seed organotypic brain slices. 300-µm-thick whole-brain coronal sections were collected at the level of the caudate nucleus from approximately -1.40 mm to -2.80 mm Bregma. The organotypic slices were then carefully placed on 3.0-µm membrane inserts and lymphatics characterized by monitoring morphologies, growth rates, and degree of apoptosis. Immortalized lymphatic cells penetrated the brain slices within 2-4 days. Lymphatic cells were observed in more than 50% of the brain slice by day 3, but had significantly higher rates of penetration by day 10. Typical cell morphology was spindly with bipolar and tripolar forms. A doubling time of 34.8 hours was recorded and apoptosis rates in lymphatic BSCs were not significantly different than control BSCs over time. Our model showed sustained lymphatic growth and viability in lymphatic BSCs. Despite an absence of lymphatic formations, i.e. tubes or channels, cells had morphologies similar to those found in other organs. Lymphatic cells showed minimal stress as manifested by robust cell growth and minimal apoptosis and we were able to observe cell to cell interactions in a physiologically correct 3D environment. However, since the higher order structures were not seen it is likely that any constructs, such as glymphatic vessels, would have to be closer to the boundaries outside of the parenchyma. Our BSC system provides a unique model to further study neuro-lymphatic dynamics and investigate CSF and solute clearance from the brain.

Research Topic: Neurology & Neurobiology
Funding agencies: CVRE
Grant support: N/A

22. Balance Changes Following Lumbar Drain as a Predictor of Neuropsychological Performance Following Ventriculoperitoneal Shunt Placement in a Sample of Veterans with Suspected Normal Pressure Hydrocephalus.

Hansen, Lucas [1]; Thuras, Paul [1]; Marggraf, Matthew [1]; Doane, Bridget [1]; Lamberty, Greg [1]; McGovern, Robert [1]

1. Minneapolis VA Health Care System

Abstract: Normal pressure hydrocephalus (NPH) is a disorder of cerebrospinal fluid (CSF) accumulation that causes compression of the brain resulting in motor, autonomic, and cognitive changes. Diagnosis is somewhat imprecise and often relies on clinician judgment. Improvements within this triad of symptoms, particularly changes in gait, following initial lumbar drain (LD) are often an important component of the decision whether more permanent CSF diversion (via ventriculoperitoneal shunt; VPS) would be beneficial (McGirt et al., 2005). Although significant change pre- to post-LD in neuropsychological performance was limited to finger tapping and phonemic fluency performance within this sample (Marggraf et al., 2022), analyses incorporating physical symptoms and post-VPS neuropsychological status have yet to be explored. In this study, we examined whether change in balance performance following LD predicted change in neuropsychological performance from pre-LD to post-VPS in a group of 9 Veterans with suspected NPH as part of an observational study. Patients were administered a battery of sensitive neuropsychological measures before and after the LD trial. Multilevel modeling was used for prediction analyses due to variation in follow-up timepoint measurement within the nested data. Changes in balance following lumbar drain were not predictive of changes in neuropsychological performance following VPS placement with regard to any of the neuropsychological measures administered (n=9; ps=0.189-0.646), likely due to the size and characteristics of the current sample. However, a generally consistent (yet non-significant) medium to large effect size was observed in performances of verbal fluency (r=0.33, p=0.38), dominant hand finger tapping (r=0.34, p=0.37), non-dominant hand finger tapping (r=0.43, p=0.25), and reverse digit span (r=0.42, p=0.26) when exploring the relationship between change in balance performance following lumbar drain to change in neuropsychological functioning from pre-LD to post-VPS placement. As such, continued data collection will provide further clarity regarding the utility of this modeling for future analyses.

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

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23. Understanding Substance Use Disorder and Comorbid Conditions in Veteran's Real-life Settings

Herrmann, Heather [1]; Stevenson, Brittany [2]

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

Abstract: Substance use disorders (SUDs) are common in Veterans, and have a strong tendency to coincide with comorbid symptoms like depression and PTSD. Substance use is also related to a host of other factors, like mood, social context, and urges. However, there is limited knowledge as to how all these factors connect to predict substance use. Our study aims to make those missing connections. Ecological momentary assessment (EMA) gives us the opportunity to assess all these constructs in the participant's natural environment over time. The resulting data will allow for individualized modeling of substance urges, use, and problems. We recruited Veterans seeking treatment for SUD(s) at the Minneapolis VA to take EMA surveys 4x daily for 4 weeks. Each survey started with the same questions for every participant, assessing comorbid symptoms, social context, mood, coping skills, substance urges, use, and substance-related problems. Personalized questions were added to each survey for items identified by each participant as important to their recovery and substance use patterns. At the end of the EMA, we analyzed each person's responses using causal inference algorithms followed by structural equation modeling to estimate edge strength. Each person's data is individually examined and includes a written interpretation of the model for them to better understand their results and how to use them to further their recovery. Results are presented for one of three total participants, to illustrate the detail of one person's data. This participant completed 100% of the surveys. Their personalized items were sleep, thoughts about their recovery, exercise, interpersonal approval, and amount of time spent at work. They entered treatment for alcohol use disorder but only reported nicotine use during the study period. At each assessment, their average happiness was M=2.78 (SD=0.61, range 1-4), average stress levels were M=0.73 (SD=0.61, range 0-3), average number of coping skills used was M=3.36 (SD=2.57, range 0-12), and average energy levels were M=2.14 (SD=0.91, range 0-4). Their most central symptom was happiness which means many items in the graph increased or decreased happiness or came as a result of happiness. For example, happiness led to relationship satisfaction which then led to decreased nicotine usage. This graph allows us to examine personalized items in order to start facilitating changes that may decrease substance use and improve well-being.

Research Topic: Substance Use Disorders
Funding agencies: CVRE
Grant support: N/A

24. Lung Microbiome Correlates with Lung Adenocarcinoma and Self-Reported Dental Cleaning

Hodgson, Shane [1]; Pragman, Alexa [1]; Wu, Tianhua [2]; Zank, Allison [1]; Reilly, Cavan [2]; Wendt, Chris [1-2]

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

Abstract: METHODS: We recruited 44 patients undergoing lung lobectomy for suspected lung cancer at a single Veterans Affairs hospital. Tobacco use history, lung function, medications, dental cleaning frequency, and pathologic diagnosis were recorded. One day prior to surgery, oral wash and induced sputum samples were obtained. Another oral wash sample and a nasopharyngeal sample were obtained just prior to surgery. Immediately following lobectomy, a bronchus sample and 3 separate lung parenchymal samples were obtained from the surgical specimen via swab. Samples underwent 16S rRNA V4 MiSeq sequencing. Data were analyzed using R. RESULTS: Most subjects were male (42, 95%) with a median age of 67 years. Thirty-six (82%) met spirometry criteria for COPD; 20 (56%) with mild, 14 (39%) with moderate, and 2 (6%) with severe disease. Five (11%) reported current tobacco use. Ten (23%) were edentulous, 15 (34%) reported a professional dental cleaning within the last 6 months, and 19 (43%) reported their last cleaning was >6 months prior. Twenty-six (59%) had adenocarcinoma, 14 (30%) had another malignancy, and 5 (11%) had no malignancy. Among nasopharyngeal and oral wash samples, increased age was associated with increased α-diversity (Simpson, $p=0.019$ and $p=0.022$, respectively). Among lung and bronchus samples, current tobacco use ($p<0.001$) and dental cleaning <6 months prior ($p<0.001$) were associated with an increase in α-diversity, while adenocarcinoma ($p=0.024$) was associated with a decrease in α-diversity. β-diversity (Bray-Curtis) demonstrated clustering by upper airway (oral wash, sputum) vs. lower airway (bronchus, lung) vs. nasopharyngeal sites. PERMANOVA analyses by site revealed clustering of lung samples by dental cleaning <6 months vs. >6 months prior ($p=0.027$). Dental cleaning <6 months was associated with increased Actinomyces among bronchus samples ($p=0.028$) and increased Streptococcus among lung samples ($p=0.007$). Current tobacco use was associated with decreased Granulicatella ($p=0.010$), increased Haemophilus ($p<0.001$), and increased Prevotella ($p=0.030$) among lung samples and increased Mycoplasmoides ($p=0.021$) among bronchus samples. Adenocarcinoma was associated with decreased Lawsonella among RATIONALE: The source of the lung microbiome is the oral microbiome; however, lung microbiome composition is heavily influenced by lung diseases. We determined the relationship between the upper and lower airway microbiome among patients with suspected lung cancer.

Research Topic: Oncology
Funding agencies: VA CSRD
Grant support: IK2 CX001095; I01 CX002130; NIH/University of Minnesota Clinical

25. Emerging Innovations in Rehabilitation Hospital Discharge Decision During the COVID-19 Pandemic: A Qualitative Study

Hudson, Emily [1]; Gustavson, Allison [1-2]; Miller, Matthew [3]; Boening, Natassia [1]; Wisdom, Jennifer [4]; Burke, Robert [5-6]; Woodward-Abel, Alicia [1]; Hagedorn, Hildi [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. University of California
4. Wisdom Consulting
5. Corporal Michael J. Crescenz VA Medical Center
6. University of Pennsylvania

Abstract: Objective: The purpose of this qualitative study was to identify factors influencing the emergence of innovation in rehabilitation hospital discharge decision-making during the Coronavirus 2019 (COVID-19) pandemic. Methods: Rehabilitation clinicians were recruited from the Veterans Affairs Health Care System and participated in individual semi-structured interviews guided by the Promoting Action on Research Implementation in Health Services (PARIHS) framework. Data were analyzed using a rapid qualitative, deductive team-based approach informed by directed content analysis. Identified themes were compared between pre-pandemic and COVID-19 era timepoints. Results: Twenty-three rehabilitation clinicians representing physical (n=11) and occupational therapy (n=12) participated in the study. Three primary themes were generated and compared pre-pandemic to COVID-19 era. First, the receipt of and participation in hospital discharge decision-making by patients and their care partners centered around communication changes and the complex nature of needs. Second, the environment in which the rehabilitation clinicians operated in to enact discharge decisions was influenced by the system's influence on clinical practice, the team role of rehabilitation clinicians, and pandemic-related fluctuations in practice. Third, discharge processes evolved with the onset of the pandemic with specific innovations noted by participants around team collaboration, shifts in hospital caseload prioritization, and alternative options for care delivery during the transition from hospital to the home. Conclusions: The experiences captured by rehabilitation clinicians indicate that responses to unforeseen stressors can be innovative. Future research is needed to assess the impact of innovations, remediate unintended consequences, and evaluate the implementation of promising innovations to respond to emerging healthcare delivery needs more rapidly. Impact Statement: The findings from this study highlight how adaptations in response to external stressors (pandemic) can potentially improve patient, clinician, and system-level outcomes. The findings also highlight the importance of implementation frameworks in identifying factors that facilitate innovation that improves health service delivery and patient outcomes.

Research Topic: Rehabilitative Medicine
Funding agencies: VA HSRD; UMN; CVRE
Grant support: CIN 13-406; K12 HS026379

26. Reducing Impulsive Behavior in Veterans with Traumatic Brain Injury (TBI) using Transcranial Direct Current Stimulation (tDCS) Paired with Cognitive Training Tasks

Jamal, Hamza [1]; Carson, Molly [1]; Larkin, Florence [1]; Moua, Angel [1]; Lim, Kelvin [1]; Gilmore, Casey [1-2]

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

Abstract: Impulsive behaviors arising following a TBI are one of the most common challenges facing patients and their families. We previously showed that tDCS over the prefrontal cortex paired with a decision-making training task reduced impulsive behavior on an untrained Risk Task in a clinically impulsive sample of Veterans (Gilmore et al., 2018). In the current study, we paired tDCS over DLPFC (left anodal/right cathodal) with executive functioning training tasks once per day for 5 days. 26 Veterans with a history of mild, moderate, or severe TBI and impulsive behaviors were randomized to receive active tDCS (n=14) or sham (n=12). Participants performed a battery of cognitive tasks and self-report symptom questionnaires pre-intervention, post-intervention, and at follow-ups 1, 2, and 3 months later. Here we report on preliminary analyses of the Stop Signal task, Barratt Impulsiveness Scale (BIS11) and Behavioral Inhibition/Activation System Scale (BIS/BAS) using individual growth curve models that used mixed effect models with maximum likelihood estimation. The method modeled change over time (Time: sessions), examined effects of group differences (Group: active vs sham), and tested for interactions. Significant interactions between Time and Group were found for 1) Stop Signal Task: response inhibition to stop signal trials (coef.=-0.014, p=0.03), 2) BIS11: Motor Impulsiveness (coef.=-0.327, p=0.008), and 3) BIS/BAS: BAS Fun Seeking (coef.=-0.154 ,p=0.04). Overall, these preliminary results indicate that, from pre- to post-intervention, active tDCS 1) improved the ability to inhibit responding in the Stop Signal task, 2) reduced motor impulsiveness as measured by the BIS11 (e.g. tendency to act on the spur of the moment), and 3) decreased motivation to find novel rewards spontaneously as measured by the BIS/BAS. Further, this decreased level of impulsiveness remained stable across the three month follow-up period. Consistent with our hypotheses, the active tDCS reduced impulsive behavior over time compared to sham in both self-report and objective task measures, and this result was durable. Results suggest that this approach may be an effective neuroplasticity-based intervention for patients with a history of TBI affected by impulsivity. We are continuing to explore other data collected in this study, such as the range of TBI severity of the Veterans, alternate methods of characterizing performance (e.g. reaction times), and performance on the training tasks.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: Other
Grant support: Minnesota Office of Higher Education TBI Grant 143479

