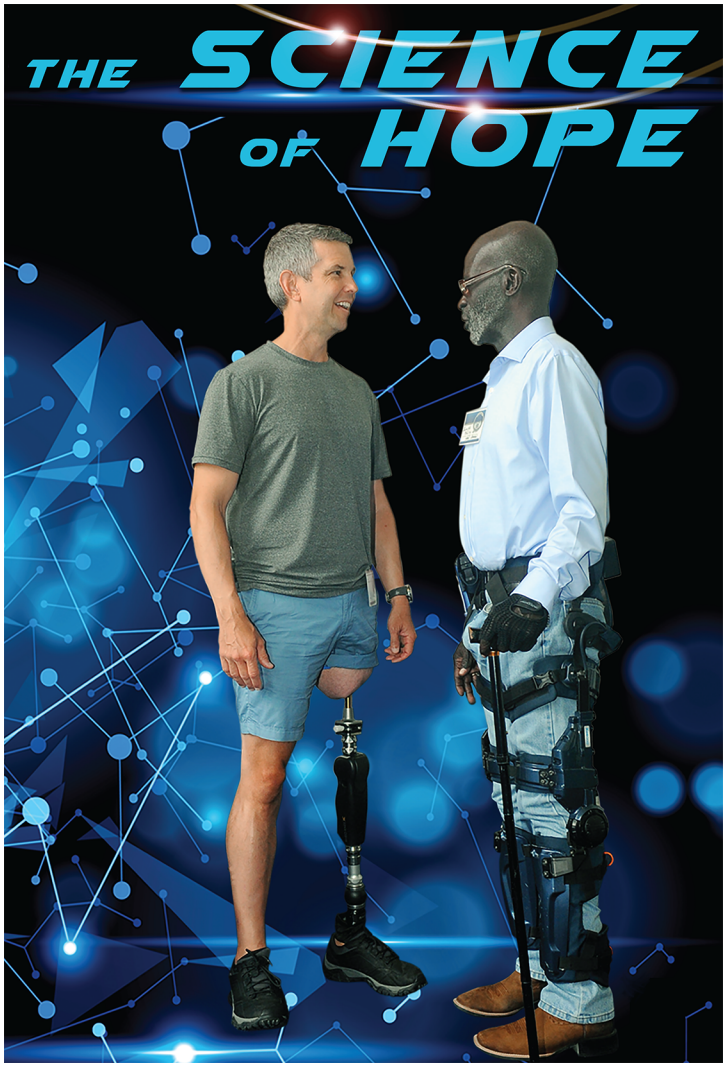
–Minneapolis VA Health Care System–

VA Research Day 2019



Program and Abstract List

(alphabetically, by author)

May 1, 2019

VA

U.S. Department of Veterans Affairs

Veterans Health Administration

Office of Research and Development

☆About Our Keynote Speaker☆

Rachel B. Ramoni, DMD, ScD, has served as the VHA Chief Research & Development Officer (CRADO) since January 2017. Dr. Ramoni was previously on the faculty at New York University College of Dentistry in the department of epidemiology and health promotion, and at Harvard Medical School in the department of biomedical informatics.

Among Dr. Ramoni's research interests are informatics, genomics, and precision medicine. Dr. Ramoni earned a Doctor of Medicine in Dentistry degree from the Harvard School of Dental Medicine, as well as a Master of Science and Doctor of Science in epidemiology from the Harvard School of Public Health. She also holds certificates in dental public health and oral epidemiology. Her publications have appeared in numerous journals, including Birth Defects Research, Epidemiology, Circulation, the Journal of the American Medical Association, and the American Journal of Human Genetics.

–Adapted from VA website at https://www.research.va.gov/about/crado.cfm

☆Program☆

1. Oral Presentations – 1st Floor Auditorium (12:00 - 1:00 pm)

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

☆**2018 Zieve Award Presentation** ..... James Johnson, MD

Recipient:
Fernando Ortiz, MD
"Utility of Nuclear Stress Imaging in Predicting Long-Term Outcomes One-Year Post CABG Surgery"

☆**2018 Lederle Award Presentation** ..... Aasma Shaukat, MD, MPH

Recipient:
Philipp Dahm, MD
"Prostate Cancer Screening with Prostate-Specific Antigen (PSA) Test: A Systematic Review and Meta-analysis"

BMJ 2018 Sep 5; 362:k3519

☆**Keynote Address** ..... Rachel Ramoni, DMD, ScD
VHA Chief Research & Development Officer

☆ *The Center for Veterans Education & Research will be providing Free Box Lunches to the first 200 attendees.*

2. Poster and Exposition Session – 2nd Floor Flag Atrium (1:00 – 3:30 PM)

☆ *Research Findings and Innovations from the Minneapolis VA Health Care System*

☆ *Popcorn provided by the Minneapolis VA Research Office*

Author Index *(first author only)*

1. CSP #592 Efficacy and Safety of ICD Implantation in the Elderly

Adabag, Selcuk [1,2]; Buelt-Gebhardt, Melissa [1]; Tholakanahalli, Venkat [1,2]; Condon, Debra [1]; Singh, Steven [3]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Washington, DC VA Health Care System

Abstract: Implantable Cardioverter-Defibrillators (ICDs) prevent Sudden Cardiac Death (SCD) by restoring normal rhythm in the event of a life-threatening ventricular tachyarrhythmia. While ICD therapy is a proven preventer of SCD in younger patients, its ability to reduce all-cause mortality in those with advanced age is unclear. ICD therapy is considered to be an under-utilized treatment option despite widely recognized safety and efficacy. Age bias is a particularly prominent theory in the effort to explain under-utilization of ICD. In major clinical trials of patients receiving ICDs over the past 15 to 20 years, the mean and median age of study populations range from 50 to 65 years of age. The proportion of potentially eligible VA patients implanted with an ICD peaks at approximately 67 years of age and declines continuously thereafter. No randomized clinical trials have focused solely on an older population. The overall aim of CSP #592 is to study the safety and efficacy of ICD implantation as a primary prevention strategy of Sudden Cardiac Death (SCD) in patients 70 years of age and older. In particular, this study is designed to compare the effectiveness of ICD, in addition to Optimal Medical Therapy (OMT), on all-cause mortality versus OMT alone. OMT includes standard intervention for chronic heart failure patients, such as disease management with neurohormonal blockade, adoption of healthy diet, and exercise. One particularly important secondary objective is to assess treatment efficacy under the conditions of high versus low co-morbidity burden. In the study, participants are randomized (1:1 ratio) to ICD + Optimal Medical Therapy (OMT), or OMT alone, stratified by participating site and co-morbidity level (Charlson score < 3 versus > 3). Follow-up will occur every 6 months until study close. We postulate that ICD + OMT will result in a 25% reduction in the hazard for all-cause mortality.

Research Topic: Cardiovascular Disease
Funding agencies: CSR&D
Grant support: Cooperative Studies Program

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

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

1. Minneapolis VA Health Care System

Abstract: The VA Cooperative Studies Program (VA CSP) Network of Dedicated Enrollment Sites (NODES) is a consortium of VA Health Care Systems that have facility-based teams dedicated to conducting VA CSP Research. The specific aims include; enhancing study performance and enrollment rates; provide a more consistent and comprehensive approach to CSP study management, quality and regulatory compliance at the VA Medical Centers; obtain center-level perspectives in the design and execution of studies; and provide opportunities for research personnel interested in supporting the VA CSP research mission. A Director, Manager, Assistant Manager (Minneapolis Only), Administrator, and Research Nurse support these efforts at each individual NODES location. NODES shares facility-derived best practices and provides local insights to VA CSP partners for efficient management and conduct of all study activities. The following achievements reflect cumulative data of the NODES sites from October 2012 – Present: *Established cross-coverage on all open CSP studies *NODES staffing incorporated as part of local CSP study teams *Created Mentorship Program for new local study investigators and coordinators *Created procedures for mobile recruiting at CBOCs *Work stream meetings on improving study design & procedures *Creation of Work groups to develop and beta test case report forms *Enhanced recruitment through Mobile Recruiting Equipment *Reduced logistical and staffing barriers *Development of Partnership between NODES and Non-NODES facilities to assist in study teams with low recruitment *Creation of VA CSP-NODES Executive Board *Creation of CSP Studies Toolbox to facilitate NODES and Non-NODES VA sites in study implementation *Creation of VA-CSP Strategic Plan Work groups to amalgamate with VHA Strategic Plan

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

3. Validation of a Sudden Cardiac Death Risk Prediction Model in Heart Failure Preserved Ejection Fraction

Adabag, Selcuk [1,2]; Langsetmo, Lisa [1,2]

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

Abstract: Sudden cardiac death (SCD) is the most common mode of death in heart failure with preserved ejection fraction (HFpEF), comprising 25% of all deaths. We previously developed a risk prediction model to identify a subset of patients with HFpEF who have a high risk of SCD. Objective: To validate the SCD risk prediction model in a large HFpEF cohort with adjudicated SCD. Methods: We validated the SCD risk model among in the publicly-available dataset of the TOPCAT trial. Of the 3445 trial participants, 615 had data on all 6 variables (age, sex, myocardial infarction, diabetes mellitus, left bundle branch block, N-terminal pro-brain natriuretic peptide) of the SCD risk prediction model. Those with a 5-year predicted risk of SCD = 10% were categorized as high risk. Results: Mean age (SD) of the 615 patients was 70.1 (9.5) and 49% were male. Over a mean 2.9 (1.3) years of follow-up, there were 23 (3.7%) SCD and 63 (10.2%) deaths from other causes. There were 216 (35.1%) participants classified as high risk for which the 5-year cumulative incidence of SCD was 15.2% (95%CI: 6.6, 27.2) vs. 2.8% (95%CI: 1.2, 5.5) for those not classified as high risk. In competing risk analysis, patients with a higher predicted risk had a 3.7-fold greater risk of SCD (HR 3.70; 95% CI: 1.6, 8.7; p = 0.003) than those classified as low risk. The SCD risk model had a Harrell's C index of 0.74. Conclusions: A SCD risk model with 6 widely-available variables can identify a subset of HFpEF patients with a higher risk of SCD. Use of this risk model will increase the feasibility of intervention trials to reduce SCD in HFpEF.

Research Topic: Cardiovascular Disease
Funding agencies: CVRE
Grant support: American Heart Association Grant no. 17GRNT33670993

4. Impact of Clostridioides difficile Stool Order Set Modification on Inpatient Inappropriate Stool Testing, Infection, and Vancomycin Consumption

Amand, Ryan [1]; Harper, Jane [1]; Narayan, Muthu [1]; DeVries, Aaron [1]

1. Minneapolis VA Health Care System

Abstract: Clostridioides difficile (C. diff) is a Gram-negative bacterium responsible for up to 500,000 cases of healthcare-associated diarrhea annually causing increased morbidity and mortality. Antibiotic exposure increases CDI risk; an estimated 30 – 50% of hospital-prescribed antibiotics are unnecessary or incorrect. A noted increase in positive C. diff tests led to a retrospective review of FY18 patients with a positive C. diff test finding 44% (25/57) did not meet published testing criteria. Inappropriate testing can lead to patients unnecessarily being treated with antibiotics. MVAHCS proposed modifying the test order to include testing criteria to determine impact on inappropriate C. diff testing. Methodology: MVAHCS uses C. diff PCR alone and multiplex enteric PCR that includes C. diff PCR. Testing criteria (> 3 loose stools in the 24 hours prior to stool sample submission and no recent laxative use) was added to the C. diff test order in CPRS on 11/15/18. Clinicians and nursing staff received additional notification via email on 12/17/18. TheraDoc was used to identify all inpatients tested for C. diff from 7/1/18-3/31/19 and reviewed for testing criteria. Theradoc was utilized to obtain oral Vancomycin therapy days from 7/1/18-3/31/19. Results: Out of 480 of the C. diff tests 79% (380) met testing criteria. Overall, 16% (76/480) were positive; of which 50% (38) of positive tests were via C. diff toxin; 50% (38) were via enteric panel. 20% (100/480) of the total did not meet the testing criteria; 48% (48/100) were on laxatives and 52% (52/100) did not have >3 loose stools in 24 hours. Comparing 7/1-11/31/18 to 12/1/18-3/31/19 the number of C. diff tests decreased from 60 to 45 tests/mo, PO vancomycin total days of therapy went from 142 to 107 per month and facility wide CDI rates decreased from 5.6 to 3.9 CDI events/10,000 Bed Days of Care. Discussion: Modification to order decreased total number of C. diff tests, Oral Vancomycin therapy days and CDI rates however last month of surveillance there was an increase. Additional time will be required to determine if these improvements will be maintained. Clinician and nursing documentation of stooling history were often inconsistent, possibly resulting in inaccurate categorization of testing criteria compliance. Testing criteria does not address patients on tube feedings (TF). This may need to be explored as patients on TF accounted for 10% of negative tests. Ongoing education may be required.

Research Topic: Infectious Diseases
Funding agencies: N/A
Grant support: N/A

5. Men with Urinary Tract Infections & Sub-Study about Bacterial Resistance to Antibiotics

Amundson, Carla [1]; Drekonja, Dimitri [1,2]

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

Abstract: Inappropriate treatment of purported urinary tract infection (UTI) is a major cause of antimicrobial overuse. This is of particular concern because such treatment often involves fluoroquinolones and other agents active against Gram-negative organisms, thus driving resistance to the few orally-available drugs still active against these organisms. An ongoing randomized controlled trial of treatment duration for men with UTI provides a unique opportunity to prospectively assess the appropriateness of UTI diagnoses and subsequent antimicrobial therapy. Methods The main objective of this trial is to randomize men with UTI to 7 vs. 14 days of treatment with ciprofloxacin or trimethoprim/sulfamethoxazole and assess for differences in rates of symptom resolution. Potential cases of UTI among men presenting to outpatient clinics and the emergency department of the Minneapolis VA Healthcare System are identified by diagnostic codes and prescriptions for the studied antimicrobials. Subsequently, medical record review and phone contact (if needed) are used to determine trial eligibility including manifestations of UTI. Qualifying UTI manifestations include dysuria, frequency, urgency, hematuria, and flank, suprapubic, or perineal pain. Results From 4/14/2014 through 4/10/18 there were 2,725 unique visits in which a man was diagnosed and treated for a UTI. A total of 759 (27.9%) had no manifestations of UTI, but still received antimicrobial therapy. Among the 1,966 men with symptoms (72.1%), 578 (29.4%) met eligibility criteria, and 144 (24.9% of eligible) enrolled. Conclusions Screening for this trial of treatment duration of male UTI allows prospective screening for manifestations of UTI, with patient contact for encounters with no (or inconsistent) documentation of signs or symptoms. We documented a high rate of misdiagnosis and inappropriate antimicrobial treatment, contributing to the emerging antimicrobial resistance crisis. This study, conducted at the Minneapolis VA Medical Center, will help to ensure that veterans receive the optimal treatment for this common condition, and help to define the potential harms of antibiotics. As of 3/28/2019, 178 patients have enrolled. Second site (Houston VAMC) started recruitment 12/2017 and have enrolled 39 participants. We look forward to presenting our results at a future Research Day.

Research Topic: Infectious Diseases
Funding agencies: CSR&D
Grant support: VA Merit Review; 1I01CX000830-01A2

6. Building and Sustaining a Veteran Engagement Panel in the VOICE Study

Amundson, Erin [1,2]; Glenn, Rosie [3]; Jensen, Agnes [1]; Krebs, Erin [1,2]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. VOICE Study Veteran Engagement Panel member

Abstract: We are part of a five-year PCORI-funded comparative effectiveness trial of two collaborative care models to improve pain and reduce opioid use among Veterans (VOICE study). Our research team is advised by a diverse ten-member Veteran Engagement Panel (VEP). The panel was formed after a multi-step recruitment process which included individual interviews with potential patient partners. The process to form the VOICE VEP included: 1) identifying patients across sites who might enjoy sharing ideas and helping others to serve as paid study advisors; 2) conducting preliminary meetings with partners to discuss potential role of the VEP and requesting a written statement of interest; 3) conducting telephone interviews with each partner and two study team members; and 4) a summary meeting by the study team to select final candidates. The final panel members were chosen based on diversity of life/pain experience, motivation for participation, diversity of military service, and traditional demographic diversity such as age/gender/geographic dispersion. The partnership launched with a one-day in-person meeting and continues with monthly phone meetings. Key lessons learned thus far are: 1) Seek early mentorship: The team's engagement knowledge was enhanced by partnering with U of Wisconsin experts to help train the team in best practices. 2) Set realistic expectations and be accountable to partners: Honest expectations from study onset are critical to the success of the collaboration. Providing specific, timely examples on how VEP input is used by the team reinforces value of the panel's contributions. 3) Encourage flexibility: Partners have competing priorities (health, family, or work) and all are living with chronic pain. The research team encourages flexibility in how feedback is provided and works around VEP member's schedules. 4) Share innovative contribution opportunities: The research team continuously seek additional opportunities for panel member input and participation. 5) Be transparent and vulnerable: The team is transparent about challenges (e.g. slow recruitment) and asks VEP members to identify strategies to overcome barriers. 6) Evaluate/check-in: VEP members provide semi-annual evaluation during individual phone calls with the study team's engagement liaison.

Research Topic: Pain
Funding agencies: N/A
Grant support: Patient Centered Outcomes Research Institute (PCORI) OPD-1511-33052

7. Assessing Resident Experience with Antimicrobial Stewardship

Andrews, Shannon [1,2]; Lynfield, Ruth [2,3]; Beaudoin, Amanda [2,3]; Drekonja, Dimitri [1,2]

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

Abstract: Inappropriate antimicrobial use is common in the outpatient setting. Antimicrobial stewardship prevents inappropriate antimicrobial prescribing and its deleterious effects. Resident physicians might benefit from directed antimicrobial stewardship efforts. Methods: Resident physicians with continuity clinic at the Minneapolis Veterans Affairs Health Care System were eligible for this study. Antimicrobial prescriptions, number of visits, and number of clinics per month were extracted from the Computerized Patient Record System from July 1, 2017 to March 31, 2018. Antimicrobial rate (prescriptions per clinics) was calculated monthly. A survey, linked to antimicrobial rate, consisted of 21 questions including demographics, attitudes regarding antimicrobial stewardship, and case-based multiple-choice knowledge questions. Results: Prescription and clinic data were available for 37 resident physicians. Average antibiotic prescribing rate was 0.3 prescriptions per clinic (range 0.02-1.17). Surveys were completed by 19 physicians (51% response rate) with a mean age of 30 years (range 26-35). Physicians were 32% female, 32% interns, and 11% international foreign medical graduates. Respondent attitudes were consistent with basic tenants of antimicrobial stewardship. Resident physicians most commonly use UpToDate to learn about antimicrobial use and resistance. They find lectures series and small-group sessions for residents the most helpful for learning regarding antimicrobials. Respondents were not confident in all areas of practice related to antimicrobial use. Knowledge was low on a quiz administered to resident physicians. Out of a total of 11 knowledge questions, the average percentage correct for all respondents was 61% with an interquartile range from 50-71%. Conclusions: There is variation in the prescribing of antimicrobials among resident physicians. Resident physicians largely agree with key concepts of antimicrobial stewardship, but they lack preparation in basic tasks related to antimicrobial prescribing and stewardship. Knowledge regarding antimicrobial prescribing was low. Targeted interventions, including lectures and small-group sessions with faculty, may help resident physicians to improve their prescribing.

Research Topic: Infectious Diseases
Funding agencies: NIH
Grant support: T32AI055433 award, NIH

8. Baseline ocular screening for hydroxychloroquine use

Armbrust, Karen [1]; Garbo, Amy [1]

1. Minneapolis VA Health Care System

Abstract: Hydroxychloroquine (HCQ; Plaquenil) is a commonly prescribed medication for the management of many autoimmune conditions. Irreversible vision loss due to retinal toxicity is a potential side effect, so regular ocular examinations with sensitive retinal screening methods should be implemented in patients taking HCQ. It is important that patients receive screening ocular examinations within the first year of starting HCQ to identify potential ocular co-morbidities that might make HCQ toxicity screening difficult and to establish baseline measurements. In this quality improvement project, we perform chart review on Minneapolis VAMC patients starting HCQ to evaluate our current practice in baseline ocular screening and identify potential areas of improvement. Although the overall ocular screening rate in HCQ users is very good, there is room for improvement. Our ultimate goal is to establish ocular screening practices that will prevent irreversible vision loss from HCQ-induced retinal toxicity.

Research Topic: Ophthalmology
Funding agencies: N/A
Grant support: not applicable

9. Creating a Standardized Approach to Evaluation & Treatment of Bone Health in Patients with Fragility Fractures at the Minneapolis VA Medical Center: The Intervention QI Project

Babcock, Corey [1]; Tranchida, Geneva [1]; Ruanpeg, Darin [2]; Sechriest, Vernon Franklin [2]; Niewoehner, Catherine [2]

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

Abstract: Osteoporosis treatment is recommended to reduce the risk of future fractures in patients with fragility fractures. Previous work at the Minneapolis VAMC documented a low rate of bone health evaluation and pharmacologic treatment of osteoporosis after hip fractures. Through collaboration amongst orthopedics, internal medicine, endocrinology, nutrition and physical therapy, we created admission and discharge order sets for bone health evaluation and treatment (laboratory evaluation, nutritional and physical function evaluation and treatment and appropriate initiation of antiresorptive therapies). The intervention was implemented February 2019 and during the first month of the intervention, we collected post-intervention rates of these evaluation and treatment modalities. In comparing pre and post-intervention bone health evaluation and treatment (Phase 1), we found an increase in the percentage of calcium and vitamin D supplementation and bone mineral density (DXA) testing. The rate of bisphosphonate or alternative osteoporosis treatment appeared to be low. In Phase 2 of this quality improvement project, the intervention has been modified to include administration of inpatient Zoledronic acid in appropriate patients per the Endocrinology team's recommendations and data collection is pending.

Research Topic: Aging
Funding agencies: N/A
Grant support: N/A

10. Is Chronic Inflammation the Underlying Cause of Gulf War Illness and Burn Pit Syndrome?

Bach, Ronald [1]; Trembley, Janeen [1]; Butterick, Tammy [1]

1. Minneapolis VA Health Care System

Abstract: Nearly 700,000 U.S. military personnel served in the 1990-91 Gulf War. Many Veterans of Operations Desert Shield and Desert Storm are now suffering from a deployment-related chronic multisymptom illness (CMI), a.k.a. Gulf War Illness (GWI). The characteristic symptoms of GWI are chronic fatigue, musculoskeletal pain, impaired cognition, gastrointestinal disorders, respiratory problems, and skin rashes. Recent research has identified exposure to environmental pollutants, such as those emitted from open-air burning of refuse on military bases ('burn pits') or other deployment-related airborne hazards as a potential cause of GWI. Exposure to complex mixtures of gasses and particles results in profound biologic consequences. Combined gasses and solid particles creates an aerosolized particle, forming a toxic delivery system that is far more dangerous than either the gasses or particles alone. The result is production of 'pulmonary shrapnel' or cellular and biochemical products that spill out of the lung and into the systemic circulation, leading to a cascade of health problems. One highly plausible theory supports chronic inflammation as the underlying pathophysiology of GWI. Our previous work identified a blood biomarker fingerprint of inflammation that differed significantly in Gulf War Veterans with and without GWI. Furthermore, all GWI-associated symptoms can be triggered by inflammation. Of note, median biomarker levels for the people with prevalent GWI were still within standard 'normal' thresholds, and thus would not have been flagged by other studies that did not include a healthy control group. Now, many Veterans of Operations Enduring Freedom (OEF) and Iraqi Freedom (OIF) are experiencing GWI-like symptoms. Therefore, we are naming this new deployment-related CMI Burn Pit Syndrome (BPS). Although the symptoms of BPS and GWI appear identical, it remains to be established whether the underlying pathophysiologies are related. Similar biomarker fingerprints across these conflicts would implicate inflammation as a potential high-value target for primary and secondary prevention of BPS morbidity and mortality.

Research Topic: Afghanistan & Iraq Veterans
Funding agencies: DOD
Grant support: Department of Defense Congressionally Directed Medical Research Programs Gulf War Illness Research Program (W81XWH-09-2-0047)

11. Impact of Gastroesophageal Reflux on Longitudinal Lung Function and Quantitative Computed Tomography in the COPDGene Cohort

Baldomero, Arianne [1,2]; Wendt, Chris [1,2]; Petersen, Ashley [2]; Gaeckle, Nathaniel [2]; Han, Meilan [3]; Kunisaki, Ken [1,2]

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

Abstract: Gastroesophageal reflux disease (GERD) is a common comorbidity in chronic obstructive pulmonary disease (COPD) and has been associated with increased risk of acute exacerbations, hospitalization, emergency room visits, costs, and quality-of-life impairment. However, it remains unclear whether GERD contributes to the development and progression of COPD as measured by lung function or quantitative computed tomography (QCT). OBJECTIVE: To determine the impact of GERD on longitudinal changes in lung function and QCT metrics of lung disease. METHODS: We evaluated 5,728 participants in the COPDGene cohort who completed baseline and follow-up visits approximately 5 years later. GERD status was based on participant-reported physician diagnoses. We evaluated associations between GERD and both lung function [forced expired volume in 1 second (FEV1) and forced vital capacity (FVC)] decline and QCT metrics of lung disease using multivariate linear regression models, adjusted for age, race, smoking, body mass index (BMI), clinical center, and FEV1 % predicted. These associations were further evaluated in the setting of GERD treatment with proton-pump inhibitors (PPI) and/or histamine-receptor 2 blockers (H2 blockers). MEASUREMENTS AND MAIN RESULTS: GERD was reported by 2101 (36.7%) participants at either baseline and/or 5-year follow-up. Compared to participants without GERD, participants with GERD had faster decline in FEV1 (difference of -3.64 mL/year; 95% CI: -6.56 to -0.728; p = 0.014), FVC (difference of -4.26 mL/year; 95% CI: -8.52 to -0.004; p = 0.05) and faster progression of air trapping (0.167 %/year; 95% CI: 0.0625 to 0.271; p = 0.0017). We observed no significant differences in the rate of change for other QCT metrics such as airway wall area/thickness or emphysema. Among those with GERD, use of PPI and/or H2 blockers was associated with faster decline in FEV1 (difference of -6.91 mL/year; 95% CI: -12.2 to -1.59; p = 0.011) and FVC (difference of -9.55 mL/year; 95% CI: -17.6 to -1.52; p = 0.02). CONCLUSIONS: GERD was associated with faster lung function decline and QCT measures of air trapping. The magnitude of the differences was clinically small, but evaluation and treatment of this common COPD comorbidity should be considered for further study. Clinical Trials Registration: NCT00608764

Research Topic: Lung Disorders
Funding agencies: NIH
Grant support: NHLBI U01 HL089897 and U01 HL089856; NCATS UL1TR000114

12. Improving Health Care for Veterans with Gulf War Illness

Baldwin, Nicole [1]; Lava-Parmele, Susan [2]; Trembley, Janeen [2]; Butterick, Tammy [2]; Bach, Ronald [2]

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

Abstract: Seven-hundred thousand U.S. military personnel were deployed to the Kuwaiti Theater of Operations in the First Gulf War (August 2, 1990 to July 31, 1991). Today, many Veterans of this conflict are reporting a complex of symptoms that we now call Gulf War Illness (GWI). There is neither a definitive etiology nor an effective treatment for GWI, and the prevalence of the disorder in this Veteran population continues to escalate. Therefore, clinical management of GWI is a growing challenge for the Department of Veterans Affairs Health Care System (VAHCS). Based on a survey of 30 Gulf War Veterans who met the Kansas case-definition for GWI, conducted at the Minneapolis VAHCS, health care provider education emerged as a primary focus of improvement. The survey results support the conclusion that there is a growing need to equip VAHCS medical personnel and trainees with updated, evidence-based GWI education and resources. One potential remedy, the creation of clinics within VAHCS focused on the diagnosis and medical treatment of symptomatic Gulf War Veterans, is examined in this report. GWI clinics would provide the interdisciplinary support required to manage this complex chronic illness and improve the health-related quality of life (HRQOL) of Veterans with GWI.

Research Topic: Gulf War Veterans
Funding agencies: DOD
Grant support: Department of Defense Congressionally Directed Medical Research Programs Gulf War Illness Research Program (W81XWH-09-2-0047)

13. Psychosocial Predictors of Cognitive Functioning In Persons with Chronic Pain

Baumgartner, Sarah [1]; Lamberty, Gregory [1]; Anderson, Carly [1]; Finn, Jacob [1]; Heideman, Paul [1]

1. Minneapolis VA Health Care System

Abstract: Chronic pain (CP) is a heterogeneous medical condition that affects more than 100 million Americans and results in $299-$335 billion in lost productivity annually (Institute of Medicine of the National Academics, 2011; Gaskin & Richard, 2012). Pain may compete with limited attentional resources and result in cognitive inefficiencies (Karp et al., 2006). Munoz and Esteve (2005) found that subjective cognitive complaints were predicted by depression, anxiety, and the rumination component of pain catastrophizing. In another study, over 62% of individuals endorsed subjective cognitive problems and 52% of the variance of these subjective complaints were explained by negative affect, physical/somatic functioning, fatigue, female sex, and pain catastrophizing (Roth et al., 2005). These findings did not include objective measures of cognition. The present study had two hypotheses: (1) Female sex, lower self-efficacy, and greater pain intensity, depressive symptoms, PTSD symptoms, pain catastrophizing will be related to worse neuropsychological functioning and (2) Neuropsychological functioning will be predicted by female sex, self-efficacy, pain intensity, depression, PTSD, and pain catastrophizing. Archival data from Veterans prior to admission to an intensive 4-week outpatient chronic pain rehabilitation program (CPRP) was examined. Data were collected from June 2014 to January 2019 and the sample included 121 veterans with CP (mean age= 53.09 years, sd = 11.47). Prior to admission to CPRP, participants completed a brief cognitive screening (OTBM) and self-report measures of pain (intensity, catastrophizing, self-efficacy to manage pain), and internalizing emotions (depression, PTSD). Pearson correlations did not reveal significant relationships between OTBM and female sex ($p = .795$), OTBM and pain intensity ($p= .659$), OTBM and PTSD ($p = .527$), OTBM and depression ($p = .347$), OTBM and pain catastrophizing ($p = .406$) or OTBM and self-efficacy ($p = .186$). A multiple regression was conducted to determine if OTBM was predicted by female sex, negative internalizing emotions (PHQ-9, PCL-5), and pain related variables (PEG, PCS, PSEQ). The overall model was not significant ($F (6, 93) = .637$, $p = .701$, $R2 = .039$). The current results did not find support for the relationship between neuropsychological functioning, female sex, pain variables (intensity, catastrophizing) or internalizing emotions (depression, PTSD). Limitations and future directions are discussed.

Research Topic: Neuropsychology
Funding agencies: N/A
Grant support: N/A

14. Aging Well with Independence using Sensors in the Environment

Benckendorf, Kurt [1,2]; Klinger, Jessica [1,2]; Bouranis, Nicole [3]; Kaye, Jeffrey [3]; Seelye, Adriana [1,2]

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

Abstract: Alzheimer's disease (AD) is a growing public health concern that has a profound negative impact on individuals living with the disease and their families, the healthcare system, and the economy. This research project will apply innovative and unobtrusive technologies directly in participants' home environments to objectively assess cognition and daily functioning among older adults with mild cognitive impairment (MCI) and older adults who have normal cognition. The goal of this research is to more effectively identify the earliest subtle declines in cognition and daily functioning that slowly emerge in MCI and ultimately threaten independence. Machine learning computational approaches will be used to examine sensor-based IADL candidate variables generated through this study to determine the relative importance of these variables for discriminating between MCI and intact cognition groups, cross-sectionally and longitudinally. The approaches used in this study will allow future researchers, physicians, and caregivers to proactively identify and monitor increasing risks for deteriorating cognitive function (progressing from normal aging to MCI and from MCI to AD) in a way that is not currently possible, transforming AD prevention trials and significantly reducing the cost and consequences of functional decline in our aging population.

Research Topic: Aging
Funding agencies: NIH
Grant support: National Institutes of Health (1R01AG058687-01A1)

15. NCI And VA Inter-agency Group to Accelerate Trials Enrollment (NAVIGATE)

Benson, Mark [1]; Meyeraan, Tacy [1]; Luikart, Sharon [1]; Klein, Mark [1]

1. Minneapolis VA Health Care System

Abstract: The National Cancer Institute (NCI) and VA Inter-agency Group to Accelerate Trials Enrollment (NAVIGATE) NAVIGATE is an opportunity for the VA and NCI to make cancer clinical trials more accessible to veterans. After completing a rigorous application process, the Minneapolis VA Medical Center was chosen as one of twelve sites to participate in NAVIGATE program. The primary objective of the NAVIGATE program is to enhance the ability of veterans to participate in cancer clinical trials carried out through NCI's National Clinical Trials Network (NCTN) and the NCI Community Oncology Research Program (NCORP). The VA Healthcare System has a robust clinical research program that includes clinical trials in cancer and other diseases at approximately 100 sites nationwide. However, VA facilities often face challenges initiating and completing trials. This program aims to overcome these challenges by establishing a sustainable infrastructure to address barriers to trial enrollment that veterans, including minority patients, often experience. In addition, NAVIGATE will increase the participation of VA investigators in clinical cancer research and provide opportunities for these researchers to identify studies that may be of particular importance to veterans with cancer. The VA's involvement in NAVIGATE is being managed through the Cooperative Studies Program (CSP), which is part of the VA's Office of Research and Development. NAVIGATE is overseen by an Executive Committee comprised of VA and NCI leadership responsible for ensuring effective coordination between the agencies to achieve program milestones. The NAVIGATE program aims to more efficiently recruit patients and accelerate cancer clinical trial enrollment. Ultimately, the timely completion of cancer clinical trials will advance cancer treatment.

Research Topic: Cancer
Funding agencies: NIH
Grant support: NCI and CSP C0008

16. Identifying and Assessing the Unique Barriers that Women Veterans Face in Substance Use Disorder Program Participation

Bertucci, Stephanie [1]; Santoo, Amy [1]; Loop, Brianna [1]; Barnard, Laura [1]; McGarry, Maura [1]; Silversmith, Daniel [1]; Sobotta, Lauren [1-3]

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

Abstract: Women face more barriers and are less likely to seek treatment for Substance Use Disorders (SUD) compared to male counterparts. Nationally, there was an 81% increase in diagnosed substance use disorders among women Veterans who receive VA care from 2005 to 2010. Despite this increase, the MPLS VAMC's primary substance use disorder treatment (IOP) has only provided 65 episodes of care to women Veterans (8.6%) out of 756 episodes of care since 2013. We also found that female Veterans are not successfully completing the IOP at a rate of 14 percentage points higher than male identifying Veterans. To identify and better understand barriers and disparities in substance use disorder treatment for the women veteran population at the MPLS VAMC, the Mental Health Social Work Research Group completed a thorough literature review on the topic, analyzed program evaluation data from 2013 to 2018 on IOP outcomes for women Veterans, and compiled data from the facility's alcohol screening (AUDIT-C). Through these reviews, we found that women often have a more rapid progression in their substance use than men. Women also tend to have a more severe clinical profile including increased rates of co-morbid mental health diagnoses, rates of trauma, and medical conditions. Specific to our site, 21.4% of all women Veterans enrolled in care at the Minneapolis VAMC scored positive on the AUDIT-C, a brief screening for alcohol misuse. Current literature does not sufficiently explore the reasons or barriers within SUD treatment that influence women Veterans' decisions to discontinue, because of this it is important to explore the phenomenon of these women dropping out of treatment programs prior to completion. History of physical and sexual trauma may be a contributing factor to female Veterans not engaging in or not completing a SUD treatment with a majority male milieu considering over three quarters of IOP's female participants reported a past trauma experience. The MPLS VAMC does not offer any women-specific SUD or MH programming. However, studies suggest that outcomes in gender-specific SUD treatments were only improved when the participant requested a women's only program. Barriers to women Veterans accessing and completing SUD interventions at the MPLS VAMC needs further study which the Mental Health Social Work Research Group will begin by surveying women Veterans using an edited version of the Allen Barriers to Care Survey.

Research Topic: Substance Abuse
Funding agencies: N/A
Grant support: N/A

17. Initial Outcomes of Mandatory Tobacco Use Intervention for Veterans Participating in Primary Treatment for Substance Use Disorders

Bertucci, Stephanie [1]; Silversmith, Daniel [1]

1. Minneapolis VA Health Care System

Abstract: Minneapolis VAMC Intensive Outpatient Program (IOP) is a 4-week abstinence-based rehabilitation program designed for Veterans with active substance use disorders (SUD). In August 2018, IOP created a mandatory tobacco use intervention (TUI) for Veterans accepted into the program with co-occurring Tobacco Use Disorders. Participants were scheduled for twice weekly, 30 minute tobacco cessation education psychotherapy groups. The groups include tobacco use assessment, education about tobacco dependence, motivational enhancement techniques, a biofeedback intervention, education on medications for tobacco use, and other interventions from VA approved tobacco cessation handbooks. Outcomes thus far suggest that participation in mandatory tobacco use intervention (TUI) enhances motivation to quit tobacco, increases likelihood that Veteran's will obtain nicotine replacement or other tobacco pharmacotherapies, and facilitates a greater percentage of Veterans to quit tobacco. Making the TUI mandatory for all nicotine dependent participants in IOP, even those who are not initially interested in changing their tobacco use habit, appears to be effective in moving those individuals towards a desire to quit through motivational interviewing and enhancement techniques, education, and a supportive group milieu. 30 participants (67%) were prescribed NRT or other nicotine pharmacotherapies while participating in the TUI. 13 participants (29%) quit tobacco/nicotine use while in the TUI. Participants also experienced significant improvement in motivation to decrease or quit tobacco use as measured by a 1-7 variable. Nicotine is a highly addictive substance and nicotine addiction is more prevalent and has even greater risk factors in populations with other substance use disorders and co-occurring mental health disorders. The TUI provides a more intensive dose of nicotine use disorder treatment compared to the typical offerings (weekly therapy, medications with case management, quit lines, online apps, etc.). Further study is needed to determine if the motivational improvements remain over time and if those who quit tobacco use remain tobacco-free.

Research Topic: Substance Abuse
Funding agencies: N/A
Grant support: N/A

18. E. coli Clone Sharing and Persistence within Households (HHs) in Relation to Fluoroquinolone (FQ) Resistance and ST131 Status

Boettcher, Jessica [1]; Clabots, Connie [2]; Porter, James [2]; Johnson, James [2]

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

Abstract: Extraintestinal E. coli infections, a perennial source of morbidity and mortality, are increasingly difficult to treat due to emerging antibiotic resistance. Within-HH sharing of E. coli strains may contribute to this problem, but is poorly understood. Accordingly, we assessed E. coli strain sharing within the HHs of veterans with a clinical E. coli isolate, including in relation to FQ resistance and ST131 status. Methods: Twenty-two veterans with a clinical E. coli isolate (11 FQ-resistant [FQ-R], 11 FQ-susceptible [FQ-S]) and their HH members underwent serial stool sampling (2-6 occasions each). Stool samples were cultured selectively for FQ-S and FQ-R E. coli. Per sample, 10 E. coli colonies underwent PCR-based profiling; 1 colony per profile underwent pulsotyping and PCR-based ST131 detection, as did all clinical isolates. Each strain's extent of within-HH sharing and colonization were calculated. Results: Of the 11 FQ-R clinical isolates, 7 were ST131 and 4 non-ST131; all FQ-S clinical isolates were non-ST131. The 22 HHs included 68 total subjects (49 humans, 19 pets), with a per-HH mean of 3 subjects, 9.5 total fecal samples, and 6.7 unique strains. The index patient's stool yielded the corresponding clinical strain in 91% of FQ-R HHs, but only 45% of FQ-S HHs. Sharing of the clinical strain occurred in 45% of FQ-R HHs (43% if ST131, 50% if non-ST131), vs. 27% of FQ-S HHs. For the 22 clinical strains, the extent of within-HH sharing and colonization was greater for FQ-R than FQ-S strains (sharing index, 0.45 vs 0.15; colonization index, 0.47 vs 0.14). The FQ-R HHs also yielded 12 additional (non-clinical) FQ-R strains, the FQ-S HHs only 1. Non-clinical FQ-R strains colonized much less extensively than FQ-R clinical strains and were not shared between HH members. Conclusion: Compared to FQ-S clinical E. coli, FQ-R clinical E. coli more frequently colonize the index patient, are shared among HH members, and co-occur with other HH FQ-R strains, all of which may drive population-level resistance. Given the potentially important clinical implications of within-HH strain sharing and colonization, better understandings are needed of its mechanisms, including characteristics of the strain, host, and gut microbiota.

