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Poster Abstracts

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Fill in the Blank: Using Standardized Templates to Improve Resident TURBT Documentation and Perioperative Chemotherapy Utilization

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Background: Guideline-adherent TURBT practices and documentation are pivotal for staging and decision-making, particularly at teaching hospitals. Residents inconsistently document TURBT elements and underutilize perioperative intravesical chemotherapy, potentially related to poor documentation and being unaware of chemotherapy candidacy.

Methods: As a quality improvement initiative, we implemented operative note templates with TURBT-specific prompts to standardize documentation and increase utilization of perioperative chemotherapy.

Results: To assess pre-intervention practices, we reviewed 188 TURBT cases performed between 1/2022-1/2023. We compared operative documentation to the AUA TURBT checklist and tallied utilization of perioperative intravesical chemotherapy. Of 137 cases with visible tumor, 67 (49%) recorded tumor size. Only 43 cases (31%) noted if resection was complete. Sixteen patients were eligible for perioperative intravesical chemotherapy, but only 2 received it. One case noted rationale for not utilizing chemotherapy; 11 cases lacked deferral reasoning.

Post-intervention data collection is ongoing. Since implementation, 14 of 30 cases utilized templates (46%). To compare pre and post-intervention arms, operative notes were assigned a score based on number of recommended AUA checklist elements recorded (maximum score 8). Pre-intervention median score was 2.9; post-intervention median was 5 (Figure 1). When including only template users for the post-intervention cohort, the new median score was 7.1 (Figure 2).

Conclusions: Standardized operative templates for TURBT's encourage thorough documentation. Longer follow-up is needed to determine if templates improve perioperative chemotherapy utilization.

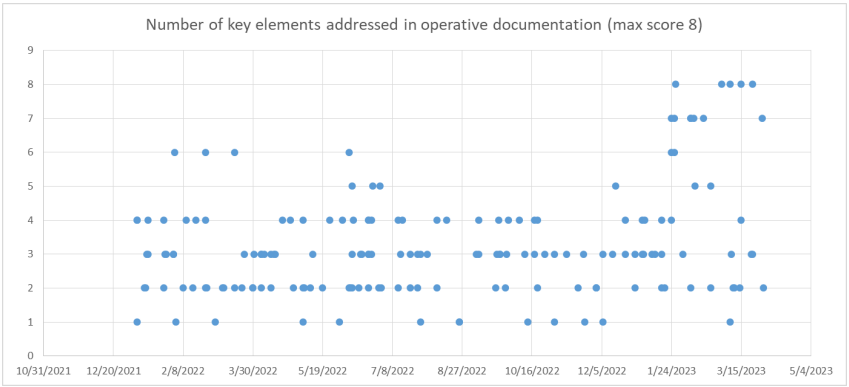

Figure 1: Run chart comparing number of elements addressed pre-intervention (1/1/22-1/22/23) vs post-intervention (1/23/23 onward) including both template users and non-adopters in the post-intervention era.

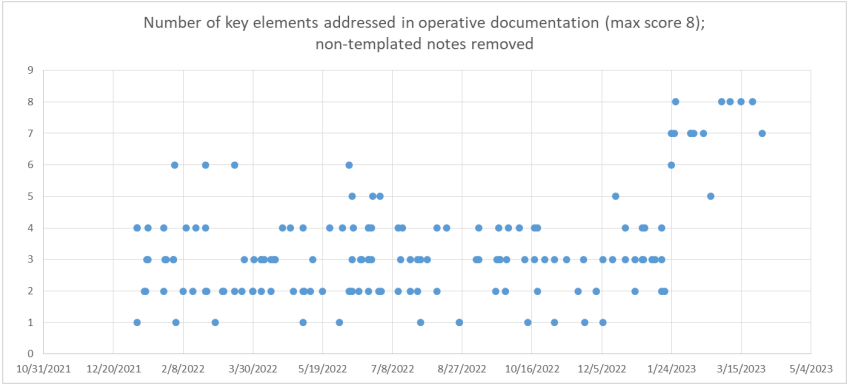

Figure 2: Run chart comparing number of elements addressed pre-intervention (1/1/22-1/22/23) vs post-intervention (1/23/23 onward) with non-template users removed.

Amateur Hour: Simulation-Based Mastery Learning for Transperineal Prostate Biopsy Technique Offers Equivalent Benefits for Novice Resident and Novice Attending Physicians

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Introduction: Simulation-based mastery learning (SBML) offers a way to build surgical skills prior to patient contact. Previous SBML studies on transperineal (TP) prostate biopsy technique have examined resident learning. Literature comparing learning curves of attendings and residents who are both novices in this technique is sparse. As part of a quality initiative to transition to transperineal biopsies, our department participated in a simulation workshop incorporating SBML to determine if learning curves of novice attendings and novice residents differ.

Methods: Participants received a lecture on TP biopsy technique followed by hands-on simulation with prostate phantoms under the supervision of experts. Subjective comfort with TP technique was assessed with pre-workshop and post-workshop surveys. Objective evaluation of biopsy technique was performed by expert graders using a standardized rubric (maximum score 12, 9 considered mastery).

Results: 23 physicians (13 residents, 10 attendings) completed subjective assessment surveys. Pre-simulation average comfort scores were 2.27 (±1.35) for residents and 4.20 (±2.64) for attendings (scale 1-10, 1 being lowest comfort). Post-workshop scores increased to 6.1(±2.23) for residents and 7.5(±0.5) for attendings.

Six physicians underwent formal SBML evaluation, 3 residents (PGY-1 to PGY-5) and 3 attendings (1st year in practice to 8th year). First simulation attempt scores were 6.33(±1.70) for residents and 6.33(±1.25) for attendings. Average second attempt scores were 9.67(±3.33) for residents and 9.33(±0.47) for attendings. Two residents and three attendings achieved mastery on their second attempt after deliberate practice.

Conclusions: Novice residents and attendings demonstrated similar trajectories and objective improvements in SBML exercises.

Effects of a rhythmic auditory stimulation-enhanced walking program on Veterans with Parkinson's disease with and without subthalamic nucleus deep brain stimulation.

Alexandria Umbarger, Sandra Kletzel, Christine Jelinek, Sadie Walker, Catherine Kestner, Kelly Krese, Blake McReavy, Frances Weaver, Theresa Pape, Kalea Colletta

Introduction: Subthalamic nucleus deep brain stimulation (STN-DBS) is an effective treatment for motor symptoms of Parkinson's disease (PD) due to mitigation of beta oscillations. Rhythmic auditory stimulation (RAS)-enhanced gait training is known to improve gait and motor dysfunction in PD through external cueing but has not been well-studied in DBS. This combination may potentially contribute to further mitigation of beta oscillations and therefore confer enhanced benefits, given internal cueing from DBS coupled with external cueing from music. The objective is to describe outcomes from a 12-week home-based RAS-enhanced walking program completed by Veterans with PD; 1 with subthalamic nucleus deep brain stimulation (STN-DBS), and 1 without.