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27. A Ventriculomegaly Feature Computation Pipeline to Improve the Screening of Normal Pressure Hydrocephalus on Computed Tomography

Kadaba Sridhar, Sharada [1-2]; Kuang, Rui [2]; Gupta, Rishabh [1]; Samadani, Uzma [1]

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

Abstract: Objective: Computational methods to quantify ventriculomegaly on Non-Contrast CT (NCCT) may enable improved detection of possible idiopathic Normal Pressure Hydrocephalus (NPH). We developed a computational pipeline to extract ventriculomegaly features and use them for NPH screening. Methods: Retrospective cohorts of NPH (n=84), Alzheimer's disease (AD) (n=97), post-traumatic encephalomalacia (PTE) (n=61), and headache control (HC, n=72) were identified on the Veterans Affairs Informatics and Computing Infrastructure. Image processing pipelines were developed to extract a novel feature capturing lateral ventricle eccentricity (MaxEccLV), a proxy-Splenial Angle (p-SA), the Evans indices (EI-x, y, z), Callosal angle (CA), third ventricle width (NMax-3VW), and CSF to brain volume ratio (CSF2BVR) from their NCCT. We used t-tests to examine group differences, and logistic regression to classify between NPH, AD, PTE, and HC. We validated our NPH v/s HC classifier on an external dataset with 13 NPH (External NPH) and 30 normal (External Control) patients to study the generalization capacity of our model. Results: When NPH was compared to HC, AD, and PTE, significant differences were seen in MaxEccLV (95% CI: [-0.17,-0.13], [-0.11,-0.07], and [-0.14,-0.1], respectively), and in all the other features. The best AUC, sensitivity, and specificity were 0.98, 98.8%, and 98.6% for NPH v/s HC; 0.9, 84.5%, and 82.5% for NPH v/s AD; 0.95, 91.7% and 86.9% for NPH v/s PTE; and 0.94, 83%, and 87% for NPH v/s rest using logistic regression under 5-fold cross validation. The NPH v/s HC model classified between the External NPH and External Control cohorts with an AUC of 0.85, sensitivity of 76.9%, and a specificity of 90%. Conclusions: Including the newly proposed MaxEccLV and the p-SA which captured significant differences between NPH and AD/PTE/HC, our framework semi-automatically computes the CA, EI-y, EI-z, NMax-3VW, and CSF2BVR from NCCT which have so far been manually measured, along with the EI-x. External validation of our NPH v/s HC classifier shows that our model generalizes well. This allows for successful screening of possible NPH from HC/AD/PTE.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: Other

Grant support: Minnesota Office of Higher Education

28. CSP #2016: National Adaptive Trial for PTSD Related Insomnia (NAP)

Kemmer, Sara [1]; Westermeyer, Joseph [1]; Swanson, Heather [1]

1. Minneapolis VA Health Care System

Abstract: VA Cooperative Studies Program (CSP) Cooperative Study #2016 is a double-blind, four-arm adaptive clinical trial to compare the efficacy of trazodone hydrochloride, eszopiclone, and gabapentin to placebo, as adjunctive therapies in the treatment of insomnia symptoms among Veterans with military-related post-traumatic stress disorder (PTSD). Many Veterans with PTSD have trouble sleeping or have frequent nightmares. So far, no medication has been approved for treatment of insomnia in PTSD. The purpose of this research study is to find out if taking medications called trazodone, eszopiclone, or gabapentin can help decrease symptoms of insomnia in patients with PTSD. PTSD is a form of intense anxiety which sometimes results from severe trauma. Symptoms may include nightmares, flashbacks, troublesome memories, difficulty sleeping, poor concentration, irritability, anger, and emotional withdrawal. Insomnia is a disorder that can make it hard to fall asleep, stay asleep or cause a person to wake up too early and not be able to fall back to sleep. The Insomnia Severity Index (ISI) is the primary outcome measure for this study. The Clinician Administered PTSD Scale for DSM-V (CAPS-5) will be the key secondary outcome measuring change in PTSD symptoms.

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

29. Improving Veterans' Telehealth Experience Through Technology Transfer Innovation

Kivi, Andrew [1]

1. Minneapolis VA Health Care System

Abstract: The COVID-19 pandemic has energized interest in telehealth modalities, including remote administration, review, and interpretation of point-of-care testing devices. Such methods have great promise to improve care for individuals with substance use disorders, who may otherwise require in-person toxicology testing multiple times per week in order to participate in medication-assisted treatment for opioid use disorder or reward-based interventions such as Contingency Management. While there is considerable interest in new technology that will unlock the potential of telehealth-based point-of-care testing, some practical challenges to implementation remain to be addressed. One key challenge to be improved upon is the qualitative visualization of test results. The MADE technology transfer assistance program (TTAP) has worked to develop a solution to meet this key challenge. Within 6 months, this new device has gone from idea to reality. Now Veterans will have better access to care from anywhere, and clinicians will be able to easily interpret test results.

Research Topic: Substance Use Disorders
Funding agencies: None
Grant support: N/A

30. A randomized trial of pain care delivery models for patients on long-term opioids in VA primary care

Krebs, Erin [1-2]; Becker, William [3]; Nelson, David [1]; Kats, Allyson [2]; Hammett, Patrick [1]; DeRonne, Beth [1]; Nugent, Sean [1]; Jensen, Agnes [1]; Amundson, Erin [1]; Seal, Karen [4]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. VA Connecticut Healthcare System
4. San Francisco VA Health Care System

Abstract: The Veterans' Pain Care Organizational Improvement Comparative Effectiveness (VOICE) trial was a 10-site pragmatic trial. The primary aim was to compare higher-intensity integrated pain team (IPT) versus lower-intensity telecare collaborative management (TCM) for improving pain and reducing opioid use. 820 VA patients with moderate-severe pain prescribed long-term opioids ≥20 mg/day were randomized to 1 of 2 12-month interventions. IPT was an interdisciplinary team intervention emphasizing multimodal therapies. TCM was a clinical pharmacist care management intervention. Both interventions provided individualized pain care and opioid tapering support. Masked assessors collected outcomes at 3, 6, 9, and 12 months. The primary outcome was pain response defined as ≥30% decrease in Brief Pain Inventory (BPI) at 12 months. From baseline to 12 months, the mean BPI score decreased from 6.7 (SD 1.5) to 6.1 (SD 1.8) in IPT and 6.6 (SD 1.6) to 6.0 (SD 1.9) in TCM. The pain response rate was 17% in IPT and 15% in TCM; the odds of pain response for IPT vs. TCM was 1.11 (95% CI 0.74, 1.66). From baseline to 12 months, the mean opioid daily dose decreased from 80 mg (SD 73) to 54 mg (SD 65) in IPT and 75 mg (SD 57) to 53 mg (SD 52) in TCM. The proportion with 50% dose reduction was 25% in IPT and 25% TCM; the odds of dose reduction for IPT vs. TCM was 1.03 (95% CI 0.75, 1.42). We concluded IPT and TCM had similar benefits for patients prescribed long-term opioids for chronic pain.

Research Topic: Pain
Funding agencies: Other
Grant support: PCORI OPD-1511-33052

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31. Effect of Opioid Dose Reduction or Discontinuation on Pain Interference with Function: Prospective Observational Study

Krebs, Erin [1-2]; Clothier, Barbara [1]; Goldsmith, Elizabeth [1]; Martinson, Brian [1]; Jensen, Agnes [1]; Hammett, Patrick [1-2]; Noorbaloochi, Siamak [1]

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

Abstract: Objective: To evaluate effects of opioid dose reduction or discontinuation on pain interference with function over two years of follow-up in a nationally representative prospective observational cohort study of VA patients prescribed long-term opioid analgesics in 2016. Methods: Of 14,160 patients invited, 9253 (65.3%) enrolled. Data were analyzed for participants in adequately sized clusters and alive at follow-up (9082 at baseline, 8825 at 1 year; 8449 at 2 years). Opioid daily dose was calculated for 60 days before each response. Opioid treatment was categorized as stable if daily dose changed <10 mg from baseline; reduced- or increased-dose if change was ≥10 mg lower/higher than baseline; and discontinued if no opioid was dispensed for 60 days. Brief Pain Inventory Interference (BPI-I) scale (0-10 score, higher=worse) outcomes were clinically relevant improvement or worsening defined as ≥1 point change from baseline. We used chi-squares to test for bivariable associations of opioid treatment with BPI-I outcomes separately for each year. To examine relationships among opioid treatment variables and BPI-I outcomes over time, we used Bayesian Network structure learning, a machine-learning method that uses directed acyclic graphs to identify conditional dependence relationships in the joint probability distribution of a set of variables. Results: The mean opioid daily dose was 50.6 mg at baseline, 40.9 mg at 1 year, and 33.2 mg at 2 years. At 1-year, 13.9% had reduced-dose opioids and 18.9% had discontinued opioids. At 2-years, 17.5% had reduced-dose opioids and 30.1% had discontinued opioids. The mean BPI-I was 6.5 (n=8956) at baseline, 6.4 (n=7211) at 1 year, and 6.4 (n=6391) at 2 years. Unadjusted bivariable comparisons at 1 year showed no association of opioid treatment with BPI-I outcome (p=0.67). At 2 years, there were slightly more improved patients in the discontinued group and slightly more worsened patients in the stable and increased-dose groups (p=0.05). In multivariable analyses, all 10 learned structures showed strong dependency among the 3 opioid treatment variables. Nine of 10 learned structures showed opioid treatment variables were independent of BPI-I outcomes; 1 showed possible weak dependency among opioid treatment variables and BPI-I outcomes. Conclusions: The probability of pain interference improving or worsening over two years was not influenced by changes in prescribed opioid treatment.

Research Topic: Pain
Funding agencies: VA HSRD
Grant support: IIR 14-295; IIR 19-083

32. Impact of Substance Use on PTSD Symptoms and Treatment Discontinuation

Lee, Jenny [1]; Stevenson, Brittany [1]; Kehle-Forbes, Shannon [1]

1. Minneapolis VA Health Care System

Abstract: Studies indicate high rates of comorbidity between substance use disorders (SUD) and posttraumatic stress disorder (PTSD). The prevalence of SUD and PTSD among military personnel and Veterans are two to four times higher than that of the general population (Petrakis et al., [2011]; Teeters et al., 2017). Recent meta-analyses have demonstrated that integrated PTSD/SUD treatment, particularly those that involve a specific trauma focus, are effective at reducing PTSD and SUD symptoms (Roberts et al., [2022]; Roberts et al., [2015]; Simpson et al., 2021). However, integrated treatments have shown smaller treatment effects than those observed in PTSD studies without the comorbidity, as well as higher rates of treatment discontinuation than treatment for either disorder alone (Roberts et al., [2016]; Roberts et al., 2022). The present study sought to examine whether ongoing substance use throughout integrated PTSD/SUD treatment would affect PTSD symptoms and treatment discontinuation. Predictors were the percentage of days with alcohol use, cannabis use, and other substance use (primarily cocaine and opioids), and average number of alcoholic drinks per drinking day. Outcomes were PTSD symptoms and treatment discontinuation at concurrent and prospective assessments. Multilevel models accounted for the nested structure of the longitudinal data. This was a secondary analysis of 183 Veterans with comorbid PTSD and SUD, as diagnosed by DSM-IV criteria, who presented for treatment between 2011 and 2015 at either the Minneapolis or Philadelphia Veterans Affairs Medical Centers. Veterans identified as mostly Black (55%) or White (41%) and male sex (92%). The average age was 44.12 (SD=13.03). Results showed alcohol, cannabis, and other substance use did not meaningfully predict PTSD symptoms or treatment discontinuation at concurrent or prospective time points. Percentage of days using alcohol was statistically associated with PTSD symptoms when measured during the same 4-week period, however, this result was not considered clinically meaningful given the small magnitude of the effect size. These results suggest that active alcohol, cannabis, cocaine, and opioid use during treatment are not directly responsible for reduced efficacy of or higher treatment discontinuation from integrated PTSD/SUD treatment, and other factors associated with SUD need to be explored.