Research Topic: Infectious Diseases
Funding agencies: CSR&D; NIH; UMN
Grant support: 1 I01 CX000192 01, 1 I01 CX000920-01A1, 2I01CX000920-04

19. Learning to Apply Mindfulness to Pain (LAMP): A pragmatic, randomized clinical trial of two mindfulness-based interventions for chronic musculoskeletal pain

Burgess, Diana [1,2]; Allen, Kelli [3,4]; Bangerter, Ann [1]; Bronfort, Gert [2]; Cross, Lee [1]; Ferguson, John [1,2]; Haley, Alex [2]; Matthias, Marianne [5,6]; Meis, Laura [1,2]; Polusny, Melissa [1,2]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Durham VA Health Care System
4. University of North Carolina
5. Richard L. Roudebush VA Medical Center
6. Indiana University

Abstract: We describe a pragmatic trial testing the effectiveness of two Mindfulness-Based Interventions (MBIs) designed to reduce chronic musculoskeletal (MSK) pain and comorbid conditions among U.S. Veterans. There is a pressing need to provide effective, non-pharmacological treatment to the vast number of Veterans with chronic musculoskeletal pain. Mindfulness-Based Interventions (MBIs) are one such approach shown to be effective for treating chronic pain and comorbid conditions (e.g., PTSD, insomnia, depression, and substance abuse). However, the predominant MBI offered in the Veterans Health Administration and other health care systems, Mindfulness-Based Stress Reduction (MBSR), has features that pose significant implementation barriers. This work is expected to result in two approaches for delivering MBIs, which incorporate mobile application technology that will optimize engagement, adherence, and sustainability and be able to reach large numbers of Veterans. Our project also focuses on adapting interventions to fit the needs of women Veterans, a priority population that is at elevated risk for chronic MSK pain and mental health comorbidities. A 4-site 3-arm RCT (N = 750) will test the effectiveness of two MBIs compared to usual practice, for men and women, and address key implementation research questions. Effectiveness will be assessed by pain severity and interference at 6 months from baseline, as measured by change in the Brief Pain Inventory total score. Outcomes also will be assessed directly after the intervention and at 12 months. Secondary outcomes will include patient-reported measures related to pain, co-morbid mental health conditions and function, as well as measures captured in health care records. Implementation data will be collected and described, guided by the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) framework, using a multi-stakeholder, mixed methods process evaluation.

Research Topic: Pain
Funding agencies: DOD
Grant support: Department of Defense; Award No. W81XWH-18-2-0003

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20. NT-Pro BNP Levels Predict Myocardial Injury Following Elective Vascular Surgery and Can be Reduced with Preoperative Administration of CoQ10: A Randomized Double Blind Controlled Trial

Carlson, Selma [1]; Khan, Asrar [2]; Johnson, Debra [1]; Hocum-Stone, Laura [1]; Kelly, Rosemary [1,2]; Gravely, Amy [1]; Mackenzi, Mbai [1]; Garcia, Santiago [3]; Adabag, Selcuk [1]; McFalls, Edward [1]

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

Abstract: NT-Pro BNP (BNP) levels provide incremental value in perioperative risk assessment prior to major non-cardiac surgery. Whether they can be pharmacologically modified is uncertain. Hypothesis: BNP levels predict postoperative adverse cardiac outcomes among patients scheduled for an elective vascular operation and can be reduced with preoperative administration of CoQ10. Study Design: A double-blind randomized controlled trial was implemented at a single institution. Patients scheduled for an elective vascular operation were screened within 4 weeks of the operation during their preoperative vascular clinic appointment. Suitable patients who met the inclusion and exclusion criteria were randomly assigned to receive either CoQ10 (400 mg per day) versus Placebo for 3 days prior to surgery. A research pharmacist prepared the treatment tablets to maintain double-blinding assignments. Biomarkers including BNP, troponin I (Tpn-I) and C-reactive protein were obtained prior to the operation and following surgery for up to 48 hours. The primary end-point measure was preoperative NT-Pro BNP and secondary end-point measures included myocardial injury, defined by an elevated cardiac Tpn-I level and hospital time. Results: One hundred and twenty-three patients were randomized to receive either CoQ10 (N = 62) versus placebo (N = 61) for 3 days prior to elective vascular surgery. Preoperative cardiac risks included a history of coronary artery disease (N = 52), heart failure (N = 12), stroke (N = 23) and diabetes mellitus (N = 48) and the planned vascular surgical procedures included infra-inguinal (N = 78), carotid (N = 36), and intraabdominal (N = 9). There were no intergroup differences in these clinical variables. Following 3 days of treatment and just prior to surgery, BNP levels (median; IQs) in the CoQ10 and Placebo groups were 179 (75-347) and 217 (109-585) pg/ml respectively (P = 0.02). At 24 hours following surgery, BNP levels (median; IQs) in the CoQ10 and Placebo groups were 397 (211-686) and 591 (288-1433) pg/ml respectively (P = 0.02). Compared with patients without an elevated BNP, patients with an elevated BNP had a higher incidence of myocardial injury, defined by an elevated Tpn-I level (58% versus 20%; $P < 0.01$) and a longer stay in the hospital (4.4 ± 3.8 versus 2.8 ± 3.2 days; $P < 0.02$). Conclusion: BNP levels predict adverse postoperative cardiac events following vascular surgery and can be reduced by administering CoQ10 for 3 days prior to surgery.

Research Topic: Cardiovascular Disease
Funding agencies: N/A
Grant support: N/A

21. Exploring the effects of gender and stimulus emotion intensity on emotion recognition in psychosis

Chong, Li Shen [1]; Kent, Jerillyn [1]; Sponheim, Scott [1,2]

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

Abstract: Social cognition impairment, including deficits in emotion recognition, has been documented in schizophrenia. The effect of gender on social cognition in schizophrenia is understudied, and the few studies that investigated gender differences in emotion recognition yielded mixed findings. In controls, an interaction between gender and stimulus emotion intensity during an emotion recognition task has been reported, with women outperforming men in recognizing mild emotion stimuli. We examined emotion recognition in individuals with psychotic disorders and controls as a function of gender and stimulus emotion intensity. Thirty-two controls (20 males, 12 females) and 54 individuals with a psychotic disorder (33 males, 21 females) completed the Penn Emotion Recognition Task. A group by gender by intensity (mild versus extreme) repeated-measures ANOVA revealed a significant main effect of intensity and a trend towards a group difference (controls performed better than individuals with a psychotic disorder). There was a significant gender by intensity interaction; females performed significantly better than males in the mild condition only. Findings are consistent with existing literature showing emotion recognition deficits in schizophrenia and replicate previous work demonstrating gender differences in mild emotion recognition. Future work will include an increased sample size and higher-order measures of social cognition (i.e., theory of mind).

Research Topic: Psychiatry
Funding agencies: NIH
Grant support: U01MH108150, NIMH; F32MH112334 , NIMH

22. Comparing Custom and Non-Custom Receiver-In-Canal (RIC) Fittings Using Objective Measures and Patient Satisfaction

Christensen, Sara [1]; Martino, Nicholas [1]; Palmer, Glen [1]; Doelger-Leyk, Sara [1]; Lappin, Megan [1]; Busch, Carly [1]

1. St. Cloud VA Health Care System

Abstract: Fitting patients who have sharply sloping sensorineural hearing loss often creates a challenging situation for audiologists. Advancements in feedback suppression systems have given providers more options for approaching this problem. Custom molds with venting and closed dome receiver in the canal (RIC) fittings are two configurations commonly used for this patient population. Previous research has not shown if custom and closed dome RIC fittings provide comparable outcomes for these patients. This study examined if custom and closed dome RIC fittings are comparable options for patients with normal to near normal low frequency hearing sloping to moderately-severe to profound sensorineural hearing loss. Objective data were obtained using real ear measurements and subjective data collected using the International Outcome Inventory for Hearing Aids (IOI-HA) survey. A counterbalanced, cross-over, repeated-measures study design was used to examine the research objectives. IRB approval was received for this project. Fifty-one subjects with normal to near normal sloping to moderately-severe to profound sensorineural hearing loss from the St. Cloud VA Health Care System were recruited. At the first visit half of the participants were fit with a closed dome configuration and the second half were fit with custom molds. After the initial wear time of 3-4 weeks participants were then fit with the alternate configuration for an additional wear time of 3-4 weeks. Real ear measurements were obtained for both custom and dome RIC fittings. The data for each real ear measurement was recorded by frequency and compared to target. The IOI-HA survey was completed following a trial with each type of fitting and participants were asked which type of fitting was 'preferred'. The data concludes that for patients with normal to near normal hearing sensitivity in the low frequencies sloping to moderately-severe to profound sensorineural hearing loss, there is no statistical difference in the ability to reach expected gain between custom molds and closed domes.

Research Topic: Audiology & Speech Pathology
Funding agencies: N/A
Grant support: N/A

23. Predictors of Social Functioning in Schizophrenia and Bipolar Disorder

Culbreth, Adam [1]; Disner, Seth [1,2]; Olson, Emily [1]; Sponheim, Scott [1,2]

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

Abstract: Many individuals with schizophrenia and bipolar disorder experience reduced social functioning. Studies have shown cognition and symptom severity, significantly predict lower functioning in these populations and there is some evidence for mediation of the relationship between cognition and functioning by symptom severity. However, few studies have recruited transdiagnostic samples to examine these relationships. In the current project, we assessed relationships between cognition, symptom severity, and social functioning in 130 individuals (BP = 56; SZ = 74). Symptom severity and social functioning were assessed using interview-based methods, the brief psychiatric rating scale and social functioning scale respectively. Cognition operationalized by conducting a principle components analysis of several common neuropsychological measures. As hypothesized, cognition and overall symptom severity were independently associated with social functioning. These associations did not vary by diagnosis, suggesting a transdiagnostic effect. Mediation analyses did not support a model wherein, symptom severity mediated the relationship between cognitive and social functioning. Finally, supplemental analyses utilizing specific subscales of the BPRS or SFS did not reveal specific relationships for particular cognitive, symptom, or social functioning domains, suggesting general effects. Taken together, these results suggest important transdiagnostic associations between cognition, symptom severity, and social functioning in individuals with serious mental illness.

Research Topic: Mental Illness
Funding agencies: CSR&D
Grant support: 2I01CX000227

24. Cochrane Urology: 2018-2019

Dahm, Philipp [1,2]; Decker, Rourke [3]; Hwang, Eu Chang [4]; Lane, Robert [2]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Rowan University
4. Chonnam National University, South Korea

Abstract: Cochrane Urology is based at the Minneapolis Veterans Administration Medical Center. Our mission is to conduct and disseminate high-quality systematic reviews related to urological diseases. We were initially founded at this institution in 1996 as the Prostatic Diseases Urological Cancers Group and were renamed in 2015 to reflect a broader scope, that includes urology-related stone disease. Methods: We assessed the contributions made by Cochrane Urology to evidence-based urology over the last year (5/2018 to 4/2019). Results: The Cochrane Urology portfolio includes a total of 69 published reviews of interventions in the diagnosis, prevention, treatment and rehabilitation of benign and malignant prostate conditions (i.e. benign prostatic hyperplasia, prostate cancer, prostatitis), male sexual dysfunction (i.e. erectile dysfunction, undescended testes, Peyronie's disease), benign and malignant urology-related renal topics (renal cancer, stones), and other urological cancers (i.e. bladder, testicular, penile, urethral). Over the last year we published 7 protocols and 14 reviews and co-published 4 reviews. We currently have 4 protocols and 39 ongoing reviews at various draft stages. The development of comprehensive search strategies is supported through a network of 6 information specialists at six different institutions. The editorial process is overseen by an international network of twelve contact editors in eight countries, a Managing Editor, an Assistant Managing Editor, and a Coordinating Editor. We collaborate closely with the VA Evidence Synthesis Program and the UMN Evidence-Based Practice Center. We provide training research opportunities for medical students, residents and fellows and participate in biannual training workshops for guideline developers on the GRADE approach for rating the quality of evidence and developing evidence-based recommendation by the US GRADE Network. Ongoing challenges relate to the training of review authors, the timeliness of review completion and the acquisition of extramural funding. Conclusion: Systematic reviews of high-quality evidence are important tools to help patients and health care providers make decisions with the best available evidence. Cochrane Urology is dedicated to providing high-quality, accessible publications of systematic reviews to aid decision-making to support the VA's mission.

Research Topic: None indicated
Funding agencies: UMN
Grant support: Off

25. Evidence Map: reporting of results by sex or gender in randomized controlled trials with women Veteran participants (2008-2018)

Danan, Elisheva [1,2]; Ullman, Kristen [1]; Klap, Ruth [3]; Yano, Elizabeth [3,4]; Krebs, Erin [1,2]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. VA Greater Los Angeles Healthcare System
4. University of California, Los Angeles

Abstract: Higher participation of women in randomized controlled trials (RCTs) has not led to significantly improved reporting of sex-stratified results. A recent evidence map of research on women Veterans revealed that many studies did not report results by sex or gender. Objective: Compare characteristics of RCTs with women Veteran participants that did or did not report results by sex or gender. Assess how sex and gender are addressed in research with women Veterans. Methods: We extended the prior evidence map with a systematic search for RCTs with women Veterans, published 2008-2018. We compared characteristics of RCTs that reported results by sex or gender with those of RCTs that did not, and reviewed methodology and reporting of sex/gender analyses. Results: In addition to 11 studies from the prior evidence map, we assessed 1,820 abstracts for relevance and ultimately included 45 unique RCTs. Five trials included only women and 40 included both men and women (median 14.3% women). Ten studies reported results by sex or gender. These trials were larger (median study size n = 343.5 vs. n = 125.5) and included a higher median proportion of female participants (16.8% vs. 11.2%) than studies without sex/gender results. Ten of 11 trials that tested pharmacologic or device interventions did not report results by sex or gender. Conclusions: Reporting of results by sex or gender remains low in Veteran research, but may improve with larger studies and increased recruitment of women Veterans into trials. Trials of pharmacologic or device interventions may be targets for future reporting requirements. Standardization could improve attention to sex and gender in methodology and reporting.

Research Topic: Women's Health
Funding agencies: HSR&D
Grant support: VA ESP Project #09-009; VA HSR&D #RCS 05-195 (Yano); VA Women's Health Research Network #SDR-10-012 (Klap)

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26. SPRINT to an 'Intensive' Blood Pressure Target? Not so Fast!: Use Evidence-Based Drugs First!

DeCarolis, Douglas [1]; Gravely, Amy [1]; Olney, Christine [1]; Ishani, Areef [1]

1. Minneapolis VA Health Care System

Abstract: The SPRINT (Systolic Blood Pressure Intervention Trial) was a large, landmark trial in 9361 patients with high blood pressure (BP) and with, or at high risk, for cardiovascular (CV) disease. Randomization to an intensive BP target strategy (systolic BP <120mm Hg) reduced the primary composite endpoint of myocardial infarction (MI), acute coronary syndrome (ACS), stroke, heart failure (HF) events, or CV death by 25%. Questions remain whether drug class selection, which was not controlled, may have contributed to these results. In large trials, angiotensin-converting enzyme inhibitors (ACE-I) and angiotensin-receptor blockers (ARBs) have reduced CV events beyond their BP lowering effect. ACE-I and ARBs are thought to have additional protective effects on the heart, vasculature, and kidney beyond BP reduction. Based on this evidence, recommendations advise ACE-I or ARB be used in patients with, or at high risk, for CV disease. However, the use (or non-use) of ACE-I and ARBs in SPRINT varied considerably between randomization arms. Did this disparity contribute to SPRINT results, beyond randomization to BP control strategy? HYPOTHESIS The use of ACE-I and ARBs contributed to the reduced CV events in SPRINT, above and beyond intensive vs. standard BP target strategy. METHODS MPLS VA SPRINT investigators were granted access from the SPRINT Steering Committee to the expanded data set of SPRINT. Data extracted for each subject included randomization arm, systolic BP (SBP) at baseline, mean SBP at each study visit (categorized as < or = 130 mm Hg), and BP lowering medications at each visit. SBP < 130 mm Hg and ACE-I/ARB use throughout study were used as cumulative time-varying covariates categorized as: 0 to < 1 year (control); 1 to < 3 years; and = 3 years. Cox regression was utilized to examine cumulative time-varying effect of receiving ACE-I/ARB controlling for cumulative time with BP < 130, baseline SBP, and randomized treatment strategy (intensive vs. standard). The study protocol was approved by MVAHCS Research & Development Committee. RESULTS Compared to ACE-I/ARB treatment < 1 year, use > 3 years was associated with a 44% reduction (p = 0.0005) in the composite endpoint, regardless of treatment strategy (intensive vs. standard), baseline SBP, and time-varying SBP. Results were consistent among individual components of the composite endpoint. Randomization to intensive strategy was not statistically significant for reduced outcomes.

Research Topic: Cardiovascular Disease
Funding agencies: N/A
Grant support: N/A

27. 7 T MR spectroscopy across psychotic illnesses and biological relatives

Demro, Caroline [1]; Schallmo, Michael-Paul [1]; Marjanska, Malgorzata [1]; Sponheim, Scott [1,2]

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

Abstract: Psychotic symptoms span across a number of clinical diagnoses, can be conceptualized in a dimensional rather than categorical way, and may share similarities in illness pathophysiology. Heterogeneity within clinical diagnoses is well documented and may reflect multiple pathways towards psychosis. Identifying biomarker mechanisms involved in the development and maintenance of psychotic symptoms regardless of clinical category may clarify some of the inconsistent findings in the literature based on DSM categories. Biotypes that are distinct from clinical categories have been identified. Recent work suggests that transdiagnostic symptom dimensions predict biotypes more accurately than diagnoses do. Biotypes could be expanded to include neurochemical mechanisms that have been proposed to underlie psychotic symptoms, including aberrant dopamine, hypofunctioning glutamatergic NMDA receptors, and oxidative stress. It remains to be clarified whether glutamatergic metabolites fluctuate with transdiagnostic symptoms of psychosis. Further, potential genetic liability towards such neurochemical changes can be approximated using family studies. The current study examined the relation between dimensional symptom severity and neurochemical concentrations using magnetic resonance spectroscopy (1H MRS) at 7 T among individuals with psychosis and biological relatives. We found a significant effect of group such that relatives had significantly lower glutamine concentrations as compared to individuals with psychosis. Concentrations of the inhibitory neurochemical GABA shared a positive correlation with disorganization among individuals with psychosis. Findings point to possible genetically-based risk factors for psychosis that are related to the glutamatergic system and potential aberrant GABAergic neurotransmission.

Research Topic: Behavioral Sciences
Funding agencies: N/A
Grant support: U01MH108150

28. White Matter Integrity Linked to Genetic Correlates of Subjective Well-Being in Combat-Exposed Veterans

Disner, Seth [1,2]; Davenport, Nicholas [1,2]; Sponheim, Scott [1,2]

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

Abstract: Combat veterans are more likely to experience disorders characterized by abnormal white matter integrity (WMI), such as PTSD and MDD. Identifying factors that confer risk for abnormal WMI would be a critical step towards early identification and personalized treatment of trauma-related disorders. Polygenic risk scores (PRSs), which reflect the cumulative risk for a trait or condition across the genome, are a promising means to identify plausible biomarkers linked to abnormal WMI. Methods: A sample of 221 US military veterans previously deployed to Iraq and/or Afghanistan completed a clinical examination, provided a genetic sample for genome-wide characterization, and underwent diffusion tensor imaging (DTI) to assess WMI. The PRS for subjective well-being was calculated using beta weights from a large-scale genome-wide association study of 298,420 individuals. WMI was operationalized as fractional anisotropy (FA) in 24 bilateral white matter tracts. Results: Following FDR correction, the best-fit PRS was significantly associated with FA in 12 tracts, including the bilateral internal capsule, external capsule, corpus callosum, and corona radiata (all $q^* < 0.025$). Post-hoc analysis showed that PRS moderated the association between PTSD and FA in the cingulum ($p = 0.04$), with trend-level moderation in the splenium of the corpus callosum ($p = 0.06$). Conclusions: Genetic factors linked to subjective well-being are associated with WMI in combat veterans, which may moderate the deleterious association between PTSD and WMI in the cingulum. If replicated in a larger and more diverse sample, this PRS merits use as a biomarker to help guide precision medicine techniques in veterans.

Research Topic: Personalized Medicine & Genomics
Funding agencies: RR&D
Grant support: RR&D IK1RX002325 (PI: Disner), 1I01RX000622 (PI: Sponheim), 1IK2RX000709 (PI: Davenport); CDMRP W81XWH-08-2-0038 (PI: Sponheim)

29. Exploration of a Novel Web-Based Ambulatory Cognitive Assessment Tool with Community Dwelling Older Adults

Dorociak, Katherine [1]; Mattek, Nora [2]; Sharma, Nicole [2]; Beattie, Zachary [2]; Kaye, Jeffrey [2]; Imtiaz, Danish [3]; Seelye, Adriana [1,2,4]

1. Minneapolis VA Health Care System
2. Oregon Center for Aging and Technology
3. The George Washington University
4. University of Minnesota

Abstract: As the population ages, an increasing number of older adults are estimated to have dementia. A delay in onset or progression to mild cognitive impairment (MCI) and dementia has the potential to significantly reduce the number of individuals affected, costs, and caregiver burden. Subtle cognitive and functional changes may be among the earliest signals of transition to MCI. Comprehensive neuropsychological assessment is time and resource consuming and not readily available to all older adults. There is a need for cognitive screeners that are brief, cost effective, self-administered, remotely accessible, and psychometrically sound. The present study outlines the development and initial validation of the online Survey for Memory Attention, and Reaction Time 2.0 (SMART 2.0) for implementation with non-demented community dwelling older adults. The online assessment tool includes face-valid cognitive tasks modeled after clinical and/or experimental tasks in public domain, including the Trail Making Task, Stroop Color-Word Task, and a Visual Memory item. Data was collected from the Oregon Center for Aging and Technology Life Lab cohort (120 people over age 65). A total of 31 older adults completed the measure (Age = 84.96 years (SD = 6.50); Education= 16.10 years (SD = 2.99)). The sample was primarily female (67.7%) and white (93.5%). Results suggest that the SMART tasks including the Trails A Time to Completion, Trails B Time to Completion, and Stroop Color Word Time to Completion significantly correlated with global cognitive scores and individual neuropsychological measures in expected directions. After dividing the sample into a 'high' and 'low' cognitive group based on their composite z-score, logistic regression analyses suggest that the model and SMART variables did not significantly predict cognitive group membership, X2 (3), = 7.38, p = .061. Findings highlight the potential advantages of the SMART as a brief, self-administered, and valid cognitive screening tool for cognitively healthy older adults. Difficulties completing the SMART highlight the need for further development geared at refining the user interface and experience, clarifying instructions, and reducing potential technical difficulties. Further investigation is needed with a more cognitively diverse sample to explore the validity and predictive utility of the measure.

Research Topic: Aging
Funding agencies: NIH
Grant support: The Alzheimer's Association, New Investigator Research Grant (NIRG-15- 362233); NIH/NIA (P30 AG008017)

30. Evidence Review: Risk Factors and Interventions to Prevent or Delay Long-Term Nursing Home Placement for Adults With Impairments

Duan-Porter, Wei [1,2]; Ullman, Kristen [1]; Rosebush, Christina [2]; McKenzie, Lauren [1]; Greer, Nancy [1]; Ensrud, Kristine [1,2]; Ratner, Edward [1,2]; Shippee, Tetyana [2]; Gaugler, Joseph [2]; Wilt, Tim [1,2]

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

Abstract: To support the VA Secretary's Choose Home Initiative, we undertook a review of reviews to examine: 1) potentially modifiable risk factors for long-term nursing home placement (NHP); and 2) interventions to prevent or delay NHP for adults with impairments. Methods: We searched multiple databases and sought references from content experts. Eligible systematic reviews examined risk factors and/or interventions to delay NHP for adults with impairments or at risk of developing impairments. We assessed quality using modified AMSTAR-2 criteria, and abstracted study characteristics, target population(s), definitions of NHP, and risk factor or intervention. Using predetermined criteria, we prioritized a subset of reviews for abstraction of detailed results on specific risk factors or interventions: pooled effects (or qualitative summary), datasets used, NHP ascertainment, and number of unique studies. Results: Of 7014 unique citations, we found 67 eligible reviews (20 on risk factors, 47 for interventions); all addressed older adults with impairments, or at high risk for impairments. We prioritized 26 reviews (6 for risk factors, 20 for interventions) for abstraction of results for specific risk factors or interventions. Three prioritized reviews found that frailty status was associated with higher NHP. Three other reviews reported higher NHP associated with a variety of risk factors, including functional impairments, behavioral and psychological symptoms of dementia, and caregiver distress or burden. Thirteen prioritized reviews addressing interventions exclusively included randomized controlled trials (RCT); three of these showed case management and adult day clinics had no effect on NHP, and 2 reviews reported that certain models of caregiver support and preventive home visits led to delay in NHP. Two prioritized reviews that included multiple study designs (RCT and observational studies) found mixed results for case management and respite care. Conclusions: Very limited evidence suggested that high-intensity models of case management, caregiver support, and home visits may delay NHP. Although there are a variety of VA programs that seek to help Veterans with impairments, it is unlikely that most involve a similar level of participant contact over years. Policymakers should consider evaluating cost-effectiveness of current and future VA programs for improving patient and family-centered outcomes, and not solely as avoiding costs from NHP.

Research Topic: Geriatrics
Funding agencies: HSR&D
Grant support: VA ESP Project #09-009

31. Associations between the MMPI-2-RF and Organ Transplant Outcomes in a Veteran Population

Emery, Rebecca [1]; Finn, Jacob [1]; Moore, Kelly [1]; Miller, Ivy [1]; Hintz, Samuel [1]

1. Minneapolis VA Health Care System

Abstract: The present study aimed to identify personality and psychopathology dimensions associated with treatment recommendations and outcomes among Veterans seeking organ transplant. Data were collected from Veterans (N = 245) undergoing a pre-transplant screening to assess suitability for heart, kidney, liver, lung, or bone marrow transplant. As part of the pre-transplant screening, Veterans completed a psychological evaluation that included the MMPI-2-RF. Referral recommendations, referral initiation, and transplant outcomes were extracted from medical records. Referral recommendations were coded dichotomously according to whether a Veteran was referred to mental health treatment, substance use treatment, and/or neuropsychological evaluation following the pre-transplant screening. Referral initiation was coded dichotomously in accordance with a standard coding protocol. Transplant outcomes were coded dichotomously according to whether a Veteran was listed for and eventually received an organ transplant. Descriptive statistics were determined and point-biserial correlations were calculated between the MMPI-2-RF validity and clinical scales and each pair of dichotomous outcomes. Logistic regression analyses were then used to determine the ability of the MMPI-2-RF validity and clinical scales to predict each pair of dichotomous outcomes, controlling for the effects of age and transplant type. On average, Veterans were 62.04 ± 8.71 years old. The sample was predominantly comprised of White (80.4%; n = 197), male (96.7%; n = 237) Veterans seeking either kidney (35.8%; n = 88), liver (26.9%; n = 66), or bone marrow (25.3%; n = 62) transplant. Results indicated that Veterans who engaged in inconsistent responding or overreporting or endorsed a lack of positive emotions were more likely to be referred to mental health treatment whereas Veterans who engaged in underreporting or endorsed disconstrained behavior were more likely to be referred to substance use treatment. Furthermore, Veterans who reported higher levels of activation were less likely to initiate mental health treatment. Finally, Veterans who reported fewer somatic complaints were more likely to be listed for organ transplant, and Veterans who reported being less interpersonally domineering were more likely to receive an organ transplant. These findings indicate that the MMPI-2-RF is a useful screening tool to determine factors that predict treatment recommendations and outcomes among Veterans seeking organ transplant.

Research Topic: Special Populations
Funding agencies: N/A
Grant support: Grant from the MMPI publisher, the University of Minnesota Press (PI: Hintz)

32. Optimal Timing of Follow Up for Cytologically Benign Thyroid Nodules - The Minneapolis VAHCS Experience

Estrada, Allison [1]; Drake, Tyler [2]

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

Abstract: Thyroid nodules are common; studies show that 85-95% of thyroid nodules are benign. Current ATA guidelines recommend continued follow up of FNA benign thyroid nodules within 24 months, due to a 0-3% false negative rate. Some studies show safety and efficacy of longer follow up periods, however these studies are comprised of mostly younger females. Within our VA, we sought to analyze the long term follow up data for FNA benign thyroid nodules to see if follow up within 24 months was necessary to provide safe and effective detection of false negative thyroid cancers in our mostly older, male population. This was a retrospective chart review involving all patients at our institution who had a new FNA benign thyroid nodule diagnosed between 2010 and 2017. This study collected data on 821 new benign nodules, from 604 patients over the 8 year study period. 488 of the 821 nodules (59%) were followed up with US, repeat FNA or thyroidectomy, while 333 (41%) had no dedicated follow up. Eighty-eight percent of nodules that had follow up received it within 24 months. In patients who received follow up, there were 6 new thyroid cancers diagnosed during the study period. Two cancers were found incidentally on thyroidectomy done for compressive symptoms, 1 cancer was found in a new nodule during follow up, and 3 were related to a false negative FNA (0.6% of all nodules). All patients with a false negative FNA were alive after a mean follow up time of 3.3 years. No patients who received first follow up at >24 months were diagnosed with thyroid cancer. Nodules that received no dedicated thyroid follow up received a mean clinical follow up time of 3.5 years, during which there was no development of clinically evident thyroid cancer. 72 patients died during the follow up time, none related to thyroid cancer. In our older, largely male population, the false negative thyroid FNA rate is low at 0.6%. No patients in this cohort died of thyroid cancer related causes during a mean follow up period of 4 years, likely related to the non-aggressive nature of most differentiated thyroid cancers. No patients who received dedicated nodule follow up after 24 months were found to have thyroid cancer, and of the 333 benign nodules that had no dedicated follow up, none presented with any evidence of clinically significant thyroid cancer during a mean follow up of 3.5 years. Based on this evidence, it appears safe to extend the follow up time of benign thyroid nodules to over 24m.

Research Topic: Cancer
Funding agencies: N/A
Grant support: N/A

33. Naturally Occurring Osteoarthritis in Male Mice with an Extended Lifespan

Ewart, David [1]; Harper, Lindsey [2]; Gravely, Amy [1]; Carlson, Cathy [2]; Loeser, Richard [3]

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

Abstract: The goal of this investigation was to evaluate whether pharmacologic treatments or genotypes shown to prolong murine lifespan reduced the severity of age-associated osteoarthritis. Materials and Methods: Male UM-HET3 mice were fed diets containing 17-a-estradiol, acarbose, nordihydroguaiaretic acid, or control diet per the National Institute on Aging Interventions Testing Program (ITP) protocol. Long-lived male Ames dwarf mice were compared to age-matched non-dwarf littermate controls. Stifles were analyzed histologically with Articular Cartilage Structure (ACS) and Safranin O scoring as well as with quantitative histomorphometry. Results: Depending on the experimental group, ITP mice were between 450-1150 days old at the time of necropsy and 12-15 animals were studied per group. Two age groups (450 and 750 days) with 16-20 animals per group were used for Ames dwarf experiments. No differences were found in the ACS or Safranin O scores between treatment and control groups in the ITP study. There was high variability in most of the histologic outcome measures and post-hoc power analysis revealed that the study was under powered. 17-a-estradiol mice had larger areas and widths of subchondral bone relative to controls. Dwarf mice had lower Safranin O but not ACS scores, less subchondral bone area and width, and less articular cartilage necrosis than non-dwarf controls. Conclusions: UM-HET3 mice developed age-related OA but with a high degree of variability, limiting the ability to detect significant effects from the ITP treatments. High variability was also seen in the Ames dwarf mice but differences in several measures suggested some reduction in age-associated OA.

Research Topic: Aging
Funding agencies: NIH
Grant support: National Institute on Aging (RO1 AG044034)

34. Clinical Significance of Infectious, Inflammatory and Structural Pulmonary Incidental Findings Identified on Initial Lung Cancer Screening Exams

Fabbrini, Angela [1]; Melzer, Anne [1,2]; Rice, Kathryn [1,2]; Clothier, Barbara [1]; Bangerter, Ann [1]; Do, Tam [1]; Fu, Steven [1,2]

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

Abstract: Pulmonary incidental findings (IFs) are sometimes noted on low-dose CT (LDCT) for Lung Cancer Screening (LCS), but are of unknown clinical significance. We sought to quantify the frequency, type, workload, and clinical outcome of pulmonary IFs on LCS-LDCTs. Methods: We reviewed a retrospective sample of all initial LCS LDCTs performed at the Minneapolis VA Health Care System from 2015-2017 with at least six months follow-up, recorded IFs using prespecified categories of pulmonary infectious/inflammatory and structural findings. IFs were characterized as potentially significant (SIFs) if follow-up was deemed necessary by reviewing physician, recommended by clinical guidelines, or by radiologist recommendation in the report. We defined notification as any form of communication of the result to patient. An evaluation was defined as resulting medical treatment or diagnostic evaluation, including follow-up testing, clinician documentation that evaluation was unnecessary, or evidence that SIFs had been previously addressed. The clinical outcome was defined as any new acute or chronic diagnosis related to SIFs. Results: We reviewed the charts of 108 patients: 96% male, 79% smokers, mean age 66 years. 37% of patients had a pulmonary SIF. There were 54 pulmonary IFs, 17 infectious or inflammatory and 37 structural lung abnormalities. All of the infectious/inflammatory IFs were considered SIFs. Of the infectious/inflammatory SIFs: 41% ground glass opacities, 35% micronodules/bronchial thickening, 6% interstitial findings, 12% mucous plugs, 6% mosaic attenuation. 47% of those findings had evidence of patient notification. Of the structural IFs, 92% were SIFs: 44% mild/moderate emphysema, 9% severe/diffuse emphysema, 18% enlarged lymph nodes, 15% pleural plaques/thickening, 12% bronchiectasis, and 3% pleural effusions. 24% of structural SIFs had evidence of patient notification. In total, there were 10 new chronic diagnoses of indeterminate clinical significance, (mucus plugging, interstitial) and 7 structural (emphysema, pleural thickening, bronchiectasis). Conclusions: Although pulmonary IFs were common, few generated additional workload or generated new diagnoses. It is likely that the majority of pulmonary IFs on LCS are not clinically significant.

Research Topic: Respiration & Pulmonary Disease
Funding agencies: N/A
Grant support: N/A

35. Diagnosis and Treatment of Clinical Alzheimer's-type Dementia (CATD): A Systematic Review

Fink, Howard [1]; Hemmy, Laura [1]; Silverman, Pombie [1]; Linskens, Eric [1]; MacDonald, Roderick [1]; McCarten, J. Riley [1]; Talley, Kristine [2]; Desai, Priyanka [2]; Forte, Mary [2]; Miller, Margaret [1]; Brasure, Michelle [2]; Nelson, Victoria [2]; Dysken, Maurice [1]; Taylor, Brent [1]; Ng, Weiwen [2]; Ouellette, Jeannine [2]; Greer, Nancy [1]; Sheets, Kerry [3]; Wilt, Timothy [1]; PhD, Mary Butler, [2]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Hennepin County Medical Center

Abstract: Objective. To summarize evidence on: (1) the diagnostic accuracy of brief cognitive tests for clinical Alzheimer's-type dementia (CATD), and biomarkers for Alzheimer's disease (AD); and (2) the benefits and harms of prescription drugs and supplements for cognition, function, and behavioral and psychological symptoms of dementia (BPSD) in patients with CATD. Data sources. Electronic bibliographic databases to August 2018; ClinicalTrials.gov; systematic review bibliographies. Review methods. Cognitive test studies used explicit CATD diagnostic criteria and a non-CATD control group. Biomarker studies used neuropathologic criteria to define AD cases and non-AD controls. All trials enrolled participants with CATD; those evaluating BPSD enrolled individuals with CATD and BPSD. Minimum study duration was 2 weeks for agitation, aggression, psychosis, and disinhibited sexual behavior, and 24 weeks for other outcomes. Two reviewers rated risk of bias (ROB) and strength of evidence. One reviewer extracted data; a second checked accuracy. We analyzed English-language studies with low or medium ROB. Results. We included 66 diagnostic accuracy studies (42 cognitive testing, 15 brain imaging, 9 cerebrospinal fluid (CSF) testing) and 60 trials of CATD treatment (49 reporting cognition or function, 11 reporting BPSD). Multiple cognitive screens, brief batteries, memory, and verbal fluency tests were highly sensitive and specific in distinguishing CATD from normal cognition, but less so for distinguishing mild CATD from normal cognition, or CATD from MCI. For distinguishing autopsy-confirmed AD from non-AD dementia, amyloid positron emission tomography (PET) and fluorodeoxyglucose (FDG)-PET may modestly improve accuracy beyond clinical evaluation. Combinations of CSF tests may have a higher combination of sensitivity and specificity than individual CSF tests, and may improve accuracy for distinguishing AD from FTLD beyond a clinical evaluation. Regardless of CATD severity, cholinesterase-inhibitors produced small improvements in cognition and function compared with placebo, but increased withdrawals due to adverse events. For mild-to-moderate CATD, memantine and placebo did not differ for function and evidence was insufficient for cognition, while for moderate-to-severe CATD, memantine inconsistently improved cognition, but not function. In patients with CATD and BPSD, mostly insufficient strength evidence suggested neither prescription drugs nor supplements differed from placebo for effects on agitation, aggression, psychosis, or disinhibited sexual behavior. Limitations. Diagnostic studies were small, methodologically heterogeneous, and rarely reported data on harms. Few studies compared accuracy between diagnostic tests, evaluated whether biomarkers improved diagnostic accuracy added to clinical evaluation alone. Few studies defined clinically meaningful differences for treatment outcomes. Few trials exceeded 6 months; most longer trials had high attrition. Conclusions. Brief cognitive tests accurately distinguished CATD from normal cognition, but less accurately distinguished smaller clinical differences. Whether biomarkers improve diagnostic accuracy when added to clinical evaluation needs verification, but clinical benefits of this testing are limited by the lack of effective treatments for AD and non-AD dementias. Cholinesterase-inhibitors slightly outperformed placebo for cognition and function, but evidence of whether drug treatments improved BPSD was largely insufficient.

