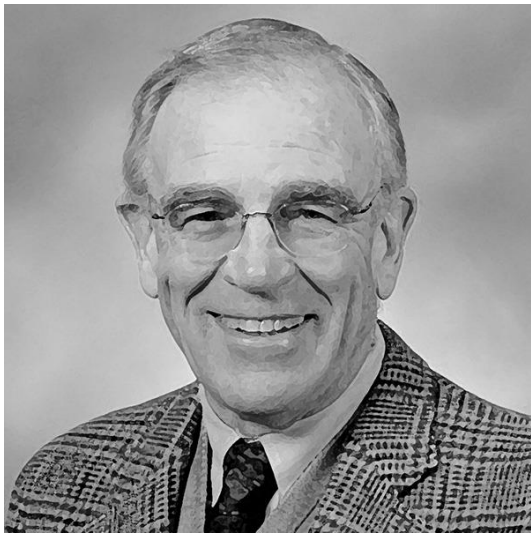


Minneapolis VA Health Care System VA Research Week 2024



Joseph J. Westermeyer, MD, MPH, PhD
1937–2024



Sean M. Nugent, BA
1964–2024

In memory of our friends and esteemed colleagues

Program and Abstract List

(alphabetically, by author)

May 28–30, 2024

VA



U.S. Department of Veterans Affairs

Veterans Health Administration
Office of Research and Development

Program:

Tuesday May 28

1. Mentor Networking 11:00 am – 12:00 pm, 3Q-128

2. Research Coordinator Resource Fair 1:00 – 3:00 pm, Auditorium

Wednesday May 29

1. CVRE Meet and Greet..... 11:00 am – 12:00 pm, 3Q-128

2. Oral Abstract Presentation Session..... 1:00 – 3:00 pm, Auditorium

1:00 ***Characterizing Tobacco Use among a National Cohort of Veterans with COPD***

Alyssa Anton*, Anne Melzer, Chris Wendt, Ken Kunisaki, Adams Dudley, Arianne Baldomero

1:15 ***Results from the Learning to Apply Mindfulness to Pain Study: A Pragmatic Clinical Trial***

Diana Burgess*, Collin Calvert, Emily Hagel Campbell, Kelli Allen, Ann Bangerter, Kimberly Behrens, Mariah Branson, Gert Bronfort, Lee Cross, Roni Evans, John Ferguson, Jessica Friedman, Alexander Haley, Brent Leininger, Mallory Mahaffey, Marianne Matthias, Laura Meis, Melissa Polusny, J. Greg Serpa, Stephanie Taylor, Brent Taylor

1:30 ***Artificial Intelligence-Assisted Colonoscopy Failed to Increase Adenoma Detection Rate: An Implementation Study***

Tessa Herman*, Daniela Guerrero Vinsard, Morgan Freeman, Anders Westanmo, Amy Gravely, Mohammad Bilal, Brian Hanson

1:45 ***Veteran Engagement Infrastructure and Practices Among VA HSR&D Research Networks***

Tracy Sides*, Erin Amundson, Malloree Argust, Diana Burgess, Laura Meis, Erin Krebs

2:00 ***Exploring the genomic link between hidradenitis suppurativa and cardiovascular disease***

Zachary Wendland*, Craig Teerlink, Kathryn Pridgen, Sydney Lo, Christopher Sayed, KR Van Straalen, Catherine Tcheandjieu, Scott Damrauer, Philip Tsao, Kyong-Mi Chang, Li Yun, Karen Mohlke, Quan Sun, Julie Lynch, Noah Goldfarb

2:15 ***Trends in the surgical management of hidradenitis suppurativa***

Zachary Wendland*, Ziou Jiang, Noah Goldfarb

****Presenting Author***

Thursday May 30

1. Clinical Research Wing Grand Opening 10:15 – 11:15 am, 3Q-100

2. Keynote Session..... 12:00 noon – 1:30 pm, Auditorium

Introductions and Welcome Steven Fu, MD, MSCE
Associate Chief of Staff, Research Service

Lederle Award PresentationDimitri Drekonja, MD, MS

Recipient:

Ariane Baldomero, MD, MS

“Guideline-discordant inhaler regimens after COPD hospitalization: associations with rurality, drive time to care, and fragmented care– a United States cohort study”

Lancet Reg Health Am. 2023 Sep 21:26:100597.

Ahmed Basic Science Paper of the Year AwardThomas Griffith, PhD

Recipient:

Vijaya Mavanji, PhD

“Changes in sensorimotor cortex oscillatory activity by orexin-A in the ventrolateral preoptic area of the hypothalamus reflect increased muscle tone”

J Neurosci Res. 2023 Aug;101(8):1305-1323

Early Stage Investigator AwardShannon Kehle-Forbes, PhD

Recipient:

Seth Disner, PhD

“Predicting Rehabilitation Outcomes Using DNA (PROUD)”

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

Recipient:

Hannah J. Schmit, BA, MA

Keynote Address **Ann M. Spungen, EdD**

VA Senior Research Scientist

Director, Spinal Cord Damage Research Center

James J. Peters VA Medical Center

Part 1: "Overview of the VA Cooperative Studies Program (CSP)"

Part 2: "VA CSP #2003: Exoskeletal-Assisted Walking in Persons with SCI: Impact on Quality of Life"

3. Poster Session 2:00 – 4:00 pm, 2P Education Conference Rooms

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Oral Presentations

1. Characterizing Tobacco Use among a National Cohort of Veterans with COPD

Anton, Alyssa ¹; Melzer, Anne ²; Wendt, Chris ²; Kunisaki, Ken ²; Dudley, Adams ²; Baldomero, Arianne ²

1. University of Minnesota

2. Minneapolis VA Health Care System

Abstract: Rationale: Tobacco use is the strongest risk factor for the development and progression of chronic obstructive pulmonary disease (COPD). Our goal was to use national data to describe the characteristics of Veterans with COPD who currently use tobacco to improve tailored tobacco cessation. Methods: Retrospective analysis of patients with diagnosis of COPD (= 2 ICD codes for COPD) in 2016-2019 using national Veterans Health Administration (VHA) data. Individual tobacco use status (categorized as currently used tobacco, formerly used tobacco, never used tobacco or unknown smoking status) was identified using tobacco health factors. These are retrievable electronic data fields that are updated at least annually at the time of a clinical encounter. We describe the sociodemographic and geographic characteristics of patients with COPD by tobacco use status, including age, sex, race/ethnicity, medical and psychiatric comorbidities, geographic region, rurality (rural vs. urban), and Area Deprivation Index (ADI). Rural vs. urban designations were based on Rural Urban Commuting Area codes. Multivariable logistic regression models assessed relationships between current tobacco use status and sociodemographic/geographic characteristics. Results: Of 882,292 patients with COPD, 20.1% currently used tobacco, 42.4% formerly used tobacco, 14.7% never used tobacco, and 22.8% had unknown smoking status. Among current tobacco users, 78.7% were white; 32.8% had cardiovascular disease, 20% substance use disorder, and 35.1% mental health diagnosis. A higher proportion of current tobacco users lived in a rural area compared to never smokers (42.8 vs. 38.8%). The ADI of current tobacco use (63.4 percentile) was also higher compared to former and never tobacco use (58.5 and 58.62 percentiles, respectively) indicating worse neighborhood disadvantage. In a multivariable logistic regression model, older age (= 80 vs. < 40 years); female sex; American Indian/Alaska Native, Asian, and Black/African American race (vs. White); substance use disorder; and lower ADI (less neighborhood disadvantage) were associated with higher odds of current tobacco use status. Conclusions: In this large national sample of Veterans with COPD, our findings suggest the need for additional tobacco cessation efforts tailored for COPD patients who are older, female, racial/ethnic minorities and those with cardiovascular disease or mental health diagnoses.

Research Topic: Respiration & Pulmonary Disease

Funding agencies: Other

Grant support: NCATS KL2TR002492, NCATS UL1TR002494

2. Results from the Learning to Apply Mindfulness to Pain Study: A Pragmatic Clinical Trial

Burgess, Diana ¹⁻²; Calvert, Collin ¹⁻²; Hagel Campbell, Emily ¹; Allen, Kelli ³; Bangerter, Ann ¹; Behrens, Kimberly ¹; Branson, Mariah ¹; Bronfort, Gert ²; Cross, Lee ¹; Evans, Roni ²; Ferguson, John ²; Friedman, Jessica ⁴; Haley, Alexander ²; Leininger, Brent ²; Mahaffey, Mallory ¹; Matthias, Marianne ⁵; Meis, Laura ¹⁻²; Polusny, Melissa ¹⁻²; Serpa, J. Greg ⁶; Taylor, Stephanie ⁶; Taylor, Brent ¹⁻²

1. Minneapolis VA Health Care System

2. University of Minnesota

3. Durham VA Health Care System

4. VA Greater Los Angeles Health Care System

5. Richard L. Roudebush VA Medical Center

6. VA Greater Los Angeles Health Care System

Abstract: Mindfulness-Based Interventions (MBIs) are evidence-based nonpharmacological treatments for pain. However, many MBIs have features that pose significant implementation barriers. This study compares two scalable approaches for delivering MBIs that address key patient- and system-level implementation barriers. Randomized pragmatic clinical trial with 12-month follow-up of 811 patients with moderate to severe chronic pain, recruited from three Veterans Affairs facilities. Mobile+Group Learning to Apply Mindfulness to Pain (LAMP) was delivered via videoconferencing and consisted of pre-recorded modules by a mindfulness instructor in a group setting, interspersed with discussions led by a facilitator. Mobile+Calls LAMP consisted of the same modules, was completed asynchronously by patients, and was supplemented by three individual facilitator calls. Both interventions were 8 weeks long and compared to Usual Care. The primary outcome was change in the Brief Pain Inventory interference score from baseline to 12 months (assessed at baseline, 10 weeks, 6 and 12 months). Secondary outcomes were changes in pain intensity, global improvement in pain, physical function, symptoms of anxiety, depression, and post-traumatic stress disorder, fatigue, sleep disturbance, participation in social roles/activities, and percentage reaching at least 30% improvement in pain interference. Both LAMP interventions resulted in significant reductions in pain interference compared to Usual Care over 12 months; similar results were observed for secondary outcomes. The two interventions performed similarly, except the Mobile+Calls group showed greater improvement on pain interference. Two novel, scalable approaches to delivering MBIs significantly reduced pain and biopsychosocial outcomes over the long-term in Veterans.

Research Topic: Pain

Funding agencies: DOD

Grant support: DOD W81XWH-18-2-0003

3. Artificial Intelligence-Assisted Colonoscopy Failed to Increase Adenoma Detection Rate: An Implementation Study

Herman, Tessa ¹; Guerrero Vinsard, Daniela ¹⁻²; Freeman, Morgan ¹; Westanmo, Anders ²; Gravelly, Amy ²; Bilal, Mohammad ¹⁻²; Hanson, Brian ¹⁻²

1. University of Minnesota

2. Minneapolis VA Health Care System

Abstract: Introduction: Artificial intelligence-assisted colonoscopy (AIAC) is a promising technology to improve colonoscopy quality by detecting precancerous polyps that may be missed during unassisted colonoscopy. Multiple studies have found improved adenoma detection rate (ADR) with AIAC. However, a few practical implementation studies have shown equal or decreased ADR with AIAC. Thus, more implementation studies are needed to determine the real-world impact of AIAC. Methods: In this single center, quasi-experimental, implementation study, we aimed to compare our primary endpoint (ADR) between 2 cohorts: a 6-month historical cohort of patients undergoing standard non-AI colonoscopy versus a 6-month prospective cohort undergoing AIAC. Both cohorts included colonoscopy for screening, surveillance, or positive fecal immunochemical test (FIT) indications. Secondary endpoints included sessile serrated lesion (SSL) detection rate, advanced ADR, hyperplastic polyp resection rate, and other benign, non-adenomatous lesion resection rate. Statistical analysis was performed using Pearson's chi-square or two sample T-test. Results: We evaluated 441 non-AI (November 2022-April 2023) and 604 AIAC cases (May-October 2023). ADR and SSL detection rates were higher in unassisted colonoscopy compared to AIAC: 85.3% versus 78.5% ($p = 0.0054$) and 21.3% versus 14.9% ($p = 0.0072$), respectively. Alternatively, benign lesion resection rates were higher in AIAC (31.5%) versus unassisted colonoscopy (22.9%) ($p = 0.0023$). Subgroup analysis by colonoscopy indication revealed surveillance colonoscopies largely accounted for the lower ADR (87.2 vs 78.7%; $p = 0.0032$) and the higher benign lesion resection rate with AI (22.9% versus 31.8%, $p = 0.0093$). The reduction in SSL detection rate with AIAC was most notable in FIT positive cases (30.9% versus 10.9%, $p = 0.0006$). Discussion: Our real-world implementation study shows lower ADR in AIAC compared to unassisted colonoscopy. While this unexpected result challenges prior RCT data, it is supported by recent pragmatic trials that did not show an ADR benefit with AI. Possible contributors may include a high baseline ADR for our endoscopists (historical average 63%), a lower SSL detection rate in AIAC specifically in FIT+ cases which may reflect endoscopist overreliance on AI technology, and a shift in focus to benign lesions detected with AI that would otherwise go undetected or unresected by endoscopists during unassisted colonoscopy.

Research Topic: Gastroenterology

Funding agencies: N/A

Grant support: N/A

4. Veteran Engagement Infrastructure and Practices Among VA HSR&D Research Networks

Sides, Tracy ¹; Amundson, Erin ¹; Argust, Mallorei ¹; Burgess, Diana ¹⁻²; Meis, Laura ¹⁻²; Krebs, Erin ¹⁻²

1. Minneapolis VA Health Care System

2. University of Minnesota

Abstract: BACKGROUND. Meaningful engagement of patients in the research process is a critical component of learning health systems. Engagement involves collaborative interaction between patients and researchers across all stages of the research process, where patients contribute their lived-experience expertise as partners. Over the past 20 years, momentum to engage patients as partners in the health research process has accelerated. There is a growing evidence base that patient engagement can improve the equity, feasibility, and relevance of health research, beyond satisfying a moral imperative to involve patients in the identification of research priorities and outcomes about them. VA strives to be a Veteran-centered health care system, which includes ensuring that VA-funded research reflects the needs and perspectives of Veterans. Health Services Research & Development (HSR&D) began supporting patient (Veteran) engagement (VE) in research in 2015. Since then, individual studies, research centers, and networks have reported a variety of VE activities across the VA research enterprise. Despite this proliferation of activity, no systematic assessment of the amount, type, or effectiveness of current VE activities is available to help track, evaluate, and promote engagement across the research enterprise. We sought to describe VE activities and practices among the 7 HSR&D research network to identify engagement activities and practices. We will use principles of thematic analysis and content analysis to describe engagement activities and identify promising practices, perceived impacts, and evaluation outcomes. RESULTS. We identified X engagement structures, assets, and services across networks. Each network has a unique context of research field and operational partners. All networks reported specific engagement strategies to facilitate VE in research, all emphasized equity as a core value, and most (5 of 7) have a standing VE panel. One panel documented a robust tracking and evaluation system. CONCLUSION. This work provides an important resource for the research community to explore and adapt VE strategies across peers and tie those strategies to outcomes in future research. It also highlights ways that research networks can help advance equity in VA health care by fostering engagement of Veterans with diverse backgrounds and experiences in the research process.

Research Topic: Health Equity

Funding agencies: VA HSRD

Grant support: HSR SDR 24-121

5. Exploring the genomic link between hidradenitis suppurativa and cardiovascular disease

Wendland, Zachary ¹⁻²; Teerlink, Craig ³⁻⁴; Pridgen, Kathryn ³⁻⁴; Lo, Sydney ²; Sayed, Christopher ⁵; Van Straalen, KR ⁶; Tcheandjieu, Catherine ⁷; Damrauer, Scott ⁸⁻⁹; Tsao, Philip ^{7, 10}; Chang, Kyong-Mi ⁸⁻⁹; Yun, Li ¹¹; Mohlke, Karen ¹¹; Sun, Quan ¹¹; Lynch, Julie ³⁻⁴; Goldfarb, Noah ¹⁻²

- | | |
|---|---|
| 1. Minneapolis VA Health Care System | 6. Erasmus University Medical Center Rotterdam |
| 2. University of Minnesota | 7. VA Palo Alto Health Care System |
| 3. VA Informatics and Computing Infrastructure (VINCI), VA Salt Lake City Healthcare System | 8. University of Pennsylvania Perelman School of Medicine |
| 4. University of Utah | 9. Corporal Michael Crescenz VA Medical Center |
| 5. University of North Carolina, Chapel Hill | 10. Stanford University School of Medicine |
| | 11. University of North Carolina, Chapel Hill |

Abstract: Background: Data from family and twin studies suggests that hidradenitis suppurativa (HS) has a hereditary component with autosomal dominant inheritance patterns in some families. 30-40% of HS patients report at least one first degree relative with HS, and twin studies have suggested a familial risk of up to 73 times the background population. While ~5-6% of HS patients have been found to have causative loss-of-function mutations in the gamma-secretase complex, genome-wide association studies, looking for single-nucleotide polymorphisms (SNPs), have thus far not found any results. We performed a genome-wide association study (GWAS) of patients in the VA's Million Veteran Program (MVP) with a diagnosis of HS. Objective: To gain insight into a potential underlying genetic driver(s) of HS pathogenesis. Methods: We performed a GWAS study of patients with a diagnosis of HS defined as at least one instance of ICD9 705.3 or ICD10 L73.2 from participants in the VA's Million Veteran Program (MVP). MVP is a national program evaluating how military experience, exposures, lifestyle, and genetics influences. MVP currently has full genome sequencing data on more than 950,000 Veterans. Conventional genome-wide significance threshold 5×10^{-8} was used to declare study-wide significance. Only SNPs with minor allele frequency $> 0.1\%$ were included in the analysis (INFO > 0.30). Results: In total, 597,819 participants were analyzed and 4,959 cases with HS were identified (African ancestry (AA): 1,931; European ancestry (EA): 7,982; Hispanic ancestry (HA): 435). When evaluating all Veterans from various ancestral backgrounds in a meta-analysis, SNPs in two genes were associated with HS; GL000251 on chromosome 6 (32 NPS) and SOX9 on chromosome 17 (12 SNPs). Discussion: HLA-DRB1 is an alternate major histocompatibility complex (MHC). SOX9 encodes a transcription factor that regulates several developmental processes expressed in the epidermal basal layer and outer root sheath (ORS) of hair follicles.

Research Topic: Dermatology

Funding agencies: N/A

Grant support: N/A

6. Trends in the surgical management of hidradenitis suppurativa

Wendland, Zachary ¹⁻²; Jiang, Ziou ²; Sayed, Christopher ³; Goldfarb, Noah ¹⁻²

- | | |
|--------------------------------------|--|
| 1. Minneapolis VA Health Care System | 3. University of North Carolina, Chapel Hill |
| 2. University of Minnesota | |

Abstract: Hidradenitis suppurativa (HS) is a chronic inflammatory skin disorder with proclivity for intertriginous anatomic sites. HS is unique in that its complementary roles of surgery combined with pharmacologic treatments. Several surgical options exist, but little research exists exploring who is performing these procedures and how this has changed over time. Our aim was to analyze trends in HS surgeries and their providers. Using data from 2009 to 2019, we found that while general surgery (27.66% [2009]) and plastic surgery (9.73% [2009]) have historically been the most common types of physicians to perform these surgeries, there has been an increase in dermatologists' involvement, particularly in the axillary region ($p < 0.001$). Despite a significant 8.5% annual rise in dermatologists performing these procedures during the study period, the overall percentage of dermatologists performing these surgeries remains low (1.75% [2019]). Conversely, general and plastic surgery had declining trends ($p < 0.001$). These findings highlight a shift in the HS surgery landscape with an increase in the role of dermatologists and a decrease in the role of the traditional surgical specialties. This study emphasizes the evolving role of dermatologists in HS surgery management.