Research Topic: Substance Use Disorders
Funding agencies: VA CSRD
Grant support: ZDA1-03-W10

33. Effect of dopamine-replacement therapy on the gambling impulsivity of Parkinson's patients

Lewis, Scott [1]; Hemmy, Laura S. [1]; Pellizzer, Giuseppe [1]

1. Minneapolis VA Health Care System

Abstract: Dopamine-replacement (DR) therapy has been associated with an increase in impulsive behavior in Parkinson's disease (PD) patients. Impulsivity has been linked to increased fall risk in PD patients and an altered quality of life. When impulsivity reaches the levels of impulse control disorders, it can lead to financial ruin, marital distress, and more generally negatively affect patients and their families quality of life and emotional well-being. For these reasons, more research is critically needed to better understand the DR-induced impulsivity in PD, and to develop more effective care. The goal of our project is to compare the outcome of behavioral tests (Iowa gambling task and go/no task) and functional brain measures in PD patients while they are ON and OFF DR. The Iowa gambling task tests decision-making abilities in a simulated card game, whereas the go/no-go task tests the ability to abort a preponderant motor response. Here we present preliminary results on the change in performance in the behavioral tasks of n=31 PD patients while in on versus off DR medications. Using a cluster analysis, we found that 58% (18/31) of PD patients had significantly more impulsive behavior in the Iowa gambling task while in ON versus OFF DR medication. They made significantly more unfavorable choices and lost significantly more play money in the ON DR medication condition compared to the OFF medication condition. In contrast, we found no significant effect of the medication condition on the go/no go task. The results show that DR medication significantly increased impulsive behavior of PD patients in a simulated gambling task. In the near future we will analyze magnetoencephalography data recorded while the patients performed the tasks to extract functional brain activity biomarkers that reflect the susceptibility to DR-induced impulsivity. We expect that the outcome will provide a better understanding of the brain mechanisms associated with impulsivity and how those are affected by DR medication in PD.

Research Topic: Neurology & Neurobiology
Funding agencies: VA CSRD
Grant support: I01 CX001773

34. A Small Molecule Orexin Agonist Induced Enhancement of Physical Activity and Cognition is Attenuated by an Orexin-1 Receptor Antagonist

Mavanji, Vijayakumar [1-2]; Shekels, Laurie [1]; Pomonis, Brianna [1]; Zhang, Dehui [3]; Zhang, Yanan [3]; Kotz, Catherine [1-2]

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

Abstract: Obesity is associated with alterations in physical activity and cognition, processes which are regulated in part by lateral hypothalamic orexin. Loss of orexin neurons and/or function is characterized by reduced physical activity, obesity and altered cognition. We hypothesized that activation of orexin receptors using newly developed small molecular weight agonists will enhance spontaneous physical activity (SPA) and cognitive function. A secondary hypothesis was that the agonist acts via orexin 1 receptor (OX1R) to enhance SPA and cognition. For the SPA study, we injected a small molecule orexin receptor agonist (RTIOXA-47, IP, 40mg/kg) in wild type male, 8-mo mice. To understand the receptors involved in agonist-induced SPA, OX1R (SB334867) or OX2R (JNJ-10397049) antagonists were injected (5mg/kg, IP) 15 min prior to injection of RTIOXA-47. Post-injection SPA was measured using an indirect calorimetry system. To determine which OXR mediates the effect of RTIOXA-47 on cognition, SB-334867 or JNJ-10397049 antagonists were injected into 12-mo male mice 15 min prior to RTIOXA-47. Injections were performed immediately after two-way active avoidance (TWAA, a memory test) training, and mice were tested for memory 24h thereafter. Peripheral injection of RTIOXA-47 enhanced physical activity up to 4h post-injection in mice. Similarly, peripheral injection of RTIOXA-47 in mice increased memory in the TWAA task, indicating improved cognition. The OX1R, but not OX2R antagonist attenuated RTIOXA-47 induced enhancement of both SPA and memory, suggesting that the small molecule orexin agonist RTIOXA-47 effects on SPA and memory are mediated by OX1R. Despite that orexin tone decreases in obesity and neurogenerative disorders, orexin receptors remain intact and orexin-based pathways can be stimulated. Future studies with specific OX1R agonists will focus on approaches to target orexin pathways with small molecule agonists to treat metabolic, sleep and cognitive disorders.

Research Topic: Obesity
Funding agencies: VA BLRD; VA RRD
Grant support: I01 BX005815; I01 RX003901

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35. Examining the Impact of Under-reporting on the MMPI-3 in the Assessment of Suicidal Ideation Among Treatment Seeking Veterans

Michal, Zachary [1]; Marquardt, Craig [1]; Arbisi, Paul [1]

1. Minneapolis VA Health Care System

Abstract: Self-report screening measures of suicide risk typically do not address the credibility of self-reported suicidal ideation. Previous research with the MMPI-2-RF suggests that under-reporting is associated with a reduced likelihood of endorsement of suicidal ideation and other relevant suicide risk factors among high-risk populations. The contemporary normative group used in the MMPI-3 demonstrates a relative increase in the likelihood of endorsement of MMPI-3 under-reporting items in the general population. As such it is important to replicate previous findings and examine the impact of under-reporting on assessment of suicide risk with the MMPI-3. The aim of this study is to assess whether under-reporting based on MMPI-3 validity scales L and K is associated with suppressed scores on the suicidal/death ideation (SUI) in a sample of treatment seeking Veterans (n=496). Additionally, we examine whether correlations between the MMPI-3 SUI scale and collateral measures of suicidal ideation such as number of past suicide attempts and clinician suicide risk ratings show weaker associations among under-reporting Veterans as compared to non-under-reporting Veterans. T-tests were used to examine mean differences for SUI and other scales relevant to suicidal behaviors across groups classified as under-reporting and not under-reporting. Results found significant group differences such that Veterans classified as under-reporting via L or K validity scales possessed significantly lower scores on SUI (Hedges' g=0.60). Similar group difference effects were observed across other scales relevant to suicide risk, e.g., demoralization, disconstraint (Hedges' g=0.49-1.37). The findings highlight the clinical utility of the MMPI-3 under-reporting scales with high-risk population and the added value of considering validity scales when screening for acute suicide risk.

Research Topic: Suicide Prevention
Funding agencies: Other
Grant support: University of Minnesota Press

36. Million Veteran Program

Murdoch, Maureen [1-2]; Bender, Tricia [1]; Pahl, Marissa [1]; Dorman, Christopher [1]

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

Abstract: The Million Veteran Program is the VA's largest research effort working to understand how genes, lifestyle, military experiences, and exposures affect health and wellness. Its goal it to enroll over 1 million Veterans to generate research findings that will improve health for Veterans, and ultimately everyone.

Research Topic: Genomics
Funding agencies: VA CSRD
Grant support: N/A

37. Method for Testing Prosthetic Socket Strength

Nickel, Eric [1]; Drew, Davis [1]; Layman, William [2]; Berardo-Cates, Alexander [3]

1. Minneapolis VA Health Care System
2. VA Southeast Louisiana Healthcare System
3. VA Puget Sound Health Care System

Abstract: Prosthetic sockets are the interface between the body and an artificial limb. For lower limb prostheses, these sockets distribute the forces of weight-bearing to the tissues of the residual limb, transferring forces and torques to the soft tissues of the limb which then transfer those loads to the skeleton. The socket must both be structurally sound to support the loads of human movement while also fitting the unique anatomy of the user. For this reason, each socket is unique. Traditional engineered components have defined geometries that can be tested, but patient-matched shapes could be almost anything. There is no "worst case" that can be defined because there will always be one more patient with a more extreme geometry to consider. The application of current ISO test methods for engineered prosthetics components results in a failure to assess the strength and durability of the majority of the socket, succeeding only in evaluating the distal end. Recent interest in the use of 3D printing has led to questions regarding safety when applying materials and fabrication methods not traditionally part of the prosthetics industry. The absence of a standard test methodology is limiting the ability to leverage these technologies for innovations. A team including researchers at the Minneapolis VA Health Care System, an engineer with the VA Office of Advanced Manufacture and a certified prosthetist at the Southeast Louisiana VA Health Care System have partnered with representatives of the American Orthotics and Prosthetics Association, international researchers, prosthetists, industry representatives, and members of the ISO Technical Committee 168 (Prosthetics and Orthotics) to jointly develop a novel methodology that can assess the structural strength and durability of novel prosthetic socket technologies. The objective of this work is to develop a prototype methodology that will form the basis for developing an international standard for testing the strength and durability of lower limb prosthetic sockets.

Research Topic: Prosthetics
Funding agencies: Other
Grant support: VA-DoD Joint Incentive Fund

38. Comparing influenza and COVID-19 vaccine hesitancy and motivations among a cohort of flu vaccine study participants: an INVESTED Trial ancillary study

Norman, Sarah [1]; Lalani, Narlina [1]; Vardeny, Orly [1]

1. Minneapolis VA Health Care System

Abstract: Patients with CV disease are particularly vulnerable to complications from viral illness, and flu and COVID vaccines have shown to reduce adverse clinical outcomes. Factors that contribute to vaccine hesitancy in patients with heart disease are incompletely understood. We undertook a phone survey of INVESTED Trial (2016—19 flu seasons) participants from 44 sites in 2021—22. INVESTED randomized 5260 patients with recent history of hospitalization for MI or HF to high dose trivalent or standard dose quadrivalent flu vaccine and examined relative efficacy on all-cause mortality or cardiopulmonary hospitalizations. Participants completed a survey assessing incidence of COVID-like illness and related clinical and social factors, as well as vaccine hesitancy domains (trust, safety, necessity, and effectiveness for both COVID and flu vaccines). Questions were scored from 1 to 7 (1=not at all/not important, and 7=completely/very important). A total of 643 participants completed the survey. Of these, 604 (94%) indicated they received at least one COVID vaccine, 493 (77%) received the flu vaccine (in 2021—22 or 2022—23), and a total of 475 (77%) received both. Most vaccinated patients rated both vaccines a 6 or 7 in trust (78% for COVID, 77% for flu), necessity (84%, 81%), safety (83%, 88%), and effectiveness (76%, 76%). Unvaccinated participants rated trust (9% for COVID, 24% for flu), necessity (9%, 21%), safety (15%, 33%), and effectiveness (12%, 33%), and had lower scores in all categories. Vaccinated individuals rated wanting to protect those close to them highest as a factor contributing to vaccination (83% vs 36% of unvaccinated participants), followed by adherence to primary care recommendations (62% vs 12%), and wanting life to get back to normal (70% vs 9%). This group considered short-and long-term vaccine adverse effects to be the least important, with the fewest percentage of participants rating these a 6 or 7 (25% short- and 23% long-term), while these were most important factors for unvaccinated participants (48%, 55%). In summary, both groups surveyed felt similarly about COVID and flu vaccines in hesitancy domains, with lower scores from unvaccinated participants. The groups had different motivations for receiving or not receiving the COVID-19 vaccine. Further analysis is needed to better understand how vaccine attitudes of those with cardiopulmonary disease and a willingness to participate in vaccine related research compares to other group

Research Topic: Cardiovascular Disease
Funding agencies: NIH; Other
Grant support: NHLBI

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39. The relation between mental health stigma and suicidal ideation: A cross-sectional and longitudinal examination in two samples

O'Reilly, Lauren [1]; Hom, Melanie [2]; Krendl, Anne [3]; Joiner, Thomas [4]; Yu, Carol [1]

1. Minneapolis VA Health Care System
2. Stanford University School of Medicine
3. Indiana University
4. Florida State University

Abstract: Stigmatizing beliefs about mental health have been associated with numerous adverse outcomes (e.g., poor mental health outcomes); however, few studies have explored the relationship between mental health-related stigma and suicidal ideation, especially longitudinally. This investigation aimed to examine the relation between mental health-related stigma and suicidal ideation cross-sectionally and longitudinally in two US-based samples: Study 1 consisted of 286 general undergraduate students who completed self-report assessments at baseline, one-month follow-up, and two-month follow-up, and Study 2 consisted of 237 undergraduates with recent suicidal ideation who completed self-report assessments at baseline, two-month follow-up, and six-month follow-up. In both studies, measures of suicidal ideation, perceived stigma, barriers to seeking mental health care, suicide stigma, and stigma of help-seeking were collected at each time point. We conducted regression analyses to examine the cross-sectional and longitudinal associations between each type of stigma and suicidal ideation. We also constructed a bifactor model that captured shared variance (general factor) and unique variance (specific factors) amongst all stigma measure items to predict suicidal ideation cross-sectionally and longitudinally. Results suggested that perceived stigma and barriers to care were robustly associated with suicidal ideation. Among the general sample (Study 1), suicide stigma was not predictive of suicidal ideation. Beliefs glorifying or normalizing suicide were associated with suicidal ideation only among the higher-risk sample (Study 2). The shared variance among the stigma measures was predictive of suicidal ideation in both samples. The results highlight the potential role of mental health stigma, especially glorification and normalization of suicide, in suicide risk.