Research Topic: Alzheimer's Disease
Funding agencies: N/A
Grant support: AHRQ, contract # HHSA290201500008I/HHSA29032005T

36. Personality and Rehabilitation Engagement in Veterans with Mild TBI: Preliminary Findings from the Outpatient TBI Program

Finn, Jacob [1]; Lamberty, Greg [1]

1. Minneapolis VA Health Care System

Abstract: Traumatic brain injury (TBI) is one of the signature injuries of the OEF/OIF conflicts, and 82.3% of those TBIs are classified as mild (mTBI). Individuals who experienced a mTBI may seek VA outpatient rehabilitation services. Rehabilitation engagement predicts functional improvement during and after treatment. Despite the benefits of engagement, almost one-third of civilian rehabilitation samples demonstrate poor or questionable engagement, and to our knowledge, no research has examined engagement in VA rehabilitation. The current study used a model of medical rehabilitation engagement to examine the association between personality and willingness to engage. Within this model, willingness to engage is impacted by perceived need for treatment, treatment outcome expectations, and perceived self-efficacy. Veterans were recruited from the Minneapolis VA's outpatient TBI rehabilitation clinic if they 1) had a history of mTBI only (i.e., no moderate/severe TBIs), 2) were referred to at least one active therapy, and 3) enrolled in the study within two weeks of their first rehabilitation appointment. Out of the 149 Veterans meeting the criteria, 44 (29.5%) have been enrolled in the study. At time of analyses, 41 participants had completed their initial session – largely male (85.4%), largely Caucasian (87.8%), and having an average age of 46 years. Only 31 of 41 participants (75.6%) completed the study's personality measure due to fatigue and time constraints. On average, participants described their personalities as distressed and pessimistic, suspicious and mistrustful of others, preferring to be alone, and preferring excitement over safety. Regarding willingness to engage, 1) denial of illness was associated with social dominance and unwillingness to let others take charge; 2) positive treatment expectations were associated with higher optimism and well-being; and 3) self-efficacy was associated with being optimistic and cheerful, being dominant and assertive, working hard and being ambitious, taking risks, and being imaginative and fantasy-prone. The current findings suggest that personality is correlated with factors impacting engagement in care and could be used to identify individuals at risk for poor engagement. Future work should identify mechanisms underlying these associations and develop tailored interventions to ensure Veterans are getting optimal outcomes from their VA rehabilitation services.

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

37. NightWare: A Breakthrough Treatment for Nightmares in Veterans with Posttraumatic Stress Disorder

Fleming, Cassandra [1]; Harris, J. Irene [1]; Evans-Lindquist, Mary [1]; Davenport, Nicholas [1]

1. Minneapolis VA Health Care System

Abstract: Nightmares are a common problem in clinical populations and are often associated with posttraumatic stress disorder (PTSD). Approximately 80% of Veterans with PTSD have nightmares, with 30% of veterans having nightmares lasting longer than 3 months. Few effective medical or behavioral treatments are available for reducing nightmares in Veterans with PTSD. NightWare is a system consisting of a smartwatch and smartphone app that monitors sleep for signs of a nightmare and provides a vibration to rouse, but not awaken, the Veteran out of the distressing dream. According to preliminary data from 31 Veterans, 85% reported improved sleep within 1 month of using the NightWare System. We have initiated a series of larger studies, including a double-blind, randomized sham-control trial, to better characterize efficacy and safety.

Research Topic: Mental Health
Funding agencies: N/A
Grant support: NightWare, Inc.

38. Early Life Trauma and the Association with Chronic Internalizing Disorders in OEF/OIF Veterans

Fleming, Cassandra [1]; Nazarova, Kristina [1]; Hansen, Clare [1]; Davenport, Nicholas [1,2]

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

Abstract: Adverse childhood experiences (ACE), originally defined as 'abuse and household dysfunction during childhood' prior to age 18, are well-known to have lasting impacts into adulthood in the forms of both physical and mental health. Effects can even be seen in brain developmental differences, specific to enduring changes in the stress response as well as the nervous and immune systems. ACEs are relatively common and are seen in higher rates among veterans. However, little is understood of how these early life experiences impact late-life health and functioning specific to veterans who have also experienced combat. Even less is known of how early life traumas and adversity, compounded with the traumas of war, are expressed and clinically presented in the long-term functioning of combat veterans. In a study of 168 OEF/OIF/OND veterans, we conducted a medical chart review of documented instances of ACEs by utilizing the ACE Questionnaire to collect data in references to specific instances. A multivariate analysis of variance was used to compare the presence and absence of ACE scores and their relationships to current symptoms of posttraumatic stress disorder (PTSD), depression, and alcohol use. Our analysis demonstrated a relationship between individuals with symptoms of chronic PTSD and depression, and a history of at least one ACE. This review calls for the need of a more-rigorous measure of early life traumas as well as the consideration of early life trauma in the medical and psychological assessments and treatments of combat veterans.

Research Topic: Mental Health
Funding agencies: RR&D; DOD
Grant support: I01RX002171-01; W81XWH-13-2-0095

39. Escherichia coli clonal subtypes, virulence genes, and antibiotic resistance predict fecal colonization behavior within households

Fox, Teresa [1]; Clabots, Connie [2]; Porter, Stephen [2]; Thuras, Paul [1,2]; Johnson, James [1,2]

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

Abstract: Extraintestinal Escherichia coli infections are an ongoing source of morbidity and mortality. Certain clonal lineages and virulence genes are recognized as important in the pathogenesis of such infections, the management of which is now complicated by emerging antibiotic resistance. The intestinal tract is the main reservoir for clinical E. coli strains; therefore, E. coli fecal colonization patterns and their determinants are of interest. Accordingly, we assessed specific clonal subtypes, virulence factors, and antibiotic resistance markers as predictors of colonization behaviors within households (HH). We recruited 22 veterans with an E. coli clinical isolate (11 flouroquinolone [FQ]-resistant, 11 FQ-susceptible) and their HH members for serial stool sampling. Stools were screened for total and FQ-resistant E. coli. Unique E. coli strains were resolved by genomic profiling of 10 colonies per sample. One colony per strain per sample underwent PCR-based clonal subtyping, virulence genotyping, and antimicrobial susceptibility testing, and was compared with the HH's index clinical isolate. Using the Wilcoxon rank-sum test, the fecal strains' characteristics were assessed as predictors of (i) within-HH strain-sharing, (ii) persistence within the HH, (ii) overall within-HH colonization prevalence, and (iv) predominance within the fecal sample. From the 22 veterans and their 46 HH members, we recovered 143 unique fecal E. coli strains. In total, 88 bacterial traits were evaluated (16 clonal subtypes, 48 virulence genes, and 24 resistance markers). Of these, 58 occurred in = 5 fecal strains each, so could be analyzed statistically. The proportion of candidate predictor variables that was significantly associated with = 1 outcome variable was 5/7 (71%) for clonal subtypes, 18/37 (49%) for virulence genes, and 7/14 (50%) for resistance markers. Fecal strains matching the index clinical isolate were associated with significantly greater sharing, persistence, and overall colonization. The studied E. coli traits were significantly associated with fecal colonization behavior within HHs, supporting the concept that 'virulence factors' may be better considered as 'colonization factors.' Fecal strains matching clinical isolates were the most extensively colonized, suggesting that increased colonization is related to increased likelihood of causing infection. This suggests that future interventions that disrupt colonization behavior could prevent E. coli infections.

Research Topic: Infectious Diseases
Funding agencies: CSR&D; NIH
Grant support: VA Merit Review grant, Intramural Bridge Grant, Medical School and University Medical Foundation (University of Minnesota), NIH ARLG grant

40. Outcomes of Elderly Patients Diagnosed with Nonmelanoma Skin Cancer

Freeman, Thomas [1]; Ravishankar, Adarsh [1]; Gravely, Amy [2]; Goldfarb, Noah [1,2]

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

Abstract: The Charlson comorbidity index (CCI) has been used in several studies as a co-morbidity instrument for nonmelanoma skin cancers (NMSC) CCI and age are key predictors of death in patients with NMSC. An age-adjusted CCI instrument has been created to combine age and CCI into a single tool to predict mortality. This model named the age-adjusted CCI (ACCI) adds one point to the CCI for every decade over 40 years of age. A recent study using ACCI found it predicted increased risk of death with increasing scores. The objectives of this retrospective cohort study were to (1) evaluate the risk 1-5 year mortality in elderly patients presenting with NMSC, and (2) compare the CCI with the ACCI in predicting 2-year mortality. We reviewed all elderly Veterans (as defined by age 75 years or older) diagnosed with a new NMSC in January of 2006 at the Minneapolis VA Healthcare System. Demographics, co-morbidities, NMSC type and location, method of treatment and complications were obtained for each patient. We then determined whether elderly patients with multiple co-morbidities (CCI ≥3 or ACCI ≥ 7) were more likely to have (1) a specific type of NMSC, (2) multiple NMSCs, (3) differences in NMSC location, or (4) increased complication rates compared to those without multiple co-morbidities (CCI < 3 or ACCI < 7). We also determined whether elderly patients with multiple co-morbidities were managed differently than those without multiple co-morbidities. We then evaluated which co-morbidity index was better at predicting death at 2 years after diagnosis of NMSC by comparing logistic regression receiver operating characteristic (ROC) curves. Finally, we evaluated whether a cut off of ≥ 7 ACCI could predict mortality better than CCI ≥ 3 There were no significant differences between the elderly patients with multiple co-morbidities compared to those without multiple co-morbidities in number of NMSCs, NMSC type, NMSC locations, complication rates or how they were managed. We had fairly high rates of death within 2 years of diagnosis of NMSC in elderly patients with multiple co-morbidities (39% died within 2 years with ≥ 3 CCI compared to 17% with < 3 CCI ($p = 0.1163$), and 41% died with an ACCI ≥ 7 ACCI compared to only 5% < 7 ACCI. No patients died from NMSC. ACCI predicted death over and above CCI ($p = 0.0087$), but the comparison of the logistic regression ROC curves did not meet statistical significance ($p = 0.2378$)

Research Topic: Dermatology
Funding agencies: N/A
Grant support: N/A

41. Progressive Functional and Structural Neurodegeneration in Veterans with Mild Traumatic Brain Injury

Gilmore, Casey [1,2]; Kardon, Randy [3,4]; Ledolter, Johannes [3,4]; Fenske, Alicia [1,2]; Thorsrud, Gavin [2]; Poolman, Pieter [3,4]; Garvin, Mona [3,4]; Hendrickson, Timothy [5]; Armstrong, Michael [2]; Lim, Kelvin [1,2,5]

1. Defense and Veterans Brain Injury Center
2. Minneapolis VA Health Care System
3. Iowa City VA Health Care System
4. University of Iowa
5. University of Minnesota

Abstract: Mild traumatic brain injury (mTBI) may predispose individuals to progressive neurodegeneration and the development of dementia. This study aimed to identify evidence of neurodegeneration through longitudinal evaluation of structural and functional changes in the visual and central nervous system in Veterans with a history of mTBI. Our long-term objective is to identify biomarkers that can be used for early identification of those Veterans at risk for future functional decline. Methods: 69 veterans with mTBI and 70 age-matched control veterans received evaluations at 6 month intervals of visual function, cognition, and Optical Coherence Tomography (OCT), and of magnetic resonance imaging (MRI) at 18 months. A linear trend statistical model was used to estimate slopes of change over time in subjects' retinal nerve fiber layer (RNFL) thickness, visual acuity, contrast sensitivity, and tests of cognitive function. Changes in structural MRI (cortical thickness) over 18 months was completed in 100 of the subjects. Results: Compared to controls, Veterans with mTBI showed significantly greater thinning of the RNFL. There was an average loss of 1.5 microns/year in mTBI and of 0.35 microns/year in controls ($p = 0.004$, Cohen's $d = .56$). This was associated with a small, but significant loss of visual acuity of one letter loss/year ($p = 0.04$), low spatial frequency contrast sensitivity ($p = 0.008$), and visual field mean sensitivity of 0.5 decibels loss per year ($p = 0.03$) compared to controls. A mildly significant increase in errors on the Groton Maze Learning Test (GMLT) was found in the mTBI group compared to controls ($p = 0.05$). Greater RNFL tissue loss was associated with this worsening performance on the GMLT ($r = -0.28$, $p = 0.002$). Finally, a significant decrease in percent change in cortical thickness at primary visual cortex (V1) was found for the mTBI vs. control group ($t = -2.23$, $p = 0.02$). Conclusions: We found evidence for significant, progressive neural degeneration over time in Veterans with mild TBI, with the greatest significant change in RNFL thinning in veterans with mTBI, indicating that retinal thickness analysis may be a useful biomarker for predicting neurodegeneration. Functional tests of vision showed small, but significant changes over the current time period of study. Continued evaluation of subjects will determine if the extent of functional deterioration in the visual and cognitive pathways follow structural loss in the retina and visual cortex.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: RR&D; DOD
Grant support: VA RR&D and Department of Defense through the Chronic Effects of Neurotrauma Consortium (CENC); Defense and Veterans Brain Injury Center

42. Mobility-in-Standing Manual Wheelchair

Goldish, Gary [1,2]; Voss, Gregory [1]; Morin, Steve [1]; Slater, Billie [1]; Johnson, Dan [3]; Fairhurst, Stuart [1]; Nickel, Eric [1]; Stein, Crystal [1]; McCracken, Patricia [1]; Hanowski, Kristin [1]; Sauerbrey, Matthew [1]; Sauerbrey, Bethany [1]; Hansen, Andrew [1,2]

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

Abstract: There are numerous standing devices; however, there are no manual standing wheelchairs on the market that allow mobility-in-standing. Giving persons with spinal cord injuries (SCI) the ability to move while standing has obvious benefits for expanding functional reach and satisfaction, but also has the potential to provide numerous health benefits, including a practical way to achieve sustained skin pressure relief. A recent mobility-in-standing manual wheelchair (MiS-MW) prototype was improved in this study (with VA funding) using a Veteran-centric, experience-based design process. The primary goals of the redesign were to reduce the physical width (31 inches) and weight (75 lbs) of the initial prototype to make it more commercially viable. These design iterations were conducted with feedback from Veterans with SCI, SCI clinicians, and an industry partner (LEVO). The MiS-MW was then tested by three Veterans with SCI using a subset of the Wheelchair Skills Test as well as collection of Veterans' predicted uses of the wheelchair in their daily lives. Mobility speed was measured during the 100-meter roll test with each participant's ultralight wheelchair (seated), the MiS-MW in seated mode, and the MiS-MW in standing mode. The width and weight of the MiS-MW were reduced to 28 inches and 65 lbs through iterative design efforts. The revised MiS-MW was tested by three Veterans with SCI (injury levels T5-6, T11, T3; ages 57, 69, 30 years). Mobility speeds were highest with the Veterans' usual ultralight wheelchairs (1.79 ± 0.63 m/s), followed by the MiS-MW during seated ambulation (1.11 ± 0.33 m/s), and lastly the MiS-MW during standing operation (0.79 ± 0.30 m/s). Although slower than the usual ultralight wheelchairs, Veterans using the MiS-MW in standing mode moved at a speed that is three times the average mobility speed of persons with SCI walking with exoskeletons. One Veteran noted that, in contrast to exoskeletons, the stability of the design allowed him to operate the MiS-MW independently and with hands-free in a standing position. Veterans who tested the MiS-MW were also able to demonstrate stability in both sitting and standing postures while ascending and descending 5-degree slopes (which exceeds ADA-compliant slopes), rolling across a 5-degree side slope, and going over thresholds. Veterans indicated that they would like to use the MiS-MW for activities at work, at home, and in the community.

Research Topic: Spinal Cord Injury
Funding agencies: RR&D
Grant support: A1826-R

43. Non-pharmacological therapy use for chronic pain among U.S. military veterans on long-term opioids

Goldsmith, Elizabeth [1,2]; MacLehose, Richard [2]; Jensen, Agnes [1]; Clothier, Barbara [1]; Noorbaloochi, Siamak [1]; Donaldson, Melvin [2]; Krebs, Erin [1,2]

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

Abstract: Chronic pain is a major cause of disability in the US, and opioid prescriptions rose amid limited availability and awareness of other pain therapies. Though many non-pharmacological therapies (NPT) are effective for chronic pain, little is known about NPT use patterns among people prescribed opioid analgesics. We examined NPT use within a national sample of US military veterans on long-term opioid therapy for chronic pain. Methods: The Effects of Prescription Opioid Changes in Veterans (EPOCH) study established a national cohort of 271,892 Veterans Affairs patients prescribed long-term opioid therapy for chronic pain. A representative sample received a survey including questions about past-year use of non-pharmacological therapies to treat or cope with chronic pain. We use descriptive statistics and latent class analysis to describe patients' self-reported NPT use patterns and to examine associations of NPT use with demographic and clinical characteristics and with patient-centered pain measures. Results: 8,891 (65%) of 13,660 invitees completed the NPT questionnaire. Female sex and younger age were associated with use of every non-pharmacological therapy for chronic pain. Higher pain-related functional interference, higher prescribed opioid dose, and psychiatric diagnoses (depression, anxiety, PTSD) were associated with psychological skills-related NPT (meditation, relaxation, psychotherapy). Lower pain-related functional interference and lower physical comorbidity were associated with movement skills-related NPT (aerobic exercise, stretching/strengthening). Lower physical comorbidity was associated with manual therapy (acupuncture, chiropractic adjustment or manipulation, massage). Conclusions: Findings can inform implementation and clinical research on non-pharmacological therapies for chronic pain, and raise questions about health system-related factors. Further analyses will examine how participants' NPT use relates to pain-related functional interference, opioid dosing, and quality of life outcomes over time.

Research Topic: Pain
Funding agencies: HSR&D
Grant support: HSR&D IIR #14-295

44. Normal microbial exposure increases sepsis-induced cytokine storm and mortality through TLR4 sensitization

Griffith, Thomas [1,2]; Sjaastad, Frances [2]; Huggins, Matthew [2]; Pierson, Mark [2]; Kucaba, Tamara [2]; Jensen, Isaac [3]; Danahy, Derek [3]; Badovinac, Vladimir [3]; Hamilton, Sara [2]

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

Abstract: It is poorly understood how natural microbial exposure alters the immune response to future challenges. We have leveraged a novel mouse model where exposure to multiple naturally acquired infections generates an experienced immune system – mimicking a critical aspect of human biology – to investigate the immune response during sepsis. Female C57BL/6 (B6) or pet store mice (purchased from local pet stores) were cohoused for 60 d to facilitate microbe transfer. Serum was collected before and after 60 d of cohousing for serology and cytokine/chemokine quantitation. Sepsis was induced by cecal ligation and puncture. Alternatively, a rodent model of endotoxemia was used (10, 5, or 1 mg/kg LPS from E. coli O111:B4 i.p.). Similarly, some mice were challenged with a single dose (10 mg/kg i.p.) of Pam3CSK4. After cohousing, B6 mice acquire many of the microbes carried by pet store mice. Importantly, this physiological microbial exposure resulted in global changes to the immune status of the cohoused mice. Inflammatory serum cytokine and chemokine levels were elevated in cohoused mice, relative to SPF mice. While total blood cell numbers were not affected, cohousing did alter the composition of circulating immune cells. There were increased frequencies of CD44hi and KLRG1+ and decreased frequencies of CD62L+ CD4 and CD8 T cells in the blood of cohoused mice – indicating a transition of naïve T cells to Ag-stimulated effector/memory T cells as a result of microbial exposure. Moreover, the innate immune cell compartment was significantly expanded following cohousing, with increases in both the frequency and number of circulating monocytes and neutrophils. When polymicrobial sepsis was induced by CLP, cohoused mice exhibited increased morbidity and mortality. The increased morbidity/mortality in the cohoused mice correlated with an exacerbated cytokine storm, marked by elevated IL-6, IFNg, and TNF (among other cytokines/chemokines). Further investigation of cohoused mice revealed an increased frequency of TLR2+ and TLR4+ phagocytes, enhancing the ability to recognize infection through pattern recognition receptors. However, the response to Pam3CSK4 (TLR1/2 ligand) was muted in cohoused mice whereas the response to LPS (TLR4 ligand) was greatly increased, suggesting complexity to innate immune education. Our data illustrate how normalized microbial exposure can increase the risk of immunopathology from a sepsis-induced severe cytokine storm.

Research Topic: Infectious Diseases
Funding agencies: BLR&D
Grant support: I01BX001324 (T.S.G.), R01GM115462 (T.S.G.), R01AI116678 (S.E.H.), R01AIGM113961 (V.P.B.), T32CA009138 (F.V.S.), T32AI007485 (I.J.J.)

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45. The Minnesota Multiphasic Personality Inventory-2 Restructured Form and Social Participation within the Context of Mild Traumatic Brain Injury

Hachiya, Kiki [1]; Finn, Jacob [1,2]; Gilmore, Casey [3]; Lim, Kelvin [1-3]; Kardon, Randy [4,5]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Defense and Veterans Brain Injury Center
4. Iowa City VA Health Care System
5. University of Iowa

Abstract: Acute symptoms of mild traumatic brain injury (mTBI) are likely to resolve for individuals within three months post-injury; however, research regarding recovery following mTBI continues to be helpful in identification of factors that may influence meaningful outcomes, such as adjustment and social participation. This study examined three groups of veterans to better understand the psychological associations that may impact social participation. The groups in this study were: (1) control: denied any history of TBI; (2) symptomatic: individuals who self-reported a history of mTBI but the reported event(s) was judged unlikely to meet criteria for a mTBI by an expert consensus review; and (3) mTBI: individuals who self-reported a history of mTBI and the reported event(s) was judged likely to meet criteria for a mTBI by an expert consensus review. All participants completed the MMPI-2-RF and the Mayo-Portland Adaptability Inventory-4's social participation subscale. Valid MMPI-2-RF protocols (CNS < 18; VRIN-r or TRIN-r < 80T; F-r < 120T; and Fp-r < 100T) for 76 control, 34 symptomatic, and 62 mTBI were used in this study. Numerous Restructured Clinical (RC) scales differentiated between control and mTBI groups, but only RCd differentiated between mTBI and symptomatic groups, with the symptomatic group having the highest mean score, followed by mTBI, and then controls. For mTBI and symptomatic participants, RC1 was a significant predictor of social participation with MLS predicting incrementally; however, no other somatic/cognitive specific problem scales added incrementally. For control participants, RC1 was a significant predictor of social participation with MLS and COG predicting incrementally. Identification of a general sense of malaise, in addition to a heighten proclivity to somatization, as a predictor of decreased social participation has clinical implications for psychological treatment, regardless of patient's mTBI history.

Research Topic: Traumatic Brain Injury (TBI)
Funding agencies: RR&D; DOD
Grant support: 1) VA RR&D and Department of Defense through the Chronic Effects of Neurotrauma Consortium (CENC); 2) Defense and Veterans Brain Injury Center

46. Advancing Pharmacologic Therapy for Opioid Use Disorders (ADaPT-OUD) in Low Prescribing VA Clinics

Hagedorn, Hildi [1]; Kenny, Marie [1]; Clothier, Barb [1]; Bangerter, Ann [1]; Noorbaloochi, Siamak [1]; Ackland, Princess [1]; Salameh, Hope [1]; Gordon, Adam [2]

1. Minneapolis VA Health Care System
2. VA Salt Lake City Health Care System

Abstract: Given the rise in opioid use disorder (OUD) and overdose, increasing Veteran access to medication addiction treatment for OUD (M-OUD) is a VA priority. While VA operations' effort have enhanced access to M-OUD, many facilities remain low-adopters. Eight low-adopter sites were recruited to receive intensive external facilitation. Four sites have received the intervention for at least 6 months. We sought to examine the initial barriers and facilitators of M-OUD implementation in these low adopting facilities. Furthermore, we reported on the interim progress of four facilities enrolled in an external facilitation intervention to improve M-OUD implementation. Methods: Eight VA sites were randomly selected from sites with low M-OUD prescribing rates (<21%) to receive the intervention which consisted of a developmental evaluation, a site visit and twelve-monthly facilitation calls. These sites were matched to other low adopter sites (4-5 sites/intervention site) and compared on three outcomes (number of buprenorphine-waivered prescribers, number of patients prescribed buprenorphine; percent of patients with OUD receiving M-OUD) at baseline and 6 months post-intervention kick-off. Results: Of the eight sites enrolled, four selected sites have received the intervention for at least 6 months. At baseline, three of the four intervention sites had only one DEA-waivered provider and prescribed to three patients total. Within six months, these sites added multiple waivered providers and prescribed to 53 patients total. The fourth site started with more providers (5) and patients (27), added modestly to these numbers and did not outperform matched control sites. All four sites showed an increase in percent of patients with OUD receiving M-OUD, outperforming many control sites. Few facilities were able to accomplish action plan goals within the first 6 months of the intervention. Examples of barriers included: recipients (providers) did not have adequate training in M-OUD, had misconceptions about OUD and its treatment, and did not feel they could prescribe without ample nursing and/or pharmacy support. Conclusions: All intervention sites increased their number of prescribers, patients and percent of patients receiving M-OUD over six months. Intensive external facilitation appears to be an effective add-on strategy to improve performance in facilities that have not responded to ongoing operational-level efforts.

Research Topic: Substance Use Disorders
Funding agencies: HSR&D
Grant support: IIR 16-145 HSR&D Study

47. Serious Mental Illness and Smoking Cessation Treatment Utilization: The Role of Healthcare Provider Interactions

Hammett, Patrick [1]; Lando, Harry [2]; Taylor, Brent [1]; Widome, Rachel [2]; Erickson, Darin [2]; Fu, Steven [1]

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

Abstract: The US is facing widening mental health disparities in smoking prevalence. Evidence suggests that low rates of physician-delivered cessation care for patients with serious mental illness (SMI) may contribute to this problem. The aim of this study was to examine how healthcare providers influence cessation treatment utilization among smokers with SMI. Data for this study were taken from OPTIN, a trial that demonstrated the effectiveness of proactive outreach for promoting smoking abstinence among low-income smokers enrolled in the publicly-subsidized Minnesota Health Care Programs (MHCP). ICD-9 codes consistent with schizophrenic disorders, psychotic disorder, bipolar disorders, and severe or recurrent major depressive disorder were used to categorize participants as having SMI (n = 939); remaining participants were non-SMI (n = 1382). Analyses assessed whether the association between SMI and treatment utilization at 12-month follow-up was mediated by baseline measures of doctor-delivered cessation treatment advice and healthcare provider bias. SMI was associated with higher rates of cessation treatment utilization at 12-month follow-up. In adjusted analyses, treatment advice and healthcare provider bias did not significantly mediate the relationship between SMI and treatment utilization. However, individual regression analyses revealed strong positive associations between treatment advice and treatment utilization (β: 0.13 – 0.30), regardless of SMI status. The strong association between doctor-delivered advice to use cessation treatments and subsequent treatment utilization, among smokers with and without SMI, highlights the important role that healthcare providers play in the cessation process. Findings suggest that expansion of publicly-subsidized insurance programs, including Medicaid, may reduce treatment utilization barriers and promote abstinence among socioeconomically disadvantaged smokers.

Research Topic: Health Care Delivery
Funding agencies: NIH
Grant support: National Cancer Institute (1R01CA141527-01 and 2T32CA163184)

48. Improving Footwear Options for Women and Men Veterans with Amputations

Hansen, Andrew [1,2]; Voss, Gregory [1]; Hein, Emily [1,2]; Nickel, Eric [1]

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

Abstract: Changing footwear for different occasions and environments is important for self-image and walking comfort, and can facilitate participation in social activities, life roles and gainful employment (e.g., required uniforms for certain occupations). While the human foot and ankle accommodates easily to changes in footwear, commercially available prosthetic feet are extremely limited in their ability to accommodate shoes of different heel heights and widths. The vast majority of prosthetic feet are aligned for a specific heel height shoe, with a potentially de-stabilizing effect on gait if the user decides to wear footwear with different heel heights. Although there are a small number of 'heel-height adjustable' feet on the market, the shapes of the plantar surfaces of these feet do not change to match the interior of different footwear, restricting the range of shoes that can be used without instability of the foot within the shoe. Additionally, alignment changes for different footwear are performed by the user rather than by a certified prosthetist, increasing the likelihood of sub-optimal alignment. Lastly, there are no commercially available prosthetic feet that can adjust to shoes of different widths, further limiting footwear options. In order to maximize the participation and functional mobility of Veterans with leg amputations, the Minneapolis VA is developing a prosthetic foot/ankle system that can accommodate a diverse range of footwear and can be changed easily and quickly by the user while retaining the clinically optimal alignment determined by the prosthetist. The purpose of this project is to develop a new ankle-foot prosthesis system that will allow Veterans with amputations to choose any footwear with heel heights between 0-100 mm (0-4 inches), and to be able to easily switch between these footwear without needing to change the alignment of their prosthesis. Prosthetic ankle-foot systems will also be developed to cover a range of sizes between 22 and 28 cm (men's sizes 3-12, or women's sizes 4.5-13.5). This project is funded by the Department of Veterans Affairs Rehabilitation Research and Development Service Project A2634-R.

Research Topic: Prosthetics
Funding agencies: RR&D
Grant support: A2634-R

49. Communication Between Soldiers and Partners During Deployment Affects Service-Member and Relationship Wellbeing

Hansen, Lucas [1]; Polusny, Melissa [1]; Balderrama-Durbin, Christina [2]; Erbes, Christopher [1]

1. Minneapolis VA Health Care System
2. State University of New York, Binghamton

Abstract: The potential benefits and costs of the more real-time, frequent, and prominent communication between service members and their spouse/partners during combat deployments to Iraq and Afghanistan in the recent wars have been debated but seldom studied. We analyzed data from a subset of 400 National Guard Soldiers and their spouse/partners who were in the RINGS-2 study, which assessed soldiers and partners over the course of a deployment to Iraq and Kuwait during Operation New Dawn in 2011-2012. Soldiers and their partners completed measures of relationship functioning (including the brief Dyadic Adjustment Scale -7 and a brief Negative Communication Scale) and distress (including the PTSD Checklist for soldiers and the PHQ-8 Depression scale for partners) before and after deployment. In addition, during deployment, partners completed the Deployment Communication Inventory (DCI) assessing Frequency, Assurance/Support, Problem Solving, Conflict, and perceived Costs and Benefits of their communication with soldiers. Regression analyses suggest that changes in all outcomes (relationship satisfaction, negative communication, soldier PTSD, and partner depression) were significantly predicted by the set of DCI scales (incremental variance accounted for was between .30 and .37). In addition, Conflict discussions, reported by partners during the deployment on the DCI, uniquely predicted deterioration in all outcomes assessed (the magnitude of partial correlation coefficients was between .11 and .22). In contrast, frequency of communication was not associated with change in any outcomes. During-deployment communication involving conflict may lead to a reduction in otherwise important coping resources but may also specifically impair resilience processes needed to promote healthy outcomes from stressful situations. Results suggest that interventions that can curtail during-deployment conflictual communication between soldiers and their loved ones may impact outcomes for soldiers, their spouses/partners, and their relationships overall.

Research Topic: Afghanistan & Iraq Veterans
Funding agencies: HSR&D
Grant support: HSR&D SDR 10-398

50. The Exclusion from Medical Research of People Living with Serious Mental Illness

Hanson, Devin [1]; Harris, J. Irene [1,2]; Leskela, Jennie [1,2]

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

Abstract: People who manage serious mental illness live with multiple disparities in their health and well-being. This is evidenced in the rate of mortality which is well established as being in excess when compared to the general population (Das Munshi et al., 2017; Colton & Manderscheid, 2006). Specific mechanisms of health disparity for people with SMI include the unequal provision of healthcare (Lawrence & Kisely, 2010). Research has shown problems with accurate diagnosis, the receipt of appropriate care, and provider issues such as stigma, therapeutic pessimism, and diagnostic overshadowing (Shefer et al., 2014). A lesser known problem that likely contributes to the disparity in health is the exclusion of people who manage serious mental illness from medical research. This study seeks to explore the rate and type of exclusion of people who manage serious mental illness from clinical trials registered on ClinicalTrials.Gov between 2015 and 2017. The first 100 trials of interventions targeting high disease burden conditions (Ischemic Heart Disease, Chronic Pain, and Substance Use Disorders) were coded for full, partial, or non-exclusion of people with serious mental illness with comparisons to depression, post-traumatic stress disorder, and substance use disorders. This study is a replication and extension of work by Humphreys, Blodgett, and Roberts (2015) review of 20 conditions between 2002 and 2010. Comments on the progress made since and recommendations for improvements are presented.

Research Topic: Mental Illness
Funding agencies: N/A
Grant support: N/A

51. Utilization of Ki-67 as an Ancillary Marker in Barrett's Esophagus and Low-Grade Dysplasia Identifies Patients at Low Risk for Malignant Progression

Hayat, Umar [1]; Mesa, Hector [2]; Henn, Andrew [1]; Song, Kevin [1]; Gravely, Amy [2]; Shaukat, Aasma [2]; Hanson, Brian [2]

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

Abstract: The degree of dysplasia in Barrett's esophagus (BE) is an important determinant of management that may include endoscopic eradication therapy (EET) or surveillance. Correct diagnosis of low grade dysplasia (LGD) remains challenging because of low inter and intra-observer agreement among pathologists with many patients labeled as indefinite for dysplasia (IND). Correct identification of LGD in BE patients would limit unnecessary surveillance and target patients for therapy who are high risk for progression to HGD or esophageal adenocarcinoma (EAC). AIM: We evaluated the efficacy of Ki-67 surface over-expression in determining the risk of progression in LGD patients. METHODS: Several immuno-histochemical markers were applied to selected slides of 20 endoscopic resection cases of BE. Ki-67 surface expression proved to have the highest discriminative power and greatest improvement in the kappa inter-observer agreement. A total of 163 BE patients were identified within the Minneapolis VA pathology database from 2006 to 2016 and underwent Ki-67 staining. A new 'consensus' diagnosis using Ki-67 was established after re-evaluation of these slides by a panel of pathologists. All patients were followed for progression to HGD/EAC. RESULTS: The sensitivity, specificity, PPV and NPV for progression in the original consensus LGD diagnosis was 44, 58, 33 and 78% respectively when compared to IND patient population where as it was 91, 53, 30 and 96% respectively in the new consensus diagnosis when compared to those patients who were categorized as NDBE. CONCLUSION: A new consensus diagnosis by a panel of pathologist utilizing Ki-67 surface expression as an ancillary tool has improved reproducibility and a high NPV for progression to HGD/EAC. Thus, it can help identify low risk patients who are less likely to benefit from EET.

Research Topic: Gastroenterology
Funding agencies: N/A
Grant support: N/A

52. Community Engagement Studios: Improving Research through Community Input

Hendricks, Deborah [1]; Fu, Steven [1,2]; Hickle, Andrea [1]; Amelang, Miriam [1]; Eder, Milton [1]

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

Abstract: Community engagement is central to the success of research in improving health and addressing health disparities and is increasingly being recognized by researchers, and required by funders, as critical in research design and implementation. Multiple obstacles can make community and patient engagement challenging, including academic policies and culture, training and experience gaps among researchers, and time considerations, while communities' previous negative experiences may lead to lack of trust in academic research institutions and research in general. The Community Engagement Studio model, developed by Vanderbilt University, offers researchers the opportunity to seek feedback from Community Experts on any aspect of their research. Patient and community stakeholders benefit from a safe and comfortable environment in which to share their perspectives. Similar to a focus group, the discussion is guided by a trained facilitator, while the researcher listens to community input and recommendations. Since 2016, the University of Minnesota Clinical and Translational Science Office of Community Engagement to Advance Research and Community Health has conducted six Studios based on requests from multidisciplinary faculty researchers on various topics and involving diverse Community Experts. Data are collected via three surveys, with Community Experts providing immediate feedback and researchers completing surveys within one month of the Studio and again one year later. Community Experts and researchers identify multiple contributions of Studios to the research projects including increased understanding of community, enhanced sensitivity to community concerns, new ideas for sharing results, feasibility considerations, and recruitment approaches. Research teams report changing various aspects of studies as a result of Studio input such as asking questions that are more patient-centered and culturally-relevant, revising data collection and data interpretation processes, adapting recruitment or retention strategies, and making plans to disseminate results more broadly to patients and community stakeholders. Next steps include increasing promotion to faculty, launching facilitation training for Community Experts, engaging Community Experts in additional research-related activities, and strengthening and expanding community partnerships.

Research Topic: Health Equity
Funding agencies: NIH
Grant support: NIH, UL1TR002494

53. With Your Help We Can Improve Your Healthcare: A Collaboration between University of Minnesota's Clinical and Translational Science Institute and Minneapolis VA Health Care System

Hendricks, Deborah [1]; Jensen, Agnes [2]; Amelang, Miriam [1]; Eder, Milton [1]

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

Abstract: To improve healthcare, we have to improve the quality of information we use to make decisions. One important goal in developing a collaboration between the University of Minnesota's Clinical and Translational Science Institute Office of Community Engagement to Advance Research and Community Health (CTSI CEARCH) Minneapolis VA's Center for Care Delivery and Outcomes Research (CCDOR) is to create new community roles and responsibilities for participating in research and to expand the evidence available to inform daily decisions about healthcare and health. We hypothesize that developing a program to encourage engagement of community members will contribute to resolving three current problems: 1) Improving representation or the relationship between participants in studies and the population in care. 2) Exploring complexity within healthcare and health by examining the relationship between healthcare, research, and the outcomes experienced by individual patients. 3) Addressing trust and ethical research conduct in communities. The community engagement program we are developing includes new community research roles and relationships: 1) A Management Council or coordinating group to help shape the strategic direction of the program and it use of resources. 2) Work groups to develop implementation strategies around research, education and the translational challenge of connecting clinical research to clinical care. 3) Community Engagement Studios to bring community voices and perspectives to the research community. 4) "Driven to Disseminate" to engage researchers in the life of communities to report on studies with an emphasis on sharing results in meaningful ways. 5) #MNResearchLink - a U of Minnesota/Mayo Clinic Facebook group to support broad public engagement in conversations about health and research.

Research Topic: Health Equity
Funding agencies: NIH
Grant support: University of Minnesota's NIH Clinical and Translational Science Award: UL1TR002494

54. Risk of Dysplastic Progression in Patients with Barrett's Esophagus Indefinite for Dysplasia: A Systematic Review and Meta-Analysis

Henn, Andrew [1]; Moscoso, Carlos [1]; Hayat, Umar [1]; Bongiorno, Connie [1,2]; Sultan, Shahnaz [1,2]; Shaukat, Aasma [1,2]; Hanson, Brian [1,2]

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

Abstract: Barrett's esophagus (BE) is a pre-malignant condition with 0.68% annual incidence of progression to high grade dysplasia and/or esophageal adenocarcinoma (EAC). Rates of progression are known to increase with increasing degree of dysplasia (low grade dysplasia [LGD], high grade dysplasia [HGD]). The focus of our review is Barrett's esophagus – indefinite for dysplasia (BE-IND). It is defined as intestinal metaplasia with associated crypt dysplasia with either uninvolved, denuded or actively inflamed surface epithelium making definitive diagnosis of dysplasia difficult. BE-IND incidence of progression to EAC has not been well characterized. Our aim is to determine the rate of progression from BE-IND to HGD/EAC. Methods: A systematic review was performed in Embase, Cochrane Central Register for Controlled Trials, Medline, and Scopus from individual database inception until February 8th, 2018 for studies assessing the risk of progression of BE-IND to HGD/EAC and LGD/HGD/EAC. All studies with BE-IND that evaluated progression to LGD or HGD/EAC with at least one year of follow up met inclusion criteria. Results: Nine studies were identified reporting on 1,378 patients with BE-IND with over 4,146 patient-years follow up and 273 patients showing progression. Five studies evaluated incidence data of 1,072 patients with BE-IND. These studies had 3,718 patient-years of follow up and 221 incident cases of progression. The pooled annual incidence rate of HGD/EAC and LGD/HGD/EAC in patients with BE-IND were 1.3 % (95% CI 0.9-1.6%, 5 studies) (figure 1) and 3.8% (95% CI 0.5-7.1%, 5 studies), respectively. No heterogeneity was present in studies evaluating progression to HGD/EAC ($I2 = 0\%$); however, significant heterogeneity was present considering rates of progression to LGD/HGD/EAC ($I2 = 96\%$). Explanations for this heterogeneity could include interobserver variability in pathology interpretation and study design. Conclusions: The annual incidence of HGD/EAC and LGD/HGD/EAC in patients with BE-IND are 1.3% and 3.8%, respectively. These findings support the conclusion that BE-IND progression rates are truly greater than non-dysplastic BE. The risk of progression in patients with BE-IND is nearly twice that of rates seen in non-dysplastic BE. Our findings support current guideline-recommended surveillance intervals in BE-IND similar to that for BE-LGD.