Research Topic: Dermatology

Funding agencies: N/A

Grant support: N/A

Poster Presentations

1. Impact of protein kinase CK2 downregulation and inhibition on oncomir clusters 17~92 and 106b~25 in prostate, breast, and head and neck cancers

Ahmed, Khalil¹⁻²; Kren, Betsy¹; Henzler, Christine²; Trembley, Janeen¹⁻²

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

Abstract: Background: Protein kinase CK2 is a ubiquitous and highly conserved protein Ser/Thr kinase with diverse cell functions. CK2 is upregulated in various cancers and affects numerous aspects of their underlying pathobiology. The important role of microRNAs (miRNAs) referred to as oncomirs is also recognized in various cancers. Elevation of both CK2 and altered miRNA expression in cancers raised the question whether there was a connection between CK2 function and oncomirs in cancer. Methods: PCR array analysis was used to examine the effects of CK2 siRNA-mediated downregulation on miRNA levels in C4-2 prostate cancer cells. We employed prostate cancer, breast cancer, and head and neck squamous cell carcinoma (HNSCC) cells as well as a prostate cancer xenograft orthotopic tumor model to examine the effects of CK2 siRNA-mediated downregulation or chemical inhibition on oncomir cluster miR-17~92 and miR-106b~25 constituent miRNAs by quantitative reverse-transcriptase stem-loop PCR. Pri-miRNAs were measured in cancer cell lines by quantitative reverse-transcriptase PCR. Protein levels were assessed by western blot. PC3-LN4 prostate cancer orthotopic xenograft tumors and blood were collected from nude mice following repeated treatments with tenfibgen ligand nanocapsules containing RNAi-CK2 or RNAi-Control cargoes. Results: PCR array analysis demonstrated effect on a subset of miRNAs following CK2 downregulation; we focused our investigation on CK2 regulation of miR-17~92 and 106b~25 oncomir clusters. Chemical inhibition or molecular downregulation of CK2 greatly reduced expression of miR-17~92 and 106b~25 in prostate, breast and head and neck cancer cells in vitro. CK2 α and CK2 α' protein levels were significantly correlated with many of the miR-17~92 and some of the miR-106b~25 constituent members in prostate cancer cells. Decreased pri-miRNA levels for the miR-17~92 gene cluster transcript were observed for 5 of 6 cancer cell lines tested following CK2 downregulation. Nanocapsule-mediated delivery of RNAi-CK2 reduced CK2 protein expression in orthotopic prostate xenograft tumors and decreased intra-tumoral and serum levels of the oncomirs. Conclusions: Targeting CK2 for the development of new cancer therapies is under active investigation in many laboratories and pharmaceutical companies. Our data suggest a new role for CK2 in cell signaling and survival in multiple cancer types through maintenance of miR-17~92 and 106b~25 biogenesis.

Research Topic: Cancer

Funding agencies: VA BLRD; NIH

Grant support: BLRD I01BX003282; BLRD I01BX005091; NIH R01CA150182

2. Extended Reality (XR) Interventions for Fibromyalgia: A Systematic Review

Anthony, Maylen¹; Thomas, David²; Zerzan, Nicholas¹; Calvert, Collin¹; Ullman, Kristen¹; Kalinowski, Caleb¹; Landsteiner, Adrienne¹; Rich, Tonya¹; Miller, Wendy³; Wilt, Timothy¹⁻²; Duan-Porter, Wei (Denise)¹⁻²; Goldsmith, Elizabeth¹⁻²; Ewart, David¹⁻²

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

Abstract: Introduction: Fibromyalgia is a chronic pain condition associated with significant disability. Pharmacologic therapies for fibromyalgia are of limited efficacy. As such, non-pharmacologic interventions may be important components of treatment. Extended reality (XR) technologies, including fully immersive virtual reality (VR) and partially or minimally immersive augmented reality (AR), could aid in the delivery of non-drug interventions for fibromyalgia. We conducted a systematic review on benefits and harms of VR and AR interventions for fibromyalgia. Methods: We searched MEDLINE, Embase, CINAHL, PsycINFO, and Scopus databases from inception to May 2023 for English-language articles of VR or AR fibromyalgia interventions. Risk of bias assessments and certainty of evidence (COE) were conducted. We classified intervention types by key content and conducted meta-analyses for = 3 sufficiently similar studies; otherwise, we provided narrative syntheses. Results: We identified 5 eligible randomized controlled trials (RCTs) (total N range 35-83). All were AR interventions and included only female participants. Most were conducted in Spain and the median follow-up period was 8 weeks (range 6-24 weeks). Four RCTs compared AR physical activity (using Microsoft Kinect or Nintendo Wii) with supervised exercises or usual care. One RCT evaluated AR-enhanced cognitive behavioral therapy (CBT) compared to usual care. All studies reported pain-related functioning and three reported pain intensity. The evidence is very uncertain on the effects of AR-enhanced CBT or AR-physical activity on pain-related functioning and pain intensity, compared with supervised exercises or usual care (very low COE). No trial reported on adverse events, and none examined VR interventions. Conclusions: The few RCTs evaluating efficacy of AR interventions for fibromyalgia were small and none reported on adverse events. Future research should involve larger RCTs that address adverse events, as well as consider comparisons with pharmacologic treatments and other non-pharmacologic interventions (e.g., non-XR CBT).

Research Topic: Pain

Funding agencies: VA HSRD

Grant support: HSR ESP 09-009

3. Geographic Disparities in Tobacco Dependence Treatment among Patients with COPD in a National Cohort

Baldomero, Arianne K.¹⁻²; Melzer, Anne C.¹⁻²; Kunisaki, Ken M.¹⁻²; Wendt, Chris H.¹⁻²; Orly, Vardeny¹⁻²; Dudley, Adams¹⁻²

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

Abstract: RATIONALE: Patients with chronic obstructive pulmonary disease (COPD) living in rural areas experience worse health outcomes compared to those in urban areas, for reasons that are not well understood. Tobacco dependence treatment (TDT) is a key part of COPD care. To assess the influence of geography in COPD management, we evaluated associations between geography (rurality and drive time to care) with receipt of TDT among Veterans with COPD. METHODS: Retrospective analysis of patients with COPD (ICD-10 codes for COPD in 2016-2019) and tobacco use at time of diagnosis using national Veterans Health Administration data. Patients who currently used tobacco were identified using ICD-10 codes and tobacco health factors, which are retrievable electronic data fields that are updated at least annually at the time of a clinical encounter. Primary outcome was receipt of TDT within 1 year of COPD diagnosis. TDT was defined as: nicotine replacement therapy, bupropion, varenicline, and/or tobacco cessation counseling. Exposure variables were derived from geocoded addresses to ascertain: 1) rurality of patient home address and 2) drive time to closest VA facility with a pulmonary specialist. Multivariable logistic regression models assessed associations between TDT, rurality, and drive times to closest pulmonary specialty care. All models were adjusted for age, sex, race/ethnicity, Area Deprivation Index, coronary artery disease, malignancy, substance use disorder, and mental health diagnosis. RESULT: Of 238,433 Veterans with COPD who currently used tobacco, 36.3% (107,374) received TDT within 1 year of COPD diagnosis. TDT rates were higher among Veterans with COPD living in urban vs. rural area (37.7% vs. 34.2%, respectively). Pharmacotherapy alone was 29.1%, pharmacotherapy+counseling 4.3%, and counseling alone 2.9%. TDTs included: nicotine patch 9.9%, bupropion 7.6%, nicotine patch+short-acting nicotine 4.2%, short-acting nicotine 4.2%, and varenicline 3.2%. Veterans living in a rural area and those with longer drive times to care had lower odds of receiving tobacco cessation therapies. CONCLUSIONS: In this national sample of Veterans with COPD who use tobacco, only a small proportion received TDT. Living in a rural area and longer drive times to care were associated with less frequent receipt of TDT. Findings suggest the need for newer care delivery models to improve tobacco cessation, especially in patients with geographic barriers to accessing care.

Research Topic: Rural Health

Funding agencies: Other

Grant support: NCATS KL2TR002492, NCATS UL1TR002494

4. Veteran social support intervention for enhancing smoking treatment utilization and cessation: results from a randomized controlled pilot trial

Branson, Mariah¹; Patten, Christi¹; Brockman, Tabetha¹; Hammett, Patrick^{1,2}; Nelson, David¹; Danan, Elisheva¹; Meis, Laura¹; Fu, Steven^{1,2}

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

Abstract: Significance: Social support interventions may enhance access and use of evidence-based tobacco cessation treatments (EBCTs) to reduce tobacco-related health disparities. We piloted a social support intervention for Veterans who smoke cigarettes. The aims were: 1) to assess the feasibility of recruiting dyads comprised of Veterans who smoke and their support person (SP), and 2) to assess the preliminary intervention effects on Veteran use of EBCT and smoking abstinence. Methods: We conducted a randomized controlled pilot trial within the national VHA health system. Veterans who smoke cigarettes, regardless of level of readiness to quit, were identified nationally and proactively recruited. To enhance recruitment among Veteran women, we received feedback from the Women's Veteran Engagement Panel on recruitment strategies. Interested Veterans were asked to identify a SP who would enroll. Participants were randomized as Veteran-SP dyads to the SP intervention (based on Cohen's theory of social support) or control condition. All Veteran and SP participants received information on EBCTs. All SP participants received support tips. SP participants in the intervention group additionally received a 1-call coaching session to encourage the Veteran to use EBCTs. Follow-up survey assessments for dyads were conducted at baseline, 1-month, and 4-months post-randomization. Veterans who self-reported abstinence completed remote biochemical verification at 1-month and 4-months. Results: Of the 605 Veterans invited to join the study, 38 Veterans were interested in participating in the study, returned a baseline survey, and nominated a SP. 27 of the 38 nominated SPs consented to participate, resulting in 27 dyads randomized. A total of 14 dyads were randomized to the intervention group, and 13 dyads to the control group (18 women Veterans, 9 male Veterans). At 4-months, Veteran intervention participants reported a higher rate of cessation medication use (57% vs. 31%) and use of EBCT (64% vs. 38%) than control participants. Veteran intervention participants reported higher rate smoking abstinence than control participants (57% vs 15%). Conclusion: The recruitment methods were feasible, especially for women Veterans. The intervention may lead to higher Veteran use of EBCT and smoking abstinence. This project including women Veterans provides preliminary evidence that a social support intervention increases use of cessation treatment among Veterans who smoke.

Research Topic: Health Services

Funding agencies: VA HSRD

Grant support: HSR I01HX003185

5. Synthesis and Evaluation of Atypical Symptom Characteristics in Peripheral Artery Disease (PAD): A Systematic Review

Brown, Rebecca^{1,2}; Treat-Jacobson, Diane²; Schorr, Erica²; Lindquist, Ruth²; Pruinelli, Lisiane³; Wolfson, Julian²

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

Abstract: Background: PAD is an underdiagnosed and undertreated disease affecting more than 230 million individuals worldwide. The majority patients with PAD experience atypical symptoms or are asymptomatic. Claudication is well described in the literature, however, atypical symptoms, though more prevalent, are not well defined. The purpose of this systematic review is to comprehensively describe the range of atypical symptom characteristics in individuals with PAD, how they are defined, and examine potential factors associated with atypical symptoms reported in the literature. Methods: A search of online electronic databases, Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily, Ovid MEDLINE and Versions® using search terms "vascular disease or arter* disease*", "atypical*", "asymptomatic", and "typical*" was conducted with consultations from the librarian and author team. Results: The systematic search yielded 502 unique studies. Twenty-four studies met inclusion criteria for review. Studies were analyzed based on methodological approach including a) questionnaire-based, b) clinician assessment, and c) qualitative interview. Atypical claudication was defined differently across studies. Definitions of atypical claudication included non-classic claudication, symptoms which resulted in cessation of physical activity versus those which allowed continuation of physical activity, leg pain during exertion and at rest. Variations in symptom descriptors, locations, and characteristics were noted as atypical. Atypical symptoms were more often associated with increased rates of comorbid diseases, coexisting conditions affecting ambulation, and a greater number of PAD risk factors. The majority of participants reported atypical symptoms. Conclusion: More research is needed to further elucidate the symptoms experienced by patients with and without PAD. A common denominator may exist across symptom subtypes, classifications, and through comorbid conditions which are clinically useful in enhancing PAD detection.

Research Topic: Cardiovascular Disease

Funding agencies: UMN

Grant support: UMN CTSI TL1/TRACT Program, NIH National Center

6. Women's Enhanced Recruitment Process (WERP) Toolkit

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2. University of Minnesota

Abstract: Women Veterans are the fastest-growing subpopulation in VA, expected to reach 18% by 2040. Adequate representation of women in VA trials is critical for generalizability of trial results to women. However, recruiting women Veterans can be challenging given the small number of women at any given VA facility, the unique healthcare needs of women, and differing sociodemographic characteristics of women Veterans. To overcome some of these barriers, the Women's Health Research Network (WHRN) was initiated to boost inclusion of women in HSR&D studies. In 2016, VA Cooperative Studies Program (CSP) partnered with WHRN to increase representation of women Veterans through an initiative called "Women's Enhanced Recruitment Process" (WERP). WERP seeks to enhance recruitment of women Veterans into large multi-site clinical trials through broad dissemination of targeted strategies to VA research staff. As a part of this effort, WERP has developed a collection of resources known as the WERP Toolkit. This collection contains resources to deepen understanding of women Veteran health, staff training suggestions, communication strategies, and tips and tools for successful recruitment and retention of women Veterans throughout the lifespan of a research study. The WERP Toolkit is hosted on CIPHER.

Research Topic: Women's Health

Funding agencies: VA CSRD

Grant support: VA CSP N0011

7. Reaching Rural Veterans: Applying Mind-Body Skills for Pain Using a Whole Health Telehealth Intervention (RAMP). Protocol for a Hybrid 2 Effectiveness-Implementation Pragmatic Clinical Trial

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1. Minneapolis VA Health Care System
2. University of Minnesota
3. Iowa City VA Medical Center
4. University of Iowa
5. Richard L. Roudebush VA Medical Center
6. VA Greater Los Angeles Healthcare System

Abstract: The RAMP project addresses the significant challenge of implementing effective, non-opioid interventions for chronic pain management among rural-dwelling Veterans Affairs (VA) patients, using evidence-based complementary and integrative health (CIH) approaches. While the VA has become a leader in advancing CIH, there remain many barriers, especially for rural patients. The Reaching Rural Veterans: Applying Mind-Body Skills for Pain Using a Whole Health Telehealth Intervention (RAMP) is a scalable intervention that incorporates multiple evidence-based CIH self-management strategies, designed to be implemented within the VA Whole Health (WH) System, using WH coaches as program facilitators. RAMP is a 13-week program including two individual sessions with a WH Coach (at the start and end of the program), and 11 group sessions including pre-recorded expert-led education videos, mind-body skill training and practice, and facilitated discussions. For the preparatory phase (UG3) we will: 1) conduct stakeholder engagement activities (n = 35-50 patients, community partners, VA healthcare system leaders/staff), guided by the RE-AIM/PRISM framework, to learn about key factors that can affect long-term adoption; and 2) conduct a pilot study of 40 rural VA patients with chronic pain to assess feasibility of delivering RAMP in terms of recruitment and engagement, intervention fidelity and adherence, data collection, and other metrics. For the UH3 Phase, we will conduct a randomized hybrid type 2 effectiveness-implementation multi-site pragmatic clinical trial of RAMP compared to Usual Care, among rural patients (n = 500) in the VA healthcare system. UH3 Aim 1 will assess the relative effectiveness of RAMP in terms of the primary effectiveness outcome of pain interference at 13 and 26 weeks and secondary outcomes including opioid use and other biopsychosocial outcomes. In UH3 Aim 2 we will work iteratively with stakeholders to evaluate intervention implementation strategies used in the trial and adapt these strategies to scale up RAMP within VA. This will include a) conducting mixed-methods assessments of stakeholder and randomized trial participant views of implementation-related barriers and facilitators, resource needs, and other RE-AIM/PRISM domains; b) working with stakeholders to co-create additional plausible strategies for overcoming barriers to implementation of RAMP and c) conducting budget impact analyses using models informed by stakeholder views.

Research Topic: Pain

Funding agencies: NIH

Grant support: NINR 1UG3NR020929

8. Automated Chronic Subdural Hematoma Segmentation with 3D U-Net

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Abstract: Traumatic brain injury (TBI) is highly prevalent within the Veteran population and can result in chronic subdural hematoma (cSDH). Veterans' projected incidence rate of cSDH was reported to be 121.4, significantly higher than that of civilians which range from 1.72 to 20.62 per 100,000 persons per year. The management of cSDHs heavily relies on computed tomography (CT) imaging, with serial scans often acquired to guide treatment decisions. In this study, our objective is to develop a machine learning model to automate cSDH segmentation to improve and assist clinical diagnosis. We train our model based on an available Veteran cohort from the Veteran Affairs New York Harbor Healthcare System (NYHHS) to account for population-specific factors when analyzing cSDH incidence trends. A total of 65 CT scans were obtained from NYHHS, identified by CPT codes 6110-61108, corresponding to Subdural Evacuating Port System (SEPS) drainage procedures. The hematoma volume ranged from 43.25 ml to 484 ml across the patients. Among these, 10 patients were presented with bilateral, while the remaining patients had unilateral cSDH. Manual segmentation of the cSDH region was carried out, confirmed by neurosurgeon assessment as ground truth. We employed a 3D U-Net architecture in our machine learning model development to automate the segmentation of cSDHs utilizing the manually segmented CT scans. This model was trained in the 3D U-Net architecture using TensorFlow that includes contracting and expanding paths with convolutional and up sampling layers, respectively, to capture features at multiple scales. Our best performing model achieved a mean IOU of 0.8743 and a DICE score of 0.9214 on the validation set. Cases where the model performed well typically exhibited clear and distinct segmentation of the cSDH region, closely aligning with the manually segmented ground truth. However, certain cases posed challenges for the model, particularly those with faintly defined hematoma boundaries. This trained 3D U-Net model's performance indicates a high level of accuracy in delineating cSDH volumes from surrounding brain tissues, providing clinicians with a valuable tool for diagnostic assistance and treatment planning. The successful implementation of the 3D U-Net model underscores its potential as a reliable and efficient method for automated segmentation of cSDH, offering promise for improved patient care and clinical outcomes in the management of this prevalent neurological condition.

Research Topic: Traumatic Brain Injury (TBI)

Funding agencies: Other

Grant support: Minnesota Spinal Cord Injury and Traumatic Brain Injury Research Grant 165646

9. Genitourinary Syndrome of Menopause: A Systematic Review

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3. VA Greater Los Angeles Healthcare System

Abstract: Background: Genitourinary syndrome of menopause (GSM) describes common physical changes and vulvovaginal, urinary, and sexual symptoms associated with menopause. Treatments include hormonal, non-hormonal, and energy-based (e.g., laser and radiofrequency) therapies. We conducted a systematic review of GSM screening, treatment, and surveillance. Methods: For hormonal, energy-based, and vaginal moisturizer interventions, we assessed study quality and provided GRADE certainty of evidence for patient-centered outcomes in moderate to high quality studies, including: dyspareunia; vulvovaginal dryness; vulvovaginal discomfort/irritation; dysuria; change in Most Bothersome Symptom (MBS); distress, bother, or interference of genitourinary symptoms; treatment satisfaction; and harms. For non-hormonal intervention studies, we created an evidence map of study characteristics without assessing study quality. Results: After assessing 107 publications for risk of bias, we extracted and synthesized outcomes from 69 publications describing moderate to high quality trials or prospective, controlled observational studies (24 estrogen publications, 35 non-estrogen, 11 energy-based, and 4 moisturizers). An additional 66 publications evaluating natural products, mind/body practices, and educational interventions, were described in an evidence map. We found evidence that some treatments may improve vulvovaginal dryness (vaginal estrogen, vaginal moisturizers, vaginal dehydroepiandrosterone (DHEA), oral ospemifene), dyspareunia (vaginal estrogen, DHEA, ospemifene), change in MBS (vaginal estrogen), distress, bother, or interference of genitourinary symptoms (DHEA), and treatment satisfaction (vaginal estrogen, ospemifene). No treatments improved vulvovaginal discomfort/irritation or dysuria. Energy-based therapies, vaginal and systemic testosterone, vaginal oxytocin, oral raloxifene, or bazedoxifene offered no benefit or had very uncertain evidence. Few studies enrolled women with a history of cancer. Harms reporting was limited. Most studies were = 12 weeks. Conclusions: This systematic review provides comprehensive information regarding GSM interventions. Little long-term data exists on efficacy, comparative effectiveness, tolerability, and safety of GSM treatments. Future research would be strengthened by standard definitions of symptoms and uniform diagnostic criteria for GSM and a common set of validated outcome measures and reporting standards.