Research Topic: Suicide Prevention
Funding agencies: None
Grant support: N/A

40. Extracting Clinically Relevant Data Using Pattern Recognition: A Non ML Approach

Ortiz, Isai [1-2]; Taylor, Olivia [1]; Taylor, Brent [1]; McPherson, Jacob [1]; Ibrahim, Hanna [1]; Raju, Srihari [1]; Nelson, David [1]; Nugent, Sean [1]; Cutting, Andrea [1]; Nayanjot, Rai [2]; Westanmo, Anders [1]; Margolis, Karen [1,3]; Muntner, Paul [4]; Shimbo, Daichi [5]; Drawz, Paul [2]; Ishani, Areef [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. HealthPartners
4. The University of Alabama at Birmingham
5. Columbia University

Abstract: The VA has a vast amount of patient data sitting in patient notes. Some clinically relevant information is buried in free form text fields waiting to be extracted. This poster presents a method using pattern recognition to extract home blood pressure measurements from patient notes. The method is agnostic to manufacturer and relies on the predictable pattern of blood pressure measurements to work. It is effective and simple requiring little overhead unlike natural language processing algorithms that require training data and are computationally heavy. This work can be extended to other telehealth proforma with similar characteristics.

Research Topic: Informatics
Funding agencies: NIH
Grant support: R01 HL157667

41. Increasing prescribing of sodium-glucose cotransporter-2 inhibitors among eligible patients in the VA: A targeted pharmacist intervention

Pestka, Deborah [1-2]; Murphy, Daniel [1]; Huynh, Pearl [1]; Rechtzigel, Jessica [1]; Kjos, Shari [1]; Ellich, Lisa Marie [1]; Atwood, Melissa [1]; Polsfuss, Beth [1]; Lee, Joseph [1]; Ishani, Areef [1-2]

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

Abstract: Background: Patients with chronic kidney disease (CKD) are at increased risk for cardiovascular disease and cardiovascular events. Multiple studies have demonstrated that sodium glucose co-transport 2 inhibitors (SGLT2i) provide several benefits, including reducing cardiovascular death and major adverse cardiovascular outcomes among patients with CKD. As a result, guidelines now recommend SGLT2i be given to all qualified patients with CKD and type 2 diabetes. The objective of this study is to evaluate the impact of a pharmacist-driven SGLT2i prescribing initiative among eligible patients with CKD and diabetes within the VA. Methods: Eligible patients will be identified through an established VA diabetes dashboard. Patients with an odd social security number will be put into the intervention arm, while those with an even social security number will serve as the control. The intervention will be implemented in a rolling fashion, beginning with patients at the Minneapolis VA Health Care System, and other VA clinics in the Midwest region will be subsequently added as outreach is being completed. Our primary outcome is the initiation of an SGLT2i. Additional outcomes include progression of CKD, all-cause hospitalizations, initiation of dialysis, and implementation outcomes, such as reach. Results: To date, the initiative has been rolled out at Minneapolis and St. Cloud VA sites, with plans to expand into Iowa, Nebraska, North Dakota, and South Dakota in the near future. A total of 1430 patients have been enrolled at both sites. Outreach has occurred with 1103 Veterans. Of those, 210 (19%) were determined ineligible, and 192 (17%) refused to participate. Of the 519 who attended a pharmacist visit, 342 (66%) were initiated on the medication, while 177 (34%) were not. Reasons for not initiating the medication include advanced age, late-stage cancer diagnosis, dementia, and others. Data collection for other outcome measures is still ongoing. Conclusion: This project tests the effectiveness of a pharmacist-driven medication outreach initiative as a strategy to accelerate the initiation of SGLT2i in a rolling fashion to eligible patients within the VA. The results of this work will not only illustrate the effectiveness of this strategy in initiating SGLT2is but may also have implications for increasing dissemination for other areas of guideline concordant care.

Research Topic: Pharmacy
Funding agencies: Other
Grant support: N/A

42. Personality and Psychopathology Characteristics Associated with Suicidal Intent and Behaviors Among Veterans

Peterson, Amanda [1]; Chu, Carol [1]

1. Minneapolis VA Health Care System

Abstract: Rates of suicide among U.S. Veterans have steadily increased in the past two decades. Much of the literature on suicide prevention has focused of risk factors for suicidal thinking (Franklin et al., 2017); less has examined the transition from suicidal thinking to suicide attempts. Data analysis was conducted on pre-existing information taken from chart reviews to examine demographic and personality variables that contribute to the transition from suicidal thinking to suicide attempts in a sample of Veterans receiving care at the Minneapolis VAHCS. Longitudinal data was extracted from 196 Veteran's charts with suicide behavior and overdose reports (SBOR) and Minnesota Multiphasic Personality Inventory-2-Revised Form (MMPI-2-RF) records from 2016—2021. Multivariate analysis of variance (MANOVA) was utilized to explore study hypotheses. Results indicated MMPI-2-RF variables did not significantly predict suicidal intent and attempt status in this sample. Future directions for research will be discussed.

Research Topic: Suicide Prevention
Funding agencies: None
Grant support: N/A

43. CSP #597 Diuretic Comparison Project: Chlorthalidone vs. Hydrochlorothiazide for Hypertension–Cardiovascular Events

Raju, Srihari [1]; McPherson, Jacob [1]; Taylor, Olivia [1]; Ishani, Areef [1]; Cushman, William [2-3]; Leatherman, Sarah [4-5]; Lew, Robert [4-5]; Woods, Patricia [4]; Glassman, Peter [6-7]; Taylor, Addison [8-9]; Hau, Cynthia [4]; Klint, Alison [4]; Huang, Grant [10]; Brophy, Mary [4-5]; Fiore, Louis [4]; Ferguson, Ryan [4-5]

1. Minneapolis VA Health Care System
2. Lt. Col. Luke Weathers, Jr. VA Medical Center
3. University of Tennessee
4. VA Boston Healthcare System
5. Boston University
6. VA Greater Los Angeles Healthcare System
7. University of California Los Angeles
8. Michael E. DeBakey VA Medical Center
9. Baylor College of Medicine
10. VA Office of Research & Development

Abstract: Whether chlorthalidone is superior to hydrochlorothiazide for preventing major adverse cardiovascular events in patients with hypertension is unclear. We randomly assigned VA patients 65 years of age or older who had been receiving 25 or 50 mg hydrochlorothiazide daily to continue therapy with hydrochlorothiazide or to switch to chlorthalidone at a daily dose of 12.5 or 25 mg. The primary outcome was a composite of nonfatal myocardial infarction, stroke, heart failure resulting in hospitalization, urgent coronary revascularization for unstable angina, and non–cancer-related death. Safety was also assessed. A total of 13,523 patients underwent randomization. The mean age was 72 years. At baseline, hydrochlorothiazide at a dose of 25 mg per day had been prescribed in 12,781 patients (94.5%). The mean baseline systolic blood pressure in each group was 139 mm Hg. At a median follow up of 2.4 years, there was little difference in the occurrence of primary-outcome events between the chlorthalidone group (702 patients [10.4%]) and the hydrochlorothiazide group (675 patients [10.0%]) (hazard ratio, 1.04; 95% confidence interval, 0.94 to 1.16; p=0.45). There were no between-group differences in the occurrence of any of the components of the primary outcome. The incidence of hypokalemia was higher in the chlorthalidone group than in the hydrochlorothiazide group (6.0% vs. 4.4%, p<0.001). In this large pragmatic trial of thiazide diuretics at doses commonly used in clinical practice, patients who received chlorthalidone did not have a lower occurrence of major cardiovascular outcome events or non–cancer-related deaths than patients who received hydrochlorothiazide.

Research Topic: Cardiovascular Disease
Funding agencies: Other
Grant support: VA CSP

44. Validity of the Eating Concerns (EAT) Scale: A Study with National Guard Soldiers and Their Romantic Partners

Ramberg, Caitlyn [1]; Menton, William [1]; Arbisi, Paul [1]; Polusny, Melissa [1]; Marquardt, Craig [1]

1. Minneapolis VA Health Care System

Abstract: The development and validation of screening tools for eating disorders is crucial for effective early intervention and treatment. Researchers have recently developed a new Eating Concerns (EAT) scale for the MMPI-3, which is designed to capture various general aspects of problematic eating behavior. Our study examined the utility of the EAT scale by comparing it to well-established based multidimensional markers of eating disorders. The study involved 375 National Guard soldiers and their romantic partners who completed both the MMPI-2-RF-EX and the Eating Pathology Symptoms Inventory (EPSI). Results showed that the EAT scale was effective in capturing EPSI domains of body dissatisfaction, binging, purging, and restricting. However, there was no association found between excessive exercise and EAT. Similar to Va.ousov? and colleagues' study using EAT and the EPSI among college undergraduates (2022), our use of hierarchical regressions demonstrated the added usefulness of EAT as a screening measure for some aspects of dysfunctional eating behavior; we found that the EAT scale better predicted EPSI scores than other scales from the MMPI-3 (e.g., HO, RC, PSY-5). The new EAT scale increases the scope of the MMPI-3 by allowing for the assessment of maladaptive attitudes and self-reported behaviors not previously encompassed by the MMPI-2 or the MMPI-2-RF. Overall, the findings support the incremental and convergent validity of the new EAT scale for select facets of disordered eating. It provides researchers and clinicians with a valuable screening tool to assess problematic eating behaviors and potentially facilitate effective early intervention and treatment for individuals with eating disorders.

Research Topic: Mental Health
Funding agencies: Other
Grant support: University of Minnesota Press

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45. Heat and cold waves increase risk of mortality among U.S. Veterans with Chronic Obstructive Pulmonary Disease

Rau, Austin [1]; Baldomero, Arianne [2]; Wendt, Chris [2]; Tarr, Gillian [1]; Alexander, Bruce [1]; Berman, Jesse [1]

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

Abstract: Chronic obstructive pulmonary disease (COPD) is a heterogeneous pulmonary disease affecting 16 million Americans. Individuals with COPD are susceptible to environmental disturbances including heat and cold waves that can exacerbate disease symptoms. We collected individual level data with geocoded residential addresses from the Veteran's Health Administration on 377,545 deceased patients with COPD (2016—2021). A time stratified case-crossover study was designed to estimate the incidence rate ratios (IRR) of heat and cold wave mortality risks using conditional logistic regression models examining lagged effects up to 7 days. Attributable risks (AR) were calculated for the lag day with the strongest association for heat and cold waves respectively. Effect modification by gender and race was also explored. Heatwaves had the strongest effect on all-cause mortality at lag day 0 (IRR: 1.04, 95% CI: 1.02, 1.06) with attenuated effects by lag day 1. The AR at lag day 0 was 647 (95% CI: 324, 969) per 100,000 Veterans. The effect of cold waves steadily increased from lag day 2 and plateaued at lag day 4 (IRR: 1.04, 95% CI: 1.02, 1.07) with declining but still elevated effects over the remaining 7-day lag period. The AR at lag day 4 was 687 (95% CI: 344, 1,200) per 100,000 Veterans. Differences in risk were also detected upon stratification by gender and race. Our study demonstrated harmful associations between heat and cold waves among a high-risk population of Veterans with pre-existing COPD using individual level health data. Future research should emphasize using individual level data to better estimate the associations between extreme weather events and health outcomes for high-risk populations with pre-existing chronic medical conditions.

Research Topic: Respiration & Pulmonary Disease
Funding agencies: NIH
Grant support: KL2 TR002492; UL1 TR002494

46. Effects of Social Determinants of Health (SDOH) on Psychological Outcomes following Mild Traumatic Brain Injury

Reiten, Morgyn [1-2]; Mahr, Colette [1]; Disner, Seth [1]

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

Abstract: Traumatic brain injury (TBI) is a common public health concern with significant psychological consequences. However, the impact of TBI on psychological outcomes may vary based on social determinants of health (SDOH), such as neighborhood disadvantage, household income, or education level, and the nature of these effects are not well known. The present study aims to investigate the moderating role of SDOH in the association between TBI and psychological outcomes in US military Veterans. We recruited 276 Veterans previously diagnosed with mild TBI (mTBI) through the PROUD research study (mean age: 45.62 years [SD=12.92], 88% male). Participants completed surveys assessing PTSD, depression, neurobehavioral symptoms, and quality of life, as well as providing basic demographic and SDOH information. To measure neighborhood disadvantage, Area Deprivation Index (ADI) was determined using the Neighborhood Atlas from the University of Wisconsin-Madison, which assigned participants a national percentile ADI based on their current address. Psychological outcomes included the Beck Depression Inventory (BDI), PTSD Checklist (PCL), Neurobehavioral Symptom Inventory (NSI), and Quality of Life after Brain Injury (QOLIBRI). Moderation was tested using the interactions between number of mTBIs and each of three SDOH (income, ADI, and years of education). There was no significant moderation observed (all $p>0.05$), so interaction terms were dropped from subsequent analyses. There was a significant negative association of income on BDI and NSI severity, and a positive association on QOLIBRI (all $p<0.006$). Income was marginally associated with PCL scores ($\beta=-0.123$, $t=-1.839$, $p=0.067$). Years of education had a marginal negative association with PCL score ($\beta=-0.116$, $t=-1.731$, $p=0.085$), but was not associated with any other outcome. There were no significant associations between number of mTBIs or ADI on any of the psychological outcomes. These findings suggest that household income (a key SDOH) plays a role in psychological outcomes after mTBI, particularly for depression, neurobehavioral symptoms, and quality of life, though less so for PTSD. The association with household income far exceeds the associations with education, neighborhood disadvantage, or even number of mTBIs. Financial stability appears to be among the strongest influencers of post mTBI mental health, and is an important factor to consider in regards to post TBI assessment and treatment.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: None
Grant support: IK2 RX002922