Research Topic: Digestive Diseases
Funding agencies: N/A
Grant support: N/A

55. Adjunctive therapy with an MSC patch at the time of CABG improves mitochondrial function in hibernating myocardium

Hocum Stone, Laura [1,2]; Swingen, Cory [2]; Chappuis, Erin [2]; Wright, Christin [1,2]; McFalls, Edward [1,2]; Kelly, Rosemary [1,2]

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

Abstract: Clinical studies have shown that functional recovery of hibernating myocardium (HM) remains incomplete following surgical revascularization. Mesenchymal stem cells (MSCs) have been shown to improve cardiac function in the peri-infarct region of myocardial ischemia. Our current study tests the therapeutic efficacy of a vicryl-based stem cell patch applied to viable but ischemic myocardium at the time of surgical revascularization. METHODS: Young anesthetized swine underwent thoracotomy with placement of a constrictor around the LAD artery. At 12 weeks, off-pump revascularization was performed with a left internal mammary artery graft to the LAD artery. Animals received adjunctive treatment of either a vicryl patch seeded with MSCs ($n = 4$), or a vicryl patch alone ($n = 4$) sutured to the epicardium. 4 weeks later, MRI imaging was performed to assess cardiac function, coronary anatomy, and viability, followed by termination of the animal. MRI studies were performed at baseline and during an infusion of low dose dobutamine (5 μg/kg/min). Low dose dobutamine is used to determine functional reserve. RESULTS: Swine that received the stem cell patch at the time of revascularization showed improvement in regional wall thickening in response to inotropic stimulation ($p = 0.042$), indicating improved recovery of function as compared to revascularization alone (63.18 ± 21.5 vs 46.67 ± 1.87). Western Blots of the mitochondrial fraction from cardiac tissue showed a significant increase ($p = 0.025$) in expression of ATP synthase (4.18 ± 0.26) as compared to animals who were only revascularized (1.65 ± 0.42). CONCLUSIONS: In a novel large animal model of chronic ischemia, we show for the first time that the combination of an epicardial MSC patch and surgical revascularization results in increased functional recovery of chronically ischemic myocardium compared to revascularization alone. This restoration of function is evident at baseline and under increased workload induced by inotropic stimulation. Mitochondrial studies demonstrate an increase in expression of ATP synthase, which is a key protein involved with energy formation to the heart cells. This suggests that the mechanism of action of MSCs on enhanced function is by facilitating ATP synthesis in cardiac tissue.

Research Topic: Heart Disease
Funding agencies: BLR&D
Grant support: I01 BX000760

56. CoQ10 enhances PGC1a and increases expression of mitochondrial antioxidant proteins in chronically ischemic swine myocardium

Hocum Stone, Laura [1,2]; Wright, Christin [1,2]; Ward, Herbert [1,2]; Kelly, Rosemary [1,2]; McFalls, Edward [1,2]

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

Abstract: Expression of mitochondrial proteins within chronically ischemic, hibernating myocardium is known to be reduced. It is unclear whether administration of CoQ10 can increase expression of mitochondrial electron transport chain (ETC) and antioxidant proteins potentially via enhanced PGC1a signaling. Objective: In a swine model of chronically ischemic hibernating myocardium, administration of CoQ10 in the diet for 30 days increases PGC1a expression and enhances the expression of ETC and antioxidant proteins within the mitochondria. Methods: Twelve swine (8-10 kg) underwent a thoracotomy and were instrumented with a fixed constrictor around the LAD artery. At 3 months, transthoracic ECHO was performed to confirm the presence of a wall motion abnormality in the anterior wall. Pigs were then randomly assigned to receive daily dietary supplements of either CoQ10 (10 mg/kg/day) or placebo for 4 weeks. At 16 weeks, animals underwent a terminal procedure and tissue was harvested for nuclear and mitochondrial fractions. Expression of nuclear-bound PGC1a (Western blots) and mitochondrial proteins (Tandem Mass Tag proteomics) were determined. Results: Mitochondrial and nuclear fractions were isolated from the hibernating LAD region. Nuclear-bound PGC1a levels were >200-fold higher with administration of 4 weeks of CoQ10 treatment, with a level of 0.0007 ± 0.0002 in animals assigned to the placebo treatment and 0.044 ± 0.015 in pigs receiving CoQ10 ($P = 0.0278$). Expression of ETC proteins was increased in those animals that received CoQ10. Compared with mitochondria in the LAD region from Placebo-treated pigs, CoQ10-treated pigs had higher levels of Complex I (0.2455 ± 0.017 versus 0.8961 ± 0.27; $P = 0.027$), Complex IV (0.28 ± 0.061 versus 1.01 ± 0.2; $P = 0.01$ and Complex V (2.03 ± 0.73 versus 6.97 ± 1.66; $P = 0.03$) peptides. Conclusions: Four weeks of dietary administration of CoQ10 to pigs with a chronic stenosis on the LAD artery enhances PGC1a levels within the chronically ischemic anterior wall and increases the expression of ETC proteins within isolated mitochondria. The enhanced expression of antioxidant proteins within mitochondria might potentially mitigate the oxidant-stress within myocardial tissue, as a result of repetitive supply-demand mismatch. Future studies should determine whether such an intervention can reduce biomarker elevations within chronically ischemic heart tissue.

Research Topic: Heart Disease
Funding agencies: BLR&D
Grant support: I01 BX000760

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57. Human Leukocyte Antigen (HLA) DRB1*13 Preserves Brain Health

James, Lisa [1,2]; Georgopoulos, Apostolos [1,2]

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

Abstract: Age-related brain changes are highly variable, partly due to genetic influences. Extensive research has focused on apolipoprotein E4 (apoE4), which has been widely linked to neurodegeneration and Alzheimer's disease (AD) risk; however, increasing evidence implicates additional genes on age-related brain changes. Here we report on the effect of Human Leukocyte Antigen (HLA) DRB1*13 on age-related brain changes in 178 cognitively healthy (MoCA > 25) women. Structural magnetic resonance imaging (sMRI) and magnetoencephalography (MEG) were used to evaluate brain structure and function, respectively. Participants also provided a blood sample for genotyping. The results indicate that the absence of the DRB1*13 allele, particularly DRB1*13:02, was associated with gray matter atrophy and increased neural network variability with age. No such deleterious changes were evident in DRB1*13 carriers, regardless of apoE4 status, highlighting the robust protective effects of DRB1*13. Given the role of HLA in immune protection from foreign antigens, we suspect the protective effects observed here are related to successful elimination of specific foreign antigens that would otherwise result in neurodegeneration.

Research Topic: Aging
Funding agencies: UMN
Grant support: Kunin Professorship in Healthy Brain Aging

58. A Prospective, Randomized Trial comparing Endoscopic vs. Open Vein Grafts in CABG Surgery (REGROUP)

Johnson, Debra [1]; McFalls, Edward [1]; Zenati, Marco [2]; Bhatt, Deepak [3]; Bakaeen, Faisal [4]; Stock, Eileen [2]; Biswas, Kousick [5]; Gaziano, J. Michael [6]; Kelly, Rosemary [1]; Tseng, Elaine [7]

1. Minneapolis VA Health Care System
2. VA Boston Healthcare System
3. Brigham and Women's Hospital
4. Houston VA Health Care System
5. Perry Point VA Medical Center
6. VA Boston Healthcare System
7. San Francisco VA Health Care System

Abstract: The saphenous-vein graft is the most common conduit for coronary-artery bypass grafting (CABG). The influence of the vein-graft harvesting technique on long-term clinical outcomes has not been well characterized. METHODS: We randomly assigned patients undergoing CABG at 16 Veterans Affairs cardiac surgery centers to either open or endoscopic vein-graft harvesting. The primary outcome was a composite of major adverse cardiac events, including death from any cause, nonfatal myocardial infarction, and repeat revascularization. Leg-wound complications were also evaluated. RESULTS: A total of 1150 patients underwent randomization. Over a median follow-up of 2.78 years, the primary outcome occurred in 89 patients (15.5%) in the open harvest group and 80 patients (13.9%) in the endoscopic-harvest group (hazard ratio, 1.12; 95% confidence interval [CI], 0.83 to 1.51; P = 0.47). A total of 46 patients (8.0%) in the open-harvest group and 37 patients (6.4%) in the endoscopic harvest group died (hazard ratio, 1.25; 95% CI, 0.81 to 1.92); myocardial infarctions occurred in 34 patients (5.9%) in the open-harvest group and 27 patients (4.7%) in the endoscopic-harvest group (hazard ratio, 1.27; 95% CI, 0.77 to 2.11), and revascularization occurred in 35 patients (6.1%) in the open-harvest group and 31 patients (5.4%) in the endoscopic-harvest group (hazard ratio, 1.14; 95% CI, 0.70 to 1.85). Leg-wound infections occurred in 18 patients (3.1%) in the open harvest group and in 8 patients (1.4%) in the endoscopic-harvest group (relative risk, 2.26; 95% CI, 0.99 to 5.15). CONCLUSIONS: Among patients undergoing CABG, we did not find a significant difference between open vein-graft harvesting and endoscopic vein-graft harvesting in the risk of major adverse cardiac events.

Research Topic: Cardiovascular Disease
Funding agencies: CSR&D
Grant support: VA Cooperative Studies Program CSP #588

59. Physician Responsiveness to Positive Blood Culture Results at the Minneapolis VA

Johnson, Shaun [1]; Waisbren, Steven [1]

1. Minneapolis VA Health Care System

Abstract: The aim of this study was to determine the rate at which physicians at the Minneapolis VA Medical Center (VAMC) adjust the breadth of antibiotic coverage based on positive blood culture (PBC) results, quantify the response time for alterations to antibiotic coverage, and to bring into question what an appropriate rate and response time for alteration of antibiotic coverage would be. A retrospective medical chart review within CPRS of the VAMC database was performed for 208 positive blood cultures from July 2015 to June 2016. Time of reporting of pathogen identification and subsequent pathogen susceptibilities was compared to the time at which any alterations to antibiotic coverage were made. The width of antibiotic coverage was quantified using a linear spectrum score developed by Madaras-Kelly et al. The use of a spectrum score allowed for the reliable classification of antibiotic adjustments as either de-escalation, escalation, or no change with the added benefit of also classifying the magnitude of the change in antibiotic coverage spectrum. The percentage of cases de-escalated from a total of 208 was higher in response to physician notification of pathogen susceptibility information than in response to pathogen identification alone at 33.2% and 22.6% respectively. Overall, empiric antibiotics were not altered in response to PBC results in the majority of cases within 24 hours of physician notification. Of 208 cases explored, 70.7% and 58.6% were not altered upon PBC pathogen ID and sensitivities respectively. However, when considering the complete case from empiric antibiotics to within 24 hours of susceptibility information, 49.5% of cases were de-escalated and only 41.4% of cases had no net change in antibiotic spectrum score. Due to empirically broad antibiotics, the magnitude of de-escalations were notably larger than escalations of the coverage spectrum. The time to de-escalation of antibiotic coverage was significantly shorter ($p = .049$) when doing so based on pathogen ID as opposed to sensitivity information at 7.95 hours and 10.36 hours respectively. The response time for the physicians at the VAMC is towards the fast end compared to literature and, when considering the entire progression of each case, the de-escalation rate of 49.5% is encouraging. These results are reflective of effective practice at the VAMC and are likely aided via daily Infectious Disease staff oversight of antibiotic administration.

Research Topic: Health Care
Funding agencies: N/A
Grant support: N/A

60. A Walk Through the Dark: Pharmacogenetic Activation of Orexin Neurons in Active Night Mice

Jones, Michaela [1,2]; Bunney, Patricia [1,2]; Grace, Martha [1]; Kotz, Catherine [1,2]

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

Abstract: Overweight and obesity are defined as imbalances in energy input and energy output. Spontaneous physical activity (SPA), is non-goal directed activity, which produces non-exercise activity thermogenesis. Orexin neurons, located in the lateral hypothalamus (LH), are excitatory neuropeptides that impact multiple physiological processes including SPA. Previous studies showed that stimulation of orexin neurons increases SPA in mice during the light cycle, when these neurons are less active. While these data suggest that orexin neurons are potential therapeutic targets to counteract obesity, it is imperative to verify that targeting orexin neurons during the active (dark) cycle in mice also works to enhance SPA, since therapies for humans would need to be for use during daytime, active hours. To determine the extent to which orexin neuron activation stimulates SPA during the mouses' subjective day, we used the chemogenetic Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) approach to activate orexin neurons via peripheral (i.p.) injections of clozapine-n-oxide (CNO), either immediately preceding or 6 h after onset of the dark cycle. Hypothesis: We hypothesized that chemogenetic activation of orexin neurons will increase SPA immediately preceding and 6 h after onset of the dark cycle. Methods: Male and female orexin-Cre+/- mice (6-8 months old) were injected with a Cre-dependent AAV vector, containing the DREADD construct. Following acclimation to chambers and saline injections, mice were injected with CNO (0.25-5 mg/kg) every 48 h. Data were analyzed 2, 4, 6 and 24 h post injection. Results: DREADD-induced activation of orexin neurons robustly induced SPA. When CNO was injected immediately preceding the dark cycle, males and females exhibited an increase in SPA at 2, 4 and 6 h following injections of 1, 3, and 5mg/kg CNO ($p < 0.001$). When CNO was injected 6 hours into the dark cycle, SPA was significantly increased in females following 0.25 and 0.75mg/kg CNO at 2 h and with 1, 3 and 5mg/kg CNO at 2, 4 and 6 h post injection ($p < 0.001$). For males, there was also an increase in SPA following 0.25, 0.75, 1, 3 and 5mg/kg CNO at 2, 4 and 6 h post injections ($p < 0.001$). Conclusion: These results indicate that orexin activation significantly increases SPA in both males and females during their normal waking hours. Together, these data provide a first step in development of SPA-based therapies for obesity.

Research Topic: Obesity
Funding agencies: RR&D; NIH
Grant support: I01RX000441 (CMK), R01DK100281, and 5R01DK10

61. Diagnosis and Management of Osteomyelitis Associated with Stage IV Pressure Ulcers: Report of a Query to the Emerging Infections Network of the Infectious Diseases Society of America

Kaka, Anjum [1,2]; Beekman, Susan [2]; Gravely, Amy [1]; Polgreen, Philip [3]; Johnson, James [1,2]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Carver College of Medicine

Abstract: Despite the high prevalence of stage IV pressure ulcers, their effects on quality of life, and economic considerations for treatment there is a dearth of clinical studies to guide diagnosis and treatment of osteomyelitis in such patients. METHODS From 10 Jul to 07 Aug 2018, the Emerging Infections Network (EIN) conducted an electronic survey of adult infectious diseases physicians to determine their approach to managing such patients. RESULTS The overall response rate was 42% (558/1,332). 94/558 (17%) of the respondents had not seen such patients in the last year and opted out. Of the remaining 464 respondents, 276 (60%) usually felt confident in diagnosing osteomyelitis by physical exam, and lab or imaging results, with palpable or visible bone at the ulcer base felt to be strongly indicative of osteomyelitis. The approach to diagnosing osteomyelitis in patients with visible and palpable bone varied; 41% would assume osteomyelitis was present, 27% would trial local wound care and pressure-offloading first, 22% would pursue laboratory and imaging tests immediately, and 10% would follow another strategy. The top tests preferred when assessing for osteomyelitis were bone biopsy for culture, followed by MRI and bone biopsy for histopathology. Respondents disagreed widely regarding their favored route of antimicrobial therapy (all intravenous, partly intravenous and partly oral, or all oral) regardless of the presumed pathogen, as well as their preferred duration of antimicrobial therapy for such patients. The preferred duration of antimicrobial therapy was longer in patients who did not undergo full surgical debridement as compared to patients who did ($P < 0.001$ overall). Overall, 62% of respondents believed that osteomyelitis under stage IV pressure ulcers was usually or almost always treated with excessive antibiotics. Most respondents (59%) had suggestions for future research (average 1.6 comment/respondent), with the most common topics relating to antimicrobial durations and when to attempt antimicrobial treatment. CONCLUSIONS Physicians exhibited significant variability in in all areas of diagnosing and treating pressure-ulcer associated osteomyelitis and had concerns about excessive antibiotic use. Respondents also had multiple clinical questions which are unanswered by research to-date, and support the need for prospective trials in this field.

Research Topic: Infectious Diseases
Funding agencies: N/A
Grant support: VA Research

62. Decreased Activation in Temporoparietal Junction in Individuals with Psychotic Disorders and Biological First-degree Relatives during Implicit Theory of Mind

Kent, Jerillyn [1]; Burton, Philip [1]; Ramsay, Ian [1]; Sponheim, Scott [1,2]

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

Abstract: Individuals with schizophrenia are known to have deficits in social cognition, including theory of mind (ToM). Impaired ToM has also been reported in first degree biological relatives of individuals with schizophrenia. However, there have been only a few investigations into the neural correlates of ToM dysfunction in relatives of individuals with schizophrenia. The current study examined neural activity in individuals with psychotic disorders and first-degree biological relatives during implicit ToM, a more automatic and less cognitively demanding component of this social cognitive process. Participants were 50 individuals with a psychotic disorder, 21 biological first-degree relatives, and 29 controls. Participants underwent fMRI while completing an implicit ToM task, where 20 s animations were shown depicting two triangles, with the movement of the triangles corresponding to one of three conditions. In the Social condition, the triangles appeared to be interacting with each other and taking each other's thoughts and feelings into account. In the Physical condition, the movement of the triangles appeared related (i.e., mirror movement), but the shapes did not appear to be having a social interaction. In the Unrelated condition, the shapes' movement was not related to each other. There were 6 animations presented for each condition across 3 runs; after viewing each video clip participants selected which type of interaction they believed was going on. fMRI data were analyzed using a canonical preprocessing pipeline in FSL, and first-level GLM analyses modeled neural activity that corresponded to viewing the different types of animations. For the Social - Physical contrast, there was significantly greater activation in controls compared to both individuals with psychotic disorders and relatives in the right temporoparietal junction (TPJ). There were no significant differences in activation between individuals with psychotic disorders and relatives. TPJ is involved in ToM, and abnormalities in TPJ activity have been reported in individuals with schizophrenia during ToM. Therefore, these results are consistent with previous literature, and the use of an implicit ToM task reduces the concern of confounds related to cognitive deficits. Findings of decreased TPJ activation during implicit ToM in relatives suggests that abnormal neural activity during ToM may be associated with unexpressed genetic liability for psychosis.

Research Topic: Psychiatry
Funding agencies: NIH
Grant support: U01MH108150, NIMH; F32MH112334, NIMH

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63. Pramoxine: An Under-Recognized Cause of Allergic Contact Dermatitis

Kimyon, Rebecca [1-3]; Hylwa, Sara [2,4]; Warshaw, Erin [1-3]

1. Minneapolis VA Health Care System
2. Park Nicollet
3. University of Minnesota
4. Hennepin County Medical Center

Abstract: Pramoxine is an analgesic found in many topical medications. While allergy to lidocaine and benzocaine are well-known, allergy to pramoxine is less commonly recognized. Objective: To describe recent cases of allergy to pramoxine. Methods: We reviewed records of 8 individuals with relevant reactions to pramoxine. Results: Cases were comprised of 5 women and 3 men (aged 29-73) with positive reactions to purified pramoxine hydrochloride 2% pet. 7 patients had strong reactions (++/+++), while 1 had a mild reaction (+). 6 pramoxine-containing products were also tested eliciting significant reactions (+/++). Clinical relevance was 'current' in 6 patients who were using one or more products containing pramoxine. In these patients' personal products, pramoxine was declared in triple antibiotic ointment (n = 3), topical anti-itch lotions (n = 4), hemorrhoid cream (n = 2) and hemorrhoid wipes (n = 1). Past relevance was noted for 2 patients who had likely previously used triple antibiotic ointment suspected to contain pramoxine. Discussion: These cases illustrate contact allergy to an under-appreciated allergen which is present in a variety of over-the-counter, commonly used topical medications. This case series highlights the importance of testing to this emerging allergen.

Research Topic: Autoimmune, Allergic & Hematopoietic Disorders
Funding agencies: N/A
Grant support: N/A

64. Illegal Itch Relief: Prescription-Strength Topical Corticosteroids (TCs) Sold Over-the-Counter in US Stores

Kimyon, Rebecca [1-3]; Schlarbaum, Jamie [1-3]; Liou, Yuijie [1,2]; Adler, Brandon [4]; Comstock, Jeanette [5]; Handfield, Chelsea [6]; Kopelman, Hannah; Patel, Vidhi [7]; Raffi, Jodi [8]; Kimyon, Dawson

1. Minneapolis VA Health Care System
2. Park Nicollet
3. University of Minnesota
4. Keck School of Medicine
5. University of Wisconsin
6. Duke University
7. Northwestern University
8. University of California Irvine

Abstract: TCs are a foundational treatment for inflammatory skin disorders. Hydrocortisone less than or equal to 1.0% is the only FDA-approved over-the-counter TC in the US; unmonitored use of TCs may lead to adverse effects. While there has been a report of a US store specializing in African merchandise selling a prescription-strength TC (PSTC) without a prescription, the scope of availability has not been explored. Objective: To evaluate the over-the-counter availability of PSTCs. Methods: 22 stores selling foreign wares including pharmaceuticals were visited in 8 US states. Store personnel were asked if they sold topicals for the treatment of an 'itchy rash' or 'skin lightening.' Products were then examined and tabulated. The online availability of each product was evaluated via a Google search. Results: 15/22 stores sold PSTCs without a prescription. 51 different PSTCs were found. Specific steroids found included clobetasol propionate 0.025-0.06%, betamethasone dipropionate 0.025%, betamethasone valerate 0.002%-0.1%, fluocinonide acetonide 0.025%, fluocinolone 0.05%, and dexamethasone acetate 0.025%. 27/51 PSTCs were also available for purchase online (via eBay, e-commerce beauty product websites). 31/51 were marketed to treat rash; 20 were skin lightening creams. The average cost of clobetasol propionate 0.05% in stores was $0.21/g ($6.30 for 30g). Most of the PSTCs were not expired (1 to 39 months until expiration). Conclusions: Clinicians should be cognizant that patients can obtain potent PSTCs with relative ease. These findings underscore the importance of physically examining patients' over-the-counter products. An ongoing search in cities throughout the US is underway to better characterize this problem.

Research Topic: Autoimmune, Allergic & Hematopoietic Disorders
Funding agencies: N/A
Grant support: N/A

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65. Anogenital Dermatitis in Patients Referred for Patch Testing

Kimyon, Rebecca [1-3]; Warshaw, Erin [1-3]

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

Abstract: To characterize patients with anogenital dermatitis referred for patch testing and identify implicated allergens. Methods: Retrospective, cross-sectional analysis of North American Contact Dermatitis Group (NACDG) database, 2005-2016. Results: Of the 28,481 patients tested, the anogenital area was coded as the only site involved in 449 (1.78%) (AG, anogenital only patients). Of AG, 227 (50.6% of group 1) had at least 1 positive reaction of current clinical relevance; 211 (46.99%) had allergic contact dermatitis (ACD) as one of up to three final diagnoses; 152 (33.85%) had ACD as the only diagnosis. Anogenital involvement was significantly associated with male sex ($P = 0.0009$; RR 1.37; 95%CI 1.14-1.66) and negatively associated with atopy ($P < 0.012$; RR 0.77, 95%CI 0.63- 0.94). Of AG, 227 (50.56%) had > 1 currently relevant allergen. The 10 most common were methylisothiazolinone, balsam of Peru, fragrance mix I, methylisothiazolinone/ methylchloroisothiazolinone, nickel sulfate, fragrance mix II, iodopropynyl butylcarbamate, quaternium-15, dibucaine, and neomycin sulfate. Allergens that were significantly more frequent in AG included methylisothiazolinone methylchloroisothiazolinone, dibucaine, benzocaine, triamcinolone acetonide, budesonide, lidocaine, and desoximetasone (< 0.04 for all). Common sources of relevant allergens included cosmetics, food products, wipes, steroids, unknown sources, and pain relief/analgesics/antipruitics. Conclusions: Approximately half of AGOP referred for patch testing had ACD and approximately half had at least 1 positive reaction of current clinical relevance. Specific allergens found in products which contact the anogenital area were more common in patients with anogenital dermatitis.

Research Topic: Autoimmune, Allergic & Hematopoietic Disorders
Funding agencies: N/A
Grant support: N/A

66. Deviant Perception Captured by the Sensory Gating Inventory (SGI) is Related to Deficits in Early Visual Neural Functions in Individuals with Genetic Liability for Psychosis

Klein, Samuel [1]; Longenecker, Julia [1]; Pokorny, Victor [2]; Teich, Collin [2]; Stamos, Joshua [1]; Sponheim, Scott [1,2]

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

Abstract: Perceptual anomalies have been well documented in schizophrenia, with evidence suggesting they may be associated with genetic liability for psychosis. The present investigation explored how self-reported aberrant perception captured by the Sensory Gating Inventory (SGI) was related to perceptual sensitivity (d') and neurophysiological response to targets on the Degraded Stimulus Continual Performance Test (DS-CPT) in patients with schizophrenia and their first-degree biological relatives. Patients with schizophrenia, bipolar disorder, first-degree relatives of both patient types and non-psychiatric controls were recruited from the Minneapolis VA. Participants completed the SGI and underwent structured clinical interviews. EEG was collected using 64 or 128 channel systems during the DS-CPT. Hierarchical linear regression analyses showed that d' on the DS-CPT predicted reduced N1 amplitudes at occipital sites in relatives, moderated by the Perceptual Modulation (PM) factor on the SGI ($F = 10.64$, $p < .01$). PM predicted the severity of positive symptoms in patients ($r = .44$, $p < .05$), and both d' and positive symptom severity predicted reduced P3b amplitudes at CPz ($F = 8.715$, $p < .01$). The interaction between PM and heightened perceptual sensitivity to targets on a psychophysical task is related to early neural responses during visual processing in relatives. This same index of aberrant perception is associated with greater severity of positive symptoms in patients, which coupled with perceptual sensitivity on the DS-CPT, predicts deficits in late neural responses related to context updating. Thus, self-reported aberrant perception captured by the SGI is related to early visual neural functions in individuals with genetic liability for psychosis.

Research Topic: Mental Illness
Funding agencies: CSR&D
Grant support: I01CX000227

67. 'I'm Adventuring More': Exploring the meaning of Cognitive Behavioral Therapy for Insomnia (CBT-I) for patients with pain

Koffel, Erin [1]; Wisdom, Jennifer [2]

1. Minneapolis VA Health Care System
2. City University of New York

Abstract: Insomnia is a common, persistent, and distressing symptom associated with chronic pain. Cognitive behavioral therapy for insomnia (CBT-I) is the first-line treatment for insomnia, but patient preferences and perspectives about CBT-I within the context of chronic pain are unknown. The current qualitative study sought to understand the experience of CBT-I among patients with chronic pain. We conducted individual semi-structured interviews with 17 Veterans with chronic pain and insomnia who had recently participated in CBT-I, as well as their CBT-I therapists. Thematic analysis was used to identify conceptual themes. Findings of improved sleep and functional outcomes support efforts to incorporate CBT-I into chronic pain treatment, including educating patients and providers about the strong feasibility of improving sleep and quality of life despite ongoing pain.

Research Topic: Mental Illness
Funding agencies: HSR&D
Grant support: CDA 15-063

68. Pain, function, and quality of life in long-term opioid therapy: a national survey of VA primary care patients

Krebs, Erin [1,2]; Clothier, Barb [1]; Nugent, Sean [1]; Jensen, Agnes [1]; Martinson, Brian [1,3]; Goldsmith, Elizabeth [1,2]; Rutks, Indulis [1]; Noorbaloochi, Siamak [1,2]

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

Abstract: The Effects of Prescription Opioid Changes for Veterans (EPOCH) study is a national prospective cohort study of VA patients prescribed long-term opioid therapy (LTOT). This report describes participant characteristics and associations of opioid prescription factors with pain-related function and quality of life outcomes. METHODS: Eligibility criteria included receipt of prescribed opioid analgesics for = 6 months (defined as = 150 days' supply in 180 days, with no gaps > 40 days). Patients with dementia, nursing home residence, or treatment for opioid addiction, cancer, or palliative care were excluded. The sampling frame was patients and their primary care providers from all VA facilities, restricted to providers with panels of =500 patients and =4 eligible patients. The two-stage stratified sampling design incorporated a random sample of providers selected from each facility. Patients who were randomly selected from each selected provider's panel were mailed a questionnaire and up to 3 reminders. Non-responders were offered a telephone interview. Patients who completed a questionnaire were enrolled. Primary outcome measures were Brief Pain Inventory-Interference (BPI-I) and Veterans RAND 12-item Health Survey (VR-12). Morphine-equivalent opioid daily dosage was categorized as low (<20 mg), moderate (20-49 mg), high (50-99 mg), or very high (=100 mg). RESULTS: 9,253 patients (65.3% of 14,160 invited) who completed a questionnaire or interview were included. Participants were 6.9% female, mean 63.8 years old, and had a mean pain intensity rating of 6.8. Mean opioid daily dose was 50.6 mg. Effectiveness of pain treatment was rated very good-excellent by 12.3%; quality of pain care was rated very good-excellent by 25.0%. More patients endorsed desire for a higher opioid dose (33.9%) than desire to stop or cut down on opioids (14.6%). Higher daily doses were associated with significantly worse BPI-I (mean 6.1, 6.5, 6.7, and 7.0 for low, moderate, high, and very high dose categories, respectively; $p < 0.001$) and worse VR-12 physical and mental health. Receipt of long-acting opioids was also associated with worse BPI-I and VR-12 scores. CONCLUSION: VA patients on LTOT had poorly controlled pain, overall. Higher opioid dosages and receipt of long-acting opioids were significantly associated with worse pain-related function and health-related quality of life, although differences were small.

Research Topic: Pain
Funding agencies: HSR&D
Grant support: VA HSR&D IIR #14-295

69. Substance P Expression in the DRG of Three Murine Models of Arthritis Pain: Correlation with Pain Measures and Effect of Local Neurotoxin Analgesia

Krug, Hollis [1,2]; Blanshan, Nicole [1]; Dorman, Christopher [1]; Frizelle, Sandra [1]

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

Abstract: Substance P (SP) release and binding to NK-1 produces pain transmission. Pain from arthritis is expressed as both tenderness and as loss of function. Different arthritis pain models express pain differently. This study evaluated the relationship of dorsal root ganglion (DRG) SP expression to pain using both measures of tenderness and function in 3 different models of arthritis pain. Neurotoxins (NT) that prevent release of SP, such as onabotulinum toxin (BoNT/A), and those that deplete SP, such as vanilloids (VAN), can produce analgesia in these models. We correlated effects on SP expression in the DRG with analgesic responses. Methods: C57/Bl6 male mice received intra-articular (IA) carrageenan, Complete Freund's Adjuvant (CFA) or Collagenase (COL) to produce acute inflammatory, chronic inflammatory or chronic noninflammatory arthritis respectively. IA therapies were given at appropriate intervals before examination. Twelve-week-old mice were examined after arthritis induction. Evoked (tenderness) and spontaneous (functional) pain was quantitated. DRGs were harvested for immunohistochemistry (IHC) after pain assessment. SP expression was measured as % DRG neurons expressing SP. Results: Both Evoked and Spontaneous pain in arthritic and naïve mice correlated with SP expression ($R2 = 0.981$, $\beta=1.678$ and $R2 = 0.724$, $\beta=0.653$ respectively). IA vanilloid agonists and antagonist reduced SP expression in chronic inflammatory arthritis (CFA) but did not improve pain behavior. IA BoNT/A reduced SP expression in CFA arthritis but significantly increased SP expression in COL arthritis at 4 weeks after induction but not at 6 weeks. Vanilloid (VAN) treatment normalized evoked pain and weightbearing in mice with acute arthritis pain but did not change SP expression in the DRG. None of the neurotoxins altered pain expression or SP expression in non-arthritic mice. Conclusions: SP expression correlates with both evoked and spontaneous pain behaviors in murine models of arthritis pain. Depending on the NT mechanism of action, SP expression may either increase (BoNT/A) or decrease (VAN). The effect of NT on SP expression may also depend on pathophysiology of pain production and chronicity. SP expression does not necessarily correlate with NT-induced analgesia.

Research Topic: Pain
Funding agencies: RR&D
Grant support: 160402

70. Depression screening and mental health in dialysis patients at the Minneapolis VA dialysis unit

Kuzmenko, Yekaterina [1]; Slinin, Yelena [1]; Reule, Scott [1]

1. Minneapolis VA Health Care System

Abstract: Depression is the most common psychiatric illness in patients with end-stage renal disease. The reported prevalence of depression in dialysis population varied from 22.8% (interview-based diagnosis) to 39.3% (self- or clinician-administered rating scales). Systemic review and meta-analysis of observational studies showed that depression was a significant predictor of mortality in dialysis population. Although the best methods for depression screening remain controversial, recent research has validated cutoff values for some of the more common depression screening questionnaires for evaluation in ESRD hemodialysis patients. There are limited data regarding the treatment of depression in ESRD patients. This abstract presents the data of our baseline assessment of the prevalence of depression in patients with end-stage renal disease at the Minneapolis VA dialysis unit. Methods: Study Cohort: chronic dialysis patients who attended dialysis unit in the end of February and beginning of March of 2018. Site: VA dialysis unit, Minneapolis, Minnesota. Methodology: Cross sectional, clinician-administered rating scales Patient Health Questionnaire (PHQ)-9. Manual review of medical records. Data recorded: demography, Status (outpatient/inpatient), previous history of depression, antidepressant medications, Non pharmacological treatment, established care with mental health provider, depression score by using PHQ-9. Statistical analysis: Chi-squared analyses was used to compare variables and logistic regression for odds ratio (OR) calculations. Results: A total of 50 patients were screen for depression. Discussion: Diagnosis and management of depression in dialysis patients are challenging. The use of clinician-administered rate scales may lead to over-diagnosis due to overlapping symptoms of depression and uremia. The dialysis team should take the lead to identify high-risk patients and promptly refer them to psychiatrist for formal assessment, i.e. an active patient-centered approach. Nephrologist should work closely with psychiatrists to provide regular counselling and review of patients in order to individualize treatment and optimize clinical outcomes. Conclusion: Depression is common in patients with ESRD on dialysis at Minneapolis VA dialysis unit. Patients who were on antipsychotic medications and receiving non-pharmacological treatment of depression, and followed by mental health provider had greater odds of depression.

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

71. INfluenza Vaccine to Effectively Stop Cardio Thoracic Events and Decompensated heart failure (INVESTED)

Lalani, Narlina [1]; Kosik, Nicole [2]; Lecky, Vanessa [2]; Santos, Abigail [2]; Joseph, Jacob [2]; Vardeny, Orly [1]

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

Abstract: Influenza leads to significant morbidity and mortality, particularly in patients with cardiovascular disease. Studies have suggested influenza vaccine might attenuate cardiac risk in higher risk populations. In older adults, a higher vaccine dose has been shown to elicit more pronounced protective antibody titer production and lower influenza infection rates compared to standard dose. However, influenza vaccine is widely underutilized in this population. Whether high dose vaccine portends protection from cardiovascular events in a high-risk cardiac population is unclear. INfluenza Vaccine to Effectively Stop Cardio Thoracic Events and Decompensated heart failure (INVESTED) is a multi-center, prospective, randomized double-blinded active-controlled trial of high dose trivalent influenza vaccine compared to standard dose quadrivalent in 8300 adults with high-risk cardiovascular disease. This trial has 172 sites across the United States and Canada. The primary objective is time to the occurrence of all-cause death or cardiopulmonary hospitalization within each influenza season. Secondary outcomes include total (first and recurrent) cardiopulmonary hospitalizations or death, time to first composite of cardiovascular death or cardiovascular hospitalization within each influenza season and time to first composite of death or cardiopulmonary hospitalizations across all enrolled seasons. Patients within 12 months of a myocardial infarction or 24 months of a hospitalization for heart failure will be randomized in a 1:1 fashion to receive one of the two vaccine formulations via permuted blocks of random block size, balanced by site, without stratification, except for the natural stratification by influenza season. This is a five-year trial and subjects may participate for up to three seasons. At the baseline visit, vaccine will be administered according to each participant's initial randomized strategy, medical history and current medications will be collected. Vaccine-related adverse events will be ascertained via phone calls one week after vaccination. Hospitalization and vital status will also be ascertained via phone during influenza season and the summer after vaccination. The INVESTED trial has 5,262 participants and will complete accrual in 2020. This study has the potential to inform health care policy regarding optimal vaccination strategy in patients at high risk for cardiovascular events, who are especially susceptible to influenza-related complications.

Research Topic: Cardiovascular Disease
Funding agencies: NIH
Grant support: National Heart, Lung and Blood Institute (NHLBI), Sanofi Pasteur

72. All of Us Research Program

Lapiro, Jessica [1]; Loew, Sarah [1]; McCarthy, Meaghan [2]; Klein, Mark [1,3]

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

Abstract: The All of Us Research Program is an ambitious effort to gather data (including clinical data and "panomics") from 1 million or more people living in the United States to accelerate research and improve health. The program will be open to people both healthy and sick, from all communities. Unlike a single research study focused on a specific disease or population, All of Us will serve as a national research resource to inform thousands of studies, covering a wide variety of health conditions that affect many different people. Participants will have opportunities over many years to provide data about themselves that will help researchers learn more about how individual differences in lifestyle, environment, and biological make-up can influence health and disease. By taking part, participants will contribute to an effort to advance the health of generations to come. Methods: To achieve the goal of creating a research cohort of 1 million or more U.S. participants, the NIH has engaged a number of organizations to establish the infrastructure of the All of Us. The key program components include a Data and Research Center, a Participant Technology Systems Center, Participant Center, a Biobank, and a number of Health Care Provider Organizations (HPO). The VA is a core HPO, and the Minneapolis VA Healthcare System is one of the first wave of VA sites to open for enrollment. NIH and VA have a goal to have approximately 100,000 Veterans enroll in the All of Us and MVP studies simultaneously for comparison. Enrollment Activities: Once a participant indicates interest, participants are scheduled for an appointment. At the study visit, participants learn about the program (including security regarding privacy), provide consent electronically, answer surveys electronically, and have 8 tubes of blood plus one urine sample obtained. Samples are sent to the Biobank (run by Mayo Medical Laboratories). As of March 28, 2019, the All of Us Program has enrolled 126,744 total core participants nationally. Participants will eventually have their genomic testing reported individually in addition to the overall study activities. Conclusion: The All of Us Program will provide a national panomics resource and lay a scientific foundation for Precision Medicine.