Research Topic: Women's Health

Funding agencies: Other

Grant support: AHRQ/PCORI EPC Task Order No. 75Q80122F32006

10. Unanticipated Effects of Cognitive Training on Quality of Life in Veterans with History of mTBI

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| 1. Minneapolis VA Health Care System | 4. University of New Mexico |
| 2. University of Minnesota | 5. The Mind Research Network |
| 3. Raymond G. Murphy Department of Veterans Affairs Medical Center | |

Abstract: Veterans with a history of mild traumatic brain injury (mTBI) often report persistent cognitive deficits, particularly in working memory and processing speed, that can interfere with activities of daily living and overall quality of life (QOL). Cognitive training interventions, such as Attention Process Training-3 (APT-3), have demonstrated potential to improve cognition, but less is known about downstream effects on QOL. We hypothesized that greater improvement in cognitive performance would be associated with positive changes in QOL. Participants include N = 12 combat-deployed OEF/OIF/OND Veterans (mean age = 36.6, 100% male) with a documented history of mTBI recruited by the Minneapolis and Albuquerque VA Medical Centers and their university affiliates. Measures of working memory (WAIS-IV Digit Span [DS]) and quality of life (TBI-QOL) were collected at baseline and after 16 sessions of APT-3 over the course of one month. Participants also received an active or sham version of either repetitive transcranial magnetic stimulation (rTMS) or high-density transcranial direct current stimulation (HD-tDCS) at each session according to a double-blind randomization schedule that is still intact. Of the 7 TBI-QOL scales assessed, Pain Interference scores significantly improved between baseline and post-intervention, and two scales (Self-Esteem, Emotional and Behavioral Dyscontrol) also tended to improve ($p < 0.10$). Likewise, DS Total Score also significantly improved over the course of the study. However, contrary to hypotheses, changes in DS performance were inversely related to changes on the TBI-QOL scales such that greater increases in cognitive performance were associated with smaller increases or even decreases in some TBI-QOL domains. This relationship was strongest for Pain Interference ($r = -0.72$) and Self-Esteem ($r = -0.65$). While we observed overall improvement in both cognition and QOL, these changes were inversely related, suggesting that individual participants demonstrate improvement in one area or the other but rarely both. Specifically, participants with lower baseline DS scores tended to improve on Pain Interference but not on DS, while those with higher baseline DS scores improved even further on DS but saw little improvement of Pain Interference. This pattern highlights the potential benefits of cognitive training even in “non-responders” and the potential costs of cognitive training in other areas of life functioning.

Research Topic: Traumatic Brain Injury (TBI)

Funding agencies: DOD

Grant support: DOD 81XWH2010928

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

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Abstract: The VA Cooperative Studies Program (VA CSP) Network of Dedicated Enrollment Sites (NODES) is a consortium of VA Health Care Systems that have teams dedicated to conducting VA CSP Research. NODES goals include enhancing study performance and enrollment rates; providing a consistent and comprehensive approach to CSP study management; maintaining quality and regulatory compliance; providing feedback on the design and execution of studies; and providing opportunities for research personnel interested in supporting the VA CSP research mission. NODES shares best practices and provides local insights to VA CSP partners for efficient management and conduct of all study activities. At the Minneapolis NODE site, a Director, Associate Director-Operations, Operations Manager, Administrator/Enrollment Manager and Research Assistant support these efforts. The Minneapolis CSP Node site has three strategic priorities, all aligned with the VA Office of Research and Development’s priorities of enhancing access to high quality clinical trials for Veterans and increasing the real-world impact of VA research. These priorities are: 1.) Provide efficient and cost-effective support for CSP studies to ensure successful enrollment, superior retention, and high-quality data for CSP trials. 2.) Enhance the recruitment of underrepresented Veterans in clinical research, including rural and women Veterans, across CSP and non-CSP studies. 3.) Support and grow the development of VA clinical research across the enterprise by a) increasing collaboration with the facility’s Research Office to provide support for CSP and other government-funded research; b) facilitating partnerships across the Minneapolis VAHCS, our academic affiliate, VISN23, national VA, and Veteran groups; and c) enhancing the training and mentoring of clinical investigators to conduct high-impact clinical trials. Since its inception in 2012, the Minneapolis NODE site has supported the conduct of 35 VA CSP trials. Currently the Minneapolis NODE supports 12 active CSP studies and 5 CSP studies in various stages of start-up.

Research Topic: Health Care Delivery

Funding agencies: VA CSRD

Grant support: VA CSP

12. The (Inconsistent) Link between Rehabilitation Utilization and Neurobehavioral Symptom Change in Veterans with History of Mild TBI

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Abstract: Over 440,000 OEF/OIF/OND service members have experienced a traumatic brain injury (TBI), 87.2% of which were mild TBI (mTBI). While most experienced full recovery, a subset (10-20%) experienced persistent post-concussive symptoms that prompted a National Research Action Plan between VA, DoD, and HHS emphasizing the importance of optimizing care. Improving neurobehavioral symptoms is a primary target of this effort, being identified as a key outcome by both VA and DoD. However, Veterans' rehabilitation utilization varies significantly in both the type and quantity of services used, and it is unclear how variation in utilization type and frequency is associated with neurobehavioral symptom change over time. The present study examined multifactorial predictors of score change on the Neurobehavioral Symptom Inventory (NSI) in Veterans with a history of mTBI, including demographic factors, injury history, service connection, and rehabilitation utilization. Using a subsample of the Predicting Rehabilitation Outcomes Using DNA (PROUD) study, 182 Veterans (89% male, mean age 41.69 years [SD = 9.73], mean time since most recent mTBI 11.58 years [SD = 6.162], mean service connection 76.5% [SD = 27.7%]) were given the NSI at their TBI consult visit and then again at the PROUD study visit, an average of 5.41 years later (SD = 4.62 years, range = 40 days to 15.56 years). Rehabilitation stop codes were extracted from computerized records during the window of time between the consult and follow-up NSI. Before adding rehabilitation utilization to the model, number of mTBIs ($p = 0.007$) and service connection percentage ($p < 0.001$) both were linked to higher NSI scores at follow-up. Total rehabilitation utilization (i.e. number of therapeutic visits during the window) was associated with higher follow-up NSI score ($p = 0.049$), consistent with more services being used by more symptomatic Veterans. However, when divided into rehabilitation categories, only quantity of mental health visits was associated with lower NSI severity at follow-up ($p = 0.002$), even when controlling for injury characteristics and service connection. These results suggest that increased utilization of most rehabilitation types may be emblematic of higher distress and symptomatology, but that mental health interventions uniquely show the inverse association, with improved long-term outcomes as utilization increases.

Research Topic: Traumatic Brain Injury (TBI)

Funding agencies: VA RRD

Grant support: RRD IK2RX002922

13. Neural Processing of Ambiguous Stimuli in Psychosis & Genetic Liability

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2. University of Minnesota

Abstract: Background: Predictive processing models of perception postulate a hierarchical relationship wherein visual inputs from low-level sensory cortices are shaped by top-down predictions. These top-down signals are crucial in guiding perception of information that is ambiguous, as is often the case in the environment. Psychotic psychopathology involves disruptions in feedforward and feedback neural functions supporting the integration of low-level and top-down information. Oscillatory signals of brain activity likely reflect these integrative neural functions. The present study sought to evaluate whether aspects of psychotic psychopathology are associated with atypical oscillations during the viewing of ambiguous objects. Method: Probands with psychosis ($N = 50$), first-degree relatives ($N = 19$), and comparison subjects ($N = 37$) completed the Fragmented Ambiguous Object Task, an object perception task which varies higher-level recognizability of images by presenting meaningful vs. meaningless objects while controlling for bottom-up visual features. MEG data were collected, and oscillatory power was quantified using Morlet wavelet convolution and corrected using percent-change-from-baseline in theta, alpha-beta, and delta frequencies. Dimensional psychotic symptoms were assessed using the schizotypal personality questionnaire (SPQ), and perceptual dysregulation with the sensory gating inventory (SGI). Results: Across groups, significant and marginally significant condition effects emerged for delta ($p = 0.005$) and theta ($p = 0.08$) power, respectively, with greater power following meaningful vs. meaningless images. Across conditions, greater perceptual dysregulation emerged as a predictor of lower delta power (meaningful $p = 0.027$, meaningless $p = 0.027$). Similarly, greater schizotypy was associated with lower alpha-beta suppression (meaningful $p = 0.017$, meaningless $p = 0.028$). Effects were significant after considering group. Conclusions: The present findings lend support to the relevance of alterations across hierarchical levels of visual processing to psychotic psychopathology. The nature of effects across probands, their relatives, and non-psychotic comparison subjects suggests relationships which are dimensional in nature.

Research Topic: Mental Health

Funding agencies: NIH

Grant support: NIH R01MH112583

14. Cochrane Urology: 2022-2024 Update

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Abstract: Cochrane Urology was founded at Minneapolis VAMC as “Prostatic Diseases and Urological Cancers’ Group” by Tim Wilt and was renamed to Cochrane Urology in 2015 with an expanded scope covering more urological conditions. Our mission is to develop high quality systematic reviews to support evidence-based clinical practice and train individuals (medical students, residents, nurses, fellows) in systematic review methodology. Our scope covers Urological oncology, endourology and sexual medicine. Cochrane Urology is funded by University of Minnesota and the Minneapolis VAMC. Herein we describe our projects and future plans such as enhancing the relevance of Cochrane Urology reviews for stakeholders like VA patients.

Research Topic: Urology

Funding agencies: UMN

Grant support: N/A

15. Veterans' Views of Mindfulness Programs for Pain

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2. Minneapolis VA Health Care System

Abstract: Purpose: Understanding participants’ views about interventions is critical for research translation. Methods: Our team conducted a three-group, randomized pragmatic trial, Learning to Apply Mindfulness to Pain (LAMP) testing a telehealth mindfulness based intervention (MBI) for Veterans with pain. We administered open-ended questions to a sub-sample of 142 Veterans about their views of the MBI, to assess the extent it met their capability, opportunity and motivational needs (based on the underlying theoretical model of behavior change which informed MBI development). A rapid qualitative assessment was performed by two team members using a codebook based on the theoretical model. Results: Overall, the majority mentioned the MBI enhanced their capabilities, particularly their psychological and physical skills, with the most mentioning they learned ways to apply mindfulness for pain management. Participants also shared they gained useful knowledge, and ways to regulate their pain management behaviors. A sizable number mentioned the MBI provided important opportunities and resources, with the social influence provided by the MBI facilitators most commonly cited. A smaller number noted the group support was also helpful. The majority of respondents shared the program was motivating, providing positive reinforcement that mindfulness could affect their pain. Large numbers shared the program influenced their beliefs about their own capabilities and the consequences of practicing mindfulness for pain; for some, it influenced their optimism. A smaller number shared they had negative perspectives of the MBI’s influence on their beliefs. Conclusions: Overall, these results confirm that at least in part (and from the Veteran participant perspective), the MBI achieved its goals in meeting important capability, opportunity and motivational domains required for facilitating engagement in positive pain management behaviors. Areas for improvement and optimization were also identified.

Research Topic: Pain

Funding agencies: DOD

Grant support: DOD W81XWH-18-2-0003

16. Perceptions of Phantom Limb Pain after Amputation: A Focus Group Study

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Abstract: Pain is a subjective and multifactorial experience. Phantom limb pain adds a layer of complexity, since this type of pain is perceived as originating from a limb that was amputated and no longer remains. Use of qualitative methods can allow for exploration of the ways in which phantom limb pain specifically affects daily life, revealing valuable insights about how this experience can influence participation in meaningful activities after an amputation. Therefore, the purpose of this qualitative study was to explore how individuals perceive phantom limb pain, its effects on their daily life, and its contributing factors. Focus groups were conducted virtually with individuals with major lower limb amputation across the United States. Participants were over the age of 18 and experienced at least two episodes of phantom limb pain per month. Focus groups were recorded and analyzed using thematic analysis. Thirteen individuals participated in four focus groups. Participants included women (54%) and men (46%) ranging in age from 33 to 79 (mean: 61). Time since amputation ranged from 1 to 65 years (mean: 15) and causes of amputation included trauma (46%), infection (23%), cancer (15%), vascular disease (8%), and blood clot (8%). Six themes were identified from the focus groups: 1) moving target, 2) life disruption, 3) choices and trade-offs, 4) waiting out the storm, 5) isolated and unsure, and 6) pushing forward and holding hope. Quotes from participants described specific examples of pain interference with life, both in immediate activities as well as through its lasting effects. The unpredictability of phantom limb pain discussed in these sessions gives insight as to why effective treatment can be so difficult. Participants commonly experienced self-doubt, since the pain is perceived from a limb that they no longer have and since many participants did not remember receiving education about phantom limb pain following their amputation. This uncertainty highlights the importance of clinician-initiated discussions and assessment of amputation-related pain. Participants reported a multitude of factors that were perceived to contribute to their pain. The themes identified in these focus groups illustrate both a sense of desperation regarding pain as well as a drive to push through pain episodes. A sense of immediate community and shared wisdom was evident during the focus group sessions, illustrating the power of connecting with others with amputation.

Research Topic: Pain

Funding agencies: NIH

Grant support: NIH 1F31NS134186

17. Impact of the COVID-19 pandemic on the rate of lower limb amputation in Veterans

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Abstract: The COVID-19 pandemic led to changes in health care, including postponement of nonurgent appointments. These changes, combined with overall decreased activity levels, may have placed individuals with vascular disease at increased risk for skin ulceration and amputation. The objective of this retrospective chart review was to determine the rates of lower limb amputation in Veterans due to complications of diabetes and/or vascular disease in the year following onset of the COVID-19 pandemic (March 2020–March 2021) compared to the previous 3 years (March 2017–March 2020). We reviewed medical records of Veterans with a vascular consult appointment note at the Minneapolis Veterans Affairs Health Care System between March 1, 2017, and February 28, 2021. The primary outcome was lower limb amputation rate in the year following onset of the COVID-19 pandemic compared to the previous 3 years. Secondary outcome was the rate of lower limb wounds in the same time frame. We hypothesized that rates of lower limb amputation and wounds increased during the pandemic. In reviewing vascular consult appointments ($n = 4183$) between March 1, 2017, and February 28, 2021, significantly higher rates of amputation (7.52% vs. 5.19%; $p = 0.006$) and wound presence (16.77% vs. 11.66%; $p < 0.001$) were found 1 year postpandemic compared to the previous 3 years. Amputation and wound rates did not significantly increase between pairs of consecutive years prior to the pandemic but significantly increased between the year preceding the pandemic and the first year of the pandemic (amputation $p = 0.047$; wound $p = 0.004$). Increased rates of amputation and wounds in Veterans following the onset of the COVID-19 pandemic are likely due to disruption of care, lifestyle changes, and other pandemic-related factors. Awareness of COVID-19-related negative health effects is imperative for health care providers to ensure appropriate allocation of resources and alternate models for care delivery for amputation and preventative care as part of disaster response.

Research Topic: Vascular Surgery

Funding agencies: N/A

Grant support: N/A

18. Characterization of Service Member and Veteran Participants of the Department of Veterans Affairs Polytrauma Intensive Evaluation and Treatment Programs

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3. James A. Haley VA Health Care System
4. Central Virginia VA Health Care System

Abstract: Mild traumatic brain injury (mTBI) remains the signature injury of the global war on terrorism and is associated with chronic physical and mental health comorbidities. Polytrauma Intensive Evaluation and Treatment Programs (IETPs) were developed for active-duty Service Members and Veterans (SMVs) with mTBI to address symptoms, comorbidities, and functional limitations. These IETPs are residential, inpatient programs that provide comprehensive, interdisciplinary rehabilitation at the five VA Polytrauma Rehabilitation Centers (PRCs). To date, the participants of these IETPs and their healthcare needs have not been described. The purpose of this study was to characterize the SMVs with mTBI served by the IETPs. Using the VA TBI Model Systems (TBIMS) national database, we performed descriptive analyses on participants who were admitted to one of the five IETPs. Data were collected from participants at study enrollment (i.e., during their IETP participation). SMV characteristics examined included sociodemographics, military service history, injury descriptives, prevalence of comorbidities, and mental health service utilization. Across the five VA PRCs, 821 SMVs (86.3% of the programs' participants) were enrolled in the VA TBIMS longitudinal study. IETP participants were predominantly white (81.1%), non-Hispanic (82.3%), married (77.2%), men (97.6%) who had military service histories that included combat deployments (91.8%), membership in the Special Forces (74.2%), and had their index mTBI while deployed (52.9%). The most common life-time medical comorbidities included chronic pain (88.7%) and sleep apnea (53.8%). One-quarter of the participants reported a pre-injury history of mental health treatment utilization. The IETPs serve unique individuals with distinctive needs that are different from other inpatient rehabilitation programming. These descriptive results further our understanding of SMVs participating in these programs and their unique needs, informing future program development and refinement. Future work will also capitalize on the longitudinal design of VA TBIMS to examine long-term outcomes for these SMVs.

Research Topic: Traumatic Brain Injury (TBI)

Funding agencies: DOD; Other

Grant support: VA Central Office Special Purpose Funding; Department of Defense Defense Health Agency

19. Effectiveness of intravitreal faricimab in a United States Veteran population

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2. Minneapolis VA Health Care System

Abstract: The purpose of this study is to evaluate the effectiveness of intravitreal faricimab in alleviating disease burden in a US Veteran population. Chart review was performed for all patients with at least one intravitreal faricimab injection recorded in the US Veterans Health Administration's Corporate Data Warehouse in 2022 (n = 572 eyes of 451 patients at 33 sites). Exclusion criteria included intervening intravitreal injection of a different medication, cataract extraction in the study time frame, or incomplete chart notes at key follow-up visits. The primary study outcome was control of disease activity in the subset of eyes that received = 3 doses of aflibercept followed by = 3 doses of faricimab. Secondary outcomes included treatment interval length and adverse events. Differences were assessed using Fisher's exact and paired t-tests. For the results, mean±SD age was 74.2 ± 8.9 years. Most patients were male (97%) and white (80%). Treatment indications were exudative age-related macular degeneration (AMD) in 314 eyes (55%) and diabetic macular edema (DME) in 219 eyes (38%). Adverse events occurred in 5 eyes (1%). Of the 212 eyes (167 patients) in the aflibercept/faricimab comparison subcohort, reasons for the medication switch included inadequate disease control in 88 eyes (42%) and desire to extend treatment interval in 65 eyes (31%). Inactive disease was documented in 22 eyes (10%) at the time of first faricimab injection. Following the first faricimab injection there were significantly more eyes with inactive disease in the setting of AMD (p < 0.001) but not DME (p = 1), although there were significantly more DME eyes with disease improvement (p = 0.004). Short term treatment interval duration was stable: mean±SD interval between the last aflibercept dose and the first faricimab dose was similar to the interval between the third and fourth faricimab doses for the comparison subcohort (46.5 ± 26.8 days, 44.3 ± 22.0 days, p = 0.29) and the subset with desired interval extension (44.2 ± 20.4 days, 44.1 ± 18.4 days, p = 0.97). In conclusion, faricimab may facilitate disease control in exudative AMD recalcitrant to aflibercept. Ongoing follow-up of this study cohort will assess the feasibility of long-term treatment interval extension with faricimab.