Methods: Participants were instructed to walk 30-45 minutes, three times per week, listening to a personalized RAS-enhanced music playlist and wearing a FitBit to track activity. Weekly phone calls were made by an exercise coach to assess safety and compliance during the intervention. Motor and neuropsychological assessments were collected pre- and post-intervention.

Results: The MDS-UPDRS Motor III Subscale score improved by 54% in both participants (59 to 27 in DBS; 37 to 17 in non-DBS). Timed Up and Go (TUG) improved by 19% in our DBS patient and 8% in our non-DBS patient. The seven-day average Total Step Count reported by the FitBit increased from 8000 to 12,000 (69% improvement) in our DBS patient, and from 4000 to 6000 (62% improvement) in our non-DBS patient. Self-reported scores in the Activities-Specific Balance Confidence Scale (ABC Scale) increased by 17% in our DBS patient and 9% in our non-DBS patient. Pre-intervention, cognitive processing speed measured by the Symbol Digit Modalities Test (SDMT) was in the normal range for the non-DBS patient and was in the mild impairment range for the DBS patient; post intervention, only the DBS patient improved in processing speed (Z score pre: DBS -1.8, non-DBS 0.3; Z score post: DBS -1.4, non-DBS 0.35).

Conclusions: A 12-week home-based, personalized RAS-enhanced walking program was safe and contributed to an improvement in motor function in both DBS and non-DBS PD Veterans, while increasing overall activity. Our DBS patient demonstrated superior overall improvements on TUG, ABC scale, SDMT, and overall activity suggesting potential enhanced benefits of DBS plus RAS-enhanced gait training.

Cognitive effects of high frequency rTMS to the prefrontal cortex in a patient with atypical parkinsonism

Blake McReavy, Alexandria Umbarger, Sadie Walker, Rama Alsakaji, Kalea Colletta, Theresa Pape, Sandra Kletzel

Introduction: Atypical parkinsonisms are characterized by gait dysfunction, motor, cognitive, and non-motor features, including depression and apathy. The cognitive profile includes deficits in executive function, visuospatial function, verbal fluency, and processing speed. There is a paucity of effective treatments for these cognitive and behavioral impairments. rTMS is a noninvasive approach to modulate brain activity. It is an FDA-approved treatment for depression; research indicates it potential utility for cognitive enhancement in neurodegenerative diseases.

Methods: rTMS was targeted with neuronavigation to the left DLPFC. 15Hz rTMS was delivered at 110% resting motor threshold (5sec/train, 40 trains/session). Neuropsychological assessments were collected pre and post intervention and at 1-month follow-up. Safety measures were collected before and after each TMS session.

Results: Baseline cognitive profile fit the typical presentation of executive dysfunction, with notable deficits in the Wisconsin Card Sorting Task, verbal fluency, Trails B and the Symbol Digit Modality Test. At endpoint, anxiety was attenuated (Beck Anxiety Inventory (BAI) pre=21, post =12), but not maintained at follow-up (BAI=19). Visuospatial function and global cognitive function improved from baseline to follow-up (Hooper Visual Organization Test pre=20, post=27; Montreal Cognitive Assessment pre=23, post=28). There were no serious or unanticipated adverse events.

Conclusions: The is the first report demonstrating the utility of rTMS to improve cognitive function and attenuate anxiety in a Veteran with atypical parkinsonism. Treatment was safe and well tolerated.

Seizure risk associated with the use of transcranial magnetic stimulation for coma recovery in individuals with disordered consciousness after severe traumatic brain injury

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Background: Advances in medical care have resulted in improved survival for individuals with traumatic brain injury. Concomitantly, many people now survive to live with disorder of consciousness (DoC) following traumatic brain injury. Clinicians continue to look for new treatment options for DoC. Repetitive Transcranial Magnetic Stimulation (rTMS) is an emerging treatment to improve level of consciousness for these individuals. However, there is limited evidence about the safety of this intervention for individuals with DoC.

Methods: Data derived from three separate rTMS studies that each enrolled unique participants in states of DoC after TBI were evaluated for associations with adverse events, such as seizures. Subjects received rTMS to the dorsolateral prefrontal cortex (DLPFC) in all three studies. The relationship between adverse events and rTMS was examined using logistic regression. The relationships between both seizure occurrence (SO) and each seizure risk factor/predictor variable were also examined using Pearson correlation. For the significant correlations, contingency chi-square tests were computed with the same variables to confirm significance. Variables with Pearson correlations larger than 0.25 or significant with chi-square tests were included in the logistic regression models as predictors. Specifically, a logistic regression model for each SO outcome was conducted using the group variable (Active rTMS and Placebo rTMS) and variables with correlations > 0.25 or that were significant.

Results: Three subjects were noted to have experienced seizures during the protocols. Two of the seizures occurred during the treatment phase of protocol and one during the placebo phase. Both subjects who experienced seizures during active rTMS treatment were noted to have ventriculoperitoneal shunts. One of these episodes was a subclinical seizure only. There were are no associations between these variables and SO-any day. There was one significant correlation with SO-rTMS day: which was the presence of a VP shunt. There were no associations with any other adverse event.

Conclusion: In this evaluation of safety of rTMS in individuals with DoC following TBI, there was no statistical difference between active and placebo groups with the occurrence of seizures. There was a strong association between the occurrence of seizure during rTMS with the presences VP shunts for hydrocephalus. rTMS appears to be safe and well-tolerated in this patient population. More evidence is needed regarding the efficacy of this intervention.

Age and Sex Impact the Role of Thrombospondin-2 in Response to Hindlimb Ischemia

Ashley Penton MS MD, Melissa Rangel MD, Corinne Bunn MS MD, Sharon Wang MD, Kristopher Maier PhD, Vivian Gahtan MD

Introduction: Angiogenesis and arteriogenesis are physiologic responses to chronic limb ischemia. Gaps in knowledge exist regarding age, sex, and thrombospondin-2 (TSP2, an endogenous inhibitor of angiogenesis) on these processes. Hypotheses: (1) TSP2 will inhibit angiogenesis regardless of age; (2) angiogenesis will be increased in TSP2 null ($TSP2^{-/-}$) compared to wild-type (WT) mice, males compared to females, and young compared to old; (3) arteriogenesis will increase to compensate for decreased angiogenesis.

Methods: *In vitro,* young (passage 2-3) or old (>passage 14) aortic endothelial cell (EC) tubules were formed overnight using a matrigel-based assay. TSP2 was added, incubated overnight and tubule branch points recorded. *In vivo*, male and female WT or $TSP2^{-/-}$ young (14-16 weeks), middle (MA, 58-64 weeks) or old (105-110 weeks) mice underwent femoral artery ligation. Laser Doppler confirmed >50% decrease in blood flow ($p<0.05$). After 14 days, angiogenesis (CD31) and arteriogenesis (αSMA) were quantified using immunohistochemistry. Two-way ANOVA with post hoc testing was performed ($p<0.05$ for significance).