47. The association of long-term PM2.5 exposure and all-cause mortality in COPD

Robichaux, Camille [1]; Baldomero, Arianne [2]; Wendt, Chris [2]; Bangerter, Ann [2]; Gravely, Amy [2]; Berman, Jesse [1]

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

Abstract: Long-term exposure to ambient fine matter (PM2.5) increases the risk of premature death. The US Environmental Protection Agency has set National Ambient Air Quality Standards (NAAQS) for annual average PM2.5 at 12µg/m3. The risk of poor health outcomes related to PM2.5 in people with COPD at any level of long-term PM2.5 exposure is understudied. We extracted health and demographic data from all patients with an ICD-9 or -10 diagnosis of COPD from the VHA system between 2016-2019, including sex, race, date of death, smoking status, significant comorbidities, and geocoded residential address. Using the residential address, we spatially assigned neighborhood level socioeconomic status, and census tract level urbanicity. We used publicly available data from NASA to determine annual PM2.5 modeled concentrations with a 1km resolution. Using a series of nested logistic regression models, we evaluated the odds of all-cause mortality associated with 5-year average PM2.5 exposure stratified into three levels (less than 8, 8 to less than 12, and greater than 12µg/m3. We adjusted for age, sex, latitude, and longitude (Model 1), Model 1 plus race and smoking status (Model 2), and Model 2 plus socioeconomic status and rurality (Model 3). These models represent individual factors, social factors, and environmental factors respectively. We then stratified by comorbidities known or hypothesized to be associated with poor outcomes from COPD or PM2.5 exposure. Our cohort consisted of 1.12 million people with COPD with a 34% mortality rate from January 2016 to December 2021. Average PM2.5 exposure between 8 and <12 µg/m3 is associated with a 9% (95% CI 8-10%) higher odds of all-cause mortality compared to levels below 8 in our fully adjusted model; whereas exposure to levels 12 µg/m3 and greater is associated with a 15% (95% CI 10-21%) higher odds of all-cause mortality compared to levels below 8µg/m3. Asthma, congestive heart failure, and chronic kidney disease were especially sensitive to higher levels of PM2.5 exposure. In previous metanalysis, a 10 µg/m3 increase in average PM2.5 exposure was associated with an 8% higher HR of mortality in the overall population, including those with and without COPD. People with COPD include a significant proportion of the US population. This study provides evidence that COPD patients—and particularly those with additional comorbidities—may benefit from lower PM2.5 levels compared to the full population. These findings should be consider

Research Topic: Respiration & Pulmonary Disease
Funding agencies: NIH

Grant support: NHLBI T32 HL007741; NIH NCATS KL2 TR002492; NIH NCATS UL TR002494

48. Immunosuppression Associated Dermatophytosis with Microvascular Invasion within the Veterans Affairs Health Care System

Rypka, Katelyn [1-2]; Davis, Michael [1]; Wendland, Zachary [1]; Buechler, Connor [1]; Solomon, Robin [1]; Kaka, Anjum [1]; Goldfarb, Noah [1]

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

Abstract: Trichophyton, Microsporum, and Epidermophyton species are common dermatophytes that typically infect the stratum corneum. In extremely rare circumstances dermatophytes have been reported to cause deep dermal invasion, pseudomycetoma, and disseminated infections. To our knowledge, there is a single report of deep dermal dermatophyte infection with microvascular invasion. This rare phenomenon has only been reported in immunocompromised patients. We present a case of angioinvasive dermatophyte infection in an immunosuppressed patient. A 69-year-old male with a past medical history of recurrent tinea corporis, immune thrombocytopenia, and chronic lymphocytic leukemia presented via inpatient consult to dermatology for a tender, pruritic, eruption on his right lower extremity (RLE) that had been present for less than a week. On examination, there was a well-demarcated, pink-red plaque with a trailing edge of scale and scattered hemorrhagic, dusky purple papules within the plaque. Potassium hydroxide preparation demonstrated a heavy burden of branching hyphae. Topical terbinafine was initiated with close follow-up. Four days later, the patient was readmitted for worsening sharp, burning pain of the RLE. Computed tomography imaging was negative for emphysema or abscess formation. Necrotizing fasciitis was diagnosed via surgical consult and a four-compartment fasciotomy with debridement was performed. Tissue culture grew Trichophyton spp (2+) as well as pan-sensitive Staphylococcus aureus (3+), Enterococcus faecalis (1+). Blood cultures were negative. Histopathology demonstrated purulent inflammation with numerous branching, septate fungal hyphae extending into subcutaneous fat and thrombosed blood vessels. Appropriate antibiotics and a 12-week course of daily oral terbinafine 250mg was initiated with resolution by the 12-week follow-up. Immunosuppressive therapies are commonly implicated with non-dermatophyte fungal infections, and are predisposing factors for deep dermal invasion, as seen in our patient. We propose that in immunosuppressed patients with tinea corporis, a dusky appearance and/or pain out of proportion to exam should raise the concern for invasive dermatophytosis. Therapeutic management should include treatment of invasive fungal infection and cessation/decrease of immunosuppression as able.

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

49. Bridging the Gap: Investigating Health System Factors and the Delivery of Evidence-Based Psychotherapies for Depression

Salameh, Hope [1]; Brent, Taylor [1]; Cutting, Andrea [1]; Spoont, Michele [1]; Clothier, Barbara [1]; Nugent, Sean [1]; Ibrahim, Hanna [1]; Degerstrom, Rose [1]; Hudson, Emily [1]; Ackland, Princess [1-2]

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

Abstract: Background: Depression is a highly prevalent mental health disorder that carries a heavy disease burden. It is the 2nd leading risk factor for suicide among Veterans. Evidence-based treatment for depression includes medications such as selective-serotonin reuptake inhibitors, and psychotherapies—cognitive behavioral therapy for depression (CBT-D), acceptance and commitment therapy for depression (ACT-D), and interpersonal psychotherapy (IPT). No studies have examined provision of evidence-based psychotherapies (D-EBPs) in VA or reasons underlying infrequent delivery, leaving a critical gap in depression care delivery. System factors are a known driver of EBP use, and unique factors related to how depression care is organized warrant an empirical investigation. As part of a larger study, we quantitatively examined the association between health system factors and D-EBP delivery. Methods: We identified VA patients seen in FY22 in a general mental health clinic or behavioral health interdisciplinary team (GMH/BHIP) with a diagnosis of depression. We identified patients who received at least one session of D-EBP, depression medication prescription releases, and comorbid mental health diagnoses. We also extracted facility size, determined by the total number of patients seen by GMH/BHIP clinics within each parent facility and associated CBOCs. Findings: 635,653 patients diagnosed with depression were seen in VA GMH/BHIP clinics in FY22. Only 2.8% (n=17,588) had a D-EBP session. Only 4 out of the 139 VA GMH/BHIP clinics had a D-EBP reach of 10% or above. Comparatively, 79.5% of patients with depression received a depression medication in FY22. Patients with depression most frequently had a comorbid diagnosis with PTSD (47.8%), anxiety (43.5%) and SUD (26.2%). Of the 568,247 GMH/BHIP patients who did not have a depression diagnosis associated with any FY22 GMH/BHIP encounter, 0.6% (n=3,655) had at least one FY22 D-EBP session. The total number of patients seen in GMH/BHIP in FY22 ranged from 1097 to 25,354. Conclusions: The majority of VA GMH/BHIP clinics are delivering D-EBPs to less than 10% of their patients with depression. Therapists may also be using a D-EBP with patients without a diagnosis of depression, suggesting inappropriate use of national templates. The qualitative portion of this study will expand on these findings to identify how system and other factors impact whether D-EBPs are delivered and how their use is measured at 10 VA facilities.

Research Topic: Depression
Funding agencies: VA HSRD
Grant support: N/A

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50. The Journeys Program: An Evaluation of the Combined Implementation of PE and DBT

Schachter, Jacob [1]; Voller, Emily [2]; Andrews Wiebusch, Lindsay [2]; Kaler, Matthew [2]; Marquardt, Craig [2]

1. Augsburg University
2. Minneapolis VA Health Care System

Abstract: Among Veterans with borderline personality disorder (BPD), comorbidity with posttraumatic stress disorder (PTSD) is frequent. Clinicians are often hesitant to treat PTSD symptomatology among this population given the elevated risk associated with suicidality. The purpose of this project was to examine the effectiveness of a twelve-week dialectical behavior therapy (DBT) and prolonged exposure (PE) combined intensive outpatient program at the Minneapolis VAHCS. The full model of DBT was provided from 2012 through [2018]; PE was provided twice weekly for approximately 6 weeks of the program. Symptom reduction was measured for posttraumatic distress, borderline features, depression, anxiety, and subjective stress. Changes in self-reported DBT skills were also calculated. 178 Veterans started the treatment program and 130 Veterans successfully completed the program (73%). Most participants met criteria for PTSD and BPD. Results showed that 43-51% of participants experienced a partial response to treatment (at least 30% reduction of scores on one of the five symptom measures) and 27-34% of participants experienced a full response (at least 50% reduction). Furthermore, 18-36% of participants experienced full remission (meeting the normative cutoff of scores on each of the five symptom measures) and 30-48% experienced partial remission (mild or normative cutoff). Lastly, large pre- to post-treatment effect sizes were found for decreases in posttraumatic distress (d=1.36), borderline features (d=0.86), and depression (d=0.81) as well as increases in DBT skills (d=0.83). Medium effect sizes were found for decreases in anxiety (d=0.72) and subjective stress (d=0.66). The results of this evaluation suggest that PTSD can be safely and effectively treated among Veterans with comorbid symptoms of borderline personality disorder through the joint administration of intensive DBT and PE on an outpatient basis.

Research Topic: Posttraumatic Stress Disorder (PTSD)
Funding agencies: None
Grant support: N/A

51. Post Weight-Loss Energy Gap in a Rat Model of Polygenic Obesity

Shekels, Laurie [1]; Mavanji, Vijayakumar [1]; Pomonis, Brianna [1]; Kotz, Catherine [1]

1. Minneapolis VA Health Care System

Abstract: Current obesity interventions result in significant weight loss, but the weight loss is typically not maintained long-term. Individuals that lose weight often have an Energy Expenditure Gap (EEgap) post-weight loss, such that considerably less energy is required to maintain the new weight compared to that required prior to their weight loss as well as compared to weight-matched individuals who have never been obese. This EEgap may be due to compensatory reductions in basal EE (BEE), which makes it difficult to support a lower body weight and leads to weight regain. Obesity prone (OP) rats are a polygenic animal model ideal for studying human obesity. These rats gain weight even when fed a low-fat diet ad lib. The neuropeptide orexin promotes spontaneous physical activity (SPA) and energy expenditure (EE) and could be a therapeutic target for minimizing the EEgap. We hypothesized that diet restriction will result in weight loss in OP rats and that weight-reduced animals will exhibit an EEgap in the weight-reduced state. We used 12-month-old male OP and obesity resistant (OR) rats for this study (n=8 for each group). After acclimation and a baseline measurement of spontaneous physical activity (SPA) and energy expenditure measures from indirect calorimetry chambers (Sable Promethion), the OP rats were restricted to 60% of their ad lib food intake, while the OR rats were allowed ad lib food intake for 7 weeks. Our results show that a 7-week caloric restriction reduced body weight in the OP rats to the level seen in the age-matched OR rats. Further, the 24h EE was significantly lower in the weight-reduced OP rats compared to their baseline EE as well as compared to the EE of the OR rats at the same body weight. Our results suggest that the OP rat is a suitable model to study the EEgap following weight loss. This continuing study will focus on the potential for small molecule orexin agonists to reduce the EEgap to prevent weight regain following weight loss.

Research Topic: Obesity
Funding agencies: VA BLRD; VA RRD
Grant support: N/A

52. WNT/β-Catenin Activation has a role in Preventing Obesity-induced Cognitive Impairment

So, Simon [1-2]; Nixon, Joshua [1-2]; Bernlohr, David [2]; Butterick, Tammy [1-2]

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

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. Microglial fatty-acid binding protein 4 (FABP4) is a regulator of neuroinflammation. We hypothesized that the link between lipid metabolism and inflammation indicates a role for FABP4 in regulating high fat diet (HFD)-induced cognitive decline. We have previously shown that obese FABP4 knockout mice exhibit decreased neuroinflammation and cognitive decline. FABP4 knockout and wild type mice were fed 60% HFD for 12 weeks starting at 15 weeks old. Hippocampal tissue was dissected and RNA-seq was performed to measure differentially expressed transcripts. Reactome molecular pathway analysis was utilized to examine differentially expressed pathways. Results showed that HFD-fed FABP4 knockout mice have a hippocampal transcriptome consistent with neuroprotection, including associations with decreased proinflammatory signaling, ER stress, apoptosis, and cognitive decline. This is accompanied by an increase in transcripts upregulating neurogenesis, synaptic plasticity, long-term potentiation, and spatial working memory. Pathway analysis revealed that mice lacking FABP4 had changes in metabolic function that support reduction in oxidative stress and inflammation, and improved energy homeostasis and cognitive function. Analysis suggested a role for WNT/β-Catenin signaling in the protection against insulin resistance, alleviating neuroinflammation and cognitive decline. Collectively, our work shows that FABP4 represents a potential target in alleviating HFD-induced neuroinflammation and cognitive decline and suggests a role for WNT/β-Catenin in this protection.