Research Topic: Ophthalmology

Funding agencies: UMN; Other

Grant support: VitreoRetinal Surgery Foundation Grant, UMN Medical Student Research Grant

20. Neural response to reward and loss are significantly reduced following Basic Combat Training

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2. University of Minnesota

Abstract: The brain's ability to respond to rewarding stimuli is essential for adaptive functioning while deficits in neural reward processing have been linked to the transdiagnostic symptom of anhedonia. Prior studies have shown that experiencing acute or prolonged stressors may negatively impact neural reward responses; however, few studies have been able to empirically test whether experiencing real-world naturalistic stressors predicts a reduction in the brain's responses to rewards. Therefore, the present pre-registered analysis (<https://osf.io/f6e8w>) used data from the ARMOR project to assess whether undergoing basic combat training, a demanding and stress-inducing 10-week program, led to significant reductions in electrophysiological measures of neural reward response in Army National Guard recruits. Study participants completed a virtual gambling task while electroencephalogram (EEG) was recorded both before and after completing basic combat training. Mean EEG activity in the time window of the Reward Positivity (RewP; 200–325 ms post feedback at FCz) was averaged separately for the win and loss condition as was delta- and theta-band frequency power. We found that neural response to both win and loss feedback in the time-window of the RewP was significantly reduced following basic training, relative to baseline ($F_{(1, 64)} = 9.154$, $p = 0.004$, $d = 0.125$). However, delta- and theta-band power in response to win and loss feedback did not change from pre- to post-basic training. Similarly, we did not find evidence that the level of perceived stress experienced during basic training mediated change in reward response. These findings suggest that experiencing the stress of basic combat training is associated with a significant reduction in neural feedback processing; however, this is not specific to reward or loss responses.

Research Topic: Mental Health

Funding agencies: NIH

Grant support: NIH UH3AT009651

21. Reducing impulsivity in Parkinson's disease patients with a transcranial direct current stimulation (tDCS) plus cognitive training intervention

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2. University of Minnesota

Abstract: Background. Dopamine-replacement (DR) therapy used to treat symptoms of Parkinson's disease (PD) has been associated with an increase in patients' impulsivity, which has been linked to increased fall risk, financial problems, marital distress, and a generally reduced emotional well-being of patients and their families. The main approach for reducing excessive impulsivity in PD is to decrease the dosage of DR medication. However, this medication reduction undermines the motor symptom benefits of the treatment. Here, we report on a pilot study to test the feasibility and initial effectiveness of a neuroplasticity-based intervention using transcranial direct current stimulation (tDCS) combined with cognitive training tasks selected to functionally target impulsive behavior, cognitive control, and brain circuits underlying impulsivity. Methods. To date, we have enrolled 3 Veterans (mean age 74.6 years; all men) who showed increased impulsivity in a previous, companion study investigating biomarkers of impulsivity in PD. The intervention was 5 sessions of tDCS (2 mA open label active, 20 minutes, left prefrontal anode/right prefrontal cathode) paired simultaneously with a battery of computer training tasks that required aspects of cognitive control for successful performance (e.g. set-shifting, working memory, inhibition). We collected both self-report (QUIP-RS, BIS-11) and untrained computer task (Iowa Gambling Task [IGT], Stop Signal, Delay Discounting) measures of impulsivity at a pre-intervention baseline assessment, a post-intervention assessment, and a 1 month follow-up visit. Results. Preliminary results suggest that the intervention successfully reduces impulsive behavior in these patients with PD. The scores of the self-reported questionnaires were lower, and scores on the untrained gambling game (IGT) showed an increase in the number of favorable choices, at the post-intervention and 1-month follow-up sessions relative to the baseline session. These changes indicate decreased impulsive behavior. Discussion. While these pilot data are from just 3 Veterans, they are very promising with respect to our intervention's ability to reduce impulsivity in patients with PD without the need to reduce DR medication dose. Our preliminary results, so far, provide support for the feasibility of the intervention, and suggest that tDCS plus cognitive training provides appreciable benefits with regard to decreasing impulsivity in PD patients.

Research Topic: Parkinson's Disease

Funding agencies: VA CSRD

Grant support: CSRD I01CX001773

22. CD115+ monocytes protect microbially experienced mice against E. coli-induced sepsis

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Abstract: Uropathogenic E. coli (UPEC) is a primary organism responsible for urinary tract infections and a common cause of sepsis. Microbially experienced laboratory mice, generated by cohousing with pet store mice, exhibit increased morbidity and mortality to polymicrobial sepsis or lipopolysaccharide challenge. By contrast, cohoused mice display significant resistance, compared with specific pathogen-free mice, to a monomicrobial sepsis model using UPEC. CD115+ monocytes mediate protection in the cohoused mice, as depletion of these cells leads to increased mortality and UPEC pathogen burden. Further study of the cohoused mice reveals increased TNF- α production by monocytes, a skewing toward Ly6C+ CD115+ “classical” monocytes, and enhanced egress of Ly6C+ CD115+ monocytes from the bone marrow. Analysis of cohoused bone marrow also finds increased frequency and number of myeloid multipotent progenitor cells. These results show that a history of microbial exposure impacts innate immunity in mice, which can have important implications for the preclinical study of sepsis.

Research Topic: Infectious Diseases

Funding agencies: VA BLRD

Grant support: BLRD I01BX001324; BLRD IK6BX006192; R35GM134880

23. Predictors of Treatment Engagement in Primary Care-Mental Health Integration

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2. University of Minnesota

Abstract: The Patient Aligned Care Team (PACT) utilizes a patient-driven, interdisciplinary team-based approach to deliver efficient, comprehensive, and continuous care to Veterans in the VA Health Care System (VAHCS). The PACT consists of a teamlet, which includes primary care providers and nurses, as well as discipline specific team members, including Primary Care-Mental Health Integration (PC-MHI). PC-MHI integrates mental health staff into each PACT with the goal of integrating high-quality, collaborative, brief behavioral health interventions into routine primary care to improve individual and population-level Veteran health. With the growing need for PC-MHI services within the VAHCS, this study examined patient-level predictors of treatment engagement in PC-MHI. Treatment engagement during an episode of care between October 2022-February 2024 was defined as 1) utilizing services, 2) total number of sessions attended, 3) no-shows, and 4) late cancellations. Patient-level predictors included demographic variables, mental health diagnoses, and medical diagnoses. Logistic regression models evaluated the binary outcome of service utilization and negative binomial regression models evaluated number of sessions attended, no-shows, and late cancellations. All relevant predictors were entered into one model for a total of four main effect models. After adjusting for all relevant predictors, results suggested that older adult Veterans (aged 65+) utilized services the least and attended fewer sessions compared to their younger peers, OR's = 0.53-0.84, p 's < 0.05. Female Veterans and Veterans with sleep and anxiety disorders demonstrated the highest engagement (utilized services and attended more sessions), OR's 1.15-1.80, p 's < 0.01. Findings suggest that older adult Veterans may be less likely to utilize PC-MHI services, highlighting the need to address potential barriers and internalized mental health stigma in our aging Veteran population. Veterans who identified as Black/African American were more likely to no-show or late cancel, OR's 2.26-2.36, p 's < 0.05; findings are consistent with health disparities literature that suggests Black/African American Veterans report lower healthcare utilization. These results support the need to increase engagement in Black/African American Veterans by finding ways to reduce no-shows and late cancellations, such as through focusing on rapport-building, multicultural competence, and identifying potential barriers to utilizing care.

Research Topic: Mental Health

Funding agencies: N/A

Grant support: N/A

24. Hospitalized acute exacerbations of chronic obstructive pulmonary disease and beta-blocker use indications: A single center, retrospective study.

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2. Minneapolis VA Health Care System

Abstract: Purpose: Beta-blockers are commonly prescribed in the United States and have clear benefit for persons with certain indications, but guidelines no longer support beta-blockers for hypertension. A randomized controlled trial (BLOCK-COPD) showed that metoprolol increased the risk for hospitalized acute exacerbation of COPD (AECOPD) in persons without strong indications. There are limited data on clinical indications for beta-blockers in people with COPD. In this study we analyzed beta-blocker indications and markers of cardiac stress among persons hospitalized for AECOPD. Methods: We performed a retrospective cohort analysis of Veterans admitted to the Minneapolis VA Medical Center with a primary diagnosis of AECOPD between December 2022 and November 2023. Upon admission all participants were interviewed by a pharmacist who documented prescriptions and indications. Charts were reviewed for class I beta-blocker indication (heart failure with reduced ejection fraction, atrial fibrillation, and coronary artery disease with recent myocardial infarction). Brain natriuretic peptic (BNP) and troponin from admission were extracted. Proportions were compared using Chi-squared tests. Results: 79 persons with AECOPD were included, and 29 (38.1%) were on beta-blockers at admission. Of these, 16 (55%) were on beta-blockers for class I indications. The remaining 13 persons on beta-blockers were prescribed for hypertension (10, 34%) or other reasons (3, 10%). After excluding 16 persons with a class I indication for beta-blockers, BNP concentration was checked on admission in 45 persons and was elevated in 18. Persons on beta-blockers for hypertension or other indications had similar rates of BNP elevation to persons not on beta-blockers (16% vs 22%; $p = 0.65$). Troponin was measured in 38 persons and elevated in 9. Those not on beta blockers were numerically more likely to have an elevated troponin based on direct percentage comparison (31% vs 11%; $p = 0.23$), however this was not statistically significant due to low power. Conclusions: Rates of non-guideline adherent beta-blocker use are high among persons hospitalized for AECOPD and may be a contributor to admission. Larger studies are needed to determine possible cardioprotective effects of beta blockers during the acute exacerbation phase requiring hospitalization. Clinicians should be aware that beta-blockers can have deleterious effects on COPD and should consider deprescribing in the absence of a strong indication.

Research Topic: Cardiovascular Disease

Funding agencies: N/A

Grant support: N/A

25. Implementation of Centralized Support for Community Care Lung Cancer Screening

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2. Minneapolis VA Health Care System

Abstract: Introduction: Approximately 10% of Veterans across the Midwest region of the VA network are eligible for lung cancer screening (LCS). Most LCS is performed at VA medical centers, but Veterans living far from VA centers can access LCS through the community. These patients are not managed using the centralized processes VA utilizes to ensure high-quality LCS, placing them at risk of fragmented and less timely care. We performed an implementation intervention at the Minneapolis VA Health Care System (MVAHCS) to improve this process. Methods: A community care LCS nurse coordinator (NC) was hired who served as implementation champion. She gathered the implementation team and developed the program manual. We created a community care LCS referral with consults routed to the NC for review of eligibility for LCS and community care. NC offered screening at the MVAHCS, obtained imaging results, and ensured follow up per LUNG-RADS guidelines including pulmonary consultation. We conducted a pre- (10/2022-12/2022) and post- (10/2023-12/2023) implementation chart review of key quality metrics. Outcomes included timeliness of results reporting and pulmonary consult completion and location. Data analysis was performed using a t-test comparing mean days. Results: During the pre-implementation period, 233 patients completed LCS in the community of whom 6.9% were ineligible. Post-implementation, NC received 1247 consults after program launch, of whom 14.7% were ineligible and imaging was not completed. Many patients eligible for care in the community and LCS elected to receive LCS at the MVAHCS (121/600, 25%), and 241 received LDCT during the post- review period. Time from consult to obtaining CT report decreased by 23 days ($p = 0.0001$), driven by a faster turnaround time from CT completion to report received. All patients found to have high-risk nodules were referred to pulmonology. Pre-implementation, one patient declined and 6/8 consults were referred to community pulmonologists. Post-implementation, 11/12 consults were completed at the MVAHCS. Conclusion: Implementation of a centralized process for coordinating LCS between the MVAHCS and community providers resulted in significant improvements in timeliness adherence to eligibility criteria. More care was recaptured into the VA system which is a surrogate for decreased care fragmentation. Incorporating community LCS patients into structured VA programs should be considered across all sites to improve quality of LCS.

Research Topic: Respiration & Pulmonary Disease

Funding agencies: VA HSRD

Grant support: HSR IK2HX003067

26. Identifying Patient, Care Partner and Clinician Needs for Functional Recovery Following Hospitalization when Dementia is Present

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2. Wisdom Consulting
3. Creighton University
4. University of California
5. University of Minnesota

Abstract: Persons with dementia are frequently hospitalized, which threatens their ability to return to and live at home. Current post-acute paradigms tend to default to short-term rehabilitation in a nursing home. Still, alternative post-acute care models are crucial for Veterans with dementia to recover at home. This study aims to identify the needs of Veterans with dementia, care partners, and rehabilitation clinicians in relation to home-based models of care to inform the implementation and adaptation of models to the post-acute context. Semi-structured interviews were conducted across three groups (Veterans with dementia, care partners, and rehabilitation clinicians) and analyzed using a rapid qualitative approach guided by the Practical, Robust Implementation and Sustainability Model (PRISM). Veterans with a dementia diagnosis hospitalized and their care partners were recruited from the Minneapolis VA Health Care System (MVAHCS). Rehabilitation clinicians were recruited from within the Veteran Health Administration (VHA). Participants included 11 Veterans with dementia, 13 care partners, and 23 rehabilitation clinicians. We identified three themes from the interviews: (1) collaborative decision-making and planning are crucial to high-quality care, (2) follow-through is necessary to ensure needs are met when transitioning from hospital to home, and (3) alternative care options, including technology use, are important when optimizing transitions of care. Alternative options for home care after hospital discharge may enhance patient and family-centered outcomes. Future research must identify evidence-based models that can be collaboratively adapted or developed to provide effective, safe, and feasible post-acute care to optimize independence in the home and quality of life.

Research Topic: Rehabilitative Medicine

Funding agencies: VA HSRD; NIH

Grant support: AHRQ/PCORI K12HS026379; NIH KL2TR002492; HSR I50HX001228; RRD I50RX004836

27. Chlorthalidone compared with Hydrochlorothiazide for the prevention of renal events in patients with hypertension with long-term follow up: Secondary Analysis from the Diuretic Comparison Project (DCP)

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3. VA Greater Los Angeles Healthcare System
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5. Lt. Col. Luke Weathers, Jr. VA Medical Center

Abstract: Background: Hypertension is risk factor for the development and progression of chronic kidney disease (CKD). Thiazides reduce blood pressure (BP) in those with CKD. Prior observational studies have suggested a greater rate of progression of eGFR and a greater incidence of CKD with chlorthalidone(CTD) compared to hydrochlorothiazide(HCTZ). This analysis evaluates renal outcomes comparing CTD and HCTZ in patients with hypertension in the Diuretic Comparison Project(DCP) trial. Methods: In the DCP trial, participants were randomized to either continue HCTZ or switch to CTD at pharmacologically comparable doses. For this analysis the primary outcome was progression of CKD, defined as a doubling of creatinine, a terminal eGFR < 10 mL/min or kidney failure requiring treatment (KFRT). Additional analysis included an alternate definition of progression (40% reduction in eGFR, eGFR < 10 mL/min or KFRT), the total slope of eGFR and incident CKD were evaluated. Adverse events of acute kidney injury and hypokalemia were also evaluated. Extended follow up for this analysis was through December 31, 2023. Results: Overall, 12,265 (91%) had a baseline and at least one follow-up creatinine measurement with a mean duration of follow up 3.9 ± 1.2 years. Baseline median eGFR was 71.2 mL/min (IQR 58.8-84.6 mL/min), with no difference between CTD compared to HCTZ. There was no difference in the primary composite renal outcome between the CTD (369/6,118; 6.0%) and the HCTZ groups (396/6,147; 6.4%) (HR 0.95 (0.82-1.09), $p = 0.44$). There was no difference between interventions when a reduction of 40% of eGFR was substituted for doubling of Cr in the above outcome (CTD 12.7% vs HCTZ 13.3%; HR 0.97 (0.88-1.07), $p = 0.53$). There was no difference in any of the components of the primary composite outcome. There was also no difference in the incidence of CKD between the CTD and the HCTZ groups(40.2% vs 39.0%; $p = 0.18$). There was no difference between groups in the incidence of acute kidney injury requiring hospitalization between groups (CTD 6.4% vs HCTZ 6.2%; $p = 0.63$). There was an increased incidence of total hypokalemia events in the CTD compared to the HCTZ group (CTD 8.9% vs HCTZ 6.9%; $p < 0.001$). Conclusion: Overall results from DCP suggest similar effects of CTD to HCTZ for renal outcomes. There is a greater tendency for hypokalemia in those randomized to CTD compared to HCTZ even in those with CKD. Clinicians should feel confident in using either agent for the treatment of hypertension.

Research Topic: Nephrology

Funding agencies: VA CSRD

Grant support: CSP 597

28. Combined transcranial direct current stimulation (tDCS) and cognitive training improves inhibitory control in clinically impulsive patients with Traumatic Brain InjuryJamal, Hamza¹; Camchong, Jazmin²; Lim, Kelvin¹⁻²; Gilmore, Casey¹⁻²

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2. University of Minnesota

Abstract: Background. Impulsive behaviors arising following traumatic brain injury (TBI) are a common challenge facing patients and their caregivers. We previously showed that a neuromodulation-based intervention, using transcranial direct current stimulation (tDCS) over prefrontal cortex paired with a decision-making training task, reduced impulsive behavior in a clinically impulsive sample of Veterans (Gilmore et al., 2018). Here, we report on a follow-up study to test the effectiveness of this neuroplasticity-based intervention using tDCS combined with a battery of cognitive training tasks in Veterans with a history of TBI. Methods. 25 Veterans with a history of mild (n = 18), moderate (n = 4), or severe (n = 3) TBI and clinical history of impulsive behavior were randomized to receive either active tDCS (n = 13; mean age = 58.8 years; 1 woman) or sham (n = 12; mean age = 62.9 years; 1 woman). The intervention was 5 sessions of prefrontal tDCS (2 mA, 20 minutes, left anode/right cathode) paired simultaneously with a battery of four computer training tasks, administered via the online BrainHQ portal, that required aspects of cognitive control for successful performance. Participants performed a battery of self-report and untrained cognitive tasks pre-intervention, post-intervention, and at follow-ups 1, 2, and 3 months later. Here we report on analyses of the untrained Stop Signal Task, a test of inhibitory control. Outcome measure was the percentage of times participants responded incorrectly to a 'stop signal' (i.e. failed to successfully inhibit a response). Results. For the BrainHQ training tasks, individual growth curve analysis (IGC) examining individual variation of the growth rates over the 5 intervention sessions showed no significant variations in individual trajectory changes over time. For the untrained Stop Signal Task, IGC showed that the active tDCS group had a significant 67% decrease in failed inhibitory responses from pre- to post-intervention, which persisted through the 1-, 2-, and 3-month follow-up sessions. The sham tDCS group showed no significant change in performance over time. Discussion. tDCS over prefrontal cortex paired with executive function training tasks effectively improved inhibitory control in a group of Veterans with a history of TBI and clinically-relevant impulsivity. Results suggest that this approach may be an effective non-pharmacological neuroplasticity-based intervention for patients who suffer a TBI and are affected by impulsivity.

Research Topic: Traumatic Brain Injury (TBI)

Funding agencies: Other

Grant support: MN State Office of Higher Education TBI grant 143479

29. Epidural Spinal Cord Stimulation Mapping: Targeted Restoration of Volitional Movements and Autonomic Function in Patients with Spinal Cord Injury

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2. Minneapolis VA Health Care System

Abstract: Introduction: Epidural spinal cord stimulation (eSCS) has been shown as a promising modality for restoring motor and autonomic functions in spinal cord injury (SCI) patients. Optimizing stimulator parameters and electrode configurations to enhance therapeutic outcomes is a critical yet underexplored area of research. Our study focuses on establishing a correlation between specific eSCS settings and therapeutic benefits. Methods: Stimulator settings were collected in PulseShare.org, a web-based database designed by our lab for secure storage and communication with all personal health information de-identified to maintain confidentiality. Follow-up interviews via phone or video, medical chart reviews, and the Mayo Clinic SCI Questionnaire were utilized to collect data on patient functional outcomes. Welch's t-tests and Benjamini/Hochberg correction with a false discovery rate of 0.1 were utilized to test for significant differences between average parameters that showed improvements in walking, standing, core stability, spasticity, bowel and bladder function versus those that did not. The average electrode configurations were visually examined for each outcome among programs that showed improvement. Results: Of the 58 patients, 67% (35 patients) reported at least one type of functional improvement after eSCS. Notably, a pulse frequency (Hz) difference of 19.06 Hz resulted in improvements for walking ($p < 0.001$), 18.90 Hz for standing ($p < 0.001$), and 15.75 Hz for reduced spasticity ($p < 0.05$). A pulse frequency difference of 16.10 Hz ($p < 0.01$) also resulted in increased core stability. When comparing the average values of the programs that showed improvements with those that did not, pulse frequency (Hz) of was lower for core, walking, standing ($p < 0.001$), pulse width (μs) was lower for bowel ($p < 0.1$), maximum (mA) was lower for spasticity, walking, and bowel ($p < 0.1$), and comfort (mA) was lower for spasticity and bowel ($p < 0.1$). Furthermore, average electrode configurations with central cathodes near the stimulator's base and anodes at the top showed correlations with improved bowel and bladder functions. Conclusions: This study establishes correlations between specific eSCS parameters, their average electrode configurations, and functional improvements in SCI patients, providing essential guidelines for programming stimulators to meet distinct rehabilitation goals.