Results: *In vitro:* (1) TSP2 treated ECs had reduced tubule formation in all groups; (2) young ECs formed more tubules than old ECs. *In vivo:* (1) see Table 1; (2) young and MA $TSP2^{-/-}$ male and females had more angiogenesis than old $TSP2^{-/-}$ males and females, respectively ($p<0.05$); (3) there was no difference in arteriogenesis between age groups for either male or female $TSP2^{-/-}$.

Conclusions: TSP2 is an inhibitor of angiogenesis. Animals devoid of TSP2: (1) had increased angiogenesis in young aged and in males; (2) permitted compensatory arteriogenesis compared to WT.

		ANGIOGENESIS	ARTERIOGENESIS
^ = **increased, p<0.05** **$TSP2^{-/-}$ vs. WT**	Young ♂	^	
	Middle ♂		^
	Old ♂		^
	Young ♀	^	
	Middle ♀	^	
	Old ♀		^
$TSP2^{-/-}$ vs $TSP2^{-/-}$	Young ♂ vs ♀	^	
	Middle ♂ vs ♀	^	^
	Old ♂ vs ♀		

Cellular Immunotherapy for Type 1 Diabetes

Shafiya Imtiaz Rafiqi, DVM, PhD, Shahnawaz Imam, DVM, PhD, Juan C Jaume, MD

We recently developed pancreatic beta-cell, antigen-specific, Chimeric Antigen Receptor (CAR) T regulatory cell (Tregs) (1) and explored their therapeutic potential against Type 1 Diabetes (T1D) in our humanized mouse model (2). Ours was the first successful, antigen-specific CAR-Treg treatment of T1D in a mouse model that closely resembles the human disease.

Based on our mice data, we believe treatment with pancreatic beta-cell, antigen-specific CAR-Tregs will allow for recovery and reconstitution of beta cells in human T1D patients as well. Therefore, we studied the biological behavior of Glutamic Acid Decarboxylase, 65 kD isoform (GAD65)-CAR human (h)Tregs over diabetogenic, human (h) cytotoxic T lymphocytes (CTLs) from T1D patients, in the presence of human islets while in culture.

Having shown that GAD65-CAR mouse Tregs are able to find their cognitive antigen in pancreatic islets and proliferate in-vivo, we designed the following experiment to test the hypothesis that anti-inflammatory GAD65-CAR hTregs could suppress diabetogenic, hCTLs attacking heterologous human pancreatic islets ex vivo.

We first isolated hTregs and hCTLs (CD8 and CD4 T cells) from peripheral blood of T1D patients (n=3). A batch of those hTregs was used to generate GAD65-CAR hTregs. GAD65-CAR hTreg and naïve hTregs were also made to express GFP for tracking. Separately, pancreatic tissue was being collected from donors undergoing pancreatectomy for some other clinical indication (i.e. cancer). Pancreas was processed for islet separation using standard collagenase method. GAD65-CAR hTregs and naïve hTregs were then co-cultured with activated autologous CTLs (CD8 T and CD4 T cells) all from T1D patients in the presence of heterologous human pancreatic islets. GAD65-CAR Treg homing and islet viability was monitored daily while in culture using IncuCyte S3 Live-Cell System (Sartorius), and hCTL suppression was assessed by FACS at the end of a 7-day cycle. Supernatant cytokines were assessed by ELISA.

In presence of heterologous human pancreatic islets, GAD65-CAR hTregs homed to islets, got activated, proliferated and suppressed diabetogenic CTLs (CD8 and CD4 T cells). Flow cytometry demonstrated the superiority of GAD65-CAR hTregs over naïve hTregs in suppressing diabetogenic CTLs in the pancreatic islet microenvironment. GAD65-CAR hTregs had significantly higher ($p<0.04$) proliferative capacity compared to naïve hTregs. More importantly, the percentage of diabetogenic CTL suppression was significantly higher with GAD65-CAR hTreg than with naïve hTreg ($p<0.01$).

This work provides evidence for the use of cellular immunotherapy to reverse T1D either directly while pancreatic islets remain or indirectly when pancreatic islet replacement is needed.

Glaucomatous insults result in molecular signatures of reactive astrocytosis and elastinopathy in optic nerve head astrocytes

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Purpose: Glaucomatous optic neuropathy is the leading cause of irreversible blindness worldwide. Biochemical, biomechanical and bioenergetic changes have all been implicated in the pathophysiology of glaucoma. Here, we sought to investigate the effects of multiple disease-relevant stimuli on reactive astrocytosis in primary optic nerve head astrocytes (ONHA).

Methods: Primary rat ONHA were prepared from adult Brown Norway rats. For some experiments, ONHA were transduced with lentivirus expressing the EDN1 gene to generate endothelin-1 (ET-1) overexpressing cultures, or transfected with siRNA targeting lysyl oxidase like-1 (Loxl1) to generate Loxl1-deficient ONHA. Cultures were exposed to 10% static equibiaxial strain in a FlexCell® (FlexCell International) chamber for 16 h. Actin cytoskeleton was labeled with AlexaFluor® 488 phallodin and AlexaFluor® 594 DNAse I for F-actin and G-actin, respectively. Lengths of stress fibers was quantified using Matlab software (MathWorks, Natick, MA). Sensitivity to exogenously-applied oxidative stress was quantified by MTT uptake and lactate dehydrogenase (LDH) release assays. Quantitative PCR, immunoblotting and immunocytochemistry were performed using previously validated primers and antibodies to quantify molecular phenotypes of reactive astrocytosis and elastinopathy.

Results: Mechanical strain, ET-1 overexpression and Loxl1 deficiency all resulted in reactive astrocytosis, as assessed by increases in glial fibrillary acidic protein (GFAP). Reactive astrocytosis resulted in similar changes to elastin expression in response to different glaucomatous insults. Specifically, mechanical strain resulted in a decrease in stress fiber length with a concomitant increase in G-actin immunoreactivity, suggestive of reactive astrocytosis. Furthermore, mechanical strain resulted in a significant decrease in Loxl1 (35% reduction, $P < 0.001$) and elastin (65% reduction, $P < 0.05$) expression. ET-1 overexpressing ONHA exhibited a less-differentiated morphology and significantly increased doubling times, compared with control or non-transduced ONHA. Gene expression changes were similar to those observed in response to mechanical strain for LOXL1 (48% reduction, n=3; $p<0.05$) and elastin (62% reduction; n=3; $p<0.05$). Loxl1-deficient cultures showed ~50% reduction in Loxl1, concomitant with a significant reduction in elastin expression (32% reduction, $P < 0.01$). Changes in elastin gene expression were confirmed by immunoblotting and immunocytochemistry.