Research Topic: Basic Sciences
Funding agencies: VA BLRD; NIH; UMN; CVRE
Grant support: I01 BX004146; AARGD-17-505409; UMN HFHL; NIH DK053189; NIH AG069819

53. Generalized Slowing of Resting State Neural Oscillations in People with Schizophrenia

Sponheim, Scott [1-2]; Lynn, Peter [2]; Ramsay, Ian [2]

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

Abstract: Background: Recent interest in the role of neural oscillations in the flow of information through the brain has led to partitioning electroencephalography (EEG) recordings into periodic and aperiodic components. While both contribute to conventional measures of power within EEG bands (e.g., delta, theta, alpha, beta), the periodic aspect of EEG is thought to reflect true oscillatory behavior within neural systems while aperiodic activity captures sporadic brain activity. Given past evidence of resting state EEG power abnormalities in schizophrenia, we sought to determine if the periodic aspect of neural activity was aberrant in people with schizophrenia (PSZ) after removal of aperiodic activity. Methods: EEGs were gathered during a resting state from 104 PSZ and 105 healthy control participants (HCs). We used the fitting-oscillations-and-one-over-f (FOOOF) toolbox was to remove aperiodic neural activity, and computed the cross-correlation between power spectra for individual participants and the mean power spectrum for HCs to quantify the relative speed of neural oscillations. Results: Periodic activity in PSZ was shifted toward lower frequencies compared to HCs during eyes closed rest ($t(187.86)=-3.67$, $p\leq0.001$). PSZ on average had a .50 hz shift toward oscillatory slowing compared to HCs across the frequency spectrum. Discussion: Slowed periodic activity at rest is evident in schizophrenia. A slower pace of neural oscillations may limit the transmission of information within and across brain systems. Slowed neural oscillations may contribute to poor integration of low-level perceptual and high-level cognitive functions in people with the illness.

Research Topic: Psychiatry
Funding agencies: VA CSRD
Grant support: I01 CX000227

54. Filtering of visual distractors in schizophrenia: Diminished attentional control predicts behavioral deficits

Sponheim, Scott [1-2]; Lynn, Peter [2]

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

Abstract: Attentional filtering has long been suggested to be a core deficit of schizophrenia. Recent work (Luck, Leonard, et al., 2019) has emphasized the important distinction between attentional control, which involves the voluntary selection of a particular stimulus for focused processing, and implementation of selection, which involves the mechanisms that enhance the stimulus selected via filtering processes (p. 1001). We recorded electroencephalography data from people with schizophrenia (PSZ), their first-degree relatives (REL) and healthy controls (CTRL) during performance of a resistance to attentional capture task that tapped attentional control and implementation of selection measured during a brief period of attentional maintenance. Event-related potentials (ERPs) during attentional control and maintenance of attention both yielded evidence for diminished neural responding in PSZ. But it was only the ERPs during attentional control that predicted performance on the visual attention task for PSZ – which was not the case for REL and CTRL. Visual attention performance for CTRL was best predicted by ERPs during attentional maintenance. These results support the idea that poor initial voluntary attentional control is more central to attentional dysfunction in schizophrenia than difficulty implementing selection (e.g., resistance to attentional capture by visual distractors). Nevertheless, weak neural modulations indicative of impaired early attentional maintenance in people with schizophrenia challenge notions of increased intensity of focus or "hyperfocusing" in the disorder. Improvement of the initial control of attention may be a productive target for cognitive remediation interventions for schizophrenia.

Research Topic: Psychiatry
Funding agencies: VA CSRD
Grant support: I01 CX000227

55. Posttraumatic Avoidance and Electrophysiological Markers of Posterior Attention During a Flanker Task

Stevens, Kara [1-2]; Marquardt, Craig [1]; Davenport, Nicholas [1]; Sponheim, Scott [1]

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

Abstract: We sought to quantify the associations of posttraumatic stress disorder (PTSD) symptoms and blast-related mild traumatic brain injury (mTBI) with neural markers of conflict monitoring and cognitive control. Electroencephalography recordings were collected during a Flanker task for 194 military Veterans (85 healthy controls, 37 PTSD, 38 mTBI, 33 PTSD and mTBI). Trials were coded as either Congruent (flanker stimuli same direction as target) or Incongruent (opposite direction) with respect to Current and Previous (n-1) trials. Event-related potential analyses revealed an N1 component of interest quantified between 110-200ms at posterior electrodes (average of PO7/PO8). There was an interaction between Current and Previous trial type such that Previous Congruent trials influenced N1 amplitude of the Current trial type (Current=more negative), a pattern not observed following Previous Incongruent trials. Further, analyses revealed interactions between Clinician-Administered PTSD Scale (CAPS) symptom grouping Avoidance and Current trial type at N1. Higher levels of Avoidance behaviors related to more negative N1 amplitude and an elimination of differences between Current trial types. We observed posttraumatic avoidance to be associated with posterior attentional processes and a reduction in neural discrimination between Congruent/Incongruent trial types. This suggests avoidance is involved in a disruption of stimulus-driven attentional control during conflict monitoring.

Research Topic: Posttraumatic Stress Disorder (PTSD)
Funding agencies: VA RRD
Grant support: I01 RX000622

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

Swanson, Heather [1-2]; Dickmann, Patricia [1]; Steen, Katie [1]; Westermeyer, Joseph [1]

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

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

57. Military Toxic Exposure Conference: Developing an interdisciplinary-systematic approach

Taylor, Jedidah [1]; Trembley, Janeen [2]; Tomaska, Julie [3]; Torres, Rosie [3]; Ginex, Pam [4]; Barach, Paul [5]; Lee-Wong, Mary [6]; Kirkness, Jason [7]; Covey, Andrea [8-9]; Lindheimer, Jacob [10]; Szema, Anthony [11-12]; Miller, Robert [13]; Nurkiewicz, Timothy [14]; Klein, Mark [2]; Butterick, Tammy A. [2,15]

1. Tulane University
2. Minneapolis VA Health Care System
3. Burn Pits 360 Veterans Organization
4. Stony Brook University
5. Thomas Jefferson University
6. Maimonides Medical Center
7. 4D Medical
8. Kansas City VA Medical Center
9. Kansas University
10. William S. Middleton Memorial VA
11. Donald and Barbara Zucker School of Medicine at Hofstra/Northwell
12. Stony Brook University
13. Vanderbilt University
14. University of West Virginia
15. University of Minnesota

Abstract: Background: Millions of U.S. troops were deployed to Iraq and Afghanistan from 2001 to 2011 and were exposed to either toxic airborne hazards or open-air burn pits. Ongoing research has demonstrated that these exposures may have profound biologic consequences on human health, yet there are major gaps in the establishment of robust, reproducible, and systematic research approaches for developing translational targeted therapeutics. Objectives: Our goal is to engage a learning community of preclinical, clinical experts, and Veteran advocacy groups to help improve the awareness and best practices for burn-pit Veterans. These efforts will highlight the long-term health effects of exposures to airborne hazards or open-air burn pits and outline systematic approaches for bench to bedside translational research. We have established a multi-series field-based planning meeting which aims to foster an interdisciplinary approach to a strategic toxic airborne hazard healthcare and research agenda. Utilizing a hybrid format of virtual and in person meetings, the series leverages participants with experience in pulmonology, oncology, hematology toxicology, pharmacology, physiology, kinesiology, neuroscience, and public health sciences. Key Products: This forum explores topics which: 1) address VA health care and translational challenges relating to airborne toxin exposure, 2) identify how to leverage VA and university affiliated resources and expertise, 3) innovate access improvements to the VA Burn Pit Registry for research and health care delivery. VA health care and policy is strengthened and informed by collaborative scientific knowledge, research, and innovation. Final outcomes will be utilized in a variety of ways, including to develop research solicitation, advance collaborations across the VA and with external stakeholders, and explore other funding mechanisms to support innovative and high-quality preclinical and clinical research to improve Veteran healthcare.

Research Topic: Afghanistan & Iraq Veterans
Funding agencies: VA BLRD
Grant support: I01 BX004146

58. Development of a Platform for Clinical Trials in Dialysis and its first trial: The Beta blockeR diAlyzability on cardioVascular Outcomes (BRAVO) Trial

Taylor, Olivia [1]; McPherson, Jacob [1]; Raju, Srihari [1]; Ishani, Areef [1]; Ferguson, Ryan [2]; Leatherman, Sarah [2]; Donnelly, Christopher [2]; Doros, Gheorghe [2]; Hau, Cynthia [2]; Fiotto, Jade [2]; Pierre-Antoine, Samorah [2]; Robben, Gregory [2]; Kaufman, James [3]

1. Minneapolis VA Health Care System
2. VA Boston Healthcare System
3. VA New York Harbor Healthcare System

Abstract: Dialysis patients have high morbidity and mortality yet are often excluded from clinical trials. The newly established VA Dialysis Platform (DiaP) will facilitate research on this population and help to answer important clinical questions about treating these patients. The DiaP is a master protocol infrastructure that will provide multidisciplinary support to the design, implementation, analysis, and dissemination of results of randomized clinical trials in the Veteran dialysis population. The platform will emphasize pragmatic, comparative effectiveness trials. A key feature of DiaP is a repository which will list every Veteran receiving dialysis who has consented to being contacted about dialysis-related clinical trials they may be eligible for. Hemodialysis patients come in for treatment several times per week, resulting in strong relationships with their providers. They also get routine lab monitoring. These characteristics mesh well with the elements of usual care and electronic follow-up which are typical of pragmatic trials. Beta Blocker Dialyzability on Cardiovascular Outcomes (BRAVO) is to be the inaugural trial within DiaP. Due to their cardioprotective benefits, beta blockers are some of the most common medications used by dialysis patients. There are several beta blockers, and each has different pharmacokinetic properties. Dialyzability and beta-selectivity, in particular, are characteristics that may influence the efficacy and safety of a beta blocker in dialysis patients. Observational studies have investigated the question of which types of beta blockers are associated with better cardiovascular outcomes for patients receiving dialysis, however, there have been conflicting findings. BRAVO will enroll patients from the DiaP repository who are taking a beta blocker filled by a VA pharmacy. Patients will be randomized to either metoprolol succinate (dialyzable, beta-1 selective) or carvedilol (non-dialyzable, non-selective), then proceed with their usual care. Follow-up will occur using the EMR to track study outcomes. BRAVO has an anticipated study duration of 4 years (1 year enrollment period and 3 years of follow-up for last patient enrolled) to reach 1,100 events. The primary endpoint is a composite of non-fatal major adverse cardiovascular events (MI, stroke, HF hospitalization) and all-cause mortality.

Research Topic: Nephrology
Funding agencies: Other
Grant support: VA CSP

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59. Protein kinase CK2 serum mRNA levels as a potential indicator of prostate cancer progression

Trembley, Janeen [1]; Kren, Betsy [1]; Hwang, Justin [2]; Klein, Mark [1]; Ahmed, Khalil [1]

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

Abstract: Introduction: Protein kinase CK2 regulates several biological features that are hallmarks of cancer. CK2 expression levels are significantly elevated in prostate cancer (PCa) compared to non-malignant prostate; high CK2 levels indicate worse disease status and outcome. In advanced PCa, most patients develop resistance to the currently used therapies targeting the androgen axis, with 5 year survival of ~ 30% for castration resistant (CRPC) disease. Methods: CK2 levels were determined in patient RNA-seq datasets and in xenograft tumors pre- and post-castration. IC50 values were determined in CRPC cells for CX-4945/Silmitasertib (CK2 inhibitor). Impact of increased CK2 on response to enzalutamide was measured by clonal survival. CK2. (CSNK2A1) mRNA levels in patient sera pre-prostatectomy vs. during abiraterone treatment were quantitated by RT-PCR. Results: CSNK2A1 mRNA levels significantly increased from non-malignant to hormone-sensitive and further to CRPC in patient tissues. Androgen deprivation significantly elevated CK2 protein and mRNA levels in xenograft tumors. CK2 inhibition with CX-4945 killed CRPC cells. CK2 elevation promoted CRPC cell survival post-enzalutamide treatment. We detected CSNK2A1 mRNA at significantly higher levels in advanced PCa patient serum vs. pre-prostatectomy. Conclusions: Androgen axis therapies trigger elevation of intra- and extra-cellular CK2 levels. Tumor-released CSNK2A1 mRNA in PCa patient blood could indicate aggressive disease. Blocking CK2 using CX-4945/Silmitasertib could represent an effective co-treatment strategy. Phase 1 & 2 cancer trials showed that CX-4945/Silmitasertib is safe for use. Correlation of baseline CSNK2A1 serum levels in CRPC patients with PFS could yield important data for stratifying patients likely to benefit from CK2 inhibition.