Research Topic: Spinal Cord Injury

Funding agencies: Other

Grant support: Neurosurgery Research & Education Foundation (NREF)

30. A Computational Method for Automatically Localizing Intracranial Landmarks on CT Scanning

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2. University of Minnesota

Abstract: Objective: Algorithmic identification of the standard neuroanatomical landmarks, namely the Anterior Commissure (AC) and Posterior Commissure (PC), on Non-Contrast Computed Tomography (NCCT) images of the brain is crucial for standardized comparison of neuroanatomical regions. The automatic localization of these landmarks may also find application in stereotactic neurosurgical procedures and/or radiation oncology. We present a two-step computational solution to this problem, involving coarse localization using image registration and fine localization using a deep neural network. Methods: The 3D coordinates of the AC and PC were manually identified on the central commissural line defined by the Schaltenbrand atlas on 383 axial acquisitions of NCCT scans from patients who were diagnosed with Normal Pressure Hydrocephalus (NPH, $n = 79$), Alzheimer's Dementia (AD, $n = 163$), post-traumatic encephalomalacia (PTE, $n = 61$), and headache (HC, $n = 80$). Nonlinear image registration to a standard CT template with known AC and PC coordinates was used to learn a coarse estimate of the landmarks on each NCCT scan. Next, a patch-based 3D U-Net model was trained to predict the AC and PC locations more accurately, using strategies to overcome class imbalance. Mean Radial Error (MRE) was used to evaluate model predictions for both the AC and PC. Different hyperparameter combinations were evaluated under a 4-fold cross validation scheme, repeated 5 times with 20% of the data acting as a test/hold-out set each time. The average error statistics were examined. Results: We observed a mean radial error (MRE) of 4.53 mm for the PC and 6.75 mm for the AC in the coarse localization step. In the fine localization step, we observed an average hold-out/test set MRE of 3.09 mm for both the AC and PC, 3.26 mm for the AC, and 2.92 mm for the PC based on the predictions by the 3D-UNet model. Conclusions: Despite inherent challenges of poor contrast and soft-tissue resolution, our two-stage approach to localizing the AC and PC on NCCT scans was able to achieve an average error of 3 mm. By using methods such as data augmentation and transfer learning, we seek to further reduce the localization error and produce a well-generalizable model for the task of automatic AC and PC landmark prediction on NCCT scans. Such methodologies will be valuable for the creation of automated image analysis algorithms useful for both disease screening and robotic treatment.

Research Topic: Computer Science

Funding agencies: Other

Grant support: MN State Office of Higher Education

31. Extended Reality (XR) Interventions for Osteoarthritis of the Knee and Recovery after Total Knee Arthroplasty

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Abstract: Background: Non-pharmacologic interventions are an important component in treatment of musculoskeletal pain, including knee pain. Osteoarthritis (OA) of the knee and recovery after total knee arthroplasty (TKA) have been shown to benefit from non-pharmacologic exercise-based treatment, and extended reality (XR) technology may improve the efficacy of these interventions. We conducted a systematic review to identify and synthesize current evidence on the benefits and harms of XR interventions for pain due to knee OA or after TKA. Methods: MEDLINE, Embase, CINHAL, PsycINFO, and Scopus databases were searched from inception to May 2023. Eligible studies included randomized controlled trials (RCTs) that evaluated XR interventions (of any type) to treat pain due to knee OA or aid recovery after TKA, and that reported at least one eligible outcome (e.g., pain-related functioning or interference, pain intensity, or adverse events). Risk of bias (RoB) was assessed and data abstraction was performed by one reviewer and verified by a second. We conducted narrative syntheses due to substantial variation in populations, interventions, comparators, and/or reported outcomes. We used the GRADE methodology to rate overall certainty of evidence (COE) for each outcome. Results: We identified 12 eligible RCTs addressing pain due to knee OA (k = 5) and recovery after TKA (k = 7). One study examined the use of virtual reality (VR) and 4 examined augmented reality (AR) in the OA pain group. In the post-TKA group, 2 studies examined VR and 5 examined AR. All studies were rated as having some concerns or high risk of bias. While the single study of a VR intervention for chronic pain due to knee OA suggested there may be some benefit in pain-related functioning and pain intensity, evidence on the effects of AR interventions is uncertain for all outcomes for both knee OA and recovery after TKA. Conclusions: VR interventions may improve functioning and pain in knee OA but there is limited evidence supporting the efficacy of AR for knee OA pain, or in support of either VR or AR for recovery in post-TKA patients. Evidence is limited by methodological concerns (no low RoB studies), non-standardized use of measurement tools to assess efficacy, and a lack of reporting of adverse events across studies. Future studies are needed to address these gaps and others highlighted by small sample sizes and a lack of diversity among study participants.

Research Topic: Pain

Funding agencies: VA HSRD

Grant support: N/A

32. Misclassification of Vaccination Status in Electronic Health Records: A Bayesian Approach in Cluster Randomized Trials

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1. Minneapolis VA Health Care System

Abstract: Misinformation about vaccines can cause severe public health problems through vaccine hesitancy and reduced uptake. A recent example is the SARS-CoV-2 pandemic response that encouraged mass roll-out of vaccines under an accelerated time frame. On a national scale, developing novel interventions that tackle these barriers and increase vaccine uptake rates heavily depends on trustworthy sources of routinely collected vaccine records, such as electronic health records (EHR) and insurance claims. A centralized national or state vaccination registry for adult vaccination does not exist, and the multiple available sources of EHR are prone to non-ignorable rates of misclassification, e.g., misclassifying an individual as unvaccinated when they truly are. Ignoring misclassification, evaluating a national level intervention's influence on vaccine uptake follows the structure of a cluster controlled randomized trial (CCRT), where groups of people or sites are randomly allocated to an intervention arm. Typical statistical analysis of this study's data follows the logistic mixed model, where the probability of being vaccinated is modeled as a function of patient and study-group covariates. These models explicitly attend to the multi-level nature of the CCRT by incorporating multi-level random effects. Furthermore, to make the CCRT more pragmatic, routine data collection from EHR is warranted. Importantly though, analysis strategies accounting for binary outcome misclassification in CCRTs are understudied. We propose a novel misclassification addition to Bayesian logistic regression with outcomes being fit on a group level (as in the case of CCRT designs). Our proposed method follows the same logistic regression structure with random effects for each level but also contains a step correcting the count of vaccinations and eligible participants at each study site. These latter corrections are based on investigator-elicited values of misclassification rates at each site. Based on a list of proposed misclassification rates per site a proper sensitivity analysis investigating the impacts on the estimated rates of vaccination can be carried out. We discuss an application of this method on a current VA CCRT estimating a behavioral training intervention's effect on SARS-CoV-2 vaccine uptake during 2022-2023. We also provide brief summaries of supporting simulation study results.

Research Topic: Epidemiology

Funding agencies: VA HSRD

Grant support: HSR SDR 21-141

33. Ecological Momentary Assessment with High-Risk Suicidal Veterans Following Inpatient Psychiatric Care

Kazynski, Megan¹; Li, Lillian¹; Larkin, Florence¹; Yu, Carol¹; Lim, Kelvin¹; Gilmore, Casey¹

1. Minneapolis VA Health Care System

Abstract: Background: Suicide rates are especially high in the first month after Veterans discharge from inpatient psychiatric treatment. Research examining this high-risk period has largely relied on retrospective, infrequent sampling methods and analysis at the group level. This is a significant limitation as recent research shows that suicide risk fluctuates within individuals over short time periods. Thus, ecological momentary assessment (EMA) methods, which capture real-time information through multiple brief daily surveys, could be an effective tool to understand the rapid progression of suicide risk post-discharge. Causal Discovery Analysis (CDA) is a novel analytic approach that uses high-density, longitudinal data, such as EMA, to create models that identify causal relationships between self-reported and objective risk factors and STBs that are specific to an individual. The purpose of this study was to create individualized causal models to identify potentially actionable treatment targets to reduce suicidal thoughts and behaviors (STB) among Veterans after discharge from inpatient treatment. Method: Veterans admitted to the Minneapolis VA inpatient psychiatric unit with elevated suicide risk completed 30 days of EMA surveys (2x per day) post-discharge assessing suicidal thinking and intent, as well as related risk factors, including mood, help-seeking, stress, social connection, sleep, impulsivity, hopelessness, alcohol craving, and suicide capability. After collecting completed EMA data sets from Veterans, CDA was performed to produce models identifying causes of observed symptomatology that are specific to the individual. Results: Findings based on three Veterans that have completed the EMAs, thus far, suggest that personalized causal models based on high-density data allow us to create a specific clinical suicide risk profile for each individual. These models may be used to identify and tailor existing interventions for each high-risk Veteran, and to develop novel and effective suicide prevention interventions. Conclusion: This study provided a fine-grained examination of suicide risk and related factors, and showed CDA of EMA data can be used to identify individual causal models to inform selection of more precise treatments specific to each individual's clinical needs. EMA is a promising approach to improving the short-term prediction of suicide risk in the high-acuity period after Veterans discharge from inpatient treatment.

Research Topic: Suicide Prevention

Funding agencies: VA RRD; CVRE

Grant support: RRD I21RX004104

34. Midline Frontal Theta and Trait Negative Emotionality Amongst Military Recruits

Kind, Andrew¹⁻²

1. Minneapolis VA Health Care System

2. University of Minnesota

Abstract: Negative emotionality is a broad personality construct reflecting various difficulties in emotion regulation and cognitive control. This can manifest in the context of stress-related disorders, exaggerated responses to fear, and other maladaptive experiences related to many forms of psychopathology. This study employed a simulated gambling task to explore the link between negative emotionality and feedback-related negativity (FRN) using electroencephalography among new military recruits. FRN is related to frontal midline theta-band (4-8 Hz) neural activity. Potentiated FRN and midline theta responses have been connected with exaggerated loss processing, cognitive control alterations, and individual differences in anxiety. The gambling task from this study presented participants with binary choices between risky and safe bets as well as visual feedback on the outcome of their choices. To analyze the brain components, time-frequency analysis was used to decompose the separate theta and delta (1-3 Hz) responses from FRN. General linear models compared loss versus gains feedback responses and associations with trait scales from the Multidimensional Personality Questionnaire (MPQ). I found significant negative associations between MPQ-Negative Emotionality (NEM) and both theta and delta time-frequency brain responses. The results are opposite of what was expected based on previous findings. The results provide evidence against a simple positive linear association between negative emotion dysregulation and exaggerated midline frontal brain responses to losses. I discuss potential implications for the search for neural markers of resilience capacity in military settings.

Research Topic: Neuropsychology

Funding agencies: DOD; NIH

Grant support: UH3AT009651

35. Do Lymphatic Cells Aggregate Around Blood Vessels in the Brain?

Lam, Cornelius¹; Hansen, Eric¹

1. Minneapolis VA Health Care System

Abstract: Brain slice culture (BSC) is a well-known three-dimensional model of the brain. To date lymphatic pathways have only been demonstrated in the meningeal component of the central nervous system (CNS). Brain parenchymal lymphatics have not been found and the degree of lymphatic extension following the micro-vasculature in the brain is still undefined. We test the hypothesis that the neural tissue repulses lymphatic growth as a possible cause, yet other brain constituents (e.g., blood vessels) may support such growth. 300 µm-thick whole-brain coronal sections were collected at the level of the caudate nucleus from approximately -1.40 mm to -2.80 mm Bregma and were placed in sterile media. The organotypic slices were then carefully placed on 3.0µm membrane inserts. Lymphatic cells labelled with CellTracker CM Dil C7000 were seeded onto brain slices and monitored for a period of 10 days. Brain slices were fixed in 10% formalin at three, seven, and ten days and samples were analyzed for cells displaying CM-Dil fluorescent dye using a Biorad MRC-1024 single photon confocal microscope 1024 (Biorad Cell Science, UK). To determine if lymphatic cells aggregated near blood vessels, CD31 PECAM-1 (SC-46694, Santa Cruz Biotechnology) secondarily labelled, with goat anti-mouse IgG Alexa Fluor 488 (ab150113 Abcam) was used to label vascular structures. Lymphatic cells in our model were scattered in all areas of the slice initially and overall apoptosis rates were not significantly different between lymphatic and control BSCs over time. Lymphatic migration toward blood vessels commenced on day 3, by day 7 lymphatics were observed in higher densities in close proximity to blood vessels. Lymphatics were observed in higher densities in close proximity to blood vessels. The observed migration of lymphatics to these areas may be due to a number of factors including diffusible cues (i.e. VEGF and PROX1 proteins) that promote cell proliferation along vessels or competitive interactions with other neuroectodermal cells that suppress growth in other areas of the brain. The lymphatic cells' interaction with blood vessels indicate a potential clearance role of CSF, trauma debris etc. Our BSC system provides a unique model to further study neuro-lymphatic transport dynamics.

Research Topic: Neurology & Neurobiology

Funding agencies: VA BLRD; CVRE

Grant support: BLRD I01BX001657

36. Screening for Hepatocellular Carcinoma in Adults at Increased Risk: A Systematic Review

Landsteiner, Adrienne¹; Ullman, Kristen¹; Langsetmo, Lisa¹; Zerzan, Nick¹; Kalinowski, Caleb¹; Haglund, Jennifer¹; Wilt, Timothy¹

1. Minneapolis VA Health Care System

Abstract: Background: An estimated 41,210 Americans will be diagnosed with hepatocellular carcinoma (HCC) in 2024, with 29,840 HCC deaths. Screening adults at increased risk may reduce morbidity and mortality though uncertainty remains. Objective: To update evidence on effectiveness, comparative effectiveness, and harms of imaging-based HCC screening strategies among increased risk adults. Methods: Medline and Embase (July 2020–November 2023) were searched, including citations from two systematic reviews (2014 and 2022), hand searching bibliographies, and expert recommendations, and screened for inclusion. Randomized clinical trials (RCTs) or observational studies with a comparator group, published in English, with a population of adults at increased HCC risk who received imaging-based screening with ultrasound (US), MRI, or CT were included. Abstracted independently by two reviewers with a third reviewer resolving discrepancies. Dual assessment of risk-of-bias (RoB) using Cochrane RoB 2.0 tool for RCTs and ROBINS-I for observational studies. Certainty of evidence (CoE) was based on GRADE. Results: We included 84 studies (5 RCTs); most, including 3 RCTs, had high RoB. We analyzed results from studies rated as low or some concerns ROB. Substantial clinical and methodological variation precluded meta-analysis. We provide a narrative synthesis. Two small RCTs rated as some concerns RoB compared Ultrasound (US) every 3 vs. 6 months (low CoE) and US every 6 months versus CT annually (very low CoE); neither found a mortality difference. The vast majority (71) of observational studies restricted evaluation to individuals with HCC, missing the increased-risk population. Two low RoB case-control studies of US screening versus no screening reported conflicting HCC mortality results (very low CoE). Limited information was available on the incremental effects of adding alpha-fetal protein testing to US. No studies evaluated MRI screening. Harms and costs were rarely reported. Conclusions and Discussion: Evidence is very uncertain as to the effectiveness, comparative effectiveness, harms, and costs of imaging-based HCC screening strategies. RCTs and higher methodological quality observational studies are needed. Uncertainty makes screening decisions challenging.

Research Topic: Cancer

Funding agencies: VA HSRD

Grant support: VA ESP Project 09-009

37. Colonoscopy Versus Fecal Immunochemical Test in Reducing Mortality From Colorectal Cancer (CONFIRM) Study, a Colorectal Cancer Screening Trial: Study Update 2024

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1. Minneapolis VA Health Care System

Abstract: Importance: The Colonoscopy Versus Fecal Immunochemical Test in Reducing Mortality From Colorectal Cancer (CONFIRM) randomized clinical trial sought to recruit 50,000 adults into a study comparing colorectal cancer (CRC) mortality outcomes after randomization to either an annual fecal immunochemical test (FIT) or colonoscopy. Objective: To (1) describe study participant characteristics and (2) examine who declined participation because of a preference for colonoscopy or stool testing (ie, fecal occult blood test [FOBT]/FIT) and assess that preference's association with geographic and temporal factors. Exposure: Case report forms were used to capture enrolled participant data and reasons for declining participation among otherwise eligible individuals. Main outcomes and measures: Among individuals declining participation, logistic regression was used to compare preference for FOBT/FIT or colonoscopy by recruitment region and year. Results: A total of 50 126 participants were recruited (mean [SD] age, 59.1 [69] years; 46 618 [93.0%] male and 3508 [7.0%] female). The cohort was racially and ethnically diverse, with 748 (1.5%) identifying as Asian, 12 021 (24.0%) as Black, 415 (0.8%) as Native American or Alaska Native, 34 629 (69.1%) as White, and 1877 (3.7%) as other race, including multiracial; and 5734 (11.4%) as having Hispanic ethnicity. Of the 11,109 eligible individuals who declined participation (18.0%), 4824 (43.4%) declined due to a stated preference for a specific screening test, with FOBT/FIT being the most preferred method (2820 [58.5%]) vs colonoscopy (1958 [40.6%]; $p < 0.001$) or other screening tests (46 [1.0%] $p < 0.001$). Preference for FOBT/FIT was strongest in the West (963 of 1472 [65.4%]) and modest elsewhere, ranging from 199 of 371 (53.6%) in the Northeast to 884 of 1543 (57.3%) in the Midwest ($p = 0.001$). Adjusting for region, the preference for FOBT/FIT increased by 19% per recruitment year (odds ratio, 1.19; 95% CI, 1.14-1.25). Conclusions and relevance: In this cross-sectional analysis of Veterans choosing nonenrollment in the CONFIRM study, those who declined participation more often preferred FOBT or FIT over colonoscopy. This preference increased over time and was strongest in the western US and may provide insight into trends in CRC screening preferences.

Research Topic: Preventive Medicine

Funding agencies: VA CSR D

Grant support: VA CSP 11-03

38. User Experience with a Passive Slope Adaptive Foot-Ankle Prosthesis

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1. Minneapolis VA Health Care System

2. University of Minnesota

Abstract: Few commercially available passive prosthetic feet adapt to sloped or uneven terrain. Motion Control, Inc. has partnered with the Minneapolis VA to develop a passive slope-adaptive foot-ankle prosthesis (SAF). The SAF uses a hydraulic mechanism to automatically adapt ankle alignment on varied terrain allowing energy storage to begin early in stance phase. The purpose of this pilot study was to test a prototype SAF with Veterans with unilateral transtibial amputations in their home and community environments. Six Veterans with unilateral transtibial amputation completed the study. Each participant used a prescribed energy storage and return (ESAR) foot. Participants completed the Prosthetic Limb Users Survey of Mobility (PLUS-M), Activity-Specific Balance Confidence scale (ABC), Prosthesis Evaluation Questionnaire (PEQ), regarding use of their prescribed prosthetic foot. Participants completed a take home trial with the SAF of at least one week. Participants then completed the PLUS-M, ABC, PEQ, a custom questionnaire regarding comfort and stability, and an unstructured interview focusing on user perceived advantages and disadvantages of the SAF. Scores from the PLUS-M, ABC, and PEQ were analyzed using descriptive statistics. Ratings of comfort and stability were reviewed for trends. Average self-reported outcome measure scores when using the SAF were better than those reported with their prescribed foot. On the custom questionnaire, participants rated the SAF the same or better as their prescribed foot for 11 of 12 stability questions and 8 of 8 comfort questions from the custom questionnaire. When asked about their overall rating of the SAF compared to their prescribed foot, all participants rated it 'better' or 'much better.' Within the unstructured interviews, Veterans reported decreased residual limb and knee pain, decreased phantom pain, improved navigation of slopes and stairs, fewer tripping incidents, increased participation in the home and community, and improved dressing ability using the SAF. Data collected strongly supported the development of the SAF for improved mobility on slopes and uneven terrain along with unanticipated aspects of daily living. Features of the SAF may improve the user experience in their home and community environments when compared to use of their prescribed ESAR foot.