Discussion: Our results indicate that reactive astrocytosis in ONHA is associated with molecular signatures of elastinopathy. Notably, elastinopathy phenotypes are similar between different glaucomatous insults, suggesting a unifying molecular pathway eliciting reactive astrocytosis in glaucoma.

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TARGETED DRUG DELIVERY USING LEUKOMIMETIC NANOPARTICLES IN EXPERIMENTAL AUTOIMMUNE NEURITIS, A MODEL FOR GUILLAN-BARRE SNYDROME

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Guillain–Barré syndrome (GBS) is an inflammatory demyelinating polyneuropathy and the leading cause of acute flaccid paralysis. Localized inflammation of the microvasculature within affected nerves (the blood-nerve barrier (BNB)) enables the trans-endothelial migration of circulating autoreactive leukocytes and is an essential pathogenic process for this disease. While experimental autoimmune neuritis (EAN), a well-established rat model of GBS, has progressed our understanding of the GBS pathophysiology, treatment options remain strictly palliative and ineffective. To address this gap in novel therapeutics in the GBS, previous studies demonstrated that high-dose, systemic administration of lovastatin improved EAN. Lovastatin is generally safe, and well-tolerated; however, the high doses required to achieve anti-inflammatory effects are associated with serious side effects clinically. Targeted delivery using drug-loaded nanoparticles (NPs) is a promising technique to administer therapeutics to affected tissue while avoiding systemic toxicity. To begin to investigate the application of NP mediated drug delivery to EAN, we previously demonstrated that lovastatin-loaded NPs locally injected to the sciatic nerve reduced clinical symptoms of EAN. To advance the therapeutic relevance of these findings, we are developing NPs coated with macrophage-derived plasma membrane vesicles (mNPs) as a novel drug delivery system that will promote accumulation of intravenously administered statins in inflamed tissue. The goal of this study was to investigate specificity of macrophages and macrophage-derived plasma membrane vesicles for inflamed endothelium *in vitro* and *in vivo*. Rat NR8383 macrophages are cultured in high yield (3x10^8), collected, and gently lysed using nitrogen cavitation. Plasma membrane vesicles are isolated by differential centrifugation and are shown to retain CD11 and CD18 proteins using western immunoblot. Specificity of mNPs for inflamed over quiescent endothelial cells was demonstrated *in vitro* by performing a functional adhesion assay with NR8383 cells and primary peripheral nerve microvascular endoneurial endothelial cells (PNMECs). Specificity of mNPs to inflamed nerves *in vivo* was demonstrated by administering fluorescently labeled membrane vesicles via tail vein to rats with EAN or healthy controls. Dye accumulation in nerves was qualitatively assessed ex *vivo* with an Odyssey flat bed imaging system and the sciatic nerves from rat with EAN were shown to have higher florescence than healthy control.

Beclin-1 Dependent Autophagy Improves Renal Outcomes Following Unilateral Ureteral Obstruction (UUO) Injury

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Background: Interstitial Fibrosis and Tubular Atrophy (IFTA) is the most common cause of long-term graft failure following renal transplant. One of the hallmarks of IFTA is the development of interstitial fibrosis and loss of normal renal architecture. Autophagy is a conserved cellular process that is activated secondary to cellular stress following ischemia-reperfusion (I/R) injury. In this study, we evaluated the role of Beclin-1 in protecting against post-renal injury fibrosis.

Methods: Adult male wild type (WT) C57BL/6 mice were subjected to Unilateral Ureteral Obstruction, and kidney tissue samples were harvested at 72-hour, 1- and 3-week post-injury. The UUO-injured and uninjured kidney samples were examined histologically for fibrosis, autophagy flux, inflammation as well activation of the Integrated Stress Response (ISR). We compared WT mice with mice carrying a forced expression of constitutively active mutant form of Beclin-1, *Becn1*$^{F121A/\,F121A}$.

Results: In all experiments, UUO injury induces a progressive development of fibrosis and inflammation. These pathological signs were diminished in *Becn1*$^{F121A/\,F121A}$ mice. In WT animals, UUO caused a strong blockage of autophagy flux; though LC3II staining and a 3-fold accumulation of p62 1-week post injury. However, the p62 level was not affected by UUO in *Becn1*$^{F121A/\,F121A}$ mice. Beclin-1 F121A mutants exhibited decreased pSTING signal and limited the production of IL6 and IFNγ, but had little effect on TNF-α Furthermore, activation of ISR signal was detected in UUO-injured in kidneys. Hpwever, *Becn1*$^{F121A/\,F121A}$ mice did not reveal signs of eIF2S1 and PERK activation under the same condition and had a dramatically reduced ATF level at 3-week post injury.

Conclusions: The results suggest that, following UUO, autophagy flux is not able to be completed due to a blockage at the lysosomal degradation step. Therefore, UUO causes an insufficient, maladaptive renal autophagy. Data also suggest that deregulated autophagy triggered downstream activation of inflammatory STING pathway, production of cytokines, and pathological activation of ISR, eventually leading to the development of fibrosis. Enhancing autophagy via Beclin-1 improved renal outcomes with diminished fibrosis, via underlying mechanisms of differential regulation of inflammatory mediators and control of maladaptive ISR. Further work will delineate the role of autophagy in post-injury fibrosis, which may potentially lead to novel and effective therapeutic interventions aimed at ameliorating IFTA.

Functional recovery and neuronal plasticity are enhanced in rats receiving anti-Nogo-A antibody therapy following a traumatic brain injury

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Traumatic brain injury (TBI) can cause sensory and motor functional deficits, and recovery is often slow and incomplete. Currently, there are no effective pharmacological treatments for recovery from TBI, but recent research has indicated great potential demonstrated by anti-Nogo-A antibody therapy. This antibody neutralizes Nogo-A, an endogenous protein that inhibits neuronal plasticity. We modeled TBI in adult male, Long Evans rats, using the controlled cortical impact (CCI) method, resulting in focal brain damage and motor deficits very similar to those observed in humans with a TBI. We hypothesized that treatment with anti-Nogo-A neutralizing antibodies following TBI would result in disinhibited axonal growth from the unlesioned cortex, the establishment of new compensatory synaptic connections, and improvement in functional outcome. First, rats were trained on the skilled forelimb reaching task, which requires the rats to reach through a small window to retrieve a food pellet. Rats were also assessed for baseline performance on the horizontal ladder rung walking task. Then, all rats were given a TBI and one week later were randomly divided into 3 groups: TBI only (n=7), TBI + anti-Nogo-A antibody (n=8), and TBI + control antibody (n=8). Testing on the skilled forelimb reaching task and horizontal ladder rung walking task resumed 3 days after TBI and continued until 8 weeks after TBI. Rats then received an injection of the anterograde neuronal tracer, biotinylated dextran amine (BDA), into the motor cortex contralateral to the TBI, to assess axonal plasticity. Our results indicate significant improvement on both skilled motor tasks in rats that received anti-Nogo-A antibody therapy. In addition, analysis of BDA-positive axons revealed cortico-rubral plasticity to the de-afferented red nucleus in rats in this treatment group. We conclude that anti-Nogo-A antibody treatment may improve functional recovery via neuronal plasticity to brain areas important for control of skilled movements, and this treatment shows promise to improve outcomes in humans who have suffered a TBI.