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

73. Promoting Independent Aging in Veterans Through Unobtrusive In-Home Monitoring of Daily Activities: A Feasibility Study

Leese, Mira [1]; Bouranis, Nicole [2]; Beattie, Zachary [2]; Schleper, Kassandra [1]; Hooper, Isabel [1]; Sharma, Nicole [2]; Riley, Thomas [2]; Kaye, Jeffrey [2]; Ferguson, John [1]; Seelye, Adriana [1]

1. Minneapolis VA Health Care System
2. Oregon Center for Aging and Technology

Abstract: Aging Veterans are an important and growing population who are at an elevated risk for developing mild cognitive impairment (MCI) and Alzheimer's dementia (AD), which emerge insidiously and progress gradually. Traditional clinic-based assessments are administered infrequently, making them less ideal to capture the earliest signals of cognitive decline in older adults. The Promote Independent Aging (PRIA) study is a VA Clinical Science Research and Development funded pilot project that will be exploring innovative real-world assessment approaches to reliably capture the earliest observable signals of cognitive decline in Veterans. Specifically, PRIA will gather information about how in-home and mobile technologies can be used to identify and monitor meaningful changes in instrumental activities of daily living (IADLs) that are affected in MCI, such as computer use, medication taking, physical activity and sleep. PRIA uses passive and unobtrusive technologies like a digital watch, home computer and an electronic pillbox to collect continuous (daily) data in real-time to monitor and learn more about how these daily activities relate to cognition in older adults. Currently, 30 veterans are enrolled at the Minneapolis VA for 1 year. Participants are 65 years of age or older, live independently in their homes, use a computer at least one time per week and take at least one daily medication. Knowledge gained from this pilot study will be used to help develop acceptable and effective home-based assessment tools that can be used to identify and monitor daily functioning in healthy and MCI older adults earlier than would be possible with infrequent episodic clinic visits to a physician's office, allowing for earlier intervention. Preliminary data and future directions will be discussed.

Research Topic: Aging
Funding agencies: CSR&D
Grant support: CX001669

74. Formaldehyde Release from Baby Wipes: Analysis using the Chromotropic Acid Method

Liou, Yujie [1,2]; Ericson, Marna [3]; Warshaw, Erin [1-3]

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

Abstract: Formaldehyde is a common preservative and strong sensitizer. Study Aim: To evaluate the presence of formaldehyde in baby/toddler wipes using the chromotropic acid method (CAM). Methodology: An online search of best-selling baby wipes was conducted. Fifty-one baby/toddler wipes were purchased which did not declare formaldehyde or formaldehyde releasing preservatives. Standard, CAM procedures were utilized: a 1x1 inch square of fresh wipe placed in bottle with an open vial of 4mg/1mL chromotropic acid and sulfuric acid solution, sealed, and stored for 48 hours. Formalin and water served as controls. A blinded investigator graded color change (negative, indeterminant, mild, moderate, and strong). For quality control, all positive samples were repeated and 20% of all samples were retested in a systematic manner. Results: CAM testing showed formaldehyde release from 12 (24%) of wipes (8 mild, 4 moderate/strong). Thirty (59%) were negative and 9 (18%) had indeterminant test results. Conclusion: Almost one-quarter of 'formaldehyde-free' baby/toddler wipes released formaldehyde when evaluated with CAM. Patients and clinicians should be aware of this potential source of formaldehyde.

Research Topic: Autoimmune, Allergic & Hematopoietic Disorders
Funding agencies: CVRE
Grant support: N/A

75. Allergenic Ingredients in Tattoo Aftercare Products

Liou, Yujie [1,2]; Liszewski, Walter [3]; Schlarbaum, Jamie [1-3]; Warshaw, Erin [1-3]

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

Abstract: Aftercare of a new tattoo is essential to ensure proper healing and achieve maximal cosmetic appearance. Common recommendations for aftercare are careful washing of the new tattoo and aftercare products used. Numerous products commercially available specifically designed for tattoo aftercare but information about these products are scarce. Method: In addition to the recommended emollients identified in a previous study, additional products were included after a search on Amazon using the phrase 'tattoo aftercare.' All products without a website or complete ingredient list were excluded. A survey of ingredients of each product was performed and ingredients were logged in Excel. A review of marking claims was also performed for each product. Analysis of product ingredients and comparison of ingredients to NACDG and ACDS core allergens are conducted using Excel. Results: Total of 84 tattoo aftercare products from 52 distinct brands were selected including lotions, cream, balms, and soaps. Forty-eight distinctive market claims are identified, the most common claim is regarding the use of 'natural ingredient(s).' Total of 369 distinct ingredients were listed. Products contain between 4 ingredients to 28 ingredients with average of 11.83 ± 5.5 ingredients per product. The products contain a range of 0 to 18 ACDS core allergens with average of 7.92 ± 3.87 allergens per products. Conclusion: Tattoo aftercare products are prevalently used to take care of a new tattoo; however, little is known about these products. This review of 84 products found that tattoo aftercare products contain on average of 8 ACDS 2017 core allergen list. Adverse reactions from tattoos have been increasing; allergic contact dermatitis to aftercare products used may be an important contributing factor.

Research Topic: Autoimmune, Allergic & Hematopoietic Disorders
Funding agencies: CVRE
Grant support: N/A

76. Piloting the ANNIE text messaging protocol to improve outpatient colonoscopy bowel preparation

Lou, Susan [1]; Aho, Hannah [2]; Groves, Stephen [2]; Wongboonsin, Janewit [2]; Zhang, Michael [2]; Song, Kevin [2]; Engebretson, Erik [2]; Kaczor, Jordan [2]; Obermeyer, Isaac [2]; Palaniappan, Vignesh [2]; Roberts, Stephen [2]; Danieli, Reut [1]; Shaukat, Aasma [1]

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

Abstract: Screening colonoscopy is effective in reducing morbidity and mortality associated with colorectal carcinoma. Inadequate bowel preparation leads to missed polyp/adenoma detections rates and increased resource utilization for repeat colonoscopies. Adequate bowel preparation detects all polyps >5mm in size or exposure of at least 90% of the mucosal surface, which correlates with a Boston Bowel Preparation Scale (BBPS) total score of 6 or greater. Several patient risk factors including age>60, single status, diabetes, and polypharmacy are associated with poorer bowel preparation, and are highly prevalent in the VA population. Identifying patients with greater risk factors and offering tools to facilitate the bowel preparation process has the potential to decrease healthcare costs and improve outcomes. ANNIE is a text messaging service developed for veterans, and allows for customizable text messages about their clinical care and has been used in management of hypertension and diabetes. The objective of our study was to study the effect of ANNIE messaging regarding bowel prep instructions on improvement in quality of bowel prep. Methods: We identified veterans scheduled to receive outpatient screening colonoscopies during the time period from 1/1/2019 through 3/31/2019 at the Minneapolis Veterans Affairs Medical Center. We enrolled interested veterans to receive a series of text reminders through the ANNIE software platform regarding key steps for their bowel preparation. Our primary outcome was improvement in the total Boston Bowel Preparation score in the ANNIE group compared to usual care, relative to baseline scores. Results: ANNIE text messaging intervention improved the bowel prep quality score (Mean 8.24 (1.27 SD) vs. usual care 7.89 (1.41 SD) ($p = 0.0021$). Preliminary survey data shows a very high patient satisfaction rate with the overwhelming majority of veterans indicating that they found the ANNIE text messaging service helpful and that they would like to utilize it again for future colonoscopies.

Research Topic: Gastroenterology
Funding agencies: N/A
Grant support: N/A

77. Distinctive Neurochemistry in Alzheimer's Disease via 7 T In Vivo Magnetic Resonance Spectroscopy

Marjanska, Malgorzata [1]; Crocker, Jillian [1]; McCarten, J. Riley [2]; Hemmy, Laura [2]; Terpstra, Melissa [1]

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

Abstract: This study's objective was to increase understanding of biological mechanisms underlying clinical Alzheimer's disease (AD) by noninvasively measuring an expanded neurochemical profile and exploring how well this advanced technology distinguishes AD from cognitively normal controls. We measured concentrations of 14 neurochemicals using ultra-high field (7 T) ultra-short echo time (8 ms) magnetic resonance spectroscopy (MRS) in 16 participants with mild to moderate clinical AD and 33 age- and gender-matched control participants. MRS was localized to the posterior cingulate cortex (PCC), a region known to be impacted by AD, and the occipital cortex (OCC), a control region. Participants with AD were recruited from dementia specialty clinics. Concentration of the antioxidant ascorbate was higher ($p. < .0.0007$) in both brain regions. Concentrations of the glial marker myo-inositol and the choline-containing compounds involved in membrane turnover were higher ($p = 0.0004$) in PCC of participants with AD. Ascorbate and myo-inositol concentrations were strongly associated, especially in the PCC. Random forests, using the 14 neurochemicals in the two regions, distinguished participants with AD from controls: same-sample sensitivity and specificity were 88% and 97%, respectively, though out-of-sample-values would be lower. Ultra-high field ultra-short echo time MRS identified the co-occurrence of elevated ascorbate and myo-inositol in the PCC as markers that distinguish participants with mild to moderate AD from controls. While elevated myo-inositol may be a surrogate marker of neuroinflammation, the unexpected elevation of the antioxidant ascorbate may reflect infiltration of ascorbate-rich leukocytes.

Research Topic: Alzheimer's Disease
Funding agencies: NIH
Grant support: NIH 1R01AG055591-01A1

78. N-back Performance with Trauma-Relevant Visual Distractors: Associations with Posttraumatic Stress Symptomatology

Marquardt, Craig [1]; Lissek, Shmuel [1]; Kang, Seung Suk [2]; Sponheim, Scott [3]

1. University of Minnesota
2. University of Missouri-Kansas City
3. Minneapolis VA Health Care System

Abstract: The attentional control theory (Eysenck et al., 2007) proposes that anxiety-related cognitive inefficiencies are the result of inefficient utilization of attentional resources. Anxiety is associated with greater perceptual engagement with task-irrelevant threat, which may require goal-directed attentional resources to inhibit and shift back towards primary task goals. As such, individuals with clinical anxiety should produce particularly slowed response times under high cognitive load when simultaneously managing unwanted automatic engagement with threat content. A cross-sectional sample of recently deployed military veterans with anxiety-related posttraumatic stress disorder (PTSD) symptoms were recruited (n = 128) to complete a sequential-letter N-back task (2- versus 0-back) superimposed over task-irrelevant neutral or aversive combat scenes. Participants produced slower responses under high cognitive and high affective loads, which were expected. However, the slowing effect of combat images was attenuated during the 2-back relative to the 0-back conditions. Furthermore, posttraumatic avoidance severity exhibited negative associations; individuals with greater maladaptive avoidance produced overall faster responses across all task conditions. Event-related potentials (ERPs) were also examined. Avoidance was related to larger early posterior negativities (EPNs) important for stimulus-driven attention, but was unrelated to P3b or late positive potential (LPP) waveforms relevant for high-level cognitive functioning. Thus, greater utilization of low-level perceptual attention appeared to narrow participants' focus onto the letter stimuli. Individuals with heightened posttraumatic avoidance symptomatology may have used this same attentional process to reduce interference from visual distractors. Theoretical revision may be necessary to reflect how motivated avoidance can increase cognitive efficiency in the context of potential threat.

Research Topic: Posttraumatic Stress Disorder (PTSD)
Funding agencies: RR&D
Grant support: NSF Graduate Research Fellowship Program (00039202); I01 RX000622

79. Intra-PVN orexin-A enhances physical activity and energy expenditure in orexin ataxin mice

Mavanji, Vijayakumar [1]; Grace, Martha [1]; Kotz, Catherine [1,2]

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

Abstract: The neuropeptide orexin (hypocretin) plays a key role in spontaneous physical activity (SPA), non-exercise thermogenesis (NEAT) and energy homeostasis. Earlier studies have shown that orexin A (OXA) injections into the paraventricular nucleus (PVN) of hypothalamus increases SPA and energy expenditure in a parallel and dose responsive manner in rats. The orexin ataxin (OA3) mice is a model of progressive neurodegeneration, in which the animals become deficient in orexin neurons by about 12 weeks of age. Our earlier studies have demonstrated normal orexin responsiveness to SPA in the OA3 mice, despite being OXA deficient. Here we tested the hypothesis that PVN injected OXA enhances SPA and energy expenditure in OA3 mice. To this end, we recorded SPA, EE body weight and food intake in female OA3 mice for 10 days, while the animals received daily injections of either orexin-A OXA (500 nmoles) or artificial cerebrospinal fluid (CSF) in the paraventricular nucleus (PVN) of the hypothalamus, via chronically implanted bilateral guide cannulae. Energy expenditure were measured using the Sable Promethion indirect calorimetry system. Food intake and body weight was also monitored throughout the injection period. At the conclusion of the experiments, mice were sacrificed and brains were processed for OXA immunostaining in the lateral hypothalamus (LH) area. We found that intra PVN OXA enhanced SPA and energy expenditure in OXA injected mice. However, intra-PVN OXA did not affect food intake in these animals. In addition, our immunohistochemistry revealed OXA neuron loss in aged animals. These results support the idea that OXA administration can result in negative energy balance through increasing physical activity, which might be of therapeutic potential for the treatment of weight gain.

Research Topic: Obesity
Funding agencies: BLR&D; NIH
Grant support: 1I01BX003004; 1I01BX003687; R01DK100281

80. Epidural Stimulation for Spinal Cord Injury

McCracken, Patricia [1]; Hoover, Caleb [1,2]; Ahmadi, Aliya [1,2]; Venkatesh, Shivani [2]; Goldish, Gary [1]; Darrow, David [3]; Samadani, Uzma [1,3]

1. Minneapolis VA Health Care System
2. Hennepin Healthcare Research Institute
3. University of Minnesota

Abstract: Spinal cord injury (SCI) is a devastating complication of trauma, with a prevalence of 273,000 patients in 2015. SCI can result in paraplegia or quadriplegia, carrying major, chronic medical complications and a significantly reduced quality of life and life-expectancy. A combination of immobility and autonomic dysregulation produces cardiovascular, respiratory, urinary, gastrointestinal complications in addition to complex pain syndromes, cognitive dysfunction and morbid pressure ulcers. These complications from SCI have serious effects on patients and their families. Secondary complications such as these contribute greatly to the high cost of this condition, which is estimated at $5.8 million over a lifespan. The epidural stimulator is a small device that creates a mild electrical current that travels along the paddle electrode in the spinal canal and has been used for over 50 years to treat back pain. Nearly a decade ago, eSCS was found to facilitate volitional movement in patients with SCI. The Epidural Stimulation for Spinal Cord Injury study (E-STAND) has been investigating the use of eSCS to facilitate volitional movement as measured by surface EMG through the Brain Motor Control Assessment (BMCA) in patients with chronic spinal cord injury and motor paraplegia since 2015. Autonomic function improvements with eSCS are measured with validated surveys over 13 monthly follow ups and tilt table assessments of cardiovascular and cognitive function. E-STAND uses personalized patient data to map the parameter space of epidural stimulation to create a Clinical Decision Support system for patient programming. E-STAND has enrolled 9 subjects (3 women, 6 men; 26-58 years old; and 3-17 years post SCI) at the VA Health Care System and the Hennepin Healthcare. Outcome measures tracked include: volitional movement, blood pressure, cerebral blood flow, arterial stiffness, cognitive assessments, bowel function, bladder function, sexual function, psychological health, pain, sleep, overall quality of life, sitting bicycle exercise, and spasticity. Two subjects have completed the E-STAND protocol and early data on these subjects has been published. Preliminary outcomes (N = 2) have reported partially restored volitional control of lower extremities, correction of orthostatic hypotension and cognitive function during tilt table assessments, and improvements in bowel and bladder function for patients with chronic neurologically complete spinal cord injury.

Research Topic: Spinal Cord Injury
Funding agencies: CVRE
Grant support: State of Minnesota, Office of Higher Education

81. walk2Wellness Clinical Trial

McCracken, Patricia [1]; Santa Ana, Christine [1]; Danzl, Lori [1]; Olney, Christine [1]; Oddsson, Lars [2-4]; Koehler-McNicholas, Sara [1]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. RxFunction Inc.
4. Ben-Gurion University, Israel

Abstract: Patients who lose plantar sensation from sensory peripheral neuropathy commonly experience problems with gait and balance that can increase risk of falls. The walk2Wellness clinical trial (clinicaltrials.gov, NCT #03538756) is testing a new wearable device indicated for these patients to help improve gait and balance function. The device, Walkasins® (RxFunction Inc., MN, USA), provides gentle directional tactile cues around the lower leg during standing and walking, reflecting changes in foot pressure distribution measured with an instrumented foot pad in the shoe. Patients react to these new sensory cues and incorporate them to improve gait and balance. The walk2Wellness trial investigates long-term, chronic-use effects (52 weeks) on clinical and patient-reported outcomes of balance and gait function, quality of life, physical activity/participation, and pain. The study will enroll up to 150 patients across six sites 2018-2020. Clinical outcomes include Functional Gait Assessment (FGA), Gait Speed, Timed Up & Go (TUG), 4-Stage Balance Test (4STB), Vestibular Activities of Daily Living (VADL), Activities-Specific Balance Confidence (ABC), and several PROMIS scores. Fall-rates are monitored and compared to pre-study data. To be included in the study, baseline FGA scores will be limited to <23, the cut-off for fall-risk in community dwelling elderly individuals, and performed without the use of an assistive device as an indication of sufficient motor function to act on new sensory information from the device. As of February 2019, 20 subjects (15 Male, 5 Female) have been enrolled across three sites, (average baseline scores: FGA 14.4, Gait Speed 0.80m/s, TUG 14.9s, 4STB 26.3s, ABC 61%). Six-month pre-study fall-rate was 8.3 falls/1000 patient days (11 of were 20 fallers). Seven during-study falls have occurred to date (4 slips on snow & ice, 2 slips in bathroom, 1 trip on fence line). Two falls occurred while wearing the device.

Research Topic: Prosthetics
Funding agencies: CVRE
Grant support: RxFunction Inc.

82. Identity Disruption among Veterans with Reintegration Difficulty

Mitchell, Lauren [1]; Sayer, Nina [1]

1. Minneapolis VA Health Care System

Abstract: Most research and theory on identity integration focuses on adolescents and young adults under age 30, and relatively little is known about how identity adjusts to changes later in life. The purpose of the present study was to operationalize and investigate identity disruption, or a major change in one's sense of self associated with life events, a construct relevant to identity development in adulthood. We used a mixed-methods approach to examine identity disruption among 244 Afghanistan and Iraq war veterans with reintegration difficulty who participated in an expressive writing intervention. Participants completed measures of social support, post-traumatic stress disorder (PTSD) symptom severity, satisfaction with life, and reintegration difficulty at baseline, 3 and 6 months postintervention. The expressive writing samples were coded for identity disruption. We hypothesized that identity disruption would be associated with lower social support, more severe PTSD symptoms, lower satisfaction with life, and greater reintegration difficulty at baseline. Forty-nine percent (n = 121) of the sample had at least one writing sample that was coded with an identity disruption theme. Identity disruption was associated with more severe PTSD symptoms, lower satisfaction with life, and greater reintegration difficulty at baseline, and with less improvement in social support. Identity disruption also provided incremental validity over combat exposure in predicting social support, PTSD symptoms, satisfaction with life, and reintegration difficulty. The findings suggest that identity disruption is a meaningful construct for extending the study of identity development to adult populations, and for understanding veterans' adjustment to civilian life.

Research Topic: Mental Health
Funding agencies: HSR&D; DOD; UMN
Grant support: U.S. DoD (Grant 08-2-0045), HSR&D DHI-07-150, UMN Doctoral Dissertation Fellowship

83. The Relationship Between Symptom & Performance Validity in a Veteran Sample

Morgan, Brittni [1]; Lamberty, Gregory [1]; Finn, Jacob [1]

1. Minneapolis VA Health Care System

Abstract: In neuropsychological assessment, it is widely accepted that clinicians assess the validity of performance (Heilbronner et al., 2009). Historically, symptom validity was the term used to refer to the accuracy of an examinee's self-reported symptoms and/or performance on neuropsychological measures (Bush et al., 2005). More recently, Larrabee (2012) recommended that the terms 'performance validity test' (PVT) and 'symptom validity test' (SVT) be adopted to clarify the relationship between cognitive performance measures and symptom self-report measures. Research examining the relationship between PVT and SVT performances has been limited, particularly as it relates to embedded PVT measures, and conflicting findings are likely reflective of sample characteristics (e.g., mTBI evaluation, compensation seeking). As such, the current study sought to examine the relationship between select PVT and symptom validity indicators on the Minnesota Multiphasic Personality Inventory-2-Restructured Form (MMPI-2-RF) in a general outpatient veteran sample. This study used archival data from 236 veterans (mean age 48.65, 88.1% White, mean education 13.75 years) who were referred for a neuropsychological evaluation and completed select PVTs (CVLT-II Forced Choice, Reliable Digit Span, and TOMM) and the MMPI-2-RF as part of their evaluation. Participants were classified as either probable symptom exaggeration if MMPI-2-RF validity scale T scores were above established cutoffs (N = 24), or no symptom exaggeration if performances were below established cutoffs (N = 212). Participants were classified as invalid PVT performers if scores on one or more PVTs were above pre-established cut-offs (N = 77) or valid PVT performers if all PVTs were below pre-established cut-offs (N = 159). Overall, we did not find significant group differences between individuals with valid and invalid MMPI-2-RF profiles on PVT group classification, $X2$ (1, N = 236) = 2.27, p = .13. We also did not find group differences between individuals with valid and invalid MMPI-2-RF profiles on any of the PVTs. When individuals were classified as either valid or invalid PVT, significant group differences emerged on RC2 (p = .04) and GIC (p = .05). Consistent with previous findings, results of the present study largely suggest that PVTs and SVTs each provide useful clinical information in neuropsychological evaluations but are not interchangeable, particularly in a general veteran sample.

Research Topic: Neuropsychology
Funding agencies: N/A
Grant support: N/A

84. Million Veteran Program (MVP): A Partnership with Veterans

Murdoch, Maureen [1,2]; Vang, Derek [1]; Eret, Donyal [1]; Condon, Debra [1]; Kantorowicz, Alexandra [1]

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

Abstract: The goal is to improve Veterans' health through the collection and testing of blood samples and health information to learn which genes are linked to which health characteristics. MVP is a national, voluntary research program conducted by the Department of Veterans Affairs, Office of Research & Development, that collects genetic and health information to help find new ways of prevention, early detection, and treatment of illnesses. MVP will provide a better understanding of how genes affect health and illness, with the goal of improving health care for Veterans. Genomic analyses, including SNP genotyping, whole genome sequencing, and whole exome sequencing is being conducted on MVP samples. Nationally, 661,076 Veterans have enrolled at 55 VAs with 15,646 at the MVAHCS as of 4-16-18. Methods: Participation involves: 1. Filling out two surveys through the mail 2. Completing a one-time, approximately 20 minute, study visit to provide a blood sample for the genetic testing 3. Permitting authorized MVP staff to access information in your medical record on an ongoing basis 4. Agreeing to future MVP contact Next Steps - MVP Data Analysis: The first projects approved to utilize the MVP data are focused on issues that are relevant in our Veteran community. These studies will not only provide valuable research results, but are also helping to develop and streamline the data access procedures for future researchers. Current Studies (*Coordinated by VA Boston & VA CT Health Care Systems): +The Genetics of Functional Disability in Schizophrenia and Bipolar Illness*, Bronx VAMC; Miami VAMC +Genomic Study of Posttraumatic Stress Disorder*, San Diego VAMC; VA Connecticut Health Care System +Genomics of Gulf War Illness in Veterans*, VA NJ Health Care System; VA Cooperative Studies Epidemiology Center Durham +Genetic Vulnerability of Sustained Multi-substance Use in MVP, VA Connecticut Health Care System; Philadelphia VAMC +Cardiovascular Disease Risk Factors, Prevalent Cardiovascular Disease, and Genetics in the Million Veteran Program, Atlanta VAMC; Boston VA Health Care System +Pharmacogenomics of Risk Factors and Therapies Outcomes for Kidney Disease, VA Tennessee Health Care System +Genetics of Cardio-metabolic Disease in the VA Population, VA Palo Alto Health Care System; Philadelphia VAMC +Genetic Risk for AMD in Diverse Veteran Populations, Cleveland VAMC; VA Western NY Healthcare System

Research Topic: Genomics
Funding agencies: CSR&D
Grant support: MVP 000

85. Context Processing in Individuals with Schizophrenia and Bipolar Disorder and their Biological Relatives: Exploring the Role of Disorganization Symptomatology

Myers, Evan [1,2]; Ramsay, Ian [2]; Ma, Yizhou [2]; MacDonald, Angus [2]; Sponheim, Scott [1,2]

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

Abstract: Individuals with schizophrenia and bipolar disorders show deficits in several cognitive areas, including context processing (CP). First-degree biological relatives show similar yet milder deficits. Disorganization symptomatology may relate to CP deficits in psychiatric patients, but it is less clear if this finding extends to relatives. The present study sought to test whether disorganization symptomatology predicted CP performance in individuals affected by schizophrenia (SZ), bipolar disorder (BP), and first-degree biological relatives (SZRel; BPRel). A sample comprised of 60 SZ, 38 BP, 56 SZRel, 26 BPRel, and 65 controls completed the Dot Pattern Expectancy (DPX) task, a measure of CP and were assessed using the Brief Psychiatric Rating Scale (BPRS) and the Schizotypal Personality Questionnaire (SPQ). Consistent with previous findings, SZ and BP showed deficits in CP compared to controls, but SZRel and BPRel did not differ from other groups. Analyses did not reveal expected associations between CP and disorganization symptomatology in the patient groups.

Research Topic: Mental Illness
Funding agencies: CSR&D
Grant support: 2I01CX000227

86. Aphasia Communication Outcome Measure: Minimal Clinically Important Difference Score Estimates

Nicholson, Hannele [1]; St. Jacque, Ann [1]; Hula, William [2]; Dickey, Michael [2]; Kendall, Diane [3]; Wambaugh, Julie [4]; Grzybowski, Angela [2]; Irwin, William [5]; Doyle, Patrick [2]

1. Minneapolis VA Health Care System
2. VA Pittsburgh Healthcare System
3. University of Washington-Puget Sound
4. University of Utah
5. Tennessee Valley Healthcare System

Abstract: Over the past two decades, aphasia rehabilitation has incorporated patient-reported outcomes (PROs) into clinical practice (Baylor et al., 2017; Doyle et al., 2004; Hilari & Byng, 2001). We provide initial anchor-based minimally clinically importance difference score (MID) estimates for the Aphasia Communication Outcome Measure (ACOM), a PRO measure of communicative functioning for people with aphasia. Aphasia is an acquired neurogenic disorder that may result from a brain injury or stroke that impairs speaking, listening, reading and writing. The ACOM is a 59-item tool with positive validity evidence (Doyle et al., 2008; Hula et al., 2015; Hula et al., 2017). An important function of a PRO is to provide an assessment of change to guide clinical practice and research. In order to provide evidence of change, a minimal clinically important difference score (MID), is used to estimate the smallest unit of meaningful change for a clinician or patient. Typically, MID estimates are calculated by administering the target PRO before and after treatment as part of regular care or as part of clinical trials, along with anchor measures that are used to classify individuals according to the degree of change in that health state (Revicki et al., 2008). For this analysis, MID estimates were based on data from four combined sources: clinical outcome data from an intensive comprehensive aphasia treatment (ICAP, n = 87; Winans-Mitrik et al., 2014), a trial of semantic feature analysis (SFA, n = 26; Gravier et al., 2018), a trial comparing phonomotor and SFA treatments (PM-SFA, n = 20; Kendall et al., 2015), and a trial of sound production treatment for apraxia of speech (SPT, n = 17; Wambaugh et al., 2018). All participants in these trials were 6-months post their aphasia diagnosis at initial testing. Patients in the ICAP and SFA trials completed the ACOM before treatment and at four weeks after treatment along with an anchor Comprehensive Aphasia Test (Swinburn et al., 2004). In all clinical trials, participants completed the ACOM before and after treatment along with a single-item rating scale of overall communicative ability as “very bad”, “bad”, “so-so”, “good”, or “very good”. We report correlations between the anchor and ACOM change scores that approach or exceed the minimum recommended value of 0.3 (Revicki et al., 2008). Initial MIDs ranged from 2.2 to 3.2 T-score points for the full ACOM and from 2.5 to 4.3 for a 12-item computer adaptive version of the ACOM.

Research Topic: Audiology & Speech Pathology
Funding agencies: RR&D
Grant support: VA RR&D I01RX001963

87. 3D Printed Prosthetic Sockets

Nickel, Eric [1]; Barrons, Kyle [1]; Owen, Meredith [2]; Hand, Barry [3,4]; DesJardins, John [2]; Hansen, Andrew [1,5]

1. Minneapolis VA Health Care System
2. Clemson University
3. Reify LLC
4. Extremiti3D LLC
5. University of Minnesota

Abstract: Unlike endoskeletal connectors and prosthetic feet, prosthetic sockets are not subjected to structural strength testing using internationally recognized test standards, such as ISO 10328. Definitive prosthetic sockets fabricated in the traditional manner have been shown to be inconsistent in the ability to withstand the loads applied by these standards. Persistent concerns regarding the strength and durability of 3D-printed prosthetic sockets are a barrier to clinical adoption of 3D-printing technologies in prosthetic socket fabrication. To develop a robust prosthetic socket design based on 3D-printing technology, an iterative development process was employed with integral validation testing using the ISO 10328 loading conditions performed independently by two testing centers. Materials and Methods – Twenty-four 3D-printed transtibial prosthetic sockets were tested using ISO 10328 loading conditions designed to represent the greatest atypical elevated loads a 125 kg user would be expected to place on their prosthesis without failure (ultimate strength test at the P6 load level). Several design iterations and variations were tested. One socket of a design that withstood the ultimate strength loading was reprinted and subjected to cyclic testing, up to 3 million cycles. All tests were conducted under the forefoot loading condition (Condition II of the ISO 10328 standard) which generates greater moments at the distal end of the socket than the heel loading condition. Results – Early socket designs were unable to withstand the ISO 10328 ultimate strength test to the P6 load level. Successive design improvements increased the strength until a robust final design was achieved. Variations of that final design for different suspension types and a different limb model demonstrated consistent performance. The final design was significantly stronger than the initial design ($p = 1.35x10\text{-}7$). The socket that was tested for durability completed the 3 million loading cycles at the P6 load level without damage and withstood the subsequent static proof loads. Conclusions – An iterative design process with integral structural testing can result in strong, durable prosthetic sockets made using 3D-printing technology that may be robust to variations in limb size/shape and suspension type.

Research Topic: Prosthetics
Funding agencies: DOD
Grant support: Defense Logistics Agency, SBIR contract numbers SP4701-16-C-0027 and SP4701-17-C-0037, awarded to Reify, LLC

88. Impact Testing Prosthetic Feet

Nickel, Eric [1]; Morin, Steve [1]; Koehler-McNicholas, Sara [1]; Hendershot, Brad [2-4]; Schnall, Barri [2]; Hansen, Andrew [1,5]

1. Minneapolis VA Health Care System
2. Walter Reed National Military Medical Center
3. Extremity Trauma and Amputation Center of Excellence
4. Uniformed Services University
5. University of Minnesota

Abstract: There is currently no accepted test standard for prosthetic feet to demonstrate durability to impact loading such as that encountered in physically demanding professions (e.g., construction, farming, or military service). The goal of the study was to build a system to pilot test the impact resilience of a selection of prosthetic feet marketed for high-activity prosthesis users. Materials and Methods: Three specimens each of nine prosthetic feet (n = 27 total) were selected by prosthetists at the Minneapolis VA Health Care System (with specifications in accordance with an associated human-subjects research study, n = 3). Maximum drop height without failure was used to assess impact resilience. Drop testing was performed using a custom system with an electromagnet to lift and release a weighted frame in increments of 10 cm until failure. The test specimens were organized into three sets, each with one specimen of each foot with the spring category for a particular user mass. Sets A, B, and C were tested with 45.9, 57.8, and 61.5 kg, respectively (101, 127, and 135 lb, respectively) simulating the mass of the user plus an added 22 kg (48 lb) of worn/carried load, then divided by two to represent even load distribution to both legs at impact. Results: The feet withstood drop heights without failure ranging from 20 cm to 100 cm. The type of foot was found to significantly affect maximum drop height ($P = 0.014$). Effect sizes for comparisons of individual feet range from 0.15 to 3.17 with the median effect size being 0.94, which is considered 'large.' Conclusions: The test system successfully measures impact resilience and is sensitive to foot type. Large effect sizes indicate substantial differences between prosthetic feet marketed for active prosthesis users.

Research Topic: Prosthetics
Funding agencies: DOD
Grant support: Support provided by the BADER Consortium via the CDMRP (Award # W81XWH-11-2-0222)

89. Prosthetic Ankle for Physical Therapy

Nickel, Eric [1]; Voss, Gregory [1]; Hansen, Andrew [1,2]; Koehler-McNicholas, Sara [1]

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

Abstract: Veterans with lower limb amputation undergo physical therapy to learn to use a prosthesis. Initial activities include learning to transition between sitting and standing postures and learning to shift weight onto the prosthesis for standing balance and balance confidence. During this critical learning period, Veterans with lower limb amputation must learn to use a prosthetic foot while also learning how to wear and trust a prosthesis with a host of new sensations. Gradual training is a well-established motor learning strategy that may simplify this learning process, allowing Veterans with lower limb amputation to focus on first learning to trust their prosthesis in a highly stable state, and then gradually learning to control more advanced functional tasks that require increased range of motion. Since current lower limb prosthetic feet are not capable of supporting this training method, researchers at the Minneapolis VA Health Care System have developed a prototype prosthesis with the ability to gradually unlock the ankle joint to provide targeted therapeutic range-of-motion limits. Focused interviews with rehabilitation experts (e.g., prosthetists and physical therapists who work with Veterans who have recently had an amputation) generated key design requirements for the prototype. Mechanical testing of the first-generation prototype using ISO 10328 strength tests identified structural weaknesses which have been addressed by design changes. Subsequent testing of the second-generation prototype successfully passed mechanical testing. A gradual training protocol is under development that will be trialed with Veterans with new amputation in the coming year.

Research Topic: Prosthetics
Funding agencies: RR&D
Grant support: I01 RX002267

90. Assessment of Social Cognition and Interaction Training for Individuals with Serious Mental Illness

Nienow, Tasha [1]; Schulte, Cody [1]; Tourville, Tia [1]; Spann, Desmond [1]; Strom, Thad [1]; Harris, J. Irene [1]

1. Minneapolis VA Health Care System

Abstract: Schizophrenia and bipolar disorder are profoundly disabling illnesses. Social cognitive deficits have been found to be unique predictors of community and work role functioning and have become targets of intervention. This study examined the impact of a psychotherapy group, Social Cognition and Interaction Training (SCIT), on social cognitive abilities, quality of work relationships, and role functioning. Durability of the intervention was assessed with a 3 month follow-up. Methods: Sixteen individuals with schizophrenia, schizoaffective disorder, or bipolar disorder received SCIT, a 24-session, group-based, skills training intervention. In addition, participants were provided with 30 minutes of individual training weekly to promote skill application. Impact of the intervention on social cognitive skills was assessed with the Face Emotion Identification Task (FEIT), the Bell-Lysaker Emotion Recognition Task (BLERT), the Ambiguous Intentions and Hostility Questionnaire (AIHQ), and the Awareness of Social Inference Test (TASIT). Work relationship quality was assessed with the Vocational Efficacy in Trauma Survivors Scale (VETSS) and the Mentoring and Communication Support Scale (MCSS). Social and work role functioning were assessed with the First Episode Social Functioning Scale (FESFS), the Social Skill Performance Assessment (SSPA). Results: Post-intervention, participants demonstrated significantly improved emotion recognition skills, $t(14) = 2.70$, $p < .05$, and assertiveness, $t(15) = 2.22$, $p < .05$. They also reported improved quality of work relationships with peers, $t(14) = 1.84$, $p < .01$. At follow up, gain in assertiveness and improved relationship quality were maintained, while gains in emotion recognition performance were not maintained. Discussion: Findings suggest that individuals with serious mental illness benefited from social cognitive skills training. Participants were more likely to assertively check into ambiguous social interactions after receiving the intervention and felt more supported by their colleagues at work. Results suggest that pairing SCIT with vocational rehabilitation may improve work outcomes for individuals with serious mental illness.

Research Topic: Psychiatry
Funding agencies: CVRE
Grant support: Minneapolis Veterans Medical Research and Education Foundation

91. Effect of Code Team Resuscitation Training Modality on 30-day Survival after In-Hospital Cardiopulmonary Arrest

Novak, Joseph [1]; Beard, Albertine [2]

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

Abstract: Though in-hospital cardiac arrests (IHCAs) are common nationally, with approximately 209,000 occurring each year, individual hospital staff members participate rarely enough in these stressful, high-stakes events that they must rely heavily on their training for successful performance. Training modalities for advanced cardiac life support (ACLS) have expanded recently to include online and simulation-based options. While these modalities have demonstrated equivalent efficacy in simulated environments and in end-of-training exams, there is little data comparing their efficacy in the clinical setting. METHODS: This study retrospectively examined the outcomes of 202 IHCAs occurring at the Minneapolis VA Health Care System between August 2011 and July 2017. The training of the core members of the 'Code Team' [physician code leader, ICU nurse(s), nurse anesthetist, respiratory therapist, and the patient's primary nurse] responding to these IHCAs was examined. RESULTS: Odds of survival 30 days following an IHCA was significantly improved if at least 50% of the code team's most recent ACLS training was completed online (OR 2.35; p 0.01) and significantly worse if no members of the code team completed online training (OR 0.36; p 0.02). Among individual members of the code team, there was a statistically significant increase in 30-day survival when the Rapid Response ICU nurse had completed online ACLS training (OR 3.14; p 0.01); there was no significant change in outcomes for other code team members. A strong trend towards improved odds of 30-day survival was observed if the patient's primary nurse underwent First 5 Minutes training prior to the code event (OR 1.99; p 0.08), whereas training of the Rapid Response ICU nurse showed no effect (OR 0.422; p 0.42). DISCUSSION: This research suggests that online ACLS training is not inferior to in-person ACLS training and may even improve patient outcomes. This is encouraging, given the convenience and cost savings associated with online CPR training. Simulation-based training of front-line floor nursing staff, such as First 5 Minutes, focused on preparing nurses for the first few minutes of rare critical events strongly correlated with improved patient mortality outcomes, supporting the use of this type of training.

Research Topic: Critical Care
Funding agencies: N/A
Grant support: N/A

92. Defining and Refining the M-PACE for SCI Rehab

Olney, Christine [1]; Goldish, Gary [1]; Ferguson, John [1]; Voss, Gregory [1]; Nickel, Eric [1]; Fairhurst, Stuart [1]; Stien, Crystal [1]; Scheel, Kristin [1]; Goding, Ann [1]; Hansen, Andrew [1]

1. Minneapolis VA Health Care System

Abstract: Problem: Prolonged bedrest and immobilization are standard treatments following certain surgical procedures (e.g., skin flaps), most often utilized to protect the surgical site as it heals. Unfortunately, the resultant physical inactivity often leads to poor quality of life and prolonged muscular deconditioning during the post-surgical recovery phase. Exercise is recognized as an important activity to reduce or remove the negative effects of prolonged bedrest. However, Veterans on bed rest have limited options for exercise, especially those with spinal cord injuries and disorders (SCI/D), who do not have active control of their lower limbs. To address this gap in commercially available exercise systems, the Minneapolis Adaptive Design & Engineering (MADE) Program has developed a Multi-Purpose Arm Cycle Ergometer (M-PACE). The Objective of this entire project, is to offer exercise to prevent deconditioning in this patient population. Pilot findings: Primary outcome measure: 6MAT (six-minute arm test) which is a measure of conditioning. Thirty-nine Veterans have enrolled in a pilot study over the last four years, and 30 have used the device at least on time during their recovery. Our data show a definitive stabilization of conditioning with regular use of the M-PACE. Beyond the clinical testing we have been conducting over the past four years, we have used an iterative process between clinicians, Veterans and engineers to define the necessary upgrades needed for optimal M-PACE usage. Recently we receive funding to refine the device. With these funds we will list the device with the FDA, replicate the refined device, deliver a M-PACE to each of three other VA SCI/D Centers (Palo Alto, Milwaukee and Hines). We will also create a user manual and conduct education on usage at these three sites. Future studies: We are planning to conduct a randomized clinical trial among the sites with the M-PACE to determine not only conditioning outcomes, but to learn the cost savings that are anticipated.