Research Topic: Prosthetics

Funding agencies: DOD

Grant support: W81XWH-18-C-0314

39. History of Psychological Trauma is Associated with Post-Concussive Neurobehavioral Symptoms and Quality of Life in Veterans Following Mild TBI

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2. University of Minnesota

Abstract: Traumatic experiences across the lifespan can have lasting negative impacts on both mental and physical health outcomes. A growing body of research suggests that exposure to psychological trauma may lead to increased risk of various physical health conditions including chronic pain, cardiovascular disease, and cancer. Persistent neurobehavioral symptoms are a common long-term consequence of mild traumatic brain injury (mTBI), impacting an estimated 20-48% of mTBI cases. However, the role of lifetime psychological trauma on recovery after mTBI is not well understood. The current study sought to investigate how trauma exposure across the lifespan impacts the persistence of mTBI symptoms and post-injury quality of life in MVAHCS Veterans. As part of the PROUD research study, a sample of 399 Veterans diagnosed with history of mild TBI (88% male, mean age 45 years [SD: 13.2], mean time since injury 11.2 years [8.4]) completed a battery of clinical and demographic measures. Trauma histories were assessed from childhood (using the Childhood Trauma Questionnaire [CTQ]), their military career (using the Deployment Risk and Resilience Inventory [DRRI]), and across the entire lifespan (using the Traumatic Life Experiences Questionnaire [TLE-Q]). Outcome measures included current neurobehavioral symptoms (measured using the Neurobehavioral Symptom Index [NSI]) and overall quality of life (measured using the Quality of Life after Brain Injury Questionnaire [QOLIBRI]). TBI history was accessed from VA medical records and included time since most recent injury and number of reported mTBIs injuries (divided into groups of 1, 2-3, and 4+). Multiple linear regression models evaluated the effect of TBI characteristics, age, gender, and trauma exposure for each measure on NSI and QOLIBRI. Each trauma measure was found to be significantly positively associated with NSI symptom severity (all $p < 0.004$) and significantly negatively associated with QOLIBRI life satisfaction (all $p < 0.004$) when controlling for all other predictors and correcting for multiple comparisons using false discovery rate. Injury characteristics were not significantly associated with outcomes in any model. These findings reaffirm that exposure to traumatic experiences across the lifespan likely plays a central role in the persistence of post-concussive symptoms, and assessment of trauma history should be a key component of TBI case conceptualization.

Research Topic: Traumatic Brain Injury (TBI)

Funding agencies: VA RRD

Grant support: RRD IK2RX002922

40. Fisetin as a treatment for community-acquired pathogen susceptibility during aging and obesity

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Abstract: The elderly and those with obesity are particularly vulnerable to adverse outcomes when exposed to a new pathogen. A commonality between these conditions is an increased burden of senescent (deteriorating) cells. Accumulation of senescent cells are established as drivers of aging, frailty, and many age-related chronic diseases. Fisetin, a compound found in many fruits and vegetables, reduces senescence, reverses tissue damage and age-related pathology, and extends median and maximum lifespans when administered to aged mice. In addition, aged specific pathogen free (SPF) mice subjected to environmental pathogens via exposure to the bedding of healthy pet store mice (called a normal microbial experience or NME) leads to higher mortality. Remarkably, when the aged mice were treated with fisetin, mortality was suppressed. These data suggest that senolysis (clearing of senescent cells) in old mice improves health and possibly resilience to novel stressors. We hypothesized that fisetin-induced clearance of senescent cells will ameliorate mortality and increase physical resilience in NME-exposed mice that are aged and obese. To test this, age- and weight-matched male/female young and old wild type mice (8 mo. & 24 mo.) were fed a high fat diet (HFD), or control diet for 15 weeks. Following the diet exposure period, mice were treated with fisetin (20 mg/kg) or vehicle, daily for 2 days. Next, mice were exposed to pet-store-mice bedding to induce NME or remained in control conditions. The mice exposed to fisetin continued to be exposed to fisetin via chow (500 ppm), and the remaining NME-mice were fed normal lab chow. On the 14th day mice were sacrificed, and tissue collected for analysis of senescence markers. Exposure of aged rats to NME increased mortality, which was reversed by fisetin. The HFD-feeding decreased percent survival in NME-exposed aged mice, which was reduced by fisetin. We found that aging increases the expression of the senescence marker 'p21' in the liver (p21 is a cyclin-dependent kinase inhibitor that promotes cell cycle arrest). Similarly, HFD-feeding in young mice increased the expression of liver p21, suggesting that HFD-induced obesity might increase cellular senescence. In conclusion, these data suggest that clearing senescent cells using fisetin may be a promising strategy to counter morbidity and mortality during aging, obesity and following microbial infections.

Research Topic: Aging

Funding agencies: VA BLRD; VA RRD

Grant support: RRD I01RX003901, BLRD I01BX005815

41. Attentional control, meaning-making, and distress endurance as predictors of perceived basic combat training stress: A structural mediation model

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2. University of Minnesota

Abstract: Objectives: Self-regulatory abilities associated with mindfulness, like attentional control, may facilitate meaning-making and valued action in response to stressors, encouraging resilience. We aimed to test this among military recruits exposed to basic combat training (BCT) stress. We hypothesized that greater self-regulation of attention at baseline would predict higher trait-level meaning-making and distress endurance tendencies in response to stressors, which would thereby predict lower levels of perceived BCT-related stress. Methods: National Guard recruits completed pre-BCT (N = 1201) and post-BCT (N = 770) assessments. Measures included the Penn Computerized Neurocognitive Battery continuous performance test (CPT), Attention Control Scale, Response to Stressful Experiences Scale, Multidimensional Experiential Avoidance Questionnaire-30, and Basic Training Stressors Scale (measured post-BCT). Results: According to a structural mediation analysis, greater Perceived Attentional Control (self-reported attention) predicted lower Perceived BCT Stress (frequency and impact of BCT stressors). However, unexpectedly, this relationship was suppressed by the influence of Meaningful Responses to Stress (meaning-making and distress endurance), which marginally predicted greater rather than lower Perceived BCT Stress. Additionally, greater Attentional Control Abilities (CPT performance) predicted greater rather than lower Perceived BCT Stress. Conclusions: Although some effects were unexpected, they are consistent with conceptualizations of acceptance versus threat-related attentional focus. Higher levels of perceived BCT stress among recruits with greater meaning-making and distress endurance tendencies as well as greater attentional abilities may reflect greater acceptance versus attentional focus, respectively, applied to unpleasant BCT experiences. Future research is necessary to determine if meaning-making and distress endurance tendencies mitigate the impact of BCT stress on psychological outcomes.

Research Topic: Mental Health

Funding agencies: NIH

Grant support: NIH UH3AT009651

42. Integrating Tobacco Treatment into Lung Cancer Screening: A Qualitative Assessment

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

Abstract: Background: Half of participants in lung cancer screening (LCS) currently smoke. Current evidence supports that tobacco dependence treatment (TDT) is poorly integrated into LCS. As part of a broader implementation initiative, we qualitatively assessed current practices and perceived barriers surrounding the integration of TDT into LCS. Methods: Informed by the Practical, Robust Implementation and Sustainability Model, we conducted semi-structured interviews among clinicians (n = 19) sampled from key roles in the LCS and TDT processes at six Veterans Affairs medical centers in the Midwest region. Clinicians were purposively sampled, representing LCS program staff, primary care providers (PCPs), and tobacco treatment clinicians (TTCs). Results: Clinicians in all roles felt that TDT was important for LCS participants. No site reported robust integration between TDT and LCS care. Participants utilized usual referral processes to link patients with treatment, though referrals were sometimes placed by LCS coordinators. Within TDT referral processes, clinicians noted difficulties with unclear and/or 'informal' referral pathways (e.g. reliance on calls, notifications or secure messages to refer) and insufficient options for combined behavioral and pharmacologic treatments. TTCs were often not prescribers and interviewees noted difficulty handing patients back and forth to provide medications. TDT was usually addressed at an initial shared decision-making visit but often not with subsequent rounds of screening or nodule follow-up. No site was aware that any TDT-related outcomes were tracked within their program. While the LCS clinical reminders included some aspects of tobacco use (e.g. tobacco pack-years), they did not support clinicians in offering TDT or capture outcomes and were perceived as 'checkboxes to nowhere.' This was contrasted with other clinical reminders linked to dashboards that provide feedback for important clinical outcomes (e.g. diabetes care). PCPs and LCS staff reported competing demands and limited expertise in motivational interventions as additional barriers. A dedicated team for TDT and a 'one-click referral' were perceived as key success factors. Conclusions: TDT remains poorly integrated into LCS. Addressing identified barriers will require considerable investment in TDT resources and improvements to LCS tools to support the provision of cessation support throughout the process.

Research Topic: Health Care Delivery

Funding agencies: VA HSRD

Grant support: QUERI PII, HSR IK2HX003067

43. Exploration of VA Prosthetists Interactions on Pain and Understanding of Biological Foundation of Pain

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

Abstract: Many individuals who undergo amputation will experience amputation-related pain and experiences such as phantom limb pain, phantom limb sensation, and residual limb pain¹. Phantom limb pain has a lifetime prevalence of approximately 76-87% while phantom limb sensation has an estimated lifetime prevalence of 87%.² It would be beneficial for prosthetists to understand the biological foundation of pain to provide a better standard of amputation care. The goal of this project is to explore the knowledge that VA prosthetists have on pain and amputation-related pain and experiences. This was determined to be QI by the Minneapolis VA IRB. All prosthetists within the VA were invited to participate in the voluntary, anonymous survey. Survey was created by combining questions regarding amputation-related experiences, demographics, and the Revised Neurophysiology of Pain Questionnaire (RNPQ). The RNPQ is scored with one point given for every correct answer and zero points given for incorrect or unsure answers.³ Open-ended questions were included about preferred patient education tools, furthering education, and demographics. The survey was completed through a Microsoft Teams Form. Descriptive statistics were used for demographic data; the RNPQ was scored individually, and all responses were described. There were 52 respondents, with majority reporting having a master's degree and most training on pain coming from school courses. 38% of respondents stated they bring up pain first almost always. Clinicians were asked how often they use handouts to aid in discussions, to which 38% stated 'never.' Several clinicians identified a need for additional patient education tools. Most of the respondents expressed interest in additional education. Of the 13 questions in the RNPQ, 3 of the questions had a majority answer incorrectly, with 2 of the 3 also having a high percentage respond with 'unsure.' Additionally, 6 other questions had a high percentage of 'unsure' answers. Prosthetists within the VA expressed they would like more training on amputation-related pain and experiences, as well as having more materials to use when discussing pain with Veterans. These QI results are limited as it was conducted solely with VA clinicians. Future direction could involve formalized research to better understand clinician experiences in supporting pain specific care. Local practice could be enhanced through tailored education on these topic areas and by developing materials for clinicians

Research Topic: Prosthetics

Funding agencies: N/A

Grant support: N/A

44. Million Veteran Program

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2. University of Minnesota

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

Research Topic: Genomics

Funding agencies: VA CSRD

Grant support: N/A

45. Adjusting the Fit of the Foot-Shoe Complex for Prosthetic Feet

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Abstract: Lower limb prosthesis users have a high risk of falling¹, therefore, it is essential that the prosthetist ensures the user's stability. If the prosthetic foot-shoe complex does not move as one, the user's gait will change with every step without a solution. To maintain the prosthetic foot's position, the prosthetist will use material to fill the shoe or the foot shell to decrease the unwanted motion. Many Veterans who receive care in the Prosthetics Department at the Minneapolis VA require extra-depth or extra-wide shoes to accommodate comorbidities that may result in edema, such as vascular disease, diabetes mellitus, or kidney involvement. According to an Archives of Physical Medicine and Rehabilitation study, 38% of individuals in the US living with amputations in 2005 required amputations due to dysvascular diseases, and the number is rising². It is essential for prosthetists to be able to evaluate and adjust the foot-shoe complex accordingly. This is an IRB approved QI/QA project at Minneapolis VA. Clinical and research prosthetists at the Minneapolis VA were surveyed, asking how often this type of adjustment is needed, and how they problem-solve in these situations. Participants: The survey was taken by 11 subjects. Apparatus: Survey. Procedures: The survey was asked verbally, in one-on-one interviews between the certified prosthetists and the researcher. The surveyed prosthetists' level of experience post-certification ranged from 4 months to 22 years. Two of the prosthetists consider the foot-shoe complex fit prior to dynamic alignment and fitting of the prosthesis. The prosthetists reported 'stuffing' the foot shells with various materials such as the foam that ships with liners, AliPlast, or Plastazote to achieve a snug-fitting foot shell. The volume inside of the shoe was adjusted with tongue pads, additional socks, paper towels, and a foam spacer that is included with shoes. The reported time to adjust the volume inside the foot shell averaged 14 minutes, while adjusting the volume within the shoe averaged 7 minutes. While the fit of the foot-shoe complex is not a regularly considered aspect of prosthetic care, the surveys of the clinicians at the Minneapolis VAHCS shows it is a regular occurrence in clinical practice. [1] MILLER, W.C. ARCH PHYS MED REHABIL. 82, 1031-1037, 2001. [2] ZIEGLER-GRAHAM K. ARCH PHYS MED REHABIL. 89, 422-429, 2008.

Research Topic: Prosthetics

Funding agencies: N/A

Grant support: N/A

46. Mediating Factors of Verbal Learning Deficits in Adolescents with Bipolar Disorder

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Abstract: Bipolar disorder (BD) is associated with cognitive deficits, with some of the largest deficits in verbal learning (Horn, Roessner, & Holtmann, 2011). Early-onset BD may influence the development of impaired cognitive functioning and declines in functioning during adulthood (Wegbreit et al., 2017; Lima, Peckham, & Johnson, 2018). Research identifying mechanisms leading to cognitive impairment in BD could lead to new treatment targets and options for improving functioning. Past studies identified greater number of hospitalization and mood episodes as associated with cognitive impairment in BD. No studies to date have examined whether these factors mediate cognitive deficits in BD suggesting a mechanistic relationship. The current study is a secondary analysis of an existing dataset to examine whether lifetime number of hospitalizations, IQ, and/or lifetime number of manic episodes mediate the relationship between BD diagnosis and verbal learning deficits. Verbal learning deficits were assessed by the Rey Auditory Verbal Learning Test, which includes outcome measures for total number of words learned, immediate recall, and delayed recall (Rey, 1993). A sample of 107 adolescents (50% female, 15.83 mean age, 46% with BD) completed a semi-structured diagnostic interview, questionnaires, intelligence testing, and a neurobehavioral task battery (Urošević et al., 2018). Mediation analyses found that the relationship between BD diagnosis and a total number of words learned across 5 trials was mediated by IQ. The total effect of the model was found to be significant, $B = -8.36$, $CI [-12.04, -4.68]$, $p < 0.01$. A statistically significant indirect effect was also found, $B = -2.96$, $CI [-4.79, -1.36]$. A similar significant pattern was also found for immediate and delayed recall measures. Number of hospitalizations and number of manic episodes were not significant mediators. These results suggest that individuals with BD exhibited verbal learning deficits compared to controls, which were partially mediated through lower general cognitive ability, as measured by IQ. Future longitudinal studies with larger sample sizes are needed to fully examine effects of current clinical states, such as mania, on verbal learning deficits. Limitations of the current study include sample size that was likely underpowered to detect small mediational effects and lack of direct measures for potential other mediating factors (e.g., disruption of education due to BD illness course).

Research Topic: Mental Health

Funding agencies: NIH

Grant support: NIH K01 MH093621

47. Increasing prescribing of sodium-glucose cotransporter-2 inhibitors among eligible patients in the VA: A targeted pharmacist intervention in a learning health system

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

Abstract: Background: Patients with chronic kidney disease (CKD) are at increased risk for cardiovascular disease and cardiovascular events. Multiple studies have demonstrated that sodium glucose co-transport 2 inhibitors (SGLT2i) reduce these adverse events and, as a result, guidelines now recommend that SGLT2i be given to those with mild to moderate CKD and type 2 diabetes. The objective of this study is to evaluate if a pharmacist-driven SGLT2i prescribing initiative among eligible patients with CKD and diabetes within the VA could more rapidly improve the adoption of SGLT2i. Methods: Eligible patients are being identified through an established VA diabetes dashboard. Patients with an odd social security number are put into the intervention arm, while those with an even social security number serve as the control while awaiting a second iteration of the same interventional program. The intervention has been implemented in a rolling fashion throughout VISN 23. Our primary outcome is the initiation of an SGLT2i. Additional outcomes include medication adherence and safety-related outcomes. Results: To date, the initiative has been rolled out to seven sites across VISN 23. A total of 4521 patients have been enrolled in the intervention. Of those, 3363 (74%) were determined eligible. After initial outreach, 1582 (47%) were scheduled for a pharmacist visit. Of those who attended a pharmacist visit, 824 (54%) were initiated on the medication while 698 (46%) were not. All baseline data collected, to date, are balanced with $p > 0.05$ between the intervention and control arms. Reasons for not initiating the medication include advanced age, late-stage cancer diagnosis, dementia, and others. Data collection for other outcome measures is still ongoing. Conclusion: This project tests the effectiveness of a pharmacist-driven medication outreach initiative as a strategy to accelerate the initiation of SGLT2i. The results of this work will not only illustrate the effectiveness of this strategy in initiating SGLT2is but may also have implications for increasing dissemination for other areas of guideline concordant care. Furthermore, the utilization of social security numbers to select Veterans for the first wave of this program has created a pseudo-randomized interventional trial supporting a pragmatic learning health system approach.

Research Topic: Pharmacy

Funding agencies: N/A

Grant support: N/A

48. Current Demographic Makeup of IACUC Members in the United States

Rassette, Matt¹

1. Minneapolis VA Health Care System

Abstract: Promotion of a diverse, equitable, and inclusive environment is a goal shared by many in the laboratory animal science field. Moving towards that goal requires benchmarks of the current conditions regarding diversity in multiple areas within the field, including demographics of oversight bodies such as the IACUC. However, data describing the current demographic makeup of IACUCs is limited to nonexistent. This study aims to provide initial data regarding the demographic makeup of current IACUCs in the United States by leveraging information found in a dataset created to query committee members on ethics. This dataset was created by inviting members of the AALAS Community Exchange and the NABR IACUC-Admin communities to participate in an anonymous online survey in March 2023. The survey gathered data on current members of IACUCs in the United States, including their age range, gender identity, race, ethnicity, religiosity, and political leaning. This is compared against baseline data on diversity within US academic faculty and the US overall gathered from the US Department of Education and the Census Bureau. These data show that respondents currently serving on US IACUCs ($n = 167$) predominantly identify as white (138/157, 88%), female (98/159, 62%), and leaning progressive (107/152, 70%). For comparison, data from the Department of Education on college faculty show 74% identifying as white and 47% as female. The general population of the US in the 2020 Census identified as 62% white and 51% as female. Efforts to improve diversification and inclusion within laboratory animal science should include diversifying membership on the IACUC. Further research is needed to address shortcomings in the present study, such as convenience and selection biases. However, if confirmed these results suggest that further efforts to improve IACUC diversity are needed.

Research Topic: Veterinary Medicine

Funding agencies: N/A

Grant support: N/A

49. Surveying IACUC Members on Ethical Deliberation and the Label 'Ethics Committee'Rassette, Matt¹

1. Minneapolis VA Health Care System

Abstract: Recent discussion within the laboratory animal science community has addressed the role of ethics in IACUC oversight and how best to acknowledge that role. There are clear opportunities for ethics to impact oversight, as reflected in the requirements for the IACUC to evaluate 'harm-benefit' relationships as well as refinement, reduction, and replacement. The perspectives of the IACUC members themselves are important, so this study was designed to survey current and former IACUC members for insights into the contribution of ethical considerations to their deliberative processes. The survey queried current and former IACUC members regarding whether IACUCs perform ethical deliberation and whether they would be comfortable labeling the IACUC as an 'ethics committee.' Following oversight board approval, a survey invitation was sent to members of AALAS Community Exchange and the NABR IACUC-Admin communities in March 2023. The majority of those surveyed affirmed that the work of an IACUC involves ethical deliberation (178/202; 88%) and, to a lesser extent, indicated support for the statement 'The IACUC is an ethics committee' (112/198; 56%). Subgroup means were compared based on the following dimensions: IACUC role, age, race, ethnicity, gender, religion, and political identity. While veterinarians (n = 68) affirmed the role of ethics in their considerations on the IACUC, more were hesitant to explicitly designate the IACUC an 'ethics committee' compared with those serving in other roles on the committee. These data suggest that most IACUC members believe that their deliberations on the committee involve ethics, and favor labeling the committee as an ethics committee. Questions of how to support the IACUC's consideration of ethics, and possible reasons behind hesitation about the label will be presented.