Keywords: Traumatic brain injury, Nogo, plasticity

Support: VA Polytrauma / TBI System of Care

Tight Junction Protein Expression in Human Trabecular Meshwork Cells

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Purpose: The blood-aqueous barrier (BAB) of the eye is a critical vascular unit that regulates the production, composition, and outflow of aqueous humor (AH). Established and maintained by proteins of tight-, adherens-, and gap-junctions, the BAB is largely localized to the ciliary process nonpigmented epithelium, endothelium of the iris vasculature, and inner wall of Schlemm's canal. Previous studies suggest that dysfunction of the BAB within the conventional outflow pathway contributes to elevated AH outflow resistance. Here, we investigated whether endothelial-like cells of the trabecular meshwork, which are distinct from the BAB, similarly express proteins associated with tight junctions.

Methods: Human primary TM cells were conditioned in serum-free media overnight and subsequently incubated in the absence or presence of TGF-β2 (5 ng/ml) and GAPDH-relative changes in claudin-5, occludins, JAM-1, ZO-1, Nox4, and Col1α1 mRNA expression were quantified. In some experiments, TM cells were challenged with agents previously reported to alter mRNA expression of tight junction proteins.

Results: As we have previously reported, TGF-β2 (5 ng/ml, 24h) elicited marked increases in both Nox4 (700-fold)- and Col1α1 (10-fold)-mRNA expression, consistent with oxidative remodeling of the TM extracellular matrix. TGF-β2 alone, however, did not significantly alter endogenous mRNA expression of tight junction proteins in quiescent TM cells. By comparison, TM cells incubated in the presence of db-cAMP (102 µM) / IBMX (90 µM) exhibited a 6-fold increase in claudin-5 mRNA expression with a concomitant reduction (35%) in ZO-1 mRNA expression. In contrast, co-incubating TM cells with TGF-β2 prevented cAMP / IBMX-mediated changes in claudin-5 and ZO-1 mRNA expression while concurrently potentiating Nox4 mRNA expression.

Conclusions: Cultured human primary TM cells can be induced to selectively increase mRNA for claudin-5, a well-established tight junction protein implicated in endothelial cell barrier function. TGF-β2 dependent changes in claudin-5 and ZO-1 mRNA expression represents a novel mechanism by which this profibrotic cytokine increases Nox4-dependent aqueous humor outflow resistance.

CSP# 596: Optimal Treatment of Recurrent C. difficile Infection (OpTION)

Susan Pacheco, MD; Rabeeya Sabzwari, MD; Co-I: Fritzie Albarillo; MD, Andrew Skinner, MD, SC: Lorinda Guenther-Wright, PhD; Conor McBurney, MPH; Laurica Petrella, RN

Recurrence of *C. difficile* infection (CDI) is a major clinical problem faced by clinicians and patients occurring in 20% to 30% of patients after successful treatment of the first episode. While the burden of hospital-associated CDI has decreased, the burden of first recurrences has not (Guh AY, et al N Engl J Med 2020;382:1320-30).

The IDSA/SHEA treatment guidelines for CDI were recently updated (Johnson S, et al. Clin Infect Dis 2021;73:755-7) and highlight recommendations for treatment of recurrent CDI. Either vancomycin, fidaxomicin, or vancomycin pulse/taper are still recommended options for a first recurrence of CDI, however, these are conditional recommendations based on low certainty of evidence. CSP# 596 includes these same 3 treatment options in a randomized, blinded clinical trial and will provide high quality evidence to help define optimal antibiotic treatment for these patients.

Kidney Transplantation in an elderly veteran population with HCV NAT (+) donors results in improved outcomes following prophylactic Mayvret Therapy

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Background: The average age of waitlisted veterans is 64. Recent data has shown the safety and benefits of using kidneys from HCV viremic [HCV NAT (+)] donors. However, these studies were limited to younger patients with initiation of therapy following transplant. This study aims to determine the safety and efficacy of a pre-emptive treatment protocol in an elderly veteran population.

Methods: This is a prospective, open-label trial. Our cohorts (20 DDKTs with HCV NAT (+) kidneys and 30 DDKTs with HCV NAT (-)] transplanted between 11/2020 and 3/2022. HCV NAT (+) recipients were treated with once-daily Glecaprevir/Pibrentasvir started pre-operatively and continued for 8 weeks. SVR 12 was determined by negative NAT testing. Other endpoints included patient and graft survival as well as graft function.

Results: There was no major difference in the cohorts other than increased number of DCD kidneys in the non-HCV recipients. Post-transplant graft and patient outcomes were equivalent amongst both groups. 8/20 HCV NAT (+) recipients had detectable HCV viral loads 1 day after transplant, but all were undetectable by day 7 with 100% SVR12. Calculated eGFR was improved in the HCV NAT (+) cohort at week 8 (58.26 ml/min vs 47.16 ml/min, $p<0.05$), and continued to be improved over non-HCV recipients one year following transplant (71.38 ml/min vs. 42.15 ml/min, $p<0.05$). Immunologic risk stratification was similar amongst both cohorts.

Conclusion: HCV NAT (+) transplants with a pre-emptive treatment protocol results in improved graft function with minimal to no complications in an elderly veteran population.

Comparative effectiveness of Antibiotic Therapy for Carbapenem-resistant Enterobacterales (CRE) Bloodstream Infections in Hospitalized U.S. Veterans

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Objectives: Carbapenem-resistant Enterobacterales bloodstream infections (CRE-BSI) are associated with significant mortality and have limited treatment options. Guidelines recommending newer antibiotics such as ceftazidime/avibactam were only recently published in 2020. Because these infections are rare, there is a paucity of information on effectiveness and the impact on mortality of different treatments. This study examines treatment regimens and associated mortality risk for patients with CRE-BSI.

Methods: This retrospective cohort study identified hospitalized patients within the VA between 2013-2018 with a positive CRE blood culture and antibiotic treatment within 5 days of culture date. Primary outcomes were in-hospital, 30-day and 1-year all-cause mortality. Secondary outcomes included health care costs at 30-days and one-year and *Clostridioides difficile* infection six weeks post-culture date. The propensity for receiving each treatment regimen was estimated and used in multivariable logistic regression to assess the association between treatment and outcomes.