Research Topic: Bioengineering
Funding agencies: RR&D
Grant support: Supported by the Minneapolis VA Health Care System and VA Technology Transfer Office

93. Refining the SkinSyte Camera System

Olney, Christine [1]; Goldish, Gary [1]; Ferguson, John [1]; Voss, Gregory [1]; Fairhurst, Stuart [1]; Dellamano, Cliff [1]; Rich, Tonya [1]; Sauerbrey, Matthew [1]; Hansen, Andrew [1]

1. Minneapolis VA Health Care System

Abstract: Veterans with spinal cord injury (SCI) are at high risk for pressure injury (PI). It is recommended that persons with SCI examine at-risk areas of their seated surfaces (e.g., sacrum, ischial tuberosities, coccyx area, and trochanters) at least twice a day for evidence of skin changes. Long-handled mirrors are the standard of care device used to examine the at-risk area but are of little utility when the person has impaired mobility, vision or both. Aims: 1) provide Veterans with SCI a more efficient and efficacious tool to examine their at-risk skin areas; and to 2) provide a secure and efficient communication process with their health care provider regarding areas of concern. We hypothesize that Veterans will be more confident in their ability to conduct skin assessments and in their communication with their health care provider regarding skin assessments. Methods: Using mixed methods of interviews, identifying strategic spots (color and letters), and surveys (QUEST 2.0) with Veterans, to inform engineers of needed refinements in the SkinSyte camera system, will result in a product ready to be trialed in the home environment. Results to date: Five Veterans have informed the research team of the barriers to the currently used system for skin screening (mirror or caregiver), have trialed the SkinSyte camera system, offering suggests for improvement (e.g. adding a strap to the handle, strap for the phone, would prefer a tablet rather than a phone, verbal command to enlarge the image, option to Bluetooth the connection versus a cord, extend the gooseneck). Average scores for satisfaction on the QUEST 2.0: Mirror 3.1 (1.45) versus SkinSyte 4.35 (0.89), where 1 is 'not satisfied at all' and 5 is 'very satisfied'. For identifying Color and Letter on seven strategic spots on the seated area, the average score for identifying color: Mirror 2.2 (1.48) versus SkinSyte 6.2 (1.7); the average score of identifying letters: Mirror 2 (1.41) versus SkinSyte 6.2 (1.3). Discussion: We will continue to gain feedback from our Veterans with SCI, to understand what characteristics they desire in the SkinSyte camera. Thus far, the SkinSyte camera system is highly acceptable to the user compared to using the standard of care mirror for viewing the at-risk seated area.

Research Topic: Preventive Medicine
Funding agencies: RR&D; CVRE
Grant support: VA RR&D SPiRE

94. Trunk Control Device for Veterans with Spinal Cord Injury

Olney, Christine [1]; Goldish, Gary [1]; Looft, John [1]; Fay, Brian [1]; Egginton, Jason [2]; Voss, Gregory [1]; Fairhurst, Stuart [1]; Dellamano, Clifford [1]; Johnson, Dan [3]; Hansen, Andrew [1]

1. Minneapolis VA Health Care System
2. Mayo Clinic
3. LEVO USA

Abstract: Problem: Over 300,000 people living in the USA have a spinal cord injury (SCI), with approximately 12,500 new injuries every year. It is estimated that over 10,500 Minnesota residents face the challenges of SCI. One of the significant challenges those individuals face is living and working with limited or no control of their torso or 'trunk'. This lack of trunk control significantly impacts their ability to carry out a broad range of simple daily tasks. Yet no commercially available solutions exist that allow some degree of movement, while also providing trunk support. Methods: To address the issue of limited control, with funding from the State of Minnesota Office of Higher Education and in partnership with a leading Minnesota-based company (LEVO USA), we sought to design, build and test a first iteration prototype trunk control device. Both Veterans and non-Veterans participated in focus groups (n = 8). The first focus group was conducted to learn, 1) what a trunk control system might offer to a person with SCI; 2) the desired features of a trunk control system and; 3) what would be deal breakers in a design. The data were analyzed using a rapid assessment process and used by MADE and LEVO USA engineers to brainstorm several possible designs. Five of the eight original focus group members returned to view the designs, comment on each, and then rank ordered the designs. From the preferred design, engineers built a prototype. Two original focus group members volunteered to test the prototype in our lab space. Outcomes: Feedback from the participants has yielded valuable data, allowing the MADE team to move the prototype forward towards the next phase of fund seeking and design development.

Research Topic: Bioengineering
Funding agencies: CVRE
Grant support: State of Minnesota, Office of Higher Education

95. Toolkit-guided external facilitation to improve access to evidence-based psychotherapies for PTSD

Orazem, Robert [1]; Nugent, Sean [1]; Ackland, Princess [1]; Kehle-Forbes, Shannon [1]; Noorbaloochi, Siamak [1]; Clothier, Barbara [1]; Sayer, Nina [1]

1. Minneapolis VA Health Care System

Abstract: While the efficacy of Cognitive Processing Therapy (CPT) and Prolonged Exposure (PE) for PTSD has been established, the majority of Veterans diagnosed with PTSD still do not receive either of these evidence-based psychotherapies (EBPs). We previously conducted a mixed-method study of clinic and organizational factors associated with high rates of EBP utilization of CPT and PE in outpatient PTSD teams. Now, in collaboration with the Office of Mental Health and Suicide Prevention (OMHSP) and the National Center for PTSD (NCPTSD), we are building on this by spreading the clinic practices we identified in PTSD teams with high reach of CPT and PE to teams with low reach of these EBPs. This poster presents an overview of this VA HSR&D-funded quality improvement project. OBJECTIVES: Specific aims were to: (1) Increase the reach of CPT and PE in 2 geographically diverse PTSD teams where reach of CPT and PE was low (< 15% of therapy patients with PTSD were receiving an EBP) using external facilitation and a specialized toolkit; (2) Conduct formative evaluation to inform and monitor the implementation intervention and to examine contextual factors associated with its success; and (3) Refine the toolkit and implementation intervention for broader dissemination. METHODS: This project used a quasi-experimental, repeated measure (pre-post) design. Each of 2 low-reach intervention sites was matched to 3 low-reach control sites using VHA administrative data for a total of 2 intervention and 6 control sites. The implementation intervention included a site visit and 6 months of toolkit-guided external facilitation as well as audit and feedback of reach of CPT and PE to patients with PTSD. During the 6 months post-intervention, the external facilitator will have minimal contact with the teams depending on their need. The primary implementation outcome will be CPT and/or PE reach during the 6 months before and after the 6 months of toolkit-guided external facilitation at the intervention and comparison sites. STATUS: The 6 months of intensive external facilitation at both intervention sites is complete.

Research Topic: Posttraumatic Stress Disorder (PTSD)
Funding agencies: HSR&D
Grant support: CRE 18-002

96. Utility of nuclear stress imaging in predicting long-term outcomes one-year post CABG Surgery.

Ortiz, Fernando [1]; Mbai, Mckenzie [2]; Adabag, Selcuk [2]; Garcia, Santiago [2]; Nguyen, Jennifer [2]; Goldman, Stephen [3]; Ward, Herbert [2]; Kelly, Rosemary [2]; Carlson, Selma [2]; McFalls, Edward [2]

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

Abstract: Early MPI after CABG is currently considered rarely appropriate in asymptomatic patients. This study aimed to identify prognostic value of nuclear stress-imaging post-CABG. METHODS: This was a single center prospective study looking at long-term outcomes post-CABG. Per protocol participants underwent SPECT-MPI stress testing and coronary angiogram on the same day, 1-year following CABG. Defect size was semi-quantified. The primary outcomes were the composite of death and congestive heart failure. RESULTS: Eighty-four participants underwent nuclear stress-imaging and angiography, with a median follow-up of 11.1 years. Three separate stress findings predicted the primary outcome: inability to reach stage 3 of a Bruce protocol (OR 7.3, CI 2.4-22.1, $P < 0.001$), LVEF < 45% (OR 4.0, CI 1.1-15.3, $P = 0.041$) and a moderate-large stress defect size (HR 2.31, CI 1.1-1.5, $P = 0.04$). These findings appear to be additive and strongest among patients who underwent exercise stress testing (HR 10.6, CI 3.6-30.6, $P < 0.001$). Graft disease was identified in 39 (46%) patients and compared to those individuals with no graft disease, did not predict long-term adverse outcomes ($P = 0.29$). CONCLUSION: In clinically stable patients early after revascularization with CABG, SPECT-MPI can identify patients at higher risk of heart failure and death.

Research Topic: Cardiovascular Disease
Funding agencies: N/A
Grant support: N/A

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97. Chemogenetic activation of orexin/hypocretin neurons ameliorates aging induced changes in behavior and energy expenditure

Pallais, Jean Pierre [1]; Stanojlovic, Milos [1]; Mavanji, Vijaya [2]; Kotz, Catherine [1,2]

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

Abstract: Aging affects numerous physiological processes as well as behavior. A large number of these processes are regulated, at least partially, by hypothalamic orexin neurons, and orexin tone may decrease with normal aging. In this study, we hypothesized that DREADD (Designer Receptors Exclusively Activated by Designer Drugs) stimulation of orexin neuronal activity will ameliorate the effect of aging on behavioral and metabolic alterations in young and middle-aged mice. DREADD targeting was achieved by stereotaxic injection of AAV vectors ((AAV2-hSyn-DIO-hM3D(Gq)-mCherry) into lateral hypothalamus of 5 and 12 months old orexin-cre female mice and was confirmed by immunohistochemistry (IHC) analysis of orexin A and mCherry expression. After recovery, animals were subjected to a behavioral test battery consisting of the elevated plus maze (EPM), open field test (OFT), and novel object recognition tests (NORT) to assess the effects of aging on anxiety-like behavior, general locomotion, and working memory. A comprehensive laboratory animal monitoring system (CLAMS) was used to measure spontaneous physical activity (SPA) and energy expenditure (EE). The results indicated that activation of orexin neurons mitigates aging-induced reductions in anxiety-like behavior in middle-aged mice ($p < 0.005$), and increases locomotion in both young and middle-aged mice ($p < 0.05$). Activation of orexin neurons increases SPA ($p < 0.01$) and EE ($p < 0.005$) in middle-aged mice, restoring the levels to that observed in young animals. Results from this study identify orexin neurons as potential therapeutic targets for age-related impairments in cognitive and anxiety-related behavior, and energy balance.

Research Topic: Aging
Funding agencies: NIH; RR&D
Grant support: 5R01DK100281, 5I01RX000441 (CMK)

98. Creation and Expansion of an Acute Regional Pain Service - Reduced Intra-operative Opioids and Operative time

Palm, Dustin [1,2]; Peterson, Garrett [1]; Anderson, Jeremy [1]; Lange, Jill [1]; Apostolidou, Ioanna [1,2]; Hutchins, Jacob [1,2]

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

Abstract: Veterans are more likely to die from accidental opioid overdose compared to civilians. A subset of deaths stem from post-surgical opioid prescription. Surgery itself is a risk factor for chronic opioid use that can lead to opioid use disorder, opioid overdose and death. The national opioid crisis has prompted anesthesia providers to employ alternatives to opioids to treat surgical pain. The American Society of Regional Anesthesia recommends the use of peripheral nerve blocks (PNBs) for the management of postoperative pain. Benefits of regional anesthesia include: minimizing opioids, better pain control, lower postoperative nausea and vomiting, earlier discharge, potential to decrease chronic pain and risk for substance abuse. We sought to increase the number and diversity of PNBs offered to veterans and to decrease opioid use by implementing an Acute Regional Pain Service (ARPS), staffed daily by one Anesthesiologist and one CRNA. Methods: One year following implementation and expansion of the ARPS, we evaluated regional nerve block utilization, volume and diversity, as well as intra-operative opioid use in total knee arthroplasty (TKA) and total shoulder arthroplasty (TSA); we additionally reviewed utilization of general vs regional anesthesia in TSA, and how this affected operative times. Results: We increased the number of blocks per month from 61 in May 2018, to 177 in Jan of 2019; we expanded the diversity (types) of blocks from 11 in May 2018, to 19 in Jan 2019. No patients having TKA in July-Sept 2017 received a PNB (n = 0/58) and all of the patients in July-Sept 2018 received a PNB (n = 60/60); this was associated with a decrease in the mean hydromorphone (from 0.66mg to 0.26mg/patient, 60% reduction) and fentanyl (from 262.5mcg to 190.8mcg/patient, 27% reduction). Although all patients having TSA in our sample of 2017 and 2018 received a PNB, we measured a reduction in mean intra-operative fentanyl (98mcg/patient in July-Sept 2017 vs 50mcg/patient in July-Sept 2018, 48% reduction), presumably due to more effective regional anesthesia sufficient for surgical analgesia. This was paralleled by a decrease in the percentage of cases requiring general anesthesia (53% in July-Sept 2017 vs 33% in July-Sept 2018). Employing effective regional anesthesia as the primary anesthetic, obviating the need for general anesthesia, saved an average of 7 minutes/case; at a operating room cost of $50-75/min, this equates to $350-$500/case.

Research Topic: Anesthesiology
Funding agencies: N/A
Grant support: N/A

99. Autosomal recessive transmission of psychosis in a consanguineous pedigree

Pardo, Jose [1,2]; Sheikh, Sohail [3]; Aslam, Faisa [4]; Yasim, Samina [4]; Naz, Sadaf [4]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Hawkes Bay Hospital, New Zealand
4. University of the Punjab, Pakistan

Abstract: Mental illness is widely considered a polygenic disease based on genome wide association studies (GWAS). The prevailing view is that common mental diseases arise from the blending of many common variants each with small effect size. If so, translation will bedevil clinical psychiatry. No single gene associated with a psychiatric disease has been found. However, rare loci identified are frequently polygenic, show pleiotropy, lack disease specificity, and become lost in 2-3 generations. Yet, all other branches of medicine have diseases with both rare and common gene variants. In fact, rare variants are typically the first clues toward pathophysiology. However, the complexity of psychiatric disorders and their broad genetic overlap may uniquely preclude pathogenic single genes of large effect size. If single genes (Mendelian) with high penetrance for mental disorders exist, they should be detectable particularly in consanguineous families. The variant should be rare given selection pressure. The variant segregating with the phenotype should be pathogenic based on current predictive tools such as conservation and structural impact scores. Here, homozygosity mapping in a consanguineous pedigree identified a candidate pathogenic variant for psychosis. Healthy, Pakistani, first cousins had seven children (Figure 1). After IRB approval and informed consent, psychiatric interviews and DNA were collected. Five offspring were unaffected psychiatrically, but two teenage sisters developed psychosis meeting established criteria for schizophrenia without intellectual disability, affective illness, or substance abuse. Whole-exome sequencing identified a single point mutation in USP53 meeting the following filters: MAF <0.01; homozygous in both affected individuals and heterozygous in parents; rare in public databases; conserved; exonic; predicted as protein damaging by multiple software. The variant was present in a region of shared homozygosity (Figure 2). This allele's frequency in South Asians is 5.2(10)-5 (gnomAD) without individuals homozygous for the variant. Given the rarity of the mutation, replication in another pedigree is unlikely. Causal evidence will need to accrue from converging molecular and cellular approaches. The functions of USP53 are understood poorly. BLMH, homocysteine-thiolactone hydrolase interacts with it. Homocysteine has been implicated in schizophrenia. Folate may be therapeutic.

Research Topic: Mental Illness
Funding agencies: CSR&D
Grant support: I01CX000501, Pakistan Higher Education Commission Grants # 3288 & 4352

100. A perplexing case of superficial granulomatous pyoderma with sporotrichoid-like distribution

Parker, Jordan [1]; Lizewski, Walter [2]; Merten, Ashley [3]; Gaddis, Kevin [2,4]; Pragman, Alexa [2,4]; Goldfarb, Noah [2,4]

1. University of Missouri School of Medicine
2. University of Minnesota
3. Mayo Clinic Health System
4. Minneapolis VA Health Care System

Abstract: 74-year-old male with no significant past medical history presented with a six-week history of an enlarging, tender red plaque with central ulceration on the right lower extremity and multiple red-pink nodules that extended linearly along the medial leg and thigh in a sporotrichoid-like distribution. Histopathology of the lesions demonstrated an acute and chronic suppurative and granulomatous infiltrate in the deep dermis extending down to subcutis. Over the ensuing months, several sterile biopsies were obtained for bacterial, mycobacterial and fungal cultures, which were all negative. During this time the patient was started on a five-month course of oral itraconazole for presumed sporotrichosis. The specimens were initially sent to the University of Washington for broad-range polymerase chain reaction (PCR) testing, with two attempts that failed to identify a pathogen. The specimens were finally sent to the Centers for Disease Control and Prevention (CDC) for further work-up. Special stains were noncontributory, except for an immunohistochemical stain that was cross-reactive for Mycobacterium species, but paneubacteria 16s rRNA gene PCR was positive only for Streptococcus salivarius group. These were considered a false positive and contaminant, respectively. On further review of the pathology, a 'three-layer' granulomatous inflammatory infiltrate was appreciated, with a central necrotic area with neutrophils, a second ring of histiocytes and giant cells, and an outermost ring of lymphoyctes and plasma cells. The diagnosis of superficial granulomatous pyoderma (SGP) was made and the patient was started on potent topical steroids and intralesional kenalog injections (ILK) of the nodules extending up the lower leg. After 12 months of minimal change with aggressive wound care, five of which on oral itraconazole, the ulceration finally healed after only four weeks of potent topical steroids. The nodules extending up the leg also healed with ILK. Superficial granulomatous pyoderma is a rare pyoderma gangrenosum (PG) variant not associated with underlying systemic conditions. They are typically painless ulcers on the trunk with absent undermining and a clean granulating base. The classic pathology finding is a 'three-layer granuloma' in the superficial dermis consisting of central neutrophilic inflammation and necrosis, a surrounding layer of histiocytes and multinucleated giant cells and an outer most layer of plasma cells and eosinophils.

Research Topic: Dermatology
Funding agencies: N/A
Grant support: N/A

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101. EEG Measures Reflect Diminished Visual Context Processing in Psychotic Disorders

Pokorny, Victor [1]; Schallmo, Michael-Paul [2]; Olman, Cheryl [2]; Sponheim, Scott [1,2]

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

Abstract: Schizophrenia is a heterogeneous disorder often associated with abnormal sensory processing, especially in auditory and visual domains. Such perceptual abnormalities often manifest as visual disturbances or hallucinations and are thought to reflect deviant visuocortical functioning. Impaired contour detection is a well documented visual deficit found in patients with schizophrenia which involves recognition of edges and boundaries of objects. Furthermore, the context in which contours are viewed can impact their overall perceptual salience. Recent evidence suggests that the effect of context during contour detection is weaker in patients with schizophrenia (i.e., patients with schizophrenia are less affected by contextual stimuli than healthy controls). There is debate in the literature regarding whether these contextual processing abnormalities are products of early, lower order or later, higher order sensory processes. Additionally, it is unclear whether these abnormalities extend to relatives of patients with schizophrenia and patients with bipolar disorder. The central aim of the present study was to identify neural correlates of weakened contextual processing and impaired contour integration in patients with schizophrenia (SCZ), patients with bipolar disorder (BP), first degree relatives of patients with schizophrenia (SREL) and healthy controls (CONT). More specifically, we sought to utilize the event-related potential technique to identify temporally discrete components of weakened context processing in psychosis. Our secondary aim was to clarify the degree to which contextual processing and contour integration are aberrant in BP and SREL to better understand whether abnormal contextual processing is specific to SCZ.

Research Topic: Mental Health
Funding agencies: CSR&D
Grant support: I01CX000227

102. COPD Upper Airway Microbiome Is Associated With Age And Obstruction Severity

Pragman, Alexa [1,2]; Knutson, Katherine [2]; Gould, Trevor [2]; Hodgson, Shane [1]; Isaacson, Richard [2]; Reilly, Cavan [2]; Wendt, Chris [1,2]

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

Abstract: Chronic obstructive pulmonary disease (COPD) is an inflammatory lung disorder associated with lung microbiome dysbiosis. Although the upper airway microbiome is the source of the lung microbiome, the relationships between the oral, nasal, and sputum microbiomes are incompletely understood. Our objective was to determine features that differentiate these microbiomes among subjects with stable COPD. We recruited 15 current or former smokers to provide oral and sputum samples on day 1. On day 2, another oral sample and a nasal sample were obtained. Each sample and control underwent DNA extraction, 16S V4 rRNA amplification, 16S V4 sequencing, and qPCR of 16S rRNA. Data were analyzed using dada2 and R. Most subjects were male with a mean age of 65.2. Five subjects had mild COPD, 7 had moderate COPD, and 2 had severe COPD. Three subjects (20%) were current tobacco users and 2 subjects (13%) used inhaled corticosteroids (ICS). Subjects had a mean of 49.1 pack-years of tobacco exposure. Bacterial biomass was associated with site, but no differences in biomass were observed with age, FEV1 percent predicted (FEV1pp), ICS use, smoking status, or edentulous state. Shannon index was associated with site ($p < 0.001$), but not age, ICS use, FEV1pp, tobacco use, or edentulous state. Beta-diversity was illustrated by principal coordinate analysis using Bray-Curtis dissimilarity and PERMANOVA analyses, showing sample clustering by anatomic site ($p = 0.001$) with nasal samples forming a cluster separate from the combined oral wash samples and sputum samples. Clustering was also observed with ICS use ($p = 0.029$) and edentulous state ($p = 0.019$), while FEV1pp and current tobacco use were not significant. In an ASV-level analysis of oral samples using a linear regression model with Benjamini-Hochberg correction at an FDR<0.10, 10 ASVs were associated with age while no ASVs were associated with FEV1pp or smoking status. Sputum sample analysis demonstrated that 51 ASVs (25 unique genera) were associated with age, 61 ASVs (32 genera) were associated with FEV1pp, and no ASVs were associated with smoking status. Among the upper airway microbiomes of COPD subjects, anatomic site was associated with bacterial biomass, Shannon diversity, and beta-diversity. ICS use and edentulous state were both associated with beta-diversity. Age was associated with taxa relative abundance in oral and sputum samples, while FEV1pp was associated with taxa relative abundance in sputum only.

Research Topic: Infectious Diseases
Funding agencies: CSR&D; NIH; UMN
Grant support: CSR&D 1IK2CX001095; UMN Women's Early Research Career Award; NIH 5KL2TR113, 8UL1TR000114; NIH 5T32AI055433.

103. Effectiveness of Antibiotic Formulary Policies on Clostridioides difficile Infection

Rahmathullah, Nabeelah [1]; DeVries, Aaron [1]

1. Minneapolis VA Health Care System

Abstract: Clostridioides difficile is linked to antibiotic-associated diarrhea and pseudomembranous colitis, especially following third-generation cephalosporin and fluoroquinolone use. Implementation of Antimicrobial Stewardship Programs (ASPs) have been associated with decreases in nosocomial C. difficile infection (CDI) rates. This multi-site qualitative research study aims to evaluate the implementation of acute care formulary restrictions and assess relation between antibiotic use patterns and historical CDI, identify barriers and facilitators to implementation, and develop a pilot intervention to implement effective and practical formulary restrictions. METHODS: The U.S. Department of Veterans Affairs Health Services Research & Development Service and the Centers for Disease Control and Prevention Division of Healthcare Quality Promotion partnered to establish a 15-site infection control practice-based research network (PBRN). Based on institution surveys and antibiotic consumption data, a subset of sites were chosen to be compared based on their antibiotic formulary policies and stratified based on their antibiotic stewardship practices (restricted, unrestricted, 'in transition') and their antibiotic use ('low', 'average', and 'high'). Minneapolis was classified as 'in transition'. Following consent, semi-structured recorded interviews were conducted with key personnel in each facility (ASP Physician, ASP Pharmacist, Hospitalist, ED Physician, Intensivist, Pharmacy Administrator). Interview recordings were sent to the central office (Iowa City VAHCS) for transcription and analysis. RESULTS: Preliminary analysis of the interview transcripts at the Minneapolis VAHCS revealed that all interviewees were aware and satisfied with ASP activities. All of them showed awareness of appropriate antibiotic use and associated adverse drug reactions, all reported satisfaction with Clinical Decision Support System for antibiotics, and half of the respondents expressed preference of more resources dedicated to ASP. DISCUSSION: Results of this study will be formulated with data collected at other PBRN sites and compared based on current ASP activities. Minneapolis VAHCS staff are satisfied with current activities, but some feel more resources are needed. With the aggregate data a pilot ASP intervention will be implemented at some PBRN sites. This study will provide valuable insight in aiding the implementation of high-quality ASPs in acute care settings worldwide.

Research Topic: Infectious Diseases
Funding agencies: HSR&D; CVRE
Grant support: N/A

104. Calculating Actinic Keratosis Risks to Aid in Shared Decision-Making

Ravishankar, Adarsh [1]; Maher, Ian [1]; Gravely, Amy [2]; Goldfarb, Noah [1,2]

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

Abstract: The treatment of actinic keratoses (AKs) in the elderly requires a complex shared decision-making discussion between a patient and their physician on risks/costs versus benefits, with an understanding of a patient's goals of care, age and co-morbidities. To aid in this shared decision-making process, we have designed an AK risk calculator that uses data available in the literature on AK-to-SCC transformation rates to help estimate a patient's lifetime risk of developing a squamous cell carcinoma (SCC) from AKs, using sex, birthdate, number of AK, NMSC history (download link: z.umn.edu/AKrisk_calculator). This calculator also calculates the risk reduction with the use of 5-fluorouracil with repeated annual use. This is the first known attempt at integrating risk calculations with data on life-expectancy and risk reduction with treatment for the purposes of improving shared decision-making for AKs. We chose the AK-to-SCC transformation rate of 0.096%/year for the general population,1 and a rate of 0.60 %/year for high-risk patients2 (defined by at least two NMSCs diagnosed in the previous five years, or at least 12 AKs on presentation). Using the risk calculations first conceived by Dodson et al (1991),3 given the yearly risk r of an AK transforming to either in situ or invasive squamous cell carcinoma (SCC), n number of AKs, and life expectancy l (years), the lifetime risk R of at least one AK transforming into an SCC is: R= 1-(1-r)^(n*l) Life expectancy l was obtained from the United States Social Security Administration's actuarial life table. Recent studies have shown that fluorouracil treatment reduced the risk of SCC developing by nearly 75% during the first year.5 From this data, the modified lifetime risk R_m if treatment were given for y years is: R_m= 1-(1-0.25 r)^ny*(1-r)^(n*(l-y)) We hope that this calculator will encourage shared decision-making between physicians and patients in discussing the management of AKs in the elderly. In the future, we hope to use this calculator in future studies of shared decision-making for the management of AKs in the elderly, looking at cost-savings and patients' views on quality of care.

Research Topic: Dental Implants
Funding agencies: N/A
Grant support: Off

105. The Effect of Metformin on the Risk of Recurrent Nonmelanoma Skin Cancers

Ravishankar, Adarsh [1]; Zhang, Tianshun [1,2]; Lindgren, Bruce [1,3]; Farah, Ronda [1]; Dong, Zingang [1,2]; Goldfarb, Noah [1,4]

1. University of Minnesota
2. The Hormel Institute
3. Masonic Cancer Center
4. Minneapolis VA Health Care System

Abstract: Metformin has been associated with a protective effect on the primary development of nonmelanoma skin cancer (NMSC) among type II diabetics. This raises the question of whether metformin can reduce recurrences of NMSC in patients with a history of NMSC. To answer this, we performed a retrospective cohort study of adult patients in the Veterans Affairs system with their first biopsy-confirmed NMSC between January 1 and December 31, 2003. The patients' problems and medication lists were screened for exclusion criteria, including previous NMSCs, type I diabetes, immunosuppression, arsenic or radiation exposure, genetic predisposition to NMSCs, and use of oral retinoids, contraceptives, or nicotinamide. Of the 740 patients screened, 544 patients were excluded due to prior NMSCs, and 22 were excluded for other exclusion criteria. The remaining 174 patients were placed into three cohorts: nondiabetics (n = 117), type II diabetics on metformin (n = 20), and diabetics not on metformin (n = 37). Demographics, patient characteristics, exposure history, melanoma history, atherosclerotic disease, average of three hemoglobin A1c (HgbA1c) values after enrollment, and significant medication usage were collected for enrolled patients. Dates of diagnosis, types, and locations of initial and second NMSCs were obtained from pathology reports. The primary outcome was the three-year risk of developing a second NMSC. Secondary outcomes included the three-year risk of developing BCC or SCC separately, the total number of NMSC over three years, and the time to second NMSC. Our study did not reveal a decreased risk of developing a second NMSC over the three-year period for type II diabetic patients on metformin compared to diabetics not on metformin (43.2% and 40.0%, respectively). Contrary to previous literature, we found an increased NMSC risk in nondiabetic patients compared to both diabetic cohorts ($p = 0.036$). Additionally, our results failed to demonstrate a significant effect of metformin on secondary variables including time to second NMSC ($p = 0.573$) and total number of NMSCs over three years ($p = 0.127$). Controlling for aspirin did not change the lack of significant effect of metformin on secondary NMSC risk. While metformin may be efficacious for primary NMSC prevention at higher doses over several years, its usage for secondary prevention necessitates further study.

Research Topic: Dermatology
Funding agencies: UMN
Grant support: University of Minnesota Foundation

106. MATCH: Microbiota or Placebo after Antimicrobial Therapy for Recurrent C. difficile at Home

Reinink, Andrew [1]; Lehenbauer, Kyle [1]; Anway, Ruth [1]; Belew, John [1]; Beste, Jacob [1]; Nugent, Sean [1]; Pretti, Alex [1]; Shaukat, Aasma [1]; Drekonja, Dimitri [1]

1. Minneapolis VA Health Care System

Abstract: Clostridium difficile infection (CDI) is one of the most common nosocomial Although more than 90% of patients have symptom resolution with a course of standard antimicrobial therapy, subsequent recurrence rates range from 15-30% (after the first CDI episode) to 40-50% (after the second and subsequent episodes). Fecal microbiota transplantation (FMT) has shown promise as an adjunct to standard antimicrobial therapy, reducing recurrence among FMT recipients to 15%. With the VA having a high burden of recurrent CDI, there has been considerable interest in FMT from both providers and patients. Objectives: The primary study goal is to test the efficacy of capsule-delivered FMT for the prevention of subsequent recurrent CDI, given after successful treatment of recurrent CDI with standard antimicrobial therapy. Secondary goals are to test the safety of FMT and document the changes in the colonic microbiome from pre- to post-transplant. Additionally, a novel enrollment strategy of traveling to the subject's home is being used. Research Plan: Using an innovative search for VA patients with CDI through the Corporate Data Warehouse (CDW), this study will enroll 390 participants who have: 1) Recurrent CDI, 2) Resolution or improvement of symptoms from most recent CDI episode, 3) Are within the enrollment window. Participants will be visited at home by a study nurse and be enrolled and randomized (1:1 ratio) to FMT or placebo capsules. The primary outcome is recurrent CDI (definite or possible) or death within 56 days of randomization. Preliminary results: Recruitment began in December 2018 and is ongoing. Our case-finding approach using the CDW has resulted in 264 potential cases of CDI, with 213 appearing to have recurrent CDI after review of the medical record. Among these 213 patients with recurrent CDI, 45 were eligible for participation. 33 of those eligible were able to be contacted and were offered participation, with 15 of those eligible opting to enroll. Enrolled patients are from 13 different VA medical centers in 15 states. Conclusions: Preliminary results show that conducing a VA-wide trial using a single center to identify and contact potential participants is feasible. Having study staff travel to participant's homes for enrollment offers a patient-centered approach and gives a greater number of patients access to research than does the traditional model of having designated participating VAs enroll subjects from within their area.

Research Topic: Infectious Diseases
Funding agencies: CSR&D
Grant support: CSP 2004

107. Osteoporosis Care After Hip Fracture at The Minneapolis VAMC

Ruanpeng, Darin [1,2]; Moen, Kyle [1,2]; Niewoehner, Catherine [1,2]; Diem, Susan [1,2]

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

Abstract: Pharmacologic treatment is recommended to reduce risk of future fractures and possibly reduce mortality in patients with hip fracture. We investigated osteoporosis care after hip fracture at the Minneapolis VA Health Care System to identify rates of pharmacologic treatment after hip fracture and barriers to treatment. Methods: We identified all patients admitted with a low impact hip fracture between 9/2015-4/2018. Follow-up clinical data was collected for a minimum of 12 months after hip fracture. Results: 136 patients were admitted with low impact hip fractures: 130 were male, mean age was 81.1 (SD 10.3) and 118 underwent surgery. At the time of the fracture, 35% had dementia/cognitive impairment, 29% used mobility aide, 15% had GFR <35 and 6% were on dialysis. Calcium and kidney function were measured in all patients and vitamin D was measured in 20% of patient. At discharge, 18% were prescribed calcium supplementation and 35% were prescribed vitamin D supplementation. At 1 year following hip fracture, osteoporosis medications had been prescribed in 17 (13%) of patients. 103 (79%) of the patients were seen in follow-up at our facility; 90 (69%) were seen in follow-up in our Orthopedics clinic. Six (4.4%) patients died in during the hospitalization for the hip fracture; 19 (18.4%) died within 3 months of the hospitalization and 49 (36.0%) died within 1 year. Conclusions: Osteoporosis treatment after hip fracture is suboptimal and a model of care is needed to close this care gap. Possible interventions could include administration of IV bisphosphonate during hospitalization or at post-fracture clinic follow-up with Orthopedics. In addition, hip fracture is associated with high 1-year mortality in elderly veterans.

Research Topic: Endocrinology & Metabolism
Funding agencies: N/A
Grant support: N/A

108. A Clinical Experience: Low-dose Topiramate in Obesity Treatment in A Minneapolis VA Population

Ruanpeng, Darin [1,2]; Gravely, Amy [1]; Billington, Charles [1,2]; Sibley, Shalamar [1,2]

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

Abstract: Despite concerns about side effects in doses used in clinical trials 10-15 years ago, low-dose topiramate (TPM) may be of use for obesity in those at high cardiovascular (CVD) risk. We report clinical experience of off-label TPM monotherapy in our weight-loss clinic. Methods: A retrospective cohort study included all patients seen at the Minneapolis VAMC Weight-Loss Clinic started on new medication for weight-loss from 1/2017-6/2017. Clinical data were followed up to 6 months. Results: Thirty-five patients started new medications (80% male, mean age 57 years [SD 13]). Baseline weight was 265.5 lbs (SD 40.4), BMI 39.4 kg/m2 (SD 4.3), hypertension 54%, type2 diabetes 51%, hyperlipidemia 31%, heart disease 14%, and baseline cravings/binging presence 91%. Medications started were TPM (15), phentermine/TPM (4), and others (16; phentermine 1, liraglutide 9, naltrexone 4, phentermine/bupropion 1 and bupropion 1). Weight loss was -5.1% (-13.9 lbs, SD 12.2) for mean 4 months (SD 2.0) on TPM; -3.3% (-7.7 lbs, SD 20.1) for mean 3.6 months (SD 0.8) on phentermine/TPM; and -4.7% (-12.4 lbs, SD 13.4) for mean 4.4 months (SD 1.5) on others. Among patients with baseline craving/binging, 92.3% on TPM, 100% on phentermine/TPM and 75% on other agents improved. One of 15 patients had symptoms likely TPM-related (memory problems). Three had side effects on other agents (short temper with bupropion; irritable, somnolence with naltrexone; dry mouth with phentermine). Average tolerated TPM dose was 100 mg/d (SD 54); 2 stopped TPM (memory problem and ineffective). Conclusion: In older patients at high CVD risk, low-dose TPM appears to be an effective, relatively tolerable pharmacologic weight-loss option. Specifically, we found that 43% got TPM monotherapy, weight loss was 5% which is clinically meaningful and in line with the other medication regimens, and the side effect rate was 7%, which is less than previous older studies have shown on higher doses, and in line with the other treatment options. Further research should be directed at mechanisms underlying TPM actions as a weight loss medication, including identification of factors predicting good response and side effects. Research should also be directed toward evaluating the potential role of craving and food impulsivity as factors driving obesity.

Research Topic: Other Chronic Diseases
Funding agencies: N/A
Grant support: N/A

109. Use of hierarchical measures of psychopathology to assess resilience in National Guard Recruits

Schaefer, Jonathan [1]; Erbes, Christopher [1,2]; Polusny, Melissa [1,2]

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

Abstract: The effects of most environmental stressors on psychopathology are strikingly non-specific, increasing risk of multiple mental disorders simultaneously. As a result, investigators who study these exposures are turning increasingly to latent measures of general psychopathology to capture their psychopathological effects. In this project, we first examined the structure of psychopathology in a longitudinal study of National Guard Recruits undergoing Basic Combat Training (BCT) using exploratory factor analysis. We then used confirmatory factor analysis to estimate a single latent factor (the 'p-factor') representing recruits' general liability to psychopathology. Finally, we tested whether recruits' scores on this measure were associated with scores on candidate predictors of resilience, including prior stressors, typical responses to stressful life events, social support, and personality. Our results indicated that recruits' scores on these predictor measures (most administered pre-BCT) were all significantly correlated their scores on the p-factor post-BCT. Taken together, these findings suggest that the p-factor may function as a useful measure in studies of psychological resilience in military samples.

Research Topic: Mental Illness
Funding agencies: N/A
Grant support: N/A

110. Facial Dermatitis in Males Referred for Patch Testing: Retrospective Cross-Sectional Analysis of North American Contact Dermatitis Group (NACDG) Data 1994-2016

Schlarbaum, Jamie [1-3]; Warshaw, Erin [1-3]; North American Contact Dermatitis Group

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

Abstract: Facial allergic contact dermatitis (ACD) due to women's cosmetics is well-recognized. However, little is known about men's facial dermatitis or personal care product usage. Objective: To characterize allergens and sources responsible for facial ACD in males. Methods: Retrospective cross-sectional analysis of 50,507 patients patch tested by the North American Contact Dermatitis Group (NACDG) from 1994-2016. Males with facial dermatitis (MFD) were compared to those without facial involvement (MNO). Results: 16,737 males were referred for patch testing. 1,332 (8.0%) had facial dermatitis (MFD) and 13,732 (82.0%) had non-facial dermatitis (MNO). 1,673 (10.0%) had both facial and body involvement and were excluded from analysis. Compared to MNO, MFD were associated with younger age (47 vs. 50 years), non-Caucasian race (17.7% vs. 10.8%) and non-occupationally-related skin disease (89.5% vs. 78.7%) (all p-values < 0.001). The most common facial sites were generalized face (48.9%), eyelids (23.5%), and lips (12.6%). 80 distinct allergens were clinically relevant; compared to MNO, the most common allergens in MFD included methylisothiazolinone (9.9% vs. 11.7%, $p = 0.4002$), fragrance mix (8.5% vs. 8.6%, $p = 0.9275$), and Balsam of Peru (6.8% vs. 9.1%, $p = 0.0042$). Of sources containing NACDG-allergens, 60.5% were personal care products. The most common specific sources of allergens were topical medications (10.1%) and hair care products (9.3%). Of the 139 males with occupationally-related facial dermatitis, the most common occupations were machine operators/assemblers/inspectors (28.4%), precision production workers (10.4%), and mechanics & repairers (9.7%). Conclusion: Males with facial dermatitis represent a distinct population with unique allergens and sources.