Research Topic: Cancer
Funding agencies: VA BLRD; CVRE; Other
Grant support: I01 BX003282; I01 BX005091; Brander Beacons Cancer Research

60. Examining Relationships Between Medication Taking Behaviors and Cognitive Functioning in Older Adults

Trofimova, Alexandra [1]; Kuperwajs Cohen, Anael [1]; Weaver, Destiny [1]; Beattie, Zach [2]; Liu, Yan [2]; Wu, Chao-Yi [3]; Hughes, Adriana [1]

1. Minneapolis VA Health Care System
2. Oregon Health & Science University
3. Harvard Medical School

Abstract: Accurate medication management is a critical aspect of maintaining health in older adulthood, and poor adherence increases the risk of negative health outcomes. This study investigated the relationships between cognitive functioning and pillbox use among older adults using a combination of self-report and objective data. The hypotheses included that there would be a significant discrepancy between self-reported and objectively measured pillbox use frequency and lower executive functioning, attention, and memory scores would be associated with greater variability in medication taking time of day, greater discrepancy between self-reported and objective pillbox use, and worse pillbox use adherence. The sample included 104 predominantly white (90.4%) community-dwelling older adults (58% male, M age=74.59, SD=5.71) without dementia who took at least one medication per day and independently managed their medications. At baseline, participants self-reported their medication taking behaviors and used a study provided electronically monitored pillbox for 90 days that recorded frequency and timing of pillbox use. Predictor variables included cognitive composite z-scores for memory, attention, and executive functioning. Outcome variables included variability in the first and last time of day a pillbox was opened, discrepancy between self-reported frequency of taking medications versus actual pillbox use frequency, and pillbox use adherence. Descriptive statistics, correlations, and multiple linear regressions were used. There were mean differences between self-reported and actual pillbox use, $p \leq 0.001$. Together, age, education, pain, and cognitive scores explained 9.6% of the variance in the discrepancy between self-reported and actual pillbox use, $p=0.03$. Lower executive functioning scores were associated with larger discrepancies ($p=0.01$). Attention ($p=0.75$) and memory ($p=0.36$) performances did not predict discrepancy. This study demonstrated that older adults without a diagnosis of dementia may misreport their medication taking frequency. Moreover, cognitive functioning, specifically lower executive cognitive abilities, influence this discrepancy. These findings underscore the value of cognitive assessment when evaluating and making inferences about functional abilities. It also highlights the potential value of incorporating objective measurement tools into clinical care with older adults for a more accurate understanding of daily functioning.

Research Topic: Aging
Funding agencies: NIH
Grant support: AG058687; AG058687-03S1

61. Usability Testing during In-Patient Rehabilitation of a Novel Clinical Dashboard: Improving Seating Behavior Education

Truty, Tim [1]; Belew, John [1]; Wacek, Amber [1]; Stien, Crystal [1]; Hicks, Brandon [1]; Eddy, Brandon [1-2]; Bornstein, A. Soleil [1]; Fairhurst, Stuart [1]; Goldish, Gary [1]; Hansen, Andrew [1-2]; Barrett, Benjamin [1]; Morrow, Melissa [1,3]; Vos-Draper, Tamara [1-2]; Olney, Christine [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. University of Texas, Galveston

Abstract: Background: Seating behavior education is one of the targeted strategies for pressure injury prevention for persons with spinal cord injury or disorder (SCID). Yet, the effectiveness of seating behavior education is wrought with many limitations, potentially leading to poor outcomes. Lack of access to and visualization of day-long seating behavior data linked to sitting surface pressure distribution, unknown quality of weight shift, and lack of individualization are among the many limitations. Seating specialists from across the country guided this technology development project for enhanced seating behavior education. We recently completed testing the newly developed clinical dashboard with six (n=6) Veterans with SCID who are at high risk for developing pressure injury. Objective: To describe usability of dashboard data as viewed by seating specialists, in the context of providing useful information to individualize their education to the Veteran. These dashboard data were captured by the mobile AW-Shift app, which was used for up to 10 days by six Veterans with SCID during their in-patient rehabilitation in the Minneapolis VA SCID Center. We will also describe the user's perception of the updated AW-Shift app. Methods: Veterans with SCI/D used an updated version of the AW-Shift app while sitting on the accompanying pressure mat, which was placed each morning on their wheelchair cushion. Veterans accessed the app throughout the day while seated in their wheelchair, allowing the study team members and study seating specialists to view the Veterans seating behavior during the Veteran's daily activities. Seating specialists accessed the seating behavior data on their dashboard, which was coded in formats programmed to meet the recommendations per an earlier convened expert panel. Semi-structure interviews and usability and self-efficacy surveys were completed by the therapists and patient participants before and after AW-Shift app use. Results: We will present data including demographics of participants (n=6), dashboard seating behavior metrics, qualitative feedback from seating specialists and Veteran users. Conclusions: Seating specialists were able to access data helpful in coaching to individualized seating behavior. The seating specialists also made recommendations to ensure what useful data needs to be easily accessed. Overall, the dashboard data was reported to be a great improvement for individualizing seating behavior to prevent pressure injury.

Research Topic: Spinal Cord Injury
Funding agencies: VA RRD
Grant support: I01 RX003222

62. Caregiver Needs of Service Members and Veterans with Traumatic Brain Injury (TBI)

Tsen, Jonathan [1]; Finn, Jacob [2]

1. Minneapolis VA Health Care System

Abstract: BACKGROUND: Family members play a crucial role in supporting Service Members/Veterans (SMVs) with a history of TBI. Indeed, about 80-90,0000 people with TBI report having chronic disability and caregiving needs (CDC, 2021). Caregivers of SMVs account for about $450 billion dollars per year in formal government program-related healthcare expenses (Feinberg, 2013). Given family members' critical roles in caregiving, it is imperative to examine what needs they face while caring for a SMV with TBI. OBJECTIVE: This study examined caregiver needs after a SMV's TBI using different time-based cohorts with discussion about how providers can target SMV and family post-injury needs. METHODS: Participants were family members of SMVs within the VA PRC TBI Model Systems national database who completed a follow-up survey either within the first 5 years after injury (n=562) or between 10 and 15 years post-injury (n=209). Family members completed the revised Family Needs Questionnaire, which assesses unmet needs related to health information, involvement in care, and support (i.e., instrumental, professional, emotional, and community support). Total, domain-level, and item-level descriptive data were analyzed. RESULTS: Unmet caregiver needs varied between the two cohorts, though were not significantly different (Chi-squared p-values for total and domain-level needs were all > .05). Specifically, in the first five years after injury, 59.17% reported having their needs met on the total score, compared to 56.3% of those 10-15 years after injury. Consistent in both samples, the emotional and instrumental support needs were the least met needs. CONCLUSION: Overall, emotional and instrumental support needs were consistently reported as less often met. Providers working with SMVs with TBI and their families can recommend use of interventions that meet these support needs, such as applying for respite care, joining educational and peer support groups, or enrolling in individual mental health therapy (Trail et al., 2020). While many caregivers may be aware of respite care or supportive options, they may be forced to rely on their own resources due to time constraints, technology access, or distance to community/healthcare resources, especially caregivers who have existing social identities that are marginalized (Pinquart & Sorensen, 2005).

Research Topic: Caregivers
Funding agencies: None

Grant support: N/A

63. Impact of Improving Footwear Options for Women Veterans with Amputations

Walker, Nicole [1-2]; Nickel, Eric [1]; Yun, Kelly [1]; Ackland, Princess [1]; Finn, Jacob [1]; Gravely, Amy [1]; Koehler-McNicholas, Sara [1]; Matsumoto, Molly [1]; Olney, Christine [1]; Hansen, Andrew [1-2]

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

Abstract: Women-identifying Veterans is one of the fastest growing subpopulations of military Veterans in the United States. It is anticipated that by 2050, nearly 20% of US military Veterans will identify as women. As the population of women Veterans grows, the number of women Veterans with amputations will also increase. In response, the United States Congress has mandated the appropriation of funds for "prosthetic research specifically for female Veterans." One identified area of need is for prosthetic feet that accommodate a broader range of footwear. The Minneapolis Adaptive Design & Engineering (MADE) Program at the Minneapolis VA Health Care System (MVAHCS) has developed a modular ankle-feet system allowing the use of nearly any pair of shoes. The device employs a single ankle unit, aligned once by the prosthetist, and multiple 3D printed foot shapes that are custom manufactured to fit various shoes. The technology has been licensed to the prosthetic wears company, UNYQ, and is being prepared for commercial release. Adjacent to the commercial release, we plan to conduct a take home study of the product with women Veterans. We seek to assess how improved footwear options improve perception of body image and participation among women Veterans. Previous studies of women Veterans indicate a significant correlation between perceived footwear challenges and decreased body image and ability to participate in social roles and activities. We hypothesize that access to a prosthetic device designed to improve footwear options will improve body image and the ability to participate among women Veterans with lower extremity amputations. To test these hypotheses, this study will employ a single-arm, long-term follow-up design. Recruited participants will travel to Minneapolis to be fit with three different foot shoes combinations, including three custom 3D printed foot shapes, the UNYQ ankle unit, and three pairs of shoes. Participants will be fit with and accommodate to the ankle-feet system in Minneapolis prior to traveling home and using the system in their home and community environments for six months. The study team will collect quantitative measures at baseline, one-month, and six-months. Participants will also complete a qualitative interview after six-months use of the system so we can continue to iterate and improve the design of the system.

Research Topic: Prosthetics
Funding agencies: VA RRD
Grant support: I01 RX004256

64. Prevalence of Abdominal Aortic Aneursym in Patients with Hidradenitis Suppurativa in the VA Health Care System

Wendland, Zachary [1-2]; Rypka, Katelyn [1]; Herzog, Claire [2]; Greenlund, Lindsey [2]; Fulk, Travis [3]; Gravely, Amy [1]; Westanmo, Anders [1]; Garg, Amit [4]; Goldfarb, Noah [1]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Southern Illinois University
4. Donald and Barbara Zucker School of Medicine at Hofstra/Northwell

Abstract: Background: Hidradenitis suppurativa (HS) is an inflammatory condition characterized by painful nodules, abscesses and draining tunnels involving body folds. Elevated interleukin (IL)-17 levels have been found in both the skin and blood of patients with HS (1). Abdominal aortic aneurysm (AAA), a focal dilation of the aorta, is a potentially life-threatening condition, thought to be partially driven by IL-17 inflammation (2) and has been found to have increased prevalence in patients with psoriasis, an IL-17-mediated skin disease (3). To date, no studies have explored the relationship between AAA and HS. Objective: To ascertain if a diagnosis of HS is associated with an increased prevalence of AAA compared to patients without HS within the Veterans Affair Health Care System (VAHCS) Methods: Retrospective, cross-sectional study of VAHCS patients using the VA Informatics and Computing Infrastructure (VINCI) database between January 1, 2017—December 31, 2021 Results: 7,465,613 Veterans were included in our analysis of AAA, with 43,647 Veterans having at least one diagnosis of HS by ICD9 (705.83) or 10 (L73.2). Our cohort of patients were largely white (78.0%), men (89.6%) greater than 65 years of age (52.9%). Overall, patients with HS were 1.33 times more likely than non-HS patients to have associated AAA diagnosis (adjusted odds ratio [aOR]=1.26-1.40; p<0.001) (3.82% vs. 3.66%), after adjusting for sex, age, race, obesity, tobacco use, diabetes mellitus type II and cardiovascular comorbidities. Male patients, greater than age 65, with a history of tobacco use and without a diagnosis of HS (population currently screened for AAA), had a prevalence of AAA of 9.1. This was compared to male patients, greater than age 65, with a history of HS, and without a diagnosis of tobacco use, which had a prevalence of AAA of 6.5%. Limitations: Cross-sectional study design, which limits our understanding of the cause-and-effect relationship between HS and AAA. In addition, this study only evaluated prevalence of AAA, and did not investigate the association between HS and AAA rupture and mortality. Discussion: Overall, our study demonstrates a statistically significant association between HS and AAA (aOR=1.333 [1.26-1.40]; p<0.001). Currently, the United States Preventative Services Task Force (USPSTF) recommends men ages 65-75 with a history of tobacco use to undergo a 1-time screening using ultrasonography for AAA (4). While the prevalence of AAA in this demogra

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65. Can text-reminders and self monitoring at home improve gout management in Veterans?