Results: 393 hospitalized patients with CRE-BSI were predominantly male (97%) and elderly (mean age=71.0±SD12.1). Diabetes and renal disease were the predominant comorbidities (42.7% and 46.8%, respectively). Carbapenems were the most frequently prescribed antibiotic class (47%), while ceftazidime/avibactam use increased from 9% in 2015 to 46% in 2018. In-hospital, 30-day, and one-year mortality was 37%, 36%, and 64%, respectively. In unadjusted analysis, ceftazidime/avibactam was associated with a lower likelihood of 30-day (OR=0.43 (95%CI=0.19,0.96)) and one-year mortality (OR=0.45 (95%CI=0.23,0.88)). However, after propensity score adjustment, there was no difference in mortality associated with any antibiotic treatment. Only 6% of the cohort had a positive *C. difficile* test and no difference was found in *C. difficile* incidence at six weeks post-infection by treatment. Average total 30-day health care total costs ranged from $43,695.50 for aminoglycosides to $48,352.60 for carbapenems, however there was no statistical difference at 30-days or 1-year post culture date by any treatment.

Conclusions: In hospitalized Veterans with CRE-BSI, carbapenems were used most frequently for treatment. Although ceftazidime/avibactam treatment trended towards lower 30-day and one-year all-cause mortality, after propensity score adjustment, this was not significant. During the study timeframe there were no clinical guidelines that specifically addressed treatments for CRE infections. Although the use of ceftazidime/avibactam was not statistically associated with decreased mortality in this study, this was heavily influenced by its low usage due to it only being approved halfway through the study timeframe. There was no difference in cost between any of the treatment regimens.

Impacts: This study provides information on the treatment outcomes of CRE-BSI which is a serious concern for the VA and associated with high Veteran mortality. The evidence from our study shows that there was no difference in outcome or cost for any of the treatment options evaluated suggesting that treatment regimens can be selected based on clinical success. This information can be used to update the current VA Directive and future guidelines for treatment of CRE in the VA.

This could be submitted under the: Quality, Safety, and Value of Healthcare.

Women Veterans' Experiences with Mobility Assistive Technology

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Objective: The purpose of this study was to conduct a needs assessment to learn about women Veterans' needs, priorities, preferences, and experiences with mobility assistive technology (AT). Devices studied included wheelchairs, scooters, walkers, canes, prosthetics, and orthotics.

Methods: Women Veterans receiving care from the Veterans Health Administration who received mobility AT in the last 5 years, identified from VA's corporate data warehouse, were invited to participate in an anonymous online survey. The surveys included questions regarding demographics, training, ability to participate in various activities, and three validated questionnaires that focused on functional mobility, user satisfaction, and psychosocial impact of assistive devices. A subset of Veterans volunteered to participate in semi-structured telephone interviews about their experiences with their AT. Interviews were audio recorded, transcribed, and relevant themes were coded using NVivo.

Results: 700 women Veterans participated in the survey and 11 Veterans completed telephone interviews. Respondents were 50-69 years of age (70%). The three most frequent disabilities women reported were Neuromuscular/Osteoarthritis/Rheumatoid Arthritis, Multiple Sclerosis (MS), and spinal cord injury (SCI) (60%; 27%; 17%). The primary AT most commonly used were canes, walkers, and manual or power wheelchairs. (26%; 24%; 24%). Activities for which their mobility device did not meet their needs included housework, leisure, and social activities (20%; 20%; 17%). Several themes related to patients' experiences with their mobility AT were identified. In general, patients expressed satisfaction with the durability and comfort of their mobility AT. Yet, patients identified several concerns with the procurement process including long wait times and feeling like they could not qualify for the same devices that male Veterans could. Women Veterans reported there were limited mobility AT design options for women, nothing that they feel "whoever is designing things forget that they are women." Patients described that their mobility device did not meet their needs for self-care and housework such as the inability to elevate the wheelchair to prepare food.

Conclusion: Barriers to the mobility AT procurement process, education, and design emerged as the overarching themes that underlie a need for improvement. Women Veterans felt there was a need to customize mobility equipment to better fit women's bodies and needs. Women felt they were limited by what activities they were able to do with their device. Concerns regarding vulnerability, disparities and aesthetics came out during the interviews.

Impact Statements: Issues identified with mobility devices included both gender specific and those of concern to individuals who use AT in general. Considerations specific to gender have not been addressed in the female Veteran population.

Evidence Of Terminal Digit Preference In Veterans Affairs Midwest Region Primary Care Clinics

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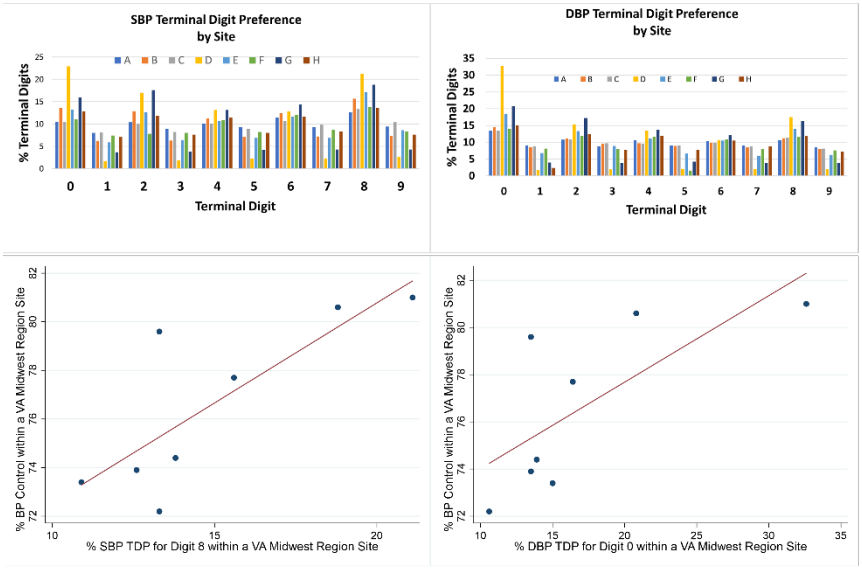
Objective: This study examined terminal digit preference (TDP) and its association with BP control in Veterans Affairs Midwest region clinics.

Methods: TDP was examined in 517, 668 BP values from 202, 781 Veterans age 18 to 85 years during primary care visits from January 1, 2019 to March 1, 2020 across eight Midwest region sites. Presence of TDP was examined using a goodness of fit test with 10 bins. BP control (<140/90 mmHg or <130/80mmHg) was assessed in 98, 433 with diagnosed hypertension based on last clinic visit vital signs. Spearman correlation coefficients examined the association of TDP with BP control.