Research Topic: Veterinary Medicine**Funding agencies:** N/A**Grant support:** N/A

50. Developing a Veteran & Caregiver Engagement Panel: Including the stakeholder voices in rehabilitation researchRich, Tonya^{1,2}; Jensen, Agnes¹; Amundson, Erin¹; Wang, Gloria¹; Krebs, Erin^{1,2}

1. Minneapolis VA Health Care System

2. University of Minnesota

Abstract: The mission of the Rehabilitation & Engineering Center for Optimizing Veteran Engagement & Reintegration (RECOVER) is to maximize Veteran participation in important lifelong roles and activities through development, evaluation, and clinical translation of practical rehabilitation interventions and technologies. Our center focuses on rehabilitation research in two populations, Veterans with amputation and Veterans with spinal cord injuries and disorders. To facilitate meaningful partnerships between Veterans with amputation or SCI and researchers across all stages of the research process, we developed a RECOVER Veteran and Caregiver Engagement Panel (VCEP). The RECOVER VCEP is modeled on the successful VA HSR&D Pain/Opioid Consortium Veteran Engagement Panel. Recruitment for the RECOVER VCEP occurred between October 2023 and January 2024. Potential candidates were identified from sources including 1) Veteran advocacy groups; 2) Veteran social media groups; 3) existing local and national Veteran Engagement Panels; and 4) Minneapolis VA staff in research, the RECOVER Center, women's clinic, and caregiver support program. Veterans and caregivers who expressed interest were interviewed by two members of the RECOVER engagement staff. The interview was an opportunity for RECOVER staff to gauge candidates' interest/suitability and for candidates to ask questions about the panel member role. We invited 12 Veterans and 1 caregiver to join the VCEP, including 5 Veterans with amputation and 7 Veterans with spinal cord injuries and disorders. The panel is diverse and includes 5 women and 8 men, age range 30s-70s, with members who are currently working, retired, and/or volunteering in the community. Several members live in rural areas of Minnesota/Wisconsin. As the VCEP is getting established, early activities are focusing on establishing a sense of community within the group, developing meeting routines, and building a shared knowledge of the research process. We are identifying shared topics relevant to research among persons with amputation and with spinal cord injuries and disorders. The VCEP has already met with research teams and provided feedback on study appeal, duration, and outcome measure selection. Planned future sessions will focus on recruitment strategies, key questions for literature reviews, and meaningful dissemination methods.

Research Topic: Rehabilitative Medicine**Funding agencies:** VA RRD**Grant support:** RRD I50RX004836

51. The effects of treatment timing in a SMART trial of tobacco longitudinal care

Rina, Horii 1; Alexander, Rothman 1; David, Vock 1; Anne, Joseph 1; Mariah, Branson 2; Anne, Melzer 1-2; Abbie, Begnaud 1; Steven, Fu 1-2

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

Abstract: Background and Objective: The Program for Lung cancer screening and TOBacco cessation (PLUTO) trial was a Sequential, Multiple Assignment, Randomized Trial (SMART) to help optimize the delivery of the tobacco longitudinal care (TLC) program. The current study reports secondary analyses of the PLUTO trial to assess the effects related to the timing of treatment delivery. Design: In Stage 1 of the trial, participants who smoked daily and were eligible for lung cancer screening were randomized to initially receive either 4 weeks or 8 weeks of TLC. At the end of Stage 1, participants' response to treatment was assessed and participants were rerandomized to either continue with TLC or receive more intensive treatment or less intensive treatment depending on their response to the initial TLC. Specifically, if participants reported continuing to smoke at the end of Stage 1, they were randomized to either continue TLC monthly or continue TLC monthly with a referral to prescription medication therapy management (MTM). If participants reported 7-day abstinence at the end of Stage 1, they were randomized to either continue TLC monthly or to receive TLC quarterly (i.e., every three months; TLC-Q). The current analyses assess the effects of the timing of the Stage 1 treatment assessment and subsequent rerandomization on 7-day point prevalence abstinence at week 12, week 26, week 52, and week 78 of the trial. Results: Participants who were randomly assigned to be assessed and re-randomized at week 4, rather than week 8, were more likely to report 7-day point prevalence abstinence at weeks 12, 26, and 52, but not 78 (p 's < 0.047). There was some evidence that among participants who did not respond to early treatment (continued to smoke at week 4), being offered a referral to MTM at week 4 did not lead to differences in abstinence, but being offered a referral to MTM at week 8 may have had an adverse effect on cessation. However, the interaction was only observed at week 52 (p < 0.06). Overall, the results provide insight about the timing of TLC program delivery suggesting that earlier treatment response assessment and re-randomization may be beneficial. Future research could assess whether there are any factors that might moderate the effects of treatment delivery timing to further optimize the TLC program.

Research Topic: Health Services

Funding agencies: NIH

Grant support: NCI R01CA196873

52. Therapist Perspectives on the Use of D-EBP Templates: Insights from Preliminary Interviews

Salameh, Hope 1; Hudson, Emily 1; Kehle-Forbes, Shannon 1; Taylor, Brent 1; Cutting, Andrew 1; Spont, Michele 1-2; Clothier, Barbara 1; Lefchak, Hanna 1; Degerstrom, Rose 1; Ackland, Princess 1-2

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

Abstract: Background: The VHA offers three evidence-based psychotherapies for depression (D-EBPs): cognitive behavioral therapy for depression (CBT-D), acceptance and commitment therapy for depression (ACT-D), and interpersonal psychotherapy (IPT). Since the D-EBP training initiatives began in 2008, nearly 2,800 therapists have been trained. Specific templates are utilized to document D-EBP sessions in medical records, aiming to standardize patient care and facilitate consistent data recording. Previous literature has explored the effectiveness of templates in tracking health outcomes and therapist perceptions of template usage across various patient conditions. However, the foundations of D-EBPs like CBT and ACT can be applied to various conditions and therapists may use those specific templates instead, use their own templates or document in other ways the details about the depression treatments used. Therapists' perceptions on using these D-EBP templates have not been previously studied. Methods: Qualitative interviews were conducted with therapists who were trained in at least one of the three D-EBPs from 10 medical centers to understand their perception of D-EBPs and their use of D-EBP templates. An interview guide was developed iteratively, and 19 therapists have been interviewed thus far. Interviews explored therapist perceptions and utility of D-EBP templates. All 19 interviews were transcribed and coded. Codes were discussed among the research team to extract preliminary themes. Findings: Therapists believe the templates are valuable but are fraught with issues such as a mismatch between the structure of the template and the therapy application. Other issues included templates being perceived as confusing, time-consuming, and cumbersome to navigate. Some therapists admitted to not using the templates at all. Additionally, some therapists indicated using alternative templates especially for patients with comorbid diagnoses and therapists may be providing the treatments even if they don't use the templates. Few therapists reported that the template saves time and are user-friendly. Conclusion: Given these provider perceptions, while D-EBP note templates offer potential benefits in standardizing patient care and ensuring consistent data recording, there are notable challenges associated with their implementation that may limit their effectiveness.

Research Topic: Depression

Funding agencies: VA HSRD

Grant support: N/A

53. A dual orexin receptor agonist, RTIOXA-47, is a candidate for preventing weight gain after acute weight loss in mice

Sandoval-Caballero, Carolina¹; Mavanji, Vijaya¹⁻²; Ward, Miranda¹⁻²; Shekels, Laurie¹⁻²; Pomonis, Brianna²; Zhang, Yanan³; Kotz, Catherine¹⁻²

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

Abstract: A synthetic dual orexin receptor agonist RTIOXA-47 increases rodent energy expenditure (EE) and body weight (BW) loss. This agonist also increases Spontaneous Physical Activity (SPA) and EE in obesity-prone (OP) rats as well as decreases BW and fat mass (FM) in New Zealand Obese mice. We hypothesized that RTIOXA-47 would maintain reduced body weight after weight loss and prevent weight gain after re-feeding in diet-induced obese (DIO) C57BL/6 mice. To test this, we are feeding male and female mice with a high-fat diet (HFD, D1245, research diets) to induce obesity. Then, half of these HFD-fed mice will be calorie-restricted to ~60% of their obese state energy intake to induce weight loss (weight gain/loss group), and the other half will be fed ad libitum with HFD (weight gain group). We will inject RTIOXA-47 in both groups, and SPA, EE, BW, and FM will be measured (outcomes). Finally, the weight gain/loss group will be re-fed with HFD to induce weight gain, and the effects of RTIOXA-47 on the outcomes will be measured again. Preliminary data show that lean (and not fat) mass significantly and positively correlates with BW in males ($R = 0.96$, $p < 0.05$) and females ($R = 0.97$, $p < 0.05$). The HFD-fed females gain weight faster than HFD-fed males, and we plan to treat each set of animals with RTIOXA-47 once they achieve a 20% increase in body weight relative to LFD-fed groups. **CONCLUSION:** Studies are in progress, but we predict that (1) RTIOXA-47 will increase SPA and EE, (2) RTIOXA-47 will decrease FM and maintain the post-weight loss BW in HFD mice, and (3) the re-exposure to HFD will result in relapse to obesity only in non-RTIOXA-47 injected mice. Together, these data will highlight the relevance of orexin agonists in driving therapies against obesity.

Research Topic: Obesity

Funding agencies: VA BLRD; VA RRD; NIH

Grant support: NIH R01DK134468, BLRD I01BX005815, RRD I01RX003901

54. RTIOXA-47, a dual orexin receptor agonist, increases energy expenditure and decreases fat mass in obesity-prone rodent models

Sandoval-Caballero, Carolina¹; Mavanji, Vijaya¹⁻²; Ward, Miranda¹⁻²; Shekels, Laurie¹⁻²; Pomonis, Brianna²; Zhang, Yanan³; Kotz, Catherine¹⁻²

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

Abstract: Orexins are neuropeptides that bind to G-protein coupled receptors 1 and 2 in brain regions that regulate body weight (BW) and energy expenditure (EE). In rodents, orexins increase physical activity (PA) and EE. We hypothesized that a synthetic dual orexin receptor agonist RTIOXA-47 prompts BW loss by increasing EE and decreasing fat mass (FM) in rodents. To test this, we injected RTIOXA-47 intraperitoneal and assessed its effects on PA, EE, food intake (FI), and FM in obesity-prone (OP) rats and New Zealand obese (NZO) mice. We showed that RTIOXA-47 (40 mg/kg): (1) increased PA without affecting FI, (2) increased 24h EE in OP rats, (3) decreased BW, and (4) decreased FM in NZO mice. These data suggest that RTIOXA-47 could maintain reduced BW after BW loss and prevent BW gain after re-feeding in mice. Preliminary data show that lean (and not fat) mass positively correlates with BW in males ($R = 0.96$, $p < 0.05$) and females ($R = 0.97$, $p < 0.05$). Females fed with a high-fat diet (HFD) gain weight faster than HFD-fed males, and we will treat each set of animals with RTIOXA-47 once a 20% increase in BW relative to low-fat diet-fed controls. Studies are in progress, but we predict that (1) RTIOXA-47 will increase PA and EE, (2) RTIOXA-47 will decrease FM and maintain the post-weight loss BW in HFD mice, and (3) the re-exposure to HFD will result in relapse to obesity only in non-RTIOXA-47 injected mice. Together, these data highlight the therapeutic potential of orexin agonists to treat obesity.

Research Topic: Obesity

Funding agencies: VA BLRD; VA RRD; NIH

Grant support: NIH R01 DK134468, BLRD I01BX005815, RRD I01RX003901

55. Investigating the Impact of Military Burn Pit Toxins on the Blood-Brain Barrier and Neuroinflammation

Shankar, Saisamyuktha¹⁻²; Taylor Poole, Jedidah³⁻⁴; Tom?ška, Julie³; Nurkiewicz, Timothy⁵; Trembley, Janeen¹⁻²; Butterick, Tammy¹⁻²

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Burn Pits 360
4. Tulane University
5. West Virginia University

Abstract: Background: Millions of post-9/11 Veterans were exposed to hazardous toxins from open-air burn pits incinerating military, medical, and industrial waste. These pits, sometimes as large as 25 acres, released harmful substances including particulate matter (PM_{2.5}), polycyclic aromatic hydrocarbons (PAH), and volatile organic compounds. Studies link these toxins to neurodegenerative conditions through neuroinflammation. This ongoing study, in collaboration with the Center for Inhalation Toxicology at West Virginia University School of Medicine, investigates the impact of burn pit toxins on the blood-brain barrier (BBB), neuroinflammation, cellular senescence, and brain health. Methods: Continuing research involves exposing male and female C57BL/6 mice to synthetic burn pit toxins via a whole-body inhalation chamber, simulating the combustion of jet fuel, wood, and plastics for five days. BBB integrity is assessed using Evans blue dye, with further analysis in brain tissue and plasma for proinflammatory biomarkers and BBB integrity proteins. We utilize western blot for tight junction proteins and matrix metalloproteinases, and cytokine levels are measured using a multiplex ELISA. Results: Preliminary data show elevated proinflammatory biomarkers such as TNF α in brain tissue and plasma, indicating both peripheral and central inflammation. Ongoing studies aim to further explore BBB permeability, protein expression changes, and cytokine profiling. Discussion: Ongoing research focuses on identifying potential therapeutic strategies to mitigate neurological complications from burn pit exposure. Emphasis is placed on studying microglia (brain immune cell) response to prolonged exposure, which may reveal their role in BBB dysfunction and targeted interventions to preserve or restore BBB function. Significance to VA Healthcare and the PACT Act: This study supports the PACT Act's goals by elucidating how burn pit toxins affect Veterans' neurological health. Insights gained may guide the development of targeted treatments, enhancing VA healthcare initiatives and fulfilling the PACT Act's mission to improve health outcomes for service-related exposures.

Research Topic: Afghanistan & Iraq Veterans

Funding agencies: VA BLRD; UMN

Grant support: BLRD Field Planning Award, BLRD I01BX004146, BLRD I01BX005091

56. The Role of Pathological Personality Traits in Outcomes from the Chronic Pain Rehabilitation Program

Stone-Bury, Lisa¹; Finn, Jacob¹⁻²; Hachiya, Kiki¹

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

Abstract: The Chronic Pain Rehabilitation Program (CPRP) is an intensive, four-week interdisciplinary outpatient program that represents a tertiary level of care for chronic pain within the VA. Because of the high number of resources required to administer the program, it is important to identify possible barriers to treatment response. This study examined relationships between pathological personality traits (defined as relatively stable, maladaptive styles of approaching the world) and pain-related outcomes among Veterans who completed CPRP. Participants consisted of 97 Veterans (M age = 52.64; 80% men) who completed the MMPI-2-RF upon admission and self-report measures surrounding pain and physical therapy assessments upon admission and discharge to CPRP. This study specifically examined relationships between the MMPI-2-RF PSY-5 scales and pain catastrophizing, pain acceptance, pain self-efficacy, and the 6-minute walk test. There were significant correlations between: pain catastrophizing at admission and discharge with AGGR, NEGE, and INTR; both pain acceptance and pain self-efficacy at admission and discharge with NEGE and INTR; and 6-minute walk at discharge with DISC. Hierarchical regression analyses revealed significant associations between admission pain-related outcomes and all five PSY-5 scales. After controlling for participants' admission scores, pain-related outcomes at discharge were not associated with any of the PSY-5 scales, indicating that personality pathology did not predict pain-related change during the program. These findings indicate that strong relationships exist between pathological personality traits and pain-related experiences among Veterans who experience chronic pain. Although casual inferences cannot be made, CPRP appeared to have contributed to improved pain outcomes regardless of baseline pathological traits. Results suggest that pathological personality traits should not be a rule-out for inclusion in intensive interdisciplinary outpatient programs targeting chronic pain.

Research Topic: Pain

Funding agencies: N/A

Grant support: N/A

57. Proceedings of the Veterans Affairs Military Toxic Exposure Research Conference

Trembley, Janeen¹⁻²; Barach, Paul³; Tom?ška, Julie⁴; Poole, Jedidah⁴⁻⁵; Ginex, Pamela⁶; Miller, Robert⁷; Lindheimer, Jacob⁸⁻⁹; Szema, Anthony¹⁰; Siddharthan, Trishul¹¹; Kirkness, Jason¹¹⁻¹²; Nixon, Joshua¹⁻²; Lopez Torres, Rosie⁴; Klein, Mark¹⁻²; Nurkiewicz, Timothy¹³; Butterick, Tammy¹⁻²

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Thomas Jefferson University
4. Burn Pits 360
5. Tulane University
6. Stony Brook University
7. Vanderbilt University
8. James A. Haley Veterans Hospital
9. University of South Florida
10. Donald and Barbara Zucker School of Medicine at Hofstra/Northwell
11. University of Miami
12. 4DMedical
13. West Virginia University School of Medicine

Abstract: Background: Millions of U.S. troops deployed to the Middle East and Southwest Asia were exposed to toxic airborne hazards and/or open-air burn pits. Ongoing research has demonstrated that these occupational exposures have profound health and wellness consequences. Major research gaps remain in fully understanding the scope of the health impacts from such exposures, developing targeted therapeutics, and establishing long term care standards. The U.S. Sergeant First Class Heath Robinson Honoring our Promise to Address Comprehensive Toxics (PACT) Act was signed into law in August 2022. This act expands the benefits and services to U.S. Veterans exposed to toxicants, requires the Veterans Health Administration to provide toxic exposure screening, and supports increased research, education, and treatment due to chronic toxic occupational exposures. Approach: We conducted a virtual plenary expert meeting and a field-based planning meeting. The goal was to foster a multi-disciplinary Community of Practice approach to improve efforts to address gaps in research and clinical care. We engaged leading experts in Veteran health care advocacy, pre-clinical and clinical scientists, clinicians, Veterans, and their families to highlight the long-term, multi-organ, and chronic health effects of repeated occupational exposures to airborne hazards. The conference was a launching point to outline a systematic road map for bench-to bedside translational research and address health and wellness gaps for Veterans exposed to military toxins as a priority research area supported by the U.S. PACT Act. Conclusion: The conference highlighted the need for continued and open collaboration among and between varied stakeholders to gather information and refine a research agenda to understand health and wellness outcomes. In these proceedings, we summarize our findings as they relate to: i) centering the Veteran voice; ii) leveraging VA-, university-, industry- and community-affiliated resources and expertise; and iii) clinical monitoring and research methods; and iv) approaches for pre-clinical research. US Veteran health care and policy are strengthened and informed by collaborative scientific knowledge, research, and innovation generated by bringing together stakeholders for effective implementation and sustained improvement of Veterans' health.