Westgard, Anne [1]; Carson, Lara [1]; Brown, Rebecca [1]

1. Minneapolis VA Health Care System

Abstract: Uncontrolled gout is very painful, leads to frequent visits to the ER and unnecessary ordering of x-rays. This project is important as we have an innovative approach to managing gout especially during the Covid-19 pandemic. 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 medication compliance. We enrolled gout patients voluntarily into our pilot gout project. Eiligibility included a diagnosis of gout and hyperuricemia. The patients were required to have a smart phone and willing to accept text messages from the VA. Patients who were enrolled in the Annie app received text messages alone. Those patients who agreed to participate with a home uric acid meter received the same gout education specific script for the Annie app and lab and home uric acid testing reminders. We queried the patients regarding gout flares (number, duration, type of therapy to abort the flare) outside medical visits, ER visits, satisfaction with Annie text messaging service alone and the home uric acid meter. We did a chart review to ascertain uric acid readings and comorbidities. We found that baseline serum uric acid (sUA) were higher in the meter group. The meter group also took longer to achieve target uric acid than the Annie text messaging group alone. We found that both groups got to target uric acid less than 6. The home meters were equally reliable to the lab testing. There was good satisfaction in both groups for the Annie app but a little less with the meter. The results need to be interpreted cautiously as the group size was small.

Research Topic: Arthritis
Funding agencies: None
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66. To the Duodenum, and Beyond! Using the BougieCap for Duodenal Stricture Dilation

Wilson, Natalie [1]; Abdallah, Mohamed [1]; McDonald, Nicholas [1]; Bilal, Mohammad [2]

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

Abstract: Introduction Benign duodenal strictures are typically caused by peptic ulcer disease, caustic ingestion, surgical anastomoses, or inflammatory bowel disease. Treatment of benign strictures usually involves endoscopic dilation using through-the-scope (TTS) balloon dilators with or without fluoroscopy. TTS balloon dilators allow visualization during dilation, but they do not provide haptic feedback. The BougieCap dilator is a newer device that attaches to the endoscope and allows direct visual and haptic feedback during dilation. While it is generally used for dilation of esophageal strictures, this report describes its use for dilation of a benign duodenal stricture. Case A 75-year-old male with stage IV non-small cell lung cancer on immunotherapy was found to have biliary dilation on imaging. He subsequently underwent endoscopic ultrasound which incidentally revealed a duodenal stricture at the junction of the first and second portions of the duodenum. The stricture was unable to be traversed with the linear echoendoscope or an adult upper endoscope. TTS balloon dilation from 8 to 12 mm was performed, however, the adult upper endoscope was still unable to traverse the stricture. Biopsies of the stricture were obtained and were negative for malignancy and gastric biopsies did not reveal any evidence of H. pylori infection. Approximately 4 months later, the patient developed progressive nausea and vomiting. Upper endoscopy again showed the duodenal stricture which was unable to be traversed. The decision was made to use the BougieCap device for dilation. The stricture was then sequentially dilated from 10 to 12 mm using the BougieCap with direct visualization of mucosal disruption during dilation as expected (Figure 1). The adult upper endoscope was then able to traverse the stricture easily. There were no procedural complications or adverse effects and the patient reported improvement in his symptoms. Discussion Benign duodenal strictures are typically treated with endoscopic dilation using TTS balloon dilators, although this method is limited by the lack of haptic feedback or complete visualization in some cases. In this case, TTS balloon dilation was ineffective for initial stricture dilation, thus the BougieCap was used for more precise dilation under direct visualization. While the BougieCap is generally used for esophageal stricture dilation, it may also serve as a safe and effective method to dilate refractory benign duodenal strictures.

Research Topic: Gastroenterology
Funding agencies: None
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67. Use of the Endoscopic Powered Resection Device for Management of Difficult Colorectal Polyps: A Multicenter Study

Wilson, Natalie [1]; Herman, Tessa [1]; S?nchez-Luna, Sergio [2]; Ahmed, Ali [2]; Peter, Shajan [2]; Obeng, George [3]; Shah-Khan, Sardar Momin [3]; Singh, Shailendra [3]; Thakkar, Shyam [3]; Azeem, Nabeel [1]; Bilal, Mohammad [4]

1. University of Minnesota
2. University of Alabama
3. West Virginia University
4. Minneapolis VA Health Care System

Abstract: INTRODUCTION Colorectal polyps with submucosal fibrosis or scarring can be challenging to resect using endoscopic mucosal resection or endoscopic submucosal dissection. The endoscopic powered resection (EPR) device (EndoRotor) is a non-thermal endoscopic resection tool that can be used for resection of complex colorectal polyps, though this data is limited. Our study aims to evaluate the feasibility, safety, and efficacy of the EPR device for resection of complex colorectal polyps. METHODS This was a multicenter retrospective study of patients who underwent endoscopic resection of a colorectal polyp using the EPR device between July 2020 and September 2022. Patient demographics, procedural data, and information regarding surveillance colonoscopy were collected. Primary outcome was technical success. Technical success was defined as complete resection of all visible polyp tissue, either using the EPR device as monotherapy or as an adjunct to other resection modalities. Secondary outcomes were rates of residual or recurrent adenoma (RRA) and adverse events. RESULTS A total of 16 patients across four institutions were included in this study. 68.8% of patients were male and the mean age was 69 years. The average polyp size was 19.6 mm and the most common location was the transverse colon. Resection was previously attempted in 14 cases (87.5%). Technical success was achieved in 100% of cases. The EPR device was used as monotherapy for polyp resection in 7 cases (43.8%) and as an adjunctive therapy in 9 cases (56.3%). The EPR device was used as an adjunctive therapy with the following modalities: full-thickness resection device (FTRD) (n=4, 44.4%), hot snare (n=3, 33.3%), and argon plasma coagulation (n=2, 22.2%). RRA was present in 2 out of the 5 patients who underwent follow-up endoscopy. Resection of RRA was performed with snare tip soft coagulation (n=1) or endoscopic full-thickness resection using the FTRD (n=1). There were no immediate or delayed adverse events. CONCLUSION The EPR device offers a safe and effective endoscopic resection method for complex colorectal polyps that may not be amenable to other resection techniques. Our preliminary findings suggest that the EPR device can be used as both monotherapy or as an adjunct to other available modalities and is a useful tool for management of complex colorectal polyps. Long-term data on residual and recurrent adenoma is needed before it can be widely incorporated into clinical practice.

Research Topic: Gastroenterology
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68. Endoscopic Full-Thickness Resection of Gastric Ulceration with Persistent Low-Grade Dysplasia Using the Full-Thickness Resection Device

Wilson, Natalie [1]; McDonald, Nicholas [1]; Abdallah, Mohamed [1]; Bilal, Mohammad [2]

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

Abstract: Introduction Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are well-established treatment methods for resection of precancerous gastric lesions and early gastric cancers. Ulcerated or scarred gastric lesions are challenging to resect with EMR or ESD due to submucosal fibrosis and scarring, and hence, carry increased risk for perforation. Endoscopic full-thickness resection (EFTR) using the full-thickness resection device (FTRD) is rapidly gaining popularity for the treatment of upper gastrointestinal tract lesions. While it has been shown to be a safe and effective treatment modality for colorectal lesions not amenable to conventional resection methods, data regarding its use in the upper GI tract is evolving. Here, we describe a patient with an ulcerated gastric lesion with persistent low-grade dysplasia who underwent successful resection of the lesion using the FTRD. Case A 75-year-old man with a history of diffuse gastric intestinal metaplasia was found to have a 1 cm ulcer in the gastric antrum (Figure 1A). Biopsies of the ulcer demonstrated low-grade dysplasia, while surrounding biopsies showed incomplete gastric intestinal metaplasia. He was started on a proton pump inhibitor with plan for repeat endoscopy for surveillance. Subsequent upper endoscopy 12 and 24 months later showed partial healing of the gastric ulcer (Figure 1B), however, biopsies showed persistent low-grade dysplasia. After a multidisciplinary discussion, the decision was made to pursue EFTR of the ulcerated lesion. An upper endoscopy was performed and the borders of the lesion were marked circumferentially with a marking probe. The FTRD was mounted on a modified therapeutic upper endoscope and the lesion was resected. The resection site was examined and demonstrated appropriate positioning of the clip and no evidence of bleeding (Figure 1C). Given the proximity of the lesion to the pylorus, the endoscope was advanced to the duodenum documenting luminal patency. The patient tolerated the procedure well and was discharged the same day. No adverse events were experienced within four weeks of the procedure. The final pathology report of the lesion confirmed focal low-grade dysplasia (Figure 1D) with negative resection margins (R0). Discussion EFTR using the FTRD device can offer a safe and effective approach to treat ulcerated or scarred gastric lesions that are not typically amenable to conventional endoscopic resection techniques.

Research Topic: Gastroenterology
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69. Through-The-Scope Helix Tack and Suture Device: Approaches to Tack Removal

Wilson, Natalie [1]; McDonald, Nicholas [1]; Megna, Bryant [1]; Abdallah, Mohamed [1]; Bilal, Mohammad [2]

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

Abstract: Introduction Malignant gastroduodenal strictures are a leading cause of gastric outlet obstruction and are often managed with endoscopic stent placement. One of the main limitations of duodenal self-expanding metal stents (SEMS) is the risk of migration. Multiple techniques have been used to prevent stent migration, including stent fixation using through-the-scope (TTS) clips, over-the-scope stent fixation devices, and endoscopic suturing. TTS suturing using the helix tack and suture device is a novel suturing method that is generally used for defect closure, though it has been rapidly gaining popularity for alternate uses. Here, we report its use as a stent fixation method in a patient with gastric outlet obstruction due to a malignant duodenal stricture. Case A 73-year-old male with pancreatic adenocarcinoma on neoadjuvant chemotherapy presented with 3 weeks of vomiting and abdominal distension. Imaging showed pancreatic adenocarcinoma with duodenal obstruction. Esophagogastroduodenoscopy (EGD) was performed and showed duodenal stenosis from tumor infiltration at the duodenal sweep. The adult upper endoscope was able to traverse the stenosis with significant resistance and the stenosis measured 2 cm in length. The patient was borderline resectable, and per institutional protocol, endoscopic ultrasound-guided gastrojejunostomy is only performed for patients who are not surgical candidates, therefore, decision was made to proceed with duodenal stent placement. A 25 mm in diameter and 10 cm in length uncovered SEMS was placed across the stenosis. Given that the upper endoscope was able to traverse the stenosis, decision was made to fixate the stent to reduce migration prior to stent expansion and tissue ingrowth to keep the stent in place. The TTS suturing device was used and the stent was fixated with four tacks placed in stent-mucosa-mucosa-stent fashion (Figure 1). A cinch was placed in the end. The patient tolerated the procedure well and no adverse events were reported within the first 4 weeks of the procedure. Discussion Duodenal SEMS are widely used in the setting of malignant gastroduodenal obstruction. While uncovered stents typically carry a lower risk of migration compared to covered stents, in this case the tissue apposition was less than desired and thus the TTS suturing device was used for stent fixation. In this report, we demonstrate that the TTS suturing device may be a safe and effective technique for duodenal stent fixation.

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70. Analysis of Reported Adverse Events Associated with the Over-The-Scope Endoscopic Suturing System: An FDA MAUDE Database Study

Wilson, Natalie [1]; Abdallah, Mohamed [1]; Jaber, Fouad [2]; Johnson, Willie Mohammed [1]; McDonald, Nicholas [1]; Baliss, Michelle [3]; Singh, Shailendra [4]; Bilal, Mohammad [5]

1. University of Minnesota
2. University of Missouri-Kansas City
3. St. Louis University
4. West Virginia University
5. Minneapolis VA Health Care System

Abstract: BACKGROUND The over-the-scope endoscopic suturing system [OverStitch™ Endoscopic Suturing System (ESS)] is one of the most widely utilized endoscopic suturing systems in current clinical practice. Since FDA approval in 2008, the device has been used for a variety of indications including closure of endoscopic resection defects, leaks, perforations and fistulas, as well as endoscopic bariatric procedures. However, data on the adverse events associated with this device is scarce. Our study aims to evaluate the adverse events associated with the over-the-scope ESS using the FDA's Manufacturer and User Facility Device Experience (MAUDE) database. METHODS We analyzed post-marketing surveillance data from the MAUDE database for the over-the-scope ESS from January 2008 through June 2022. This database collects medical device reports of suspected device-associated deaths, serious injuries, and malfunctions. The medical device reports classify events into categories based on severity, including death, injury, malfunction, or other. Our outcomes were device-related issues, patient adverse events and management of adverse events. RESULTS 83 reports were filed from January 2008 to June 2022. Adverse events were classified as device-related (n=77) and patient-related (n=87). Of 77 device-related issues, the most common was that it was difficult to remove after deployment (n=12; 15.6%). Other common device issues were mechanical problem (n=10; 13%), mechanical jam (n=9; 11.7%), or entrapment of device (n=9; 11.7%). Other less frequent device issues included failure to align, failure to fire, and broken or defective device. Of the 87 patient-related adverse events, the most common was perforation (n=19; 21.8%), followed by device embedded in tissue (n=10; 11.5%), and abdominal pain following suturing (n=8; 9.2%). Of the 19 patients who experienced perforation, two required open surgical repair and one required laparoscopic surgical repair. The rest were able to be managed conservatively, or management was otherwise unspecified. CONCLUSION The overall reported adverse events from the over-the-scope ESS remain low as evidenced by the number of reported cases since 2008. Difficulty removing the device after deployment and perforation were the most common device problems and patient-related adverse events, respectively. Identifying common and rare adverse events is important to optimize device design and improve patient outcomes.

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