Results: Mean age was 65.9 (standard deviation [SD]15.7) years, 93.9% (188, 586/202, 781) were male; race was White in 78.1% (153,372/202,781), Black or African American in 16.3% (33, 053/202,781), and Asian in 0.5% (1014/202, 781). For SBP measurements, significant TDP (P<0.001) for digit 8 was noted in all sites ranging from 12.6% (6839/54,279) to 21.2% (18,124/85,493). For DBP measurements, significant TDP was noted (P<0.001) for digit 0 ranging from 13.5% (7327/54276) to 32.7% (27,956/85,493). Among the 8 sites, BP control rates (<140/90 mmHg) ranged from 72.2% (5,947/8,237) to 81.0% (15,405/19,019) while BP < 130/80 mmHg among Veterans with high CVD risk (n=179, 074) ranged from 33.6% (4960/14,762) to 45.5% (8,204/18,233). Both SBP TDP for digit 8 (r=0.80; P<0.05) and DBP TDP for digit 0 (r=0.73; p < 0.05) were significantly and positively correlated with BP control.

Conclusion: Our data show presence of BP TDP in the Midwest region VA sites but frequency varies. The correlation of TDP with BP control rates raises concerns about ability to accurately assess BP control in these sites.

Figure 1. Top figures shows terminal digit preference for systolic (left) and diastolic BP (right) by a Midwest regional VA center. Bottom figures show the correlation between rate of BP control in a Midwest regional VA center with the SBP TDP for 8 (left) and zero (right).



Federal and State Laws Regarding Cannabis: How do VA Providers Manage their Patients?

Kelsey Berryman, MA, Julie Bobitt, PhD and Frances Weaver, PhD

Providers in the Department of Veterans Affairs (VA) healthcare system are caught between
two opposing sets of laws regarding the use of marijuana by their patients. As VA is afederal agency, it must abide by federal regulations including that the Food and Drug Administration classifies marijuana as a Schedule 1 drug (a drug that has no accepted medical use but has a high potential for abuse), and therefore, cannot recommend or help Veterans obtain it. On the other hand, 38 states have passed legislation that allows for the medical use of marijuana. This purpose of this project is to gain an understanding as to how VA providers understand and deal with the possibility that some of their patients are using marijuana in two states, one that has legalized medical marijuana (Illinois) and another that has not (Wisconsin). We surveyed providers who care for Veterans at 4 VA medical centers in two states. We sent email invitations to 433 providers across these sites, of whom 50 responded (12%). While the large majority of respondents knew whether cannabis was legal in their state (85% and 67%, respectively), there was a fair amount of confusion regarding CBD. Most providers discussed the potential impacts of using cannabis with other treatments/medications if one of their patients tested positive for THC but less than 40% would encourage the Veteran not to use cannabis or would change a prescription for a medication that might interact with cannabis. Most providers felt that cannabis might be acceptable for use in end of life (82%) or palliative care (74%). Additional guidance as what is allowed in VA, especially for CBD, is warranted.

Veteran Perceptions of the SCI/D Annual Evaluation

Smith BS, Sippel JL, Etingen B, Evans C, Kale I, Escudero G, Huo Z, Willenberg R, Stroupe KT

Objectives: The Veterans Health Administration (VHA) is the largest system of care for individuals with spinal cord injuries and disorders (SCI/D) in the world. Individuals with SCI/D require medical care to address mobility issues, as well as complications secondary to injury including pressure injuries, pain, bowel and bladder dysfunction, impaired respiratory function, and decreased psychosocial wellness. To address the needs of Veterans with SCI/D, VHA offers a comprehensive Annual Evaluation (AE). An AE can include physical exams and preventive care services for common complications that are secondary to injury. Despite the importance of prevention, as well as managing complications that result from SCI/D, only 45% of Veterans with SCI/D who receive VHA care had an AE in 2021. The objective of this quality improvement project was to collect data about Veterans' perceptions of the AE to inform the development of an intervention to increase AE receipt.

Methods: To examine Veterans' perceptions of the AE, we conducted an online survey using the Qualtrics platform. We identified approximately 8,000 Veterans with VA email addresses and sent them an email invitation to participate. Paper surveys were also mailed to 300 Veterans who did not have a VA email address. Two reminder emails were sent to non-respondents to facilitate response. Survey questions included date and location of AEs, perceptions about the value of AEs, perceived barriers to receiving an AE, and preferences about AE delivery. Overall response rate was approximately 22%. We used frequencies to describe the results.

Results: After excluding participants with missing data,1,573 Veterans were included in the analyses. Most participants (91%) were male. Mean participant age was 65, and 13% were African American and 5% were Hispanic. Of note, 90% of Veterans rated their satisfaction with the AE as excellent, very good, or good; 81% agreed or strongly agreed that the AE meets their urgent medical needs; and 80% indicated that the AE is important for their health and well-being. For Veterans who do not receive an AE every year, the most common barriers to receiving an AE were reported to be COVID-19 (58%), not being offered an AE (17%), and travel barriers (14%). Most Veterans preferred to receive their AE in-person (67%), and most (83%) Veterans indicated it was very important to receive care from an SCI/D specialty physician.

Conclusions: The majority of respondents expressed high levels of satisfaction with the AE and found many aspects of the AE to be valuable. Additional strategies are needed to address travel barriers and access challenges that resulted from the pandemic to bolster AE receipt among Veterans with SCI/D.

Impact: Veterans with SCI/D generally regard the AE as valuable and important for their health, but barriers arising from the COVID-19 pandemic and from travel need to be further mitigated for more Veterans to take advantage of their AE.

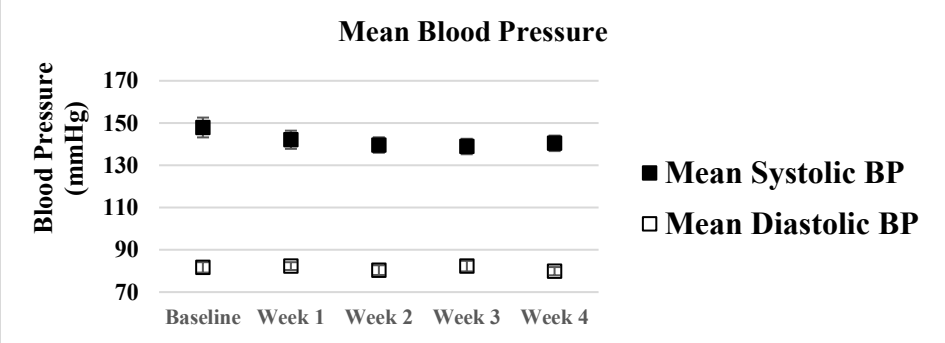
A Pilot Study to Develop A Telehealth Program For Self-Measured Blood Pressure Education And Assessment Within A Veterans Affairs Clinic

Stephanie Bercher MD; Holly Kramer MD; Michael Fayad MD; Nina Giustino BSN RB-BC; Meghan O'Halloran MD