Research Topic: Afghanistan & Iraq Veterans

Funding agencies: VA BLRD; NIH; UMN

Grant support: VA BLRD Field Planning Award, BLRD I01BX004146, CSRD IK2CX001679, CSRD I01CX002616, UMN PHDR, NIH WV-CTSI U54 GM104942, U3DMC327550100

58. The MN Pulmonary Airborne Clinical Toxin (M-PACT) Study

Trembley, Janeen¹⁻²; Barach, Paul³; Tom?ška, Julie⁴; Poole, Jedidah⁴⁻⁵; Ginex, Pamela⁶; Siddharthan, Trishul⁷; Sandri, Brian²; Klein, Mark¹⁻²; Butterick, Tammy¹⁻²

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Thomas Jefferson University
4. Burn Pits 360
5. Tulane University
6. Stony Brook University
7. University of Miami

Abstract: Over 2 million post-9/11 formerly deployed and nearly 100,000 MN Veterans were exposed to military burn pit toxins, with many becoming ill. No large-scale organized attempt has been made to study the potential profound biologic consequences on health and wellness of Veterans who breathed these emissions. The M-PACT study is intended to help Veterans suffering from respiratory ailments including cancer that were most likely caused by exposure to toxins released by trash fires on combat outposts in Afghanistan, Iraq and other countries. Veterans are at increased risk of pulmonary disease exacerbated in nearly 25% of US Veterans who live in rural communities with limited access to healthcare and where healthcare access disparities pose quality of life risks. We hypothesize that post-9/11 MN Veterans exposed to airborne toxins are at an increased risk of lung injury and cancer and we seek to identify patient-reported health outcomes. Our research goals are to 1) Determine and validate patient-reported health-related outcomes and quality of life in Veterans living in Minnesota who were exposed to airborne hazards and open-air burn pits. We will collect quantitative survey data and conduct interviews in a subset of Veterans to assess the physical and mental health as well as how well the VA manages these patient's needs. 2) Understand the symptom and system response experience and well-being of Veterans exposed to airborne hazards and burn pits, with a specific focus on poor outcomes from lung disease. We will work closely with the Veteran community organization Burn Pits 360 (BP360) and will leverage the BP360 and Veteran's Affairs Burn Pit registries to identify at risk and injured MN Veterans. Significance to US Veteran Health Care: Major research gaps remain in fully understanding the scope of the health impacts from burn pit exposures, developing targeted therapeutics, and establishing long term care standards. The U.S. Sergeant First Class Heath Robinson Honoring our Promise to Address Comprehensive Toxics (PACT) Act expands the benefits and services to Veterans exposed to toxicants, requires the Veterans Health Administration to provide toxic exposure screening, and supports increased research, education, and treatment. M-PACT has the potential to make actionable recommendations regarding chronic care management and ill health associated with burn pit exposures and improve Veterans access to healthcare.

Research Topic: Afghanistan & Iraq Veterans

Funding agencies: VA BLRD; UMN

Grant support: VA BLRD Field Planning Award, BLRD I01BX004146, University of Minnesota Program in Health Disparities Research, BLRD I01BX005091

59. Complementary and Alternative Therapies for Genitourinary Syndrome of Menopause: An Evidence Map

Ullman, Kristen¹; Diem, Susan^{1,2}; Forte, Mary²; Ensrud, Kristine^{1,2}; Sowerby, Catherine¹; Zerzan, Nicholas¹; Anthony, Maylen¹; Landsteiner, Adrienne¹; Greer, Nancy¹; Butler, Mary²; Wilt, Timothy^{1,2}; Danan, Elisheva^{1,2}

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

Abstract: Postmenopausal vulvovaginal, urinary, and sexual symptoms (i.e., genitourinary syndrome of menopause [GSM]) affect approximately 50-70% of women. Women seeking non-hormonal interventions for these symptoms may choose complementary and alternative therapies (CAM). The Agency for Healthcare Research and Quality (AHRQ) along with the Patient-Centered Outcomes Research Institute (PCORI) funded a systematic review on interventions for GSM. We searched Ovid/Medline, Embase, and CINAHL through December 11, 2023. We included RCTs of =8 weeks that evaluated the effectiveness or harms of CAM for postmenopausal women with GSM and reported =1 outcome of interest (urinary, sexual and vulvovaginal symptoms, quality of life, depression and anxiety), with =20 randomized per arm (PROSPERO CRD42023400684). We used an evidence map approach to organize trials by intervention according to the National Center for Complementary and Integrative Health (NCCIH) framework. We summarized population, study characteristics, interventions, and outcomes. We identified 57 RCTs that investigated 39 unique interventions. Studies were typically small ($n < 200$), and most were conducted in Iran ($k = 24$) or other parts of Asia ($k = 9$). Nine studies enrolled women with a history of breast or gynecological cancers. Most studies ($k = 44$) examined natural products (i.e., herbal or botanical supplements), fewer reported on mind/ body practices ($k = 6$) or educational programs ($k = 7$). Tools used to measure outcomes varied widely. Most trials reported on adverse events ($k = 33$). Of the 44 RCTs of natural products, most investigated unique phytoestrogen supplements ($k = 31$), though there were multiple RCTs of soy ($k = 5$), Pueraria mirifica ($k = 4$), and fenugreek, licorice, red clover and Tribulus terrestris ($k = 2$ each). We identified several RCTs testing a broad range of interventions. Most were small, short-term, conducted outside the US, and too heterogeneous to allow for evidence synthesis. Inconsistency in product formulation, dosing, route, and administration is a perennial challenge for evaluating natural products. Across 57 RCTs, we found few studies testing identical products, and those evaluating similar products used different compounds or doses and reported different symptom outcomes, making synthesis impossible and effectiveness estimates challenging. Detailed assessment of study outcomes and use of standardized population, intervention, comparator, and outcomes reporting in future RCTs are needed.

Research Topic: Women's Health

Funding agencies: Other

Grant support: AHRQ/PCORI

60. Trajectory of Ejection fraction among patients with heart failure with improved ejection fraction

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

Abstract: Background: As a result of the advances in the medical management of heart failure with reduced ejection fraction (HFrEF), more patients (pts) exhibit improvements in left ventricular function, increasing the population of pts with heart failure with improved ejection fraction (HFimpEF). Little is known about the frequency of subsequent regression of EF in pts with HFimpEF and the effect of EF regression on clinical outcomes compared to pts without EF regression. Methods: We examined the presence, predictors, and clinical outcomes of EF regression to = 40% in pts with HFimpEF at the Minneapolis Veterans Affairs hospital. Data were collected from electronic medical records between 2011-2023. HFimpEF was defined as a previous ICD-10 diagnosis of HFrEF with an EF = 40% determined via transthoracic echocardiogram, and a subsequent improvement of EF to > 40%. Logistic regression analysis was performed to identify characteristics associated with regression of LVEF. Kaplan-Meier or Simon Makuch survival curves, as appropriate, were used to compare the risk for all cause hospitalizations or ED visits between those with regressed compared to non-regressed LVEF using the log-rank test. Cox regression analysis was performed to determine the risk of adverse clinical outcomes by LVEF regression status. Results: Out of 5847 pts with heart failure, 1118 (19%) had HFimpEF (Table). Regression of EF occurred in 292 (26%) pts. In a multivariable model, characteristics associated with regression were EF after improvement (OR per unit 0.92, 95% CI 0.88, 0.96), BNP (OR 1.04 per 50 pg/ml, 95% CI 1.015, 1.06), BMI (OR 1.05, 95% CI 1.01, 1.10) and use of SGLT2 inhibitors (OR 0.33, 95% CI 0.16, 0.71). Compared to no regression, those with EF regression had an increased risk for HF hospitalizations (HR 2.6, 95% CI 2.12, 3.18), emergency department visits (HR 1.71, 95% CI 1.42, 2.06), and death (HR 3.48, 95% CI 2.43, 4.98). Conclusions: In a cohort of pts with HFimpEF, one in 4 faced regression of EF to = 40%. EF regression was associated with an increased risk for adverse clinical outcomes. Future research should assess potential strategies for prevention of EF regression in pts with HFimpEF.

Research Topic: Cardiovascular Disease

Funding agencies: N/A

Grant support: N/A

61. Validation of a data logger for measuring standing time and seat angles for community-based standing devices

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Abstract: Introduction: Little is understood about community-based standing device use and the impact of standing dosage on health outcomes (e.g., pressure injury) in those living with spinal cord injury and disorders (SCID). This project reports on the validity of a commercially available data logger for measuring standing time and seat angle. Methods: A standing frame and a standing manual wheelchair were instrumented with this data logger. Participants (n = 2) were able-bodied participants, and all device trials were completed in a laboratory environment. Total standing time in the standing frame was calculated from the data logger and compared to a user-recorded standing log over two, one-week periods. The standing wheelchair's seat angle was calculated using motion capture, the kinematic gold-standard, and compared to calculated seat angle from the data logger. Results: Average seat interface pressures were also captured during testing of the standing wheelchair. The data logger demonstrated high accuracy (98.27%) in determining total standing time in the standing frame when compared to a user-recorded standing log. The wheelchair seat angle calculated from the data logger demonstrated a strong linear relationship with the motion lab calculations of seat angle ($r^2 = 0.99$). The data logger seat angle results also demonstrated strong relationships to average seat pressure and rear dispersion index, measures relevant to pressure injury risk. Average seat pressure and seat angle demonstrated a generally inverse relationship with the greatest offloading of seat IP at the highest seat angle. Conclusion: This data logger appears to be a valid tool for determining standing time and seat angle in both a standing frame and standing wheelchair and could have the potential to measure prolonged periods of community-based standing. This information on standing device use may aid clinicians and researchers to better understand the use and impact of standing technologies on health outcomes.

Research Topic: Spinal Cord Injury

Funding agencies: VA RRD

Grant support: RRD I01RX003505

62. Hurley staging in patients with hidradenitis suppurativa in the VA Health Care System

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Abstract: Background: Structured datasets are available with large numbers of patients with HS for epidemiologic studies, but few, if any, include data on HS severity. Hurley staging is a widely used tool to characterize HS severity. Objective: Determine the incidence of Hurley staging and supportive documentation in the notes of patients with a new diagnosis of HS in the Veterans Affairs Health Care System (VAHCS). Methods: Retrospective, cross-sectional analysis of VAHCS patients using data from the Veterans Affairs Informatics and Computing Infrastructure (VINCI). Patients with HS were identified using at least one ICD-9 [705.83] or ICD-10 [L73.2] code between January 1, 2010 and December 31, 2021. Patients with Hurley staging at index date were identified by searching the index date notes for the term 'Hurley.' Encounters from the index date were then reviewed to identify documentation supporting the Hurley staging classification from the note (i.e., presence of scarring, presence of tunneling, diffuse involvement in an anatomic area.) Results: Of 29,483 patients with HS, 809 patients (2.7%) had Hurley staging at initial HS encounter. Of 502 patients with HS classified as Hurley I (63%), 29% and 7.9% had documentation of scarring and tunneling, respectively. None had diffuse involvement documented. Of 261 patients classified as Hurley I-II, II, or II-III in the chart (33%), 62-78%, 43-78% and 0-0.1% had documentation of scarring, tunneling, or diffuse involvement on physical exam, respectively. Of 28 patients with HS classified as Hurley III (3.5%), 75%, 79% and 39% had documentation of scarring, tunneling, or diffuse involvement on physical exam, respectively. Discussion: While there is only a small percentage of patients that have Hurley staging documented in their initial HS encounter in the VAHCS, there were more than 800 patients with Hurley staging at their index encounter that could be used to evaluate progression of HS over time.

Research Topic: Dermatology

Funding agencies: N/A

Grant support: N/A

63. Fractional concentration of exhaled nitric oxide (FeNO) by HIV status in men and women in the MACS-WIHS Combined Cohort Study

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Abstract: RATIONALE: Persons with HIV (PWH) have a high prevalence of self-reported asthma, but data are unclear whether HIV independently increases risk for asthma. A prior study in Copenhagen, Denmark reported that compared to seronegative controls, PWH had higher fractional concentrations of exhaled nitric oxide (FeNO), a marker of Th2 airway inflammation associated with asthma. Here we report FeNO interim findings from the US-based Multicenter AIDS Cohort Study ? Women’s Interagency HIV Study Combined Cohort Study (MWCCS). Our objective was to determine whether PWH have higher FeNO than those without HIV. METHODS: The MWCCS is a longitudinal, multicenter observational cohort study of men and women with HIV or without HIV. Standardized FeNO (NIOX VERO, Circassia, Morrisville, NC) was performed at 9 study clinics (3 clinics enrolling men, 6 clinics enrolling women) in consecutive MWCCS participants, without regard to prior clinical diagnoses, symptoms, or lung function test results. We performed cross-sectional analyses and compared FeNO by HIV serostatus separately in men and women. RESULTS: We collected FeNO measures in 833 unique individuals (327 men and 506 women) between May 2022 and January 2024. Median age was 58 years (interquartile range [IQR]: 50-64) and PWH composed 58% of the men and 68% of the women. Among PWH, 74% had HIV-RNA = 20 copies/mL and median CD4+ T-cell count was 747/mm³ (IQR: 500-1020). As expected, current smoking was associated with lower FeNO ($p < 0.01$); these participants ($n = 74$ men and $n = 186$ women) were excluded from further analyses. Elevated FeNO (FeNO = 25 ppb) was present in 39% of men and 19% of women but did not differ by HIV serostatus in either men ($p = 0.28$) or women ($p = 0.57$). CONCLUSIONS: In contrast to prior findings from Copenhagen, we did not observe differences in FeNO by HIV status in men or women. Reasons for this discrepancy are not clear, but our cohort differs from the Copenhagen study in its multicenter sampling, multiracial composition, and seronegative controls at risk for HIV acquisition rather than general population controls. Larger sample sizes will allow better understanding of factors associated with, and clinical consequences of, elevated FeNO in PWH. Data from other cohorts will be needed to resolve the discrepancy in findings whether HIV serostatus and FeNO measures are associated.

Research Topic: Respiration & Pulmonary Disease

Funding agencies: NIH; Other

Grant support: NHLBI NICHA, NIA, NIDCR, NIAID, NINDS, NIMH, NIDA, NINR, NCI, NIAAA, NIDCD, NIDDK, NIMHD, NIH OAR.

64. Prevalence of Sessile Serrated Lesions in Individuals with Positive Fecal Immunochemical Test Undergoing Colonoscopy: Results from a Large Nationwide Veterans Affairs Database

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Abstract: Sessile serrated lesions (SSLs) are important precursors to colorectal cancer (CRC). It is estimated that 20-30% of CRCs arise from SSLs through a pathway distinct from the traditional adenoma-carcinoma sequence. The USMSFTF recommends colonoscopy or fecal immunochemical test (FIT) as tier 1 tests for CRC screening in average risk individuals, however, the prevalence of SSLs in FIT-positive individuals is not widely known. The aim of our study is to determine the prevalence of SSLs in FIT-positive individuals using a nationwide database. Data was obtained from the VHA Corporate Data Warehouse using Structured Query Language. The cohort included individuals with a positive FIT between January 2014 and July 2022 who underwent colonoscopy in the following 12 months. Pathology records were queried using natural language processing for SSLs and traditional serrated adenomas (TSAs), tubular adenomas (TAs), tubulovillous adenomas, and adenomas with high-grade dysplasia. CRC was identified using pathologist-assigned SNOMED codes. The primary outcome was the detection of at least one clinically significant SSL (CSSL) on colonoscopy, which, for the purposes of this analysis, included TSAs and SSLs, as both serrated polyp subtypes are precursor lesions to CRC and have previously been used in studies evaluating prevalence of SSLs. A total of 52,167 individuals underwent colonoscopy within 12 months of a positive FIT. The average age was 62.5 years and 93.5% were male. At least one CSSL was found in 6.1% (n = 3,194) [M: 6.2%, F: 5.3%]. The prevalence of CSSLs increased over time from 4.6% in 2015 to 8.2% in 2022. Multivariate analysis revealed predictors for CSSLs to be female sex (OR 1.23; 95% CI [1.03-1.46], p = 0.020), smoking (OR 1.45; 95% CI [1.31-1.61], p < 0.0001), BMI = 30 kg/m² (OR 1.18; 95% CI [1.08-1.28], p < 0.0001), and presence of concomitant TA (OR 1.48; 95% CI [1.36-1.61], p < 0.0001). Lower detection of CSSLs was observed in individuals of Black race (OR 0.49; 95% CI [0.43-0.55], p < 0.0001) and Hispanic/Latino ethnicity (OR 0.78; 95% CI [0.65-0.94], p = 0.008). Overall, we found an SSL detection rate of 6.1% in FIT-positive individuals. To our knowledge, this is the largest study reporting prevalence of detected SSLs in FIT-positive individuals and provides valuable information regarding prevalence of serrated polyps in this population. These findings can be used to determine quality benchmarks for SSL detection rates in FIT based population screening programs.

Research Topic: Gastroenterology

Funding agencies: N/A

Grant support: N/A

65. Virtual Reality and Augmented Reality Interventions for Chronic Low Back Pain: A Systematic Review

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Abstract: Chronic low back pain (cLBP) is a common cause of disability. Extended reality (XR) technologies, including virtual reality (VR) and augmented reality (AR), can deliver non-drug therapies for chronic pain. We completed a systematic review on benefits and harms of VR and AR interventions for cLBP. We searched MEDLINE, Embase, CINHAL, PsycINFO, and Scopus databases from inception to May 2023 for articles of VR or AR cLBP interventions. Two independent reviewers screened abstracts, completed full-text review, assessed risk of bias (ROB), and abstracted data. We conducted quantitative meta-analyses for =3 studies that were sufficiently similar. Otherwise, we provided narrative syntheses. We used GRADE to rate overall certainty of evidence (COE). Among 10,932 unique citations, we identified 22 eligible trials assessing XR interventions for cLBP. All were rated some concerns (k = 10) or high (k = 12) ROB. Six studies evaluated varied VR intervention types for cLBP. VR psychological skills (compared with VR control or usual care) may result in greater improvement in pain-related functioning pain intensity, pain catastrophizing, and kinesiophobia in cLBP (low COE), but effects on adverse events are very uncertain (very low COE). All 16 AR studies evaluated AR physical activity cLBP interventions. The effects of AR physical activity (compared with non-AR physical activity (k = 10), medications, or usual care) on pain-related functioning, pain intensity, pain catastrophizing, kinesiophobia, and adverse events in cLBP are very uncertain (very low COE). Evidence on benefits and harms of XR interventions to treat cLBP is limited by methodological concerns, small study size, and lack of reporting on adverse events. The role of immersion in digital environments remains unclear. VR psychological skills interventions may have benefit in cLBP, but studies did not compare effects to non-VR interventions comprising similar psychological skills content. Minimally immersive AR physical activity did not demonstrate added value compared with non-AR physical activity. Fully immersive VR physical activity was not evaluated. Future work is needed to better understand how XR interventions may impact pain outcomes and add value to analogous non-XR pain interventions, particularly to overcome barriers to non-drug pain therapies in more diverse populations and settings. Larger studies informed by implementation science are important next steps to advance the field.

Research Topic: Pain

Funding agencies: Other

Grant support: VA ESP Project #09-009; 2024

66. Energy-Based Interventions for Genitourinary Syndrome of Menopause (GSM): A Systematic Review

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Abstract: Energy-based interventions for genitourinary syndrome of menopause (GSM) are gaining popularity, fueled by perceived limitations and fears related to hormonal therapies. Energy-based treatments heat tissue to induce a wound-healing response, which may result in symptom improvement. We conducted a systematic review to assess the benefits and harms of energy-based interventions for GSM symptoms to inform clinical decision making for clinicians and patients. We searched MEDLINE®, Embase®, and CINAHL® from database inception through December 11, 2023, supplemented with citation searches. Randomized controlled trials (RCTs) and prospective observational studies with a concurrent control group were eligible. Non-randomized and uncontrolled studies were eligible for long-term adverse event (AE) analysis if they reported follow-up of ≥ 12 months. We evaluated risk of bias (RoB). Data were abstracted by one reviewer and verified by a second. Outcomes of interest included eight previously identified GSM 'Core Outcomes in Menopause:' dyspareunia; dryness; discomfort/irritation; dysuria; change in most bothersome symptom; distress, bother, or interference associated with genitourinary symptoms; treatment satisfaction; and AEs. Certainty of evidence (COE) for outcomes was determined using GRADE. We identified 32 unique studies (16 RCTs; 1 quasi-RCT; 15 non-randomized). Ten RCTs and the quasi-RCT were rated low to moderate RoB. Included studies evaluated carbon dioxide (CO₂) laser (7), erbium-doped yttrium aluminum garnet (Er:YAG) laser (3), or CO₂ laser and radiofrequency (1). Studies were small, short in duration, and predominantly conducted outside the United States. Compared with sham laser, CO₂ laser may result in little to no difference in dysuria, dyspareunia, or quality of life (low COE). Compared with vaginal conjugated estrogens cream, CO₂ laser may result in little to no difference in dyspareunia, dryness, discomfort/irritation, dysuria, or quality of life (low COE). Treatment effects on other outcomes, and effects of Er:YAG laser or radiofrequency on any outcomes are very uncertain (very low COE). Studies noted few AEs and no serious AEs. CO₂ laser, Er:YAG laser, and radiofrequency energy-based therapies may offer no benefit, or have insufficient evidence, relative to any comparator for any GSM symptom. Future studies should investigate other energy-based treatments, differing protocols, and longer follow-up.

Research Topic: Women's Health

Funding agencies: Other

Grant support: PCORI/AHRQ