Research Topic: Dermatology
Funding agencies: N/A
Grant support: N/A

111. Occupationally-Related Nickel Reactions: Retrospective Cross-Sectional Analysis of NACDG Data 1998-2016

Schlarbaum, Jamie [1-3]; Warshaw, Erin [1-3]; North American Contact Dermatitis Group

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

Abstract: The epidemiology of nickel sensitivity in occupational settings is not well understood. Objective: To characterize occupationally-related nickel sensitivity (ORNS). Methods: Retrospective cross-sectional analysis of 44,378 patients patch tested by the North American Contact Dermatitis Group (NACDG) from 1998-2016. Characteristics of occupationally-related nickel reactions were compared to non-occupationally related reactions. Occupation/industry were grouped using 1990 US Census classification codes. Results: Of the 44,378 patients patch tested, 7,928 (17.9%) were positive to nickel. 268 (3.4%) had ORNS. ORNS was associated with male sex (41.0% vs. 12.9%, $p < 0.001$), a younger average age (41 years vs. 44 years), a diagnosis of irritant contact dermatitis (22.4% vs. 12.0%, $p < 0.001$), and no history of eczema (81.7% vs. 75.7%, $p = 0.0229$). The most common sites of dermatitis in individuals with ORNS were hand (39.9%, $p < 0.001$) and arm (18.1%, $p < 0.001$). 16 categories of industry and 22 categories of occupation were identified; the most common industries were durable goods manufacturing (24.6%) and personal services (15.7%) while the most common occupations were hairdressers/cosmetologists/barbers (14.3%), operators (9.4%), and healthcare workers (7.1%). Over 40% of occupations were in metalworking. Of 215 occupational sources specifically identified, instruments/phones/other equipment (16.3%), vehicles/machinery (15.9%), and tools (15.4%) were the most common. Conclusion: Occupational nickel sensitivity is distinct from non-occupational nickel sensitivity. Individuals with ORNS are more likely younger men and more likely to have hand or arm sites of involvement. Workplace sources of nickel vary, especially in regard to handheld instruments and tools.

Research Topic: Dermatology
Funding agencies: N/A
Grant support: Nickel Producers Environmental Research Association (NiPERA).

112. Contact Dermatitis to Personal Care Products in Males: Retrospective Analysis of North American Contact Dermatitis Group (NACDG) Data 1996-2016

Schlarbaum, Jamie [1-3]; Warshaw, Erin [1-3]; North American Contact Dermatitis Group

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

Abstract: Cosmetic corporations are increasingly marketing skin/hair products to men. More men than ever are using skincare and grooming products. Objective: To characterize allergic (ARs) and irritant (IR) reactions associated with personal care product (PCP) sources in males. Methods: Retrospective cross-sectional analysis of 48,472 patients patch tested by the North American Contact Dermatitis Group (NACDG) from 1996-2016. PCP sources for all ARs and IRs and were analyzed by sex. Results: Of the 17,434 individuals with 1 or more PCP-related ARs/IRs, 4,687 (26.9%) were males. Compared to females with PCP-related dermatitis, males were more likely to be older (M:52 years, F:49 years). Males with PCP-related dermatitis were also more likely to have scattered/generalized (M:21.1%, F:12.1%), hand (M:20.0%, F:15.3%), or foot dermatitis (M:5.1%, F:2.0%) but were less likely to have facial involvement (M:8.4%, F:19.2%) (all p-values<0.001). There were a total of 30,160 PCP-related ARs; 8,868 (29.4%) were in males. The most identified PCP sources of NACDG ARs for both sexes were moisturizers/lotions/creams (M:18.0%, F:14.9%) and shampoos (M:6.4%, F:8.0%). PCPs causing ACD with a high representation in males included pumice soaps (23/26), waterless hand cleansers (64/74), and deodorants (129/209). Common allergens for both sexes were methylisothiazolinone (M:28.8%, F:21.4%), fragrance mix I (M:22.2%, F:20.1%), and Balsam of Peru (M:18.4%, F:14.1%). Although many of the top allergens were relevant in both sexes, there were marked differences in frequencies. Some of the most frequent allergens found in moisturizers, shampoos, cosmetics, and soaps were different between sexes. Conclusion: Demographics of males and females with PCP-associated ARs are distinct. While many PCP-related allergens are similar, frequencies and sources of allergens differed between sexes.

Research Topic: Dermatology
Funding agencies: N/A
Grant support: N/A

113. Men's Moisturizers in the Metrosexual Era: A Comprehensive Analysis of 65 Facial Moisturizers

Schlarbaum, Jamie [1-3]; Warshaw, Erin [1-3]

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

Abstract: Manufacturers are increasingly branding personal care products specifically for men. More men than ever have started to use facial skincare regimens in this new era of men's grooming. Objective: To characterize ingredients and claims of facial moisturizers marketed to men. Methods: Moisturizers from 7 different online retailers were compared in June-September 2018. Products were included if they contained the words 'for men' and 'face.' Anti-aging products were excluded. Ingredients were grouped according to CAMP and Personal Care Product Council Ingredient Database categories. Results: 65 men's facial moisturizers marketed under 37 brands were identified. 51 (78.5%) were designated specifically for face use while 14 (21.5%) were marketed for both face and other body sites. 17 (26.2%) contained a sunscreen ingredient and 21 (32.3%) claimed to be 'paraben-free.' A total of 1929 ingredients were evaluated; the average number of ingredients per product was 30 (SD 10). The maximum number of ingredients in a single product was 61. After accounting for synonyms, there were 533 distinct ingredients, of which 234 were American Contact Dermatitis Society (ACDS) Core Allergens. The most common ACDS Core Allergens and North American Contact Dermatitis Group (NACDG) Standard Allergens were fragrances (present in 98.5% of products), phenoxyethanol (81.5%), tocopherol derivatives (69.2%), propylene glycol/derivatives (32.3%), parabens (29.2%), ethylhexylglycerin (26.2%), and glucosides (26.2%). Only 1 product contained methylisothiazolinone. Although 17 products (26.2%) claimed to be 'fragrance-free,' only 1 product was truly fragrance-free. 98.5% of products contains more than 5 ACDS Core Allergens. Conclusion: Men's facial moisturizers commonly contain fragrances and other emerging allergens. These allergens are similar but have striking differences when compared to those in unisex facial moisturizers and body moisturizers; this may reflect recent changes in personal care product preservation and ingredient usage.

Research Topic: Dermatology
Funding agencies: N/A
Grant support: N/A

114. Acceptability and Feasibility of Social Cognition and Interaction Training (SCIT) as an Intervention for Individuals with Serious Mental Illness

Schulte, Cody [1]; Tourville, Tia [1]; Nienow, Tasha [1]

1. Minneapolis VA Health Care System

Abstract: Social Cognition and Interaction Training (SCIT) is an intervention developed for individuals with serious mental illness. SCIT provides skills training with the aim of improving emotion recognition skills, reducing cognitive biases, and enhancing interpersonal effectiveness in social situations. This study examined the interest, feasibility, and acceptability of administering SCIT to veterans with serious mental illness (SMI) concurrent with maintenance of a work role. Methods: Veteran response to an advertisement offering 30 hours of social cognitive skills training was recorded. Letters were sent to 2,062 veterans with serious mental illness at the Minneapolis VAHCS. Veteran interest in the intervention was assessed through response to the advertisement and rate of study acceptance. Feasibility was assessed by examining barriers to study participation and rate of treatment uptake. Acceptability was assessed with rate of treatment completion and through recipient ratings of the intervention on the Intrinsic Motivation Inventory (IMI) after 6, 12, and 24 sessions. Results: Response to the advertisement was favorable, with only 18% of contacted veterans indicating that they were not interested in developing these skills. Among those who were eligible for the study, 81% expressed interest in study participation. Of the 18 individuals who engaged in the intervention, 16 completed it. Recipients consistently endorsed the intervention, with mean ratings on the IMI Interest and Value subscales in the 'Mostly True' to 'True' range. However, feasibility was limited. At every point in the recruitment process, veterans most frequently identified being 'too busy' as a barrier to participation. Consistent with this report, only 67% of veterans offered study enrollment progressed to the intervention phase of the study. Conclusions: Results indicate that there is interest among veterans with serious mental illness in receiving an intervention that addresses social cognitive difficulties. Importantly, veterans who received the intervention perceived it as useful and interesting. However, it was difficult for working veterans to participate in a 30-hour intervention. Offering this intervention to veterans prior to attainment of a work role may increase feasibility of participation in this type of intervention. Future research will explore pairing this intervention with vocational rehabilitation.

Research Topic: Mental Illness
Funding agencies: N/A
Grant support: CVRE

115. Quantifying Femoral Head Collapse Following Intra-Articular Corticosteroid Injections at the Minneapolis VAMC: a Quality Improvement Initiative

Schwanz, Kersten [1]; Kelly, Brandon [1]; Williams, Benjamin [1]; Sechriest, V. Franklin [1,2]

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

Abstract: Intra-articular corticosteroid injections (IACSI) are a therapeutic standard of care treatment for hip osteoarthritis symptoms. At the Minneapolis Veteran's Affairs Medical Center (VAMC), a number of patients with mild to moderate hip osteoarthritis (OA) who initially presented without radiographic evidence of femoral head collapse, underwent IACSI, and subsequently developed dramatic progression of disease (i.e. femoral head collapse) in the apparent absence of other significant risk factors. While multiple case reports of collapse exist, there is no consensus on IACSI as a cause of disease progression. There is an overall lack of practice standardization and monitoring for this problem. Currently, there is little research on how often collapse occurs, what risk factors may contribute, and what recommendations can be made to modify practice. To improve patient safety, we obtained IRB approval to quantify the burden of femoral head collapse. We are reviewing patient charts from all Minneapolis VAMC hip IACSI administered from October 2015 until February 2018. In particular, we are analyzing pre- and post-injection radiographs, IACSI doses, and pertinent patient risk factors for 423 veterans. Current analysis of reviewed data shows collapse rate of 24.17%. As we have yet to complete our review, we cannot make major conclusions at this time. We have introduced recommended guidelines for hip IACSI based on our current findings and plan to track the impact.

Research Topic: Arthritis
Funding agencies: N/A
Grant support: N/A

116. Acceptability and Feasibility of Repeated Transcranial Direct Current Stimulation (tDCS) as an Intervention for Individuals with Mild Traumatic Brain Injury

Shields, Taegan [1]; Schulte, Cody [1]; Nienow, Tasha [1,2]

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

Abstract: Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that has potential as a cognitively enhancing intervention. This project assessed the interest, acceptability, and feasibility of offering repeated tDCS as an intervention for cognitive difficulties to individuals with mild traumatic brain injury (mTBI). Methods: To accomplish this aim, veteran response to an advertisement for a 24-session clinical trial offering repeated tDCS administration concurrent with cognitive training was recorded. Letters describing the clinical trial were sent to approximately 1,000 veterans at the Minneapolis VAHCS identified through medical record review as people who had likely experienced a traumatic brain injury. Veteran interest in the intervention was assessed through response to the advertisement and rate of treatment uptake. Acceptability was assessed through the frequency with which veterans expressed concerns about this specific type of intervention. Feasibility was assessed by examining the frequency with which veterans identified barriers to participation and the frequency with which factors excluded veterans from participation. Results: Approximately 1 in 5 veterans contacted about the study expressed interest in an intervention that might enhance attention and memory skills. Among those found eligible for the study, less than 10% declined study participation due to lack of interest. TDCS was perceived as an acceptable approach to intervention, with less than 1% of veterans expressing concern about this methodology. With regard to feasibility, while incompatibility with tDCS procedures excluded less than 10% of veterans from this type of intervention, veterans frequently identified the time commitment and commute to the VA as barriers to participation in the study. Conclusions: The results of this study support interest among veterans with mTBI in receiving an intervention that addresses cognitive difficulties. The rate of response to this clinical trial among non-treatment seeking individuals suggests an unmet clinical need. Importantly, veterans perceived tDCS concurrent with cognitive training as an acceptable approach to intervention. However, this study also identified several external barriers to participation. If future research finds tDCS to be efficacious, dissemination through home care and local community clinics is likely to be critical to intervention uptake.

Research Topic: Acute & Traumatic Injury
Funding agencies: N/A
Grant support: State of Minnesota Office of Higher Learning

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117. Identification of Antidepressant Strategies by the Minneapolis VA Pharmacy Algorithm

Shiroma, Paulo [1]; Thuras, Paul [1]; Do, Annette [1]; Atkinson, David [1]; Baltutis, Eric [1]; Westanmo, Anders [1]

1. Minneapolis VA Health Care System

Abstract: The 2016 VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder offer consensus-based recommendations when response to the initial antidepressant medication is suboptimal; however, little is known about 'real-world' pharmacological strategies by providers treating depression in the Veterans Affairs Health Care System (VAHCS). We extracted pharmacy and administrative records from patients with diagnosis of depressive disorder treated at the Minneapolis VAHCS between 1/1/1999-4/10/2019. Bipolar disorder, psychosis-spectrum or dementia were excluded. An algorithm using pharmacy data was developed to identify antidepressant strategies: monotherapy (MONO); optimization (OPM); switching (SWT); combination (COM); and augmentation (AUG. The initial sample consisted of 3,968 patients. We excluded 1,706 patients who had one prescription order, were considered to initiate depression treatment outside the VA, or had a gap between fills of more than 30 days; 974 patients were excluded due to >90 days between IDD and first antidepressant prescription; in addition, fifty one patients were excluded due to lack of confirmatory diagnosis of depression within 6 months after IDD leaving a total of 1238 patients for analysis. The SSRIs with citalopram (N = 378) and sertraline (N = 254) were the most common class and antidepressants, respectively. Interestingly, sertraline, venlafaxine and mirtazapine did not achieve adequate antidepressant doses. Receiving a single antidepressant (with or without adequate doses) followed by increasing dose of initial antidepressant (OPM) were the most common antidepressant strategies representing 81.5% of total cases. There was a significant difference regarding age of patients ($F_{5,5075.6} = 3.28$; $P = 0.006$), gender of patient ($.2 = 41.14$, $df = 5$, $P = 0.001$), and gender of provider ($.2 = 278.3$, $df = 5$, $P = 0.001$), and medical service (Psychiatry vs Primary Care/Specialties) ($.2 = 215.3$, $df = 5$, $P = 0.001$) by strategies. This initial report implements an algorithm based on VA pharmacy data to identify antidepressant strategies beyond first-line agents. Increasing the dose (optimization) was the most common strategy after an initial antidepressant. Adding a psychotropic (combination and augmentation) to initial antidepressant were highly infrequent strategies. Future steps include analyzing whether strategies impacts service utilization and clinical outcomes such as hospitalization and suicidal behaviors.

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

118. Randomized, Placebo Control Study of Repeated vs Single Subanesthetic Ketamine in Treatment-resistant Depression

Shiroma, Paulo [1]; Thuras, Paul [1]; Baltutis, Eric [1]; Wels, Joseph [1]; Lim, Kelvin [1,2]; Albott, Sophia [1]; Bassett, Cody [1]; Erbes, Christopher [1]; Tye, Susannah [3]

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

Abstract: Single Ketamine at subanesthetic dose has demonstrated rapid antidepressant effects in treatment-resistant depression (TRD). Repeated Ketamine in open-label studies suggested greater antidepressant response. However, the American Psychiatric Association stated that there is no evidence to support frequent Ketamine administration. This study compared two randomized conditions: 1) six Ketamine at 0.5 mg/kg (K6) or 2) single Ketamine at 0.5 mg/kg preceded by five Midazolam at 0.045 mg/kg (active placebo) (K1) for a total of 12-day infusion-phase followed by 6-month time-to-relapse period. The primary end point is the change from baseline in the MADRS score 24 hours after the last infusion. Fifty four subjects completed all six infusions. There was no significant difference in change of MADRS scores between K1 (mean = 19.35) vs K6 (mean = 23.32) at the end of treatment ($F_{1,106.01} = 2.41$, $P = 0.13$). Nonetheless, there was a significant change in MADRS score by groups over time ($F_{1,50,97} = 1.90$, $P = 0.17$). Remission (MADRS=9) was significantly different between groups after the fourth (K6 = 68% vs K1 = 37.9%; X21df=4.86; P = 0.02) and fifth infusion (K6 = 72% vs K1 = 44.8%; X21df=4.05; P = 0.04). The time to relapse (MADRS>50% from baseline scores) was no significantly different between groups (median for K6 = 6 weeks vs median for K1 = 2 weeks; X21df=1.61; P = 0.21). Overall, results conclude that acute repeated Ketamine treatment shows greater antidepressant efficacy to active placebo, but not superior to a single Ketamine at the end of 2 weeks. These findings support the current notion that the action mechanism of Ketamine for depression does not appear to require sustained blood concentrations with antidepressant effects continuing well past the time in which it is entirely eliminated. Future studies should aim to examine the optimal balance of Ketamine treatment dosing (e.g., frequency and intervals) to obtain maximum antidepressant efficacy with minimum exposure.

Research Topic: Depression
Funding agencies: CSR&D
Grant support: 1 I01 CX001191

119. Antidepressant Effect of the Minneapolis MOVE! Program among Morbidly Obese Veterans

Shiroma, Paulo [1]; Usset, Timothy [1]; Wilhelm, John [1]; Thuras, Paul [1]; Velasquez, Tina [2]; Baltutis, Eric [1]

1. Minneapolis VA Health Care System
2. United Healthcare Group R&D

Abstract: Obesity is highly co-morbid with depression and PTSD among users of the Veteran's Health Administration (VHA) services. Weight loss and physical activity have been shown to ameliorate depression; however, specific biological, psychological, and sociological factors that facilitate treatment of depression symptoms through weight loss are unclear. The MOVE (Managing Overweight Veterans Everywhere) program is a multifaceted program that adapts interventions to the needs of participants including inpatient support, self-management classes, and on-site support groups. This pilot study sought to explore the effect of two different MOVE interventions. These interventions include: 1) the Intense MOVE! Program (IMP), which is a 2-week residential program (Monday through Friday) that includes scheduled physical activity, strict dietary intake, and behavioral modification in a controlled environment, and 2) The SMP group, which provides ten educational modules on a weekly basis on a variety of nutrition, physical activity, and behavior change topics. Fourteen subjects with morbidly obesity (BMI mean = 43.9) and depression (1/14 and mean overall duration of current depressive episode of 13.5 months) were randomly assigned to and completed either the IMP or SMP group. There was a significant change in depression severity over time ($F_{3,36.77} = 5.28$; $P = 0.004$) between both groups. In addition, the change in severity of depression measured by BDI score significantly correlated with total weight loss ($r=-0.597$; $p = 0.041$) and daily energy expenditure at 12 days ($r=-0.669$; $p = 0.012$); 6 weeks ($r=-0.587$; $p = 0.035$), and 10 weeks ($r=-0.710$; $p = 0.010$). The small sample of morbidly obese Veterans with co-morbid depression, IMP showed to be more efficacious to reduce severity of depression than the SMP group. Overall, the daily energy expenditure and weight loss correlated with mood improvement.

Research Topic: Obesity
Funding agencies: N/A
Grant support: N/A

120. 12-Month Reduction in Clinical Service Utilization Following Participation in DBT-PE Intensive Outpatient Program for Borderline Personality Disorder and PTSD

Silverman, Merav, [1]; Voller, Emily [1]; Thuras, Paul [1]

1. Minneapolis VA Health Care System

Abstract: Comorbidity rates between borderline personality disorder (BPD) and posttraumatic stress disorder (PTSD) are very high, particularly among veterans. Patients with these co-occurring disorders often experience high levels of distress and utilize a range of clinical resources, including mental health, emergency department, and inpatient hospital services. These high rates of utilization place a heavy burden on the financial and clinical resources in healthcare systems and are often ineffective at reducing the symptoms and distress associated with these disorders. Efforts to effectively treat these comorbid disorders have integrated dialectical behavioral therapy (DBT) and prolonged exposure (PE), typically on an outpatient basis, and research has shown that these integrated treatments may effectively reduce symptoms. Many facilities lack the resources to provide these treatments and patients needing these treatments often have many barriers that make engaging in these outpatient services challenging. Between 2012 and 2018, a 12-week intensive outpatient program (IOP) combining these two treatment modalities (DBT and PE) was offered at a large, Midwestern Veteran Affairs medical center for veterans with comorbid BPD and PTSD, to facilitate patients' ability to complete these two programs. 12-month pre- and post-DBT-PE-IOP treatment utilization was compared for 151 veterans for whom this information was available, to determine whether there were changes in clinical service usage prior to and following participation in this IOP. Paired sample t-tests show a significant reduction in 12-month mental health treatment utilization (mean, pre = 94.64, mean, post= 56.85, $p < .000$) and 12-month hospitalization rates (mean, pre = .729, mean, post = .351, $p < .000$). There was a non-significant reduction in emergency department visits. These findings suggest that participants in this DBT-PE IOP showed significant reductions in the most resource-intensive services (inpatient hospitalizations) and overall mental health utilization over the 12-months following their participation. These results suggest that brief, intensive treatment for individuals with these co-occurring disorders, while resource intensive, might be an effective way to treat these high needs patients while reducing long-term, ineffective service usage in hospital systems.

Research Topic: Mental Health
Funding agencies: N/A
Grant support: N/A

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121. The Veteran Amputee: A Prosthetic Sock Management Tool for Fit and Comfort

Slater, Billie Savvas [1]; Koester, Karl [1]

1. Minneapolis VA Health Care System

Abstract: Objective/Hypothesis: Prosthetic socks are used by some amputees to manage the condition of their residual limb: to avoid skin breakdown, callous formation, to maintain overall skin integrity, and to manage comfort. There may be volume changes (swelling and shrinking) in the residual limb throughout the course of the day and over time. Many patients manage the fit and comfort of the prosthetic socket, due to fluctuation in limb volume, by donning (putting on) and doffing (removing) socks of various thicknesses (ply). When Veterans repeatedly apply too many socks (over-socking), too few socks (under-socking), or have unwashed/dirty socks, problems may occur. Amputation Team Clinicians (Physiatrists, Prosthetists, Occupational and Physical Therapists) have expressed that there is a need for better education of new amputees at the time of prosthetic training, before the Veteran goes home with their new prosthetic limb. Veterans have said that they would like something to help them understand what to do with the socks once they get home, away from the clinical setting. This tool is designed to bring value to the clinicians who perform the prosthetic sock training, as well as to the Veterans who must properly utilize their socks to manage the fit and comfort of their prosthetic limbs. Clinical Significance to the Veteran Population: Clinicians working with Veterans with amputations will have a tool at their disposal that will help them teach Veterans about correct prosthetic sock use and allow for reinforcement of these instructions in multiple ways in multiple locations (in the exam room, in the waiting room, and in the Veteran's home via the infographic instruction included in the tool and the PSMT instructional video). Veterans, especially those in rural locations, will benefit from the availability of remote instruction: the infographic included in the tool, the video which will be available online, and the text message via the 'Annie' short message service (SMS). Veterans following instructions regarding appropriate prosthetic sock use will have healthier residual limbs than those who use the prosthetic socks improperly. Using the PSMT will reduce the number of clinic visits Veterans will need to make, reducing costs, and enhancing quality of life for Veterans with amputations.

Research Topic: Rural Health
Funding agencies: N/A
Grant support: VHA Innovators Network

122. Reduced Bacterial Hand Contamination with an Ergonomic Wheelchair

Slater, Billie Savvas [1]; Porter, Stephen [1]; DeVries, Aaron [1]; Johnson, James [1,2]; Clabots, Connie [1]; Hansen, Andrew [1,2]; Goldish, Gary [1]

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

Abstract: With standard wheelchairs (SWs), the co-location of hand rims and tires potentially exposes the user's hands to the tires, which continuously contact the floor. Such exposure risks contaminating the user's hands with (floor-source) bacteria, possibly increasing infection risk and disseminating resistant bacteria. For improved mechanics, our novel ergonomic wheelchair (EW) spatially separates the drive wheel and hand rims, connecting them with a chain. Objective: To determine whether our innovative EW reduces bacterial contamination of the user's hands. The Minneapolis Veterans Affairs (VA) Medical Center (MVAMC) Research and Development Committee approved this study, which was funded by the VA. Experimental Design: Volunteers wearing nitrile gloves were assigned randomly to test each wheelchair. They propelled each chair on a standardized 'run' through the hospital. The hand rims (but not the tires) of each wheelchair were cleaned thoroughly before each run. Outcomes were assessed by culturing and counting bacteria from wheelchair tires and hand rims, and from the gloved hands of volunteers. We made paired, two-tailed comparisons of gloved-hand bacterial counts. We also made overall unpaired, two tailed comparisons of hand counts between chairs (total runs, n = 19: 9 Ergonomic Wheelchair, 10 standard chair). Setting: MVAMC, a large medical center. Participants: Eleven volunteer non-wheelchair-using MVAMC employees. Intervention: The Ergonomic Wheelchair, compared with a standard manual wheelchair. Results: Post-ride hand counts were substantial, and were consistently lower with the EW than the SW: ï For riders who tested both chairs (n = 8), hand counts were significantly lower (T-test paired two-tailed p = 0.02) when using the EW versus the SW. ï For runs in which the two chairs were ridden in tandem by different users (n = 9), hand counts were also significantly lower (T-test paired two-tailed p = 0.008) when using the EW versus the SW. Pre-ride bacterial counts from cleaned hand rims, and from riders' hands, were nil. Wheelchair tires exhibited comparably high bacterial counts regardless of chair type. Conclusion: Separation of a wheelchair's hand rims and tires significantly reduces bacterial contamination of the user's hands. Clinical Relevance: These results support further studies to determine whether use of the new EW reduces users' risk of bacterial infections and dissemination of resistant bacteria.

Research Topic: Infectious Diseases
Funding agencies: N/A
Grant support: N/A

123. Outcomes of Urinary Diversion Created for Late Adverse Effects of Gynecologic Radiotherapy

Smith, Daniel [1]; Pariser, Joseph [1]; Albersheim, Jacob [1]; Moses, Rachel [2]; O'Dell, Diana [3]; Stoffel, John [3]; Myers, Jeremy [2]; Elliott, Sean [1]

1. University of Minnesota
2. University of Utah
3. University of Michigan

Abstract: Severe urinary adverse effects of radiation are seen in 17% of women treated for gynecologic malignancies. This incidence continues to climb through at least 25 years post-radiation. Reconstructive options are fraught with morbidity as surgical repair of vesicovaginal fistula and radiation-induced ureteral stricture are prone to failure due to local effects of radiotherapy. Urinary diversion represents an option for devastated anatomy, though some patients are notably frail. We sought to elucidate the risks of urinary diversion in patients with a history of radiation for gynecologic malignancy. Methods/Materials: A retrospective review was performed of patient records during the period of 2008 – 2018 from three tertiary centers. Women were identified who underwent continent or incontinent urinary diversion for urinary adverse effects of gynecologic radiotherapy. Indications for diversion included: radiation cystitis, fistula, incontinence, perineal wounds, and urinary tract stricture disease. Sarcopenia was determined by Slice-o-matic software (Tomovision, Quebec, CA) by skeletal muscle index (SMI) based on preoperative CT when available. Outcomes include any post-operative complication within 90 days of surgery as well as 30-day readmission rate. Long-term outcomes, including ureteral stenosis, stomal complications, fistula, renal dysfunction, and bowel function, were also examined. Results: A total of 34 patients from three institutions were included for analysis. The majority were white/Caucasian (73.5%). Median BMI was 24 kg/m2 (interquartile range [IQR] 19.4 – 30). 26/34 (76.5%) underwent non-continent diversion. Median EBL was 300 (IQR 150 – 500). 25/34 (73.5%) of women experienced complications within 90 days; 9/34 (26.5%) experienced high grade (> Clavien grade 3) complications. 11/34 (32.4%) of women were readmitted within 30 days. Conclusions: Urinary diversion for late adverse effects of gynecologic radiotherapy is fraught with complications. Patients and surgeons should consider risks and benefits when deciding to proceed with urinary diversion, especially in the setting of a frail patient.

Research Topic: Urology
Funding agencies: N/A
Grant support: N/A

124. Assessment of Systematic Review Quality in Urology Using AMSTAR-2

Soderberg, Leah [1]; Ding, Maylynn [2]; Jung, Jae Hung [3]; Dahm, Philipp [4]

1. University of Minnesota
2. McMaster University, Canada
3. Yonsei University, South Korea
4. Minneapolis VA Health Care System

Abstract: and Objectives: Assessment of Multiple Systematic Reviews (AMSTAR) is a validated instrument to assess systematic review (SR) methodological quality. It has been updated with more stringent expectations. AMSTAR-2 includes sixteen domains, seven of which are critical. This study investigates whether SRs published in urological literature meet these standards. Methods: We systematically searched PubMed® for SRs published in five major urology journals from 1/2016 to 12/2018 that address prevention/therapy. Two independent reviewers followed an a priori protocol to screen references and abstracted data using AMSTAR-2. Results: The literature search identified 553 studies, and 144 met inclusion criteria. The largest contributors were European Urology (53; 36.8%), Urology (36; 25.0%), and BJU International (24; 16.6%). Common topics were oncology (65; 45.1%), voiding dysfunction (32; 22.2%) and stones/endourology (14; 9.7%). The median number of studies included in SRs was 16.0 (IQR: 9, 31.0). Approximately one-third (51; 35.4%) of reviews had a registered protocol and one-third focused only on randomized trials (52; 36.11%). Nearly all SRs (139; 96.5%) searched two or more databases, but markedly fewer searched trial registries (45; 31.3%) or consulted experts (29; 20.1%). Most (120; 83.3%) screened references independently and in duplicate, but under half (65; 45.1%) reported the same for data abstraction. Few reviews (14; 9.7%) justified excluding individual studies. Conclusions: SR quality in urological literature is sub-optimal, undermining validity and value. It is important for authors, reviewers, and editors to better appreciate the underpinnings of methodologically sound, high quality SRs.

Research Topic: Urology
Funding agencies: UMN
Grant support: N/A

125. Multifocal Crohn's disease strictures are associated with an increased risk of progression to surgical resection

Song, Kevin [1,2]; Teigen, Levi [2]; Amateau, Stuart [2]; Shmidt, Eugenia [2]

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

Abstract: Crohn's disease (CD) associated intestinal stricture carries significant morbidity with the majority of patients requiring at least one surgical resection within ten years after initial CD diagnosis. Endoscopic balloon dilation (EBD) offers a safe, surgery-sparing alternative. However, the factors that affect long-term outcomes of EBD have not been sufficiently elucidated. All patients with CD-associated intestinal strictures and EBD were identified through a retrospective audit at the University of Minnesota Medical Center between 2006 and 2018. Demographic information, disease history, medications, lifestyle risk factors, endoscopy findings, basic laboratory data, and surgical information were collected. Technical success was defined as passage of the scope through the stricture after EBD. The primary endpoints of the study were need for surgery and repeat dilation. Univariate logistic regression analysis was used to identify risk factors for progression to surgery and repeat dilatation. Kaplan-Meier analysis was performed for periods free of surgery then compared using Log-rank test. During a median follow up of three years, 33 patients with CD-associated intestinal strictures underwent a total of 66 EBDs. Of these, 16 patients required repeat dilations with 11 patients requiring more than two dilations. The technical success rate was 97%. Perforation occurred in one patient during dilation and retrieval of a retained capsule endoscopy at the site of small bowel stricture with active inflammation. In total, 8 patients progressed to surgery. The presence of multifocal strictures, defined as greater than one stricture on endoscopy, was found to be a significant risk factor for the progression to surgery. Cumulative rates of progression to surgery classified by single vs. multiple strictures are demonstrated in the Figure. Moreover, 9 patients (27.3%) required repeat EBD or surgery within 6 months of index EBD. Patients who required surgery or repeat EBD within 6 months of index endoscopy had significantly smaller maximum dilation diameters compared to patients who did not require any interventions within 6 months. In this retrospective analysis, the presence of multifocal strictures at index EBD is associated with a nearly nine fold increased risk for progression to surgery. Clinicians may consider avoiding EBD in patients with multifocal CD strictures, given high likelihood of progression to surgery.

Research Topic: Gastrointestinal Health
Funding agencies: N/A
Grant support: N/A

126. Building a Nomogram with Preoperative Predictors of Early Urinary Continence Recovery After Radical Prostatectomy

Soubra, Ayman [1]; Flores, Jose [1]; Vock, David [1]; Warlick, Chritopher [1]; Weight, Christopher [1]; Nakib, Nissrine [1]; Konety, Badrinath [1]

1. University of Minnesota

Abstract: Our objectives were to determine any association between urinary continence recovery after radical prostatectomy and clinical characteristics, preoperative oncologic status, and pelvic anatomic parameters measured by magnetic resonance imaging (MRI) and to establish a nomogram with preoperative predictors to evaluate the patients√≠ baseline status to predict urinary continence recovery at 3 and 6 months after radical prostatectomy. Methods: 192 patients were evaluated. All clinical characteristics, preoperative oncological status, pelvic MRI measurements and urinary continence recovery at 3 and 6 months were assessed. A backward stepwise Logistic regression models were performed. This was fitted to evaluate the discrimination, calibration, sensitivity and positive predictive values. Nomograms were built according to the methodology described previously. A P value < 0.05 considered statistically significant. Results: A longer membranous urethra length (MUL) was the only pelvic MRI measurement statistically significant associated with urinary continence recovery at 3 and 6 months. The Logistic regression models obtained were at 3 months with MUL, the prostate anterior-posterior measurement, the bony femoral width measurement, and the midpelvic area measurement; at 6 months, diabetes mellitus, MUL and the prostate anterior-posterior measurement. The areas under ROC curves obtained were 0.691 at 3 months and 0.703 at 6 months. The c-index was 0.7 at 3 months; 0.703 at 6 months. The calibration plots between predicted and observed values were satisfactory (R2 = 0.588 at 3 months; 0.692, at 6 months). The model at 3 months had a sensitivity of 96.9% and a positive predictive value of 51.1%; at 6 months, a sensitivity of 97.1% and a positive predictive value of 77.1%. Conclusion: These are nomograms to assess preoperatively a baseline status per each patient and could help to identify potential patients with low probabilities for early urinary continence recovery.

Research Topic: Urology
Funding agencies: UMN
Grant support: N/A

127. Exoskeletal-Assisted Walking in Persons with SCI: Impact on Quality of Life

Spungen, Ann [1]; Bauman, William [1]

1. James J. Peters VA Medical Center

Abstract: Veterans with spinal cord injury (SCI) have many adverse secondary medical and quality of life (QOL) changes as a result of immobilization. Veterans with SCI who have completed rehabilitation after injury and are unable to ambulate receive a wheelchair as standard of care (SOC) for mobility. Powered exoskeletons are a technology that has recently become available as an alternate form of mobility by providing an external framework for support and computer controlled motorized hip and knee joints to assist with overground ambulation. Will Veterans with chronic SCI of =six months duration, who are medically stable and who use a wheelchair as SOC plus an exoskeletal-assisted walking (EAW) device in their home and community environments have clinically meaningful net improvements in mental health, bladder, bowel, and pain patient-reported outcomes compared with those who use only the SOC? Additionally, will the use of an EAW device for four months in the homes and/or communities of the participants result in a reduction of total body fat mass? Study Design A two-group (Intervention and Control), randomized, clinical trial will be performed with a one-year feasibility component. The Intervention group will receive SOC plus EAW. The Control group will receive SOC only. The study will require seven years in total to complete and includes fifteen VA SCI Services as study sites with one hundred-sixty participants to be randomized. The fifteen sites include: Boston, Richmond, St. Louis, Tampa, Milwaukee, Minneapolis, Dallas, Houston, Palo Alto, Long Beach, Augusta, San Antonio, Bronx, Cleveland, and Albuquerque. Of these fifteen sites, five are VA Cooperative Studies Program (CSP) Network of Dedicated Enrollment Sites (NODES).

Research Topic: Central Nervous System Injuries & Associated Disorders
Funding agencies: N/A
Grant support: CSP

128. Early sociability and social memory impairment in A53T mouse model of Parkinson's Disease are ameliorated by chemogenetic modulation of orexin neuron activity

Stanojlovic, Milos [1]; Pallais, Jean Pierre [1]; Vijayakumar, Aarthi [1]; Kotz, Catherine [1,2]

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

Abstract: Parkinson's Disease (PD) is a multi-layered progressive neurodegenerative disease. Signature motor system impairments are accompanied by a variety of other symptoms such as mood, sleep, metabolic, and cognitive disorders. Interestingly, social cognition impairments can be observed from the earliest stages of the disease, prior to the onset of the motor symptoms. In this study, we investigated age-related reductions in sociability as well as social memory in A53T mouse model of PD. Since inflammation and astrogliosis are an integral part of PD pathology and impair proper neuronal function, we examined astrogliosis and inflammation markers as well as parvalbumin expression in medial pre-frontal cortex (mPFC), part of the brain responsible for social cognition regulation. Finally, we used DREADDS (Designer Drugs Exclusively Activated by Designer Drugs) stimulation/inhibition of orexin neuronal activity to modulate sociability and social memory in A53T mice. We observed that social cognition impairment in A53T mice is accompanied by an increase in astrogliosis and inflammation markers as well as the loss of parvalbumin neurons and inhibitory pre-synaptic terminals in mPFC. Moreover, DREADD induced activation of orexin neurons restores social cognition in the A53T mouse model of PD.

Research Topic: Dementia & Neuronal Degeneration
Funding agencies: NIH; RR&D
Grant support: 5R01DK100281, D5I01RX000441 (CMK)

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129. Neural Abnormalities of Reward Processing in Adolescent Bipolar Disorders: An ERP Study

Stim, Joshua [1,2]; Maresh, Erin [2]; Van Voorhis, Abe [1]; Kang, Seung Suk [1,2]; Sponheim, Scott [1,2]; Luciana, Monica [2]; Urosevic, Snezana [1,2]

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

Abstract: Bipolar disorders (BDs) place Veterans at a high risk of completed suicide and other negative outcomes, such as homelessness and incarceration. Evidence suggests that reward dysregulation is a core dysfunction in adult BDs. However, little is known about temporal dynamics of dysregulated neural reward processing in adolescent BDs. This is an important oversight given that adolescence is a period of normative changes in neural reward systems and a common period of BD onset. Further, early onset of BDs place individuals at risk for poor prognosis in adulthood. The present study bridges this gap by using ERP analysis to examine neural abnormalities during reward processing in adolescent BDs. The ERPs of interest are the N1 and P3, which, within reward paradigms, index early selective attention and later allocation of attentional resources to reward cues, respectively. Given prior studies in adult BDs, we predict that adolescents with BDs will show enhanced P3 and N1 responses to reward cues compared to healthy adolescents. We recruited 101 adolescents (ages 13-19; 45 with BDs and 56 healthy controls [HC]). EEG data were collected using a 128-electrode net during a monetary incentive delay (MID) task. In each trial, anticipation cues signaled the opportunity to gain money, avoid losing money, or break-even, if a participant responded quickly enough to an upcoming target. Mixed models were used to assess effects of group, trial-type, sex, and age on ERP measurements at Pz for P3, and FCz and Fz for N1. Overall, the BD group had longer N1 latencies, but shorter P3 latencies, compared to HCs. There was a group-by-sex-by-trial-type interaction for N1 amplitude: sex was more predictive of N1 amplitudes in the HC group than in the BD group, but only for neutral cues. A group-by-sex-by-age interaction was also revealed for P3 latency: age was more predictive of P3 latencies for boys with BDs than for HC boys and there was no difference in age effect between BD and HC girls. Overall, the data suggests an impact of BDs in adolescence on early and later attentional processes within a reward context, but these effects appear sex-specific and not related to reward hypersensitivity in adult BDs. Neural markers of reward hypersensitivity in BDs may not appear until adulthood, when neuromaturation is complete. Longitudinal studies of adolescent BDs are needed to assess whether these sex-specific attentional abnormalities persist into adulthood and predict clinical outcomes.

Research Topic: Mental Health
Funding agencies: N/A
Grant support: NIMH K01 MH093621

130. Utilization of a Smart Water Bottle to Increase Fluid Intake in Stone Formers

Stout, Thomas [1]; Lingeman, James [2]; Krambeck, Amy [2]; Humphreys, Mitchell [3]; Zisman, Anna [4]; Borofsky, Michael [1]

1. University of Minnesota
2. University of Indiana
3. Mayo Clinic, Arizona
4. University of Chicago

Abstract: High dietary fluid intake is a cornerstone of kidney stone prevention; yet, is challenging to achieve. There is interest in using smart water bottles for this purpose but sparse data exists as to whether such technology leads to better outcomes relative to standard counseling. We sought to assess whether the addition of smart water bottle to standard dietary fluid recommendations leads to improved urine volume. Methods: IRB approval was obtained to offer voluntary enrollment into a prospective randomized controlled trial comparing the effect of standard dietary fluid recommendations to standard recommendations with the addition of a smart water bottle on 24 hour urine (24 hr U) volume. Eligible participants included those over the age 18 with a history of nephrolithiasis and low urine volume (<1.5 L) in the past 6 months. All subjects received a handout with strategies to achieve a goal urine output of 2.5 L/day. The intervention arm also received a smart water bottle (Hidrate Spark, Minneapolis, MN) with a sensor that recorded daily fluid intake, synced to the user's smartphone, and provided periodic reminders to drink. All patients completed a baseline survey to assess barriers to achieving adequate fluid intake. They then repeated a 24 hr U at 6 weeks and a repeat survey at 12 weeks. Results: 77 subjects (38 Smart-bottle arm, 39 Non-smart bottle arm) have been enrolled at the time of this 2 year interim analysis. Baseline demographics between groups are similar. Among all participants at baseline, the main reported factor limiting sufficient fluid intake is not remembering to drink (58%). 62% report being very motivated to increase fluid intake. Follow up 24 hr U are available for 42 patients. Both groups have shown increases in 24 hr U volume with mean increase being greater in the smart bottle arm (1.4L vs 0.8L). Among follow up survey respondents, both cohorts report subjective increases in fluid intake (cups/day) (0.75 Smart bottle arm vs 1.11 Non-smart bottle arm). Fewer patients in the Smart bottle arm report not remembering to drink as the main factor limiting sufficient fluid intake compared to the Non-smart bottle arm (38% vs 76%). Conclusions: Difficulty remembering to drink is a common barrier in achieving sufficient fluid intake in stone formers. Addition of a smart water bottle to dietary recommendations may lead to greater increases in 24 hr U volumes and less difficulty remembering to drink.

Research Topic: Urology
Funding agencies: UMN
Grant support: Hidrate Spark

131. Assessing the neural correlates of attentional control abnormalities in previously deployed veterans using MMPI-2-RF personality factors.

Sun, Michael [1]; Marquardt, Craig [2]; Disner, Seth [2]; Burton, Philip [3]; Lissek, Shmuel [3]; Sponheim, Scott [2]

1. University of California, Los Angeles
2. Minneapolis VA Health Care System
3. University of Minnesota

Abstract: Posttraumatic stress symptoms (PTSS) commonly co-occur with other clinical phenomena such as mild traumatic brain injuries, depression, and externalizing psychopathology. This results in complex changes to affective and cognitive processing. It is unclear how aberrant neural activity associated with PTSS maps onto quantitative models of personality and psychopathology, particularly in the context of co-morbidities. We posited that functional activation of several key brain areas underlying affective experience may reveal how neurophysiological effects of trauma can be reconceptualized within dimensional explanatory frameworks. An n-back task probed attentional control during presentations of task-irrelevant combat images resembling real world challenges faced by Military veterans (n = 87) with a history of combat deployment and PTSS. First, we regressed the time-course of task conditions onto neural activity regions-of-interest (ROIs) relevant to emotion regulation: amygdala, dorsolateral prefrontal (dlPFC), and ventromedial prefrontal (vmPFC) cortices. We examined how PTSS moderated activity to image type (neutral vs. combat scenes) and cognitive load (low [0-back] vs. high [2-back]). We then conducted multiple-mediated moderations with multilevel path modeling to explore how Higher Order (H-O) clinical scales and PSY-5 personality scales of the Minnesota Multiphasic Personality Inventory (MMPI-2-RF) mediated PTSS-relevant brain activity. When an H-O scale was found to be a significant mediator, it was broken down into its component Restructured Clinical (RC) scales. Separate models of dimensional psychopathology and quantitative personality converged in that PTSS-related amygdalar abnormalities under high cognitive load were accounted for by the related constructs of introversion and anhedonia. Furthermore, demoralization and negative emotionality independently explained additional PTSS-related amygdalar abnormalities. Cognitive performance difficulties experienced during periods of emotional dysregulation are a common clinical complaint amongst individuals with PTSS. The neural underpinnings of these complaints may exhibit specificity with distinct facets of self-reported personality. Future work may consider using the mediated moderation approach to elucidate the nature of PTSS-related biological correlates of emotional dysregulation using higher-order dimensional modeling.

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

132. Clinical Intervention for Improving Prosthetic Liner Doffing Independence and Ease

Swopes, Jensen [1]; Wood, Amber [1]; Siewert, Joseph [1]; Looft, John [1]

1. Minneapolis VA Health Care System

Abstract: Prosthetic gel liners are traditionally rolled on before prosthetic users dons their lower limb prosthesis and rolled off after the prosthesis is removed. Prosthetic users are urged to maintain proper hygiene by cleaning their gel liner every night with a mild fragrant free soap. This is due to continuous gel liner use without proper hygiene results in skin breakdown. Thus, the goal of this clinical intervention was to develop a novel doffing aid for trans-tibial prosthetic users to independently doff a prosthetic gel liner. At the Minneapolis VA Health Care System (MVAHCS), multiple patients have been observed leaving their gel liner on for extended periods of time causing skin issues. Clinicians and other members of the MVAHCS Amputation Team identified a need for a clinical intervention to benefit these patients. Our team was tasked with designing a clinical intervention that could be completed with one hand and minimal effort. Our solution used half inch width Dacron loops attached to the 3mm thermoplastic elastomer liner (TPE) liner. This loop was attached at the proximal lateral trim line and reinforced with cowhide. The cowhide reinforcement was shaped in a triangular fashion to promote rolling at the proximal edge as the liner was doffed. A dressing hook was then modified to have a hook at the end. This reach extender was able to both doff the liner using the Dacron loop as well as catch the TPE liner upon removal. Thus, preventing the TPE liner from falling to the floor and out of reach of the user. The TPE liner with the intervention demonstrated proper doffing techniques where the liner rolled down the residual limb smoothly and with minimal effort. These findings suggest this clinical intervention has the potential to increase the ease of doffing suspension sleeves and prosthetic liners for prosthetic users, and increasing proper prosthesis use and quality of life.

Research Topic: Prosthetics
Funding agencies: N/A
Grant support: N/A

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133. Abnormal Early Brain Responses in Relation to Visual Context Effects in Schizophrenia and Bipolar Affective Disorder

Teich, Collin [1]; Olman, Cheryl [2]; Pokorny, Victor [1]; Kang, Seung Suk [3]; Sponheim, Scott [1]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. University of Missouri-Kansas City

Abstract: The visual system adapts to diverse perceptual environments through using contextual factors such as relative brightness and orientation. People with schizophrenia (PSZ) show weak reliance on perceptual context. Specifically, PSZ tend to not show the expected effects of a large surrounding stimulus on perception of a center target. Weak use of perceptual context is also evident in people with bipolar disorder (PBD), but absent in biological relatives of PSZ and PBD. In the present study, we sought to extend these findings by examining neurophysiological processes elicited by a surround suppression task. We recorded EEG from PSZ and PBD, their first-degree biological relatives, and healthy controls (total n = 105) while they were shown two circular targets with larger circular surrounds and were asked to select which circular target had higher contrast. The relative contrast of the annular target without a surround and the orientation of the gratings within each annulus both varied. Preliminary analyses revealed diminished P1 and N1 amplitudes across conditions in schizophrenia and bipolar disorder. Analysis of task performance has confirmed previous findings of PSZ showing weakened surround suppression. We have yet to identify a correlation between this finding and the EEG data.

Research Topic: Mental Illness
Funding agencies: CSR&D
Grant support: 2I01CX000227

134. The Diuretic Comparison Project (DCP): A look at the best practices for informed consent recruitment in a large-scale Point-of-Care (POC) trial

Tella, Abhinav [1]; Stallman, Maddison [1]; Windschitl, Rebecca [1]; Vang, William [1]; Raju, Srihari [1]; Majkut, Alison [2]; Leatherman, Sarah [2]; Ishani, Areef [1]

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

Abstract: The DCP, the first large randomized POC trial from the Veterans Administration (VA), aims to compare the effectiveness of two thiazide-like drugs, hydrochlorothiazide (HCTZ) and chlorthalidone (CTD), in the management of hypertension. Protocol for this study outlined an over-the-phone patient recruitment and informed consent process. With the data gathered, researchers aim to identify points of improvement for recruitment and offer suggestions for future POC trials. Methods: Patients within the VA system with an HCTZ prescription were contacted after PCP permission was obtained. Patients underwent a scripted informed consent process, and their decision to participate or decline was electronically recorded. This data was analyzed to determine areas of improvement for recruitment and the study team. Results: Consent rates (number of patients consented divided by the number of patients consented and declined) varied over time. Rates had a median of 47.32% between September and March 2019 and reached a minimum of 26.35% in December (attributed to minimal calling over the holidays). March saw the highest number of consents at 505. Overall, about 5,000 patients consented to participate in the DCP. Conclusions: Researchers recorded monthly changes in aspects of recruitment and compared them to consent data. Months in which new sites were added (January through March) resulted in a higher number of consents. For studies following a similar trial design, a steady influx of new eligible patients is recommended to maximize patient consent.

Research Topic: Cardiovascular Disease
Funding agencies: N/A
Grant support: N/A

135. A Longitudinal Assessment of the Reporting Quality of Randomized Controlled Trials for Surgical Treatments of Nephrolithiasis, 2002 to 2017

Thompson, Ellen [1,2]; Lai, Andrew [3]; Morrey, Luke [2]; Dahm, Philipp [1,2]

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

Abstract: Transparently reported, high quality randomized controlled trials (RCTs) play a critical role in guiding evidence based clinical practice and informing evidence-based guidelines in patients with nephrolithiasis. Prior studies have found overall low quality in RCTs. We performed this study to assess whether the reporting of RCTs has improved over time. Materials and Methods: This study was governed by an a priori protocol. We performed a systematic literature search for RCTs analyzing nephrolithiasis treatment. Selection of eligible studies and data abstraction was performed by two of three reviewers independently and in duplicate. We developed and pilot-tested a data extraction checklist based on the Consolidated Standards of Reporting Trials (CONSORT) criteria on a scale of 0 to 25. Our primary outcome measure was the mean CONSORT score. We performed statistical hypothesis testing to compare scores between 2002-2006, 2007-2011and 2012-2017 Results: A total of 203 studies, (2002-06: 38, 2007-11: 64; 2012-17: 101), met inclusion criteria. The most common procedure types studied were percutaneous nephrolithotomy (35.1%), shockwave lithotripsy (25.4%) and ureteroscopy (22.9%). Asia contributed a rising proportion of studies (25.6%, 44.6% and 74.3%, respectively) in these three time-periods. The main journals of publication were the Journal of Endourology (23.9%), the Journal of Urology (19.5%) and Urology (8.3%). The mean ± SECONSORT summary scores were 11.4 +/-0.4, (2002 to 2006), 12.1 +/-0.3, (2007 to 2011), and 13.3 ± 0.4 ($p = 0.003$). Conclusions: While the number of RCTs investigating the use of urological devices to treat stone disease has substantially increased over time, overall reporting quality remains sub-optimal. We demonstrate some improvement over time, yet increased efforts to promote the transparent reporting of RCTs in endourology are warranted.

Research Topic: Urology
Funding agencies: N/A
Grant support: N/A

136. Investigating Perceptions and Reporting of Misconduct in the Healthcare Learning Environment

Tiryaki, Ezgi [1]; Cullen, Michael [2]; Jia, Hoa [2]; Lamm, Rik [2]; Ho, Yedam [2]; Markus-Blank, Brittany [3]

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

Abstract: To determine whether there are gender, race, and/or age-based differences in reporting of unprofessional behavior in the clinical learning environment (CLE), and to explore possible explanations. Methods: In study 1, the authors surveyed how frequently residents observed 13 unprofessional behaviors (e.g., discrimination) in the CLE. The authors analyzed gender, race, and age-based differences in reporting. In study 2, the authors conducted two part focus groups. In part 1, residents were instructed to write down incidents of 'discrimination/favoritism' and 'lack of coworker respect.' In part 2, the authors facilitated a group discussion of potential explanations to explore the gender differences in reporting identified in study 1. Results: Between 2014-2018, 1531 graduating trainees from the University of Minnesota completed this survey. Women were more likely than men to observe ten unprofessional behaviors in the CLE (ORs from 1.37 to 2.70, $p < .05$). White and younger residents were more likely than minority and older residents to observe some behaviors (ORs from 1.30 to 1.95, $p < .05$). In incidents recalled by focus group participants ($n = 38$; 47% female), women were more often cited as targets of 'discrimination/favoritism' (72.5% vs. 27.5%; $p < 0.01$) and 'lack of coworker respect' (75.0% vs. 25.0%; $p < 0.001$) while men were more often cited as the perpetrators (64.7% vs. 35.3% and 62.4% vs. 37.6%, respectively; $p < 0.01$ for both). Conclusions: Women reported unprofessional behaviors at higher rates and were more often described as targets, likely representing different lived experiences in the CLE. The authors propose strategies for institutional interventions that effectively promote professionalism.

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

137. CK2 pro-survival role in prostate cancer is mediated via its support of androgen receptor and NFκB p65 expression

Trembley, Janeen [1,2]; Kren, Betsy [1,2]; Shaughnessey, Dan [2]; Abedin, Md [2]; Ahmed, Khalil [1,2]

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

Abstract: CK2 is a broadly expressed protein Ser/Thr kinase that is highly conserved and is involved in a wide range of cellular functions in normal and disease state. In the context of cancer, two of its functions, namely, promotion of cell growth and proliferation as well as inhibition of cell death, play significant roles. CK2 has been found to be elevated in all cancers examined and its molecular or chemical downregulation results in induction of cell death. A major focus of our current research is to determine the mechanism(s) involved in the function of CK2 in promoting cell survival in prostate cancer (PCa). Here, we show that modulation of CK2 in PCa influences the expression of androgen receptor (AR) and NFκB p65 which are among the major drivers of PCa progression. For example, we have observed that elevation of CK2 in benign prostate epithelial cells (RWPE) as well as in different types of PCa cells (such as LNCaP and C4-2B) results in enhanced expression of AR and NFκB p65. cBioPortal analysis of TCGA database has indicated that AR and CK2a RNA expression are positively correlated. A correlation between RNA expression for NFκB p65 and CK2a in castrate resistant prostate cancer (CRPC) is also observed. On the other hand, blocking expression and activity of CK2 reduces AR expression in RWPE and PCa cell lines. Initial data show that AR half-life is shortened by loss of CK2 activity. Loss of NFκB p65 expression and activation is markedly reduced analogous to loss of AR on blocking CK2 activity. We have also observed that 22Rv1 tumors (model of aggressive Castration Resistant PCa) demonstrated regression and AR loss when mice were treated with an anti-CK2 therapy. Likewise, Enzalutamide- and Docetaxel-resistant PCa cells underwent reduction in viability on reduction of CK2 activity which also correlated with loss of AR. Our data suggest that loss of AR and NFκB p65 expression in response to downregulation of CK2 represent at least in part the mechanism of CK2 targeted therapeutic effect in PCa. Together, these observations have implications for PCa therapy suggesting improved therapy response to targeting both AR and CK2.

Research Topic: Cancer
Funding agencies: BLR&D; NIH
Grant support: I01 BX003282 and R01 CA150182

138. Anthrax in Gulf War Illness (GWI): Evidence for the presence of harmful anthrax antigen PA63 in the serum of veterans with GWI

Tsilibary, Effie-Photini [1]; James, Lisa [1,2]; Engdahl, Brian [1,2]; Souto, Eric [1]; Kratzke, Marian [1]; Georgopoulos, Apostolos [1,2]

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

Abstract: After the Persian Gulf War of 1990-91, about one third (>200,000) of veterans complained of a variety of chronic physical and neurocognitive symptoms, presently identified as Gulf War Illness (GWI) and traditionally attributed to possible exposures to toxic warfare chemicals (e.g. sarin). In 2016, we identified genetic vulnerability factors in GWI, when we discovered that veterans with GWI lacked one or more of 6 Human Leukocyte Antigen (HLA) class 2 alleles [1] the presence of which was associated with reduced GWI symptom severity in a dose-response fashion. Since these alleles are essential for mounting antibodies to foreign antigens, we hypothesized that veterans lacking those alleles could not make antibodies to eliminate harmful antigens which would persist and cause GWI. Such antigens could come from exposure to biological and chemical substances. A unique exposure of GW veterans was to anthrax antigen(s) contained in the vaccine [2] they received. Here we tested the hypothesis that persistent, harmful anthrax antigens are involved in GWI. Using specific, recombinant polyclonal antibodies against the PA63 and PA83 anthrax antigens contained in the anthrax vaccine, we obtained evidence for the presence of these antigens in the serum of 15 veterans suffering from GWI (and lacking all 6 HLA protective alleles), causing detrimental effects on brain cultures [3] which were eliminated when anti-anthrax antibodies were added to the serum. These findings demonstrate a direct link between anthrax vaccine and GWI.

Research Topic: Gulf War Veterans Illness
Funding agencies: UMN
Grant support: N/A

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139. Diuretic Comparison Project (DCP): Regional consent rate differences within a large randomized Point-of-Care (POC) trial

Vang, William [1]; Tella, Abhinav [1]; Windschitl, Rebecca [1]; Stallman, Maddison [1]; Raju, Srihari [1]; Majkut, Alison [2]; Leatherman, Sarah [2]; Ishani, Areef [1]

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

Abstract: The DCP study is a large nationwide Veterans Administration (VA) POC trial aimed at determining the effectiveness of two thiazide-type diuretics, hydrochlorothiazide (HCTZ) and chlorthalidone (CTD), in the prevention of cardiovascular events. There are currently 5,122 patients consented from 28 sites across the United States (U.S.). Purpose: Analyze consent rates of various geographic locations within the U.S. and factors contributing to their differences. Methods: Individual VA sites are recruited by a single coordinating research team. Primary care providers (PCPs) are given the opportunity to participate. Patients of consented PCPs who meet pre-screening eligibility are then contacted to complete the informed consent process. Consent rate is calculated as the number of patients consented divided by the number of patients who consented and declined. Results: St. Cloud, MN has the highest consent rate of 51.1% whereas the Boston, MA site has the lowest consent rate of 16.4%. Consistently higher consent rates are seen in the southern regions, with consent rates higher than 40%; Memphis, TN is an exception with a consent rate of 21.0. An overall median consent rate of 41.8% was obtained. Conclusion/Limitations: As the study recruits more VA sites and older sites lack an influx of patients to recruit, the study team adapts recruitment materials and resources in hopes to find the key to patient participation and increase future participation in VA clinical trials.

Research Topic: Cardiovascular Disease
Funding agencies: N/A
Grant support: N/A

140. Completion of Advance Directives in the Ambulatory Care Setting by Patients with Cognitive Impairment

Velin, Lauren [1]; McMahon, Siobhan [1]; Ratner, Edward [2]; McCarten, Riley [2]; Possis, Elizabeth [2]; Kavathekar, Rahul [2]

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

Abstract: Individuals with cognitive impairment particularly benefit from advance directives due to their susceptibility to lose their decision making capacity. Veterans are more likely to have some degree of cognitive impairment due to their high prevalence of military-specific risk factors. Fewer than 36% of veterans in large Midwest Veteran Affairs Medical Center (VAMC) clinic with cognitive impairment have an advance directive in the electronic health record (EHR). A multi-step intervention was created to address barriers that prevent veterans from completing an advance directive. The multi-steps included educating clinicians, mailing of an advance directive packet, and time to discuss advance care planning (ACP). The purpose of this project was to develop and evaluate a multi-step intervention to improve cognitively impaired veterans ability to complete advance directives. Methods: The multi-step intervention was implemented for 4 weeks in a primary care clinic and a memory care clinic. Patients included in the project were from the two clinic settings and had some form of cognitive impairment. Implementation of the three interventions was assessed by verification of delivery. A pre and post chart review was used to collect demographic information and measure completion/refinement rates of the advance directives. Results: All participating clinicians (100%) received ACP education before the intervention period. All 34 participating patients (100%) received step 2, a mailed informational advance directive packet. Eleven patients (32%) received step 3, an ACP conversation with a clinician. Fifty-two percent of patients had an advance directive before the intervention period and 71% of patients had an advance directive after. There was a 33% increase in completion in the memory care clinic and no increase in the primary care clinic. Conclusion: The major findings included e-mailed education to clinicians is feasible, mailing directives rarely elicits completion, and the combination of the three step intervention elicited a greater response in completion and refinement of advance directives. Limitations included the short intervention period, small sample size and inconsistent intervention implementation across clinic settings. The multi-step intervention would need to be implemented again in the primary care setting addressing complex barriers to determine its effectiveness.

Research Topic: Geriatrics
Funding agencies: N/A
Grant support: N/A

141. Visual Gaze Behavior for Two Methods of Myoelectric Prosthesis Control

Walker, Nicole [1]; Schultea, Fanny [2]

1. Minneapolis VA Health Care System
2. Baylor College of Medicine

Abstract: In intact-limb individuals, a combination of feed-forward and feed-back pathways allow for moderated and consistent control of the upper extremity during reaching and grasping tasks. For individuals with upper limb amputations, the feed-forward and feed-back pathways available to intact-limb individuals are diminished or eliminated. Users of upper limb prostheses may regain the ability to physically perform dexterous tasks, but users must rely on feedback that is not tactile or proprioceptive in nature to complete these tasks. Literature suggests that users of upper-limb prostheses rely more heavily on visual feedback to complete reaching and grasping tasks than intact-limb individuals, increasing the amount of cognitive demand associated with the completion of these tasks. There are two widely used varieties of myoelectric control of an upper limb prosthesis; direct myoelectric control, considered the standard-of-care, and pattern recognition myoelectric control, a newer variety of control. Manufacturers of pattern recognition control systems claim the system is 'easier to use' and 'more intuitive' than traditional direct myoelectric control, though this claim has not been studied in depth. The purpose of this research was to study differences in cognitive demand associated with using these two varieties of myoelectric control by comparing eye gaze behavior in a subject with an upper limb amputation while using each system.

Research Topic: Prosthetics
Funding agencies: N/A
Grant support: N/A

142. Metabolic Responses to BDNF antagonist ANA12 administered at different CNS sites in exercised animals

Wang, ChuanFeng [1,2]; Mavanji, Vijaya [1]; Grace, Martha [1]; Kotz, Catherine [1,2]

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

Abstract: Our preliminary studies found: 1) rats in running wheel exercise (RW) reduced food intake (FI) and weight gain (WG) vs. sedentary (Sed) rats; 2) mRNA for BDNF (brain-derived neurotrophic factor) in hypothalamus (HYP) was positively correlated with RW distance; 3) FI was negatively correlated with HYP BDNF mRNA; 4) BDNF protein was significantly increased in paraventricular nucleus of HYP (PVN) of RW rats. Hypothesis. HYP BDNF mediates exercise-induced reduction in feeding and weight gain. We tested the hypothesis by injecting BDNF antagonist ANA12 (ANA) in different CNS sites. Approaches. Three sets adult male SD rats were cannulated in PVN, lateral ventricle (LV) or third ventricle (3V), and divided into four groups in each setting: Sed-vehicle (Sed-Veh), Sed-ANA (10 µg), RW-Veh, and RW-ANA. The rats were injected daily 2h before dark, and monitored for FI and WG. Results. 1. PVN. Rats in RW-Veh reduced FI and WG vs. Sed-Veh, Sed-ANA increased FI and WG vs. Sed-Veh, but RW-ANA failed to antagonize RW (RW-Veh) reduced FI and WG. 2. LV. Both RW groups initially reduced FI vs. corresponding Sed rats, but at the end (62 d) they ate little more vs. Sed rats. RW-ANA initially ate a little more than RW-Veh, and at the end both groups ate same amount. Both RW groups decreased WG vs. corresponding Sed rats, and both ANA12 groups had little more WG vs. corresponding Veh rats. In energy expenditure (EE), RW-Veh had the highest total EE and EE for activity and resting, followed by RW-ANA, and two Sed groups. 3. 3V. Rats in RW-Veh reduced FI and WG vs. Sed-Veh, RW-ANA increased FI and WG vs. RW-Veh, and Sed-ANA increased FI and WG vs. Sed-Veh. Discussion. 1. An increase in FI and WG in rats in Sed-ANA with PVN injection suggests blockade of PVN BDNF-TrkB activation in sedentary rats. 2. No attenuation of exercise reduced FI and WG with PVN ANA12 (RW-ANA) suggests that exercise may activate multiple sites in CNS which could not be blocked at PVN alone. 3. The increased FI and WG in RW-ANA rats with 3V ANA12 delivery suggests blockade in multiple sites, potentially around HYP. 4. Differing from findings in 3V ANA12, RW rats with LV ANA12 had a small increase in FI and WG (vs. RW-Veh), and little reduced EE, suggesting limited ANA12 diffusion in hypothalamus. 5. The attenuation of exercise induced reduction in feeding and weight gain by antagonism of BDNF-TrkB via 3V delivery suggests hypothalamic BDNF mediates the exercise induced metabolic response.

Research Topic: Obesity
Funding agencies: BLR&D
Grant support: 5I01 BX002465

143. C16-Ceramide in CNS affects energy balance and cognition

Wang, ChuanFeng [1,2]; Mavanji, Vijaya [1]; Grace, Martha [1]; Kotz, Catherine [1,2]

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

Abstract: In a previous study, access to a high fat diet (HFD) induced obesity and cognitive decline. One of the proposed mechanisms for HFD cognitive decline may be elevated ceramides, which are lipids derived from dietary saturated fats. Reducing CNS Ceramides leads to increased energy expenditure (EE) and reduced weight gain, and increasing brain ceramides occurs with aging and dementia. In our previous studies, intraperitoneal injection of artificial C6-ceramide led to cognitive decline; whereas a reduction in CNS ceramides aligned with reduced weight gain and food intake, and possibly improved cognition in HFD fed rats. Hypothesis. Increasing CNS ceramides induces positive energy balance and cognitive deficits. Approaches. To test the hypothesis, adult male SD rats were prepared with cannulae targeting the lateral ventricle (LV) for daily injection and divided into two groups: vehicle and C16-Ceramide (C16-Ceramide conjugated with polyethylene glycerol 2000, C16-Cer-PEG, 300 µg, or 0.114 µmol). Energy balance was measured by weekly food intake, weight gain and EE; and cognition was evaluated with the Novel Object Recognition (NOR) and Two-Way Active Avoidance (TWAA) tests. Ceramide levels in hypothalamus and hippocampus were measured at study's end. Results. 1. Energy metabolism. Rats treated with C16-Cer-PEG had significantly decreased weight gain, no change in food intake, and increased total EE (both dark & light cycles), indicative of increased EE for activity and resting. 2. Cognition. Rats treated with C16-Cer-PEG had decreased cognitive performance in both NOR and TWAA tests. 3. Brain Ceramides. There were no differences in hypothalamic ceramides between the two groups. In hippocampus, rats treated with C16-Cer-PEG had elevated C16-Cer, but reductions in other individual and total ceramides. Discussion. 1. C16-Cer-PEG induces cognitive decline, accompanied by an increase in C16-Cer and reduction in other individual and total ceramides in hippocampus. 2. Unlike the changes in hippocampal ceramides, LV injection of C16-Cer-PEG did not alter hypothalamic ceramides, suggesting limited distribution of C16-Cer-PEG in hypothalamus. 3. In contrast to our expectations, C16-Cer-PEG in LV increased EE and reduced weight gain with no change in food intake, suggesting non-hypothalamic mechanism(s). 4. Future studies of delivering C16-Cer in hypothalamus (via the third ventricle) will verify if hypothalamic ceramides result in positive energy balance.

Research Topic: Nutrition
Funding agencies: BLR&D; CVRE
Grant support: CVRE, 5I01 BX002465

144. Effect of Knocking-out CA3 bdnf gene with lentiviral CRISPR-Cas9 on cognition and energy metabolism in exercised rats fed with high fat diet

Wang, ChuanFeng [1,2]; Mavanji, Vijaya [1]; Grace, Martha [1]; Kotz, Catherine [1,2]

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

Abstract: In our previous study, exercise (Exe) reversed high fat diet (HFD) induced obesity and cognitive (Cog) decline, and increased BDNF in CA3 of hippocampus. Hippocampal CA3 is an important site for Exe induced neurogenesis, Cog improvement, and BDNF function and production. Hypothesis. 1. CA3 BDNF mediates Exe induced Cog improvement. 2. CA3 BDNF may be involved in regulation of energy metabolism. We tested the hypotheses by interfering with CA3 BDNF production using lentiviral CRISPR-Cas9 for knocking-out bdnf gene (KObdnf) or scrambler (Scr) in sedentary (Sed) or running wheel (RW) rats fed with low fat diet (LFD) or HFD. Approaches. Adult male SD rats were divided into 4 groups: LFD-Sed-Scr (LSS), HFD-Sed-Scr (HSS), HFD-RW-Scr (HES), and HFD-RW-KObdnf (HEK); and were bilaterally delivered at CA3 with Scr or KObdnf (2 µl per side). After two weeks, they were assigned to LFD/HFD and Sed/RW groups. The rats were measured for Cog with Context Fear Conditioning (CFC) and Novel Object Recognition (NOR), and for energy balance with energy intake (EI), weight gain (WG), and energy expenditure (EE). Results. 1. Energy metabolism: In the first 10 days two RW groups decreased EI and WG significantly vs. two Sed groups, and KObdnf (HEK) ate more calories and lost less weight than HES. There was significant difference in EE (total EE, EE for resting and activity), and KObdnf had the highest EE followed by HES, HSS and LSS. Two RW groups had decreased beam breaks and a trend of increased distance ambulating vs. two Sed groups. 2. Cognition: For CFC in Context A (rectangular shape, associated with shock), HSS had reduced freezing latency vs. LSS, and Exe (HES) showed an improvement. KObdnf performed poorly in freezing latency and time. In Context B (round shape, no shock), KObdnf also had the lowest response in six categories. The NOR task is currently in progress. Discussion. 1. CA3 KObdnf in the initial period greatly attenuated Exe reduced EI and WG. 2. CA3 KObdnf had the highest EE, with no significance from HES. 3. Exe (HES) tended to improve HFD-induced Cog decline, while knocking out CA3 bdnf (KObdnf) prevented the improvement. 4. Future histology will verify distribution and co-localization of BDNF/green fluorescent protein for local BDNF production. 5. Conclusions. CA3 BDNF may: 1) be involved in regulation of energy metabolism, and contribute to exercise reduced energy intake and weight gain, and 2) mediate exercise induced cognitive improvement.

Research Topic: Nutrition
Funding agencies: BLR&D; CVRE
Grant support: CVRE, 5I01 BX002465

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145. Manipulation of ceramide level in CNS affects energy metabolism and cognition in animals fed with a high fat diet

Wang, ChuanFeng [1,2]; Mavanji, Vijaya [1]; Grace, Martha [1]; Kotz, Catherine [1,2]

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

Abstract: Prior studies indicate that a high fat diet (HFD) induces obesity and cognitive decline. A potential mechanism for HFD-induced disorders is by mediation of ceramides (Cer), lipid metabolites of dietary saturated fats. Hypothesis. Manipulating Cer level in CNS with Myriocin (Myr, an inhibitor for Cer de novo synthesis from saturated fats) or FTY720 (Fingolimod, an inhibitor for Cer synthesis and for its release from sphingomyelin hydrolysis) may improve energy metabolism and cognition in HFD-fed rats. Approaches. Adult male SD rats were cannulated in lateral ventricle; divided into 4 groups as low fat diet-vehicle (LFD-Veh), HFD-Veh, HFD-Myr (30 µg), and HFD-FTY720 (HFD-FTY, 1 µg); and injected every other day for 95 days. Energy intake (EI) and weight gain (WG) was monitored, and cognition tested with Novel Object Recognition (NOR), Object Place Recognition (OPR), and Two-Way Active Avoidance (TWAA). Cer levels in the hypothalamus (HYP) and hippocampus (HIP) were analyzed at the study's end. Results. 1. Energy metabolism: HFD-Veh ate more EI vs. LFD-Veh and HFD-FTY, and had more WG vs. HFD-Myr and LFD-Veh. Fat mass and delta fat mass followed a pattern similar to WG. HFD-Veh had significant heavier liver weight vs. HFD-Myr. 2. Cognition: No significant difference was found in NOR and OPR task. HFD-Veh had a trend of cognitive decline in TWAA task, showing the lowest number of escape and total responses. 3. Brain Cer: In HYP, HFD-Veh had significantly more saturated Cer vs. HFD-Myr and LFD-Veh, and more total Cer vs. HFD-Myr; and HFD-Myr rats had the lowest levels in most individual Cer, followed by LFD-Veh and HFD-FTY. In HIP, HFD-Veh had significantly more saturated and total Cer, and most individual Cer than other three groups. Discussion. 1. HFD results in obesity and possible cognitive decline, and increases Cer in both HYP and HIP. 2. Myr significantly reduces Cer production in both sites, and FTY720 shows a similarly outcome in HIP but a weak effect in HYP. 3. Myr or FTY720 reduces obesity and potentially improves cognition, with a noticeable impact on reduced WG by Myr and cognitive improvement by FTY720. 4. The weak effect of FTY720 on hypothalamic Cer might be due to its low dosage (2.9 nmol vs. 74.7 nmol of Myr) and possibly differential diffusion from lateral ventricle to HYP and HIP. 5. Conclusion: Ceramides may mediate HFD-induced obesity and cognitive decline; and reducing CNS ceramides may improve the HFD-induced disorders.

Research Topic: Nutrition
Funding agencies: BLR&D; CVRE
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146. Minneapolis VA Evidence Synthesis Program (ESP)

Wilt, Timothy [1,2]; Duan-Porter, Wei (Denise) [1,2]; Greer, Nancy [1]; MacDonald, Roderick [1]; McKenzie, Lauren [1]; Ullman, Kristen [1]

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

Abstract: Objective: Provide timely and accurate synthesis of targeted healthcare topics of particular importance to Veterans Affairs (VA) managers and policymakers as they work to improve the health and healthcare of Veterans. Methods: Each of 4 ESP sites prepares 3 systematic reviews each year. Topic nominations come from VA Central Office, VISNs, or individuals in the field (e.g. National Program Directors, Chief Consultants, leaders of VA Task Forces). The reviews are developed using standard methods for development of key questions and scope, identification of included evidence, data extraction, data synthesis, and evaluation of risk of bias and strength of evidence. A Technical Expert Panel is identified for each topic to guide topic development and assist in refining the key questions and scope of the review. Draft reports undergo peer review by content experts and policy partners. Final reports are posted on the VA HSR&D website and disseminated widely throughout VA. Management Briefs and Cyberseminars are key dissemination strategies. Results: For 2018, the Minneapolis VA ESP developed systematic reviews on the Relationship of Deployment-related Mild Traumatic Brain Injury to Posttraumatic Stress Disorder, Depressive Disorders, Substance Abuse, Suicidal Ideation, and Anxiety Disorders; Adaptive Sports for Disabled Veterans; and Modifiable Risk Factors and Interventions to Prevent or Delay Long-term Nursing Home Placement (NHP) for Adults with Impairment. Topics to date for 2019 include Deprescribing for Older Veterans and Orthobiologics. Conclusions: The Minneapolis VA ESP prepares evidence syntheses on important clinical practice topics relevant to Veterans. These reports help develop clinical policies informed by evidence, lead to the implementation of effective services to improve patient outcomes, and and guide the direction for future research to address gaps in clinical knowledge. Funding Source: Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development Key Words: Systematic reviews, evidence-based, Veterans

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

147. Diuretic Comparison Project (DCP): Provider Recruitment in a Point-of-Care Trial

Windschitl, Rebecca [1]; Tella, Abhinav [1]; Vang, William [1]; Stallman, Maddison [1]; Raju, Srihari [1]; Majkut, Alison [2]; Leatherman, Sarah [2]; Ishani, Areef [1]

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

Abstract: The DCP study is designed to compare two thiazide-type diuretics- hydrochlorothiazide (HCTZ) and chlorthalidone (CTD)- regarding the effect on long term cardiovascular outcomes often associated with hypertension. Consented patients have a 50% chance of receiving HCTZ or being randomized to CTD. Purpose: To minimize the workload of primary care providers (PCPs) by implementing a point-of-care (POC) trial design which integrates most study practices into routine patient care. Methods: VA sites are recruited by a central project management team. PCPs are contacted by mail, educated about the study, and given the opportunity to participate. Participating providers are responsible for responding to study orders (giving permission to randomize patients) entered by research staff via electronic medical record system. Therefore, randomization permission is the percent of patient orders signed by a provider. Results: 2,205 providers across 28 VA sites were approached for participation. On average of 66.9% agreed (n = 1,457). Across all sites, the Minneapolis VAMC has the highest provider participation rate (87.4%). In contrast, Washington DC, Birmingham, and Baltimore VAMCs are sites with low PCP participation, averaging 54.9%. Birmingham is the only site with PCP participation below 50%. On average, PCPs approved 90.3% of randomization orders, with the highest being Durham, NC (98.1%) and the lowest being Maddison, WI (70.0%). Interestingly, sites with low PCP consent rate show lower randomization permission. Conclusion: Provider participation is a key aspect of the DCP, as it limits the number of patients eligible to participate. For this reason, the DCP aims to maximize eligible patients by minimizing addition PCP workload.

Research Topic: Cardiovascular Disease
Funding agencies: N/A
Grant support: N/A

148. A Review of Existing Adjustable Socket Technologies and Next Steps

Zhang, Mickinney [1,2]; Voss, Gregory [1]; Laine, Myrriah [1,3]; Rich, Tonya [1]; Hanson, Andrew [1,2]; Ferguson, John [1,2]

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

Abstract: Lower limb amputees commonly experience residual limb volume fluctuation throughout the day. This can result in poor socket fit and functionality. The poor fit can cause discomfort over bony areas, skin irritation or breakdown, and decreased prosthesis proprioception and control. Volume fluctuations are most commonly managed through the addition and subtraction of plies of socks in static sockets. However frequent donning and doffing of the prosthesis can be emotionally and physically challenging for new amputees. New amputees and amputees with neuropathy may also have difficulty independently determining the fit of their prosthetic socket. In addition, adding sock plies uniformly decreases volume within the socket. Soft tissues are able to be compressed while the bones are not, creating pressure and pain over bony prominences. Adjustable socket technology could potentially resolve these issues. The fit is most often altered with a tensioning-line mechanism or an adjustable strap. However, the technology currently on the market still require the amputee to stop, adjust, and determine the fit independently. To further advance these technologies, a guided adjustment system or a self-adjusting system can be implemented. These proposed systems would modify existing sockets to address the unmet needs in socket fit.

Research Topic: Prosthetics
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