Background: Lack of education and assessment of self-measured blood pressure (BP) monitoring quality is a barrier to its widespread implementation.
Objective: To develop a pilot Veterans Affairs (VA) Telehealth Program utilizing a tool to educate and assess competencies in self-measured BP technique.
Methods: This pilot study was implemented in a single VA internal medicine primary care. Veterans aged 18 to 85 years old with an office-based BP measurement of ≥140/90 or ≥130/80 mmHg and high cardiovascular disease risk were eligible. Enrolled Veterans completed a four-week program whereby trained registered nurses (RNs) educated Veterans on self-measured BP techniques via video conferencing. At each visit, RNs conducted an 11-part assessment tool (Figure 1: top) adapted from the American Medical Association Measure accurately (M), Act rapidly (A) and Partner with patients (P) BP measurement skills assessment for patient self-measured BP technique. Scores could range from 0 (worst) to 11 (best).
Results: Forty Veterans (mean age 66 years [SD 12.6], 100% male) were referred for enrollment and twenty completed the program. In the BP measurement skills assessment, Veterans demonstrated overall high scores at each time point (Top Figure), but errors most frequently were nonadherence to avoiding stimulant use prior to BP measurement; not having an empty bladder; not resting quietly for 3-5 minutes prior to measurement; and talking or using of personal device during measurement. Mean SBP and DBP generally declined over time from a baseline mean SBP and DBP of 147.9 and 81.7 mmHg at enrollment, respectively, to a mean of 140.4 mmHg and 79.9 mmHg, respectively, at program completion, respectively (Figure 1: bottom).
Conclusions: Education and assessment of self-measured BP technique may serve as a meaningful target for future education and quality improvement efforts.

Figure 1: (Top) Veteran adherence to high quality self-measured BP monitoring competencies and (Bottom) Mean BP (95% CI) from enrollment in the telehealth program to completion

Competency Adherence, % (n)	Week 1 (n=20)	Week 2 (n=20)	Week 3 (n=20)	Week 4 (n=19)
Correct cuff size	100 (20)	100 (20)	100 (20)	100 (19)
Empty bladder	90 (18)	95 (19)	95 (19)	84 (16)
Avoided recent exercise, tobacco, caffeine, or stimulant use	85 (17)	95 (19)	95 (19)	79 (15)
Rested quietly for 3-5 minutes	100 (20)	90 (18)	95 (19)	84 (16)
No one talked or used personal device during measurement	95 (19)	90 (18)	95 (19)	89 (17)
Seated with back supported	100 (20)	100 (20)	100 (20)	100 (20)
Feet flat on the floor or foot stool	100 (20)	100 (20)	100 (20)	100 (20)
Legs uncrossed	95 (19)	100 (20)	100 (20)	100 (20)
Arm bare	100 (20)	100 (20)	100 (20)	100 (20)
Arm supported	100 (20)	100 (20)	100 (20)	100 (20)
Arm at heart level	100 (20)	100 (20)	100 (20)	100 (20)



Veteran Perspectives on the Usability of VHA's Mental Health Checkup Mobile Health Application

Lead Presenter: Bixler, FR (Center of Innovation for Complex Chronic Healthcare (CINCCH), Hines VA Hospital)

Bixler FR, Etingen BZocchi M, Higashi RT Richardson E, McMahon N, Patrianakos J, Ndiwane N, Smith BM, Hogan TP,

Objective: Measurement-based care (MBC) practices, wherein providers collect patient-reported outcome measures (PROMs) from Veterans and integrate PROM data into clinical practice, are a priority of the Veterans Health Administration (VHA). The Mental Health Checkup (MHC) mobile health application (app) was developed to support MBC in VHA, and is used to collect PROMs from Veterans remotely, in the context of their daily life. Our objective was to examine Veterans' use of MHC, and perceptions of its usability.

Methods: We completed a mixed-methods evaluation of MHC. We first fielded a mailed survey of Veterans who had logged into MHC at least twice, using a modified Dillman approach. We then completed semi-structured telephone interviews with a purposeful sample of survey respondents. Surveys and interviews asked Veterans about their use of MHC, including comfort using the app, sources of troubleshooting support, and challenges experienced with the app. Survey data were analyzed using descriptive statistics and interview data were analyzed using thematic analysis.

Results: We invited 2,690 Veterans to complete a survey and received responses from n = 533 (20% response rate). Survey respondents were predominantly male (71.0%), non-Hispanic (80.6%) White (66.2%), aged 46-55 (23.9%) or 56-65 (25.6%), and had completed at least some college (90.3%). Most respondents reported being comfortable/extremely comfortable using MHC (78.4%), and 41.2% reported not having had trouble using the app. Among those who did experience trouble using MHC, Veterans reported that, when they encountered difficulties, they sent a secure message to (32.1%) or called (21.8%) their VA providers, or called the VA Technology Help Desk (11.1%). The most frequent issues related to MHC use that Veterans reported to be somewhat or seriously challenging included: the graphs of their assessment scores were hard to understand (41.5%); they did not receive enough training when they first started using MHC (28.1%); they cannot change an answer to an assessment question if they entered it erroneously (28.0%); their provider(s) do not talk to them about their assessment scores (26.8%); and they cannot access the assessments their provider(s) asked them to complete (26.0%). Interview respondents (n = 20) further described challenges they experienced, including technical issues (e.g., links to the assessments did not work, their assessment responses did not get recorded and sent to their providers) and feeling that they had limited resources to turn to for help using the app other than their providers, which could curtail therapy time during appointments.

Conclusions: By and large, the Veterans in our sample found MHC to be easy to use. The challenges Veterans most frequently reported related to a lack of training on how to use MHC, its user interface, and limited discussions with their providers about their assessment scores.

Impacts: MHC has potential to support nationwide efforts across VHA to integrate MBC into mental health services. Efforts to make training resources available and known to Veterans regarding how to use MHC and interact with their data in the app may bolster usability and in turn, sustained use.

Post-traumatic stress disorder (PTSD) and Parkinson's disease (PD) risk in a Veteran Cohort

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ABSTRACT

Background: Stress has been proposed as a possible risk factor for Parkinson's disease (PD), but limited supportive data are available. PTSD is an increasingly recognized condition occurring in military Veterans, with an estimated prevalence up to 15% in those previously deployed. The Veterans Health Administration (VHA) electronic medical record (EMR) provides a powerful resource to investigate this relationship.

Objectives: To examine the relationship between PTSD and PD diagnosis in a large US Veteran cohort.

Methods: We studied 340,489 US Marine Corps Veterans based at Camp Lejeune, NC or Camp Pendleton, CA between 1975 and 1985. We identified Veterans who utilized any VHA health care services (10/1/99- 2/17/2021) and/or Medicare (1/1/2000- 12/31/2018) and reviewed medical records of all with ≥1 diagnostic codes for PD (ICD9 332.0 or ICD10 G20) to validate and determine incident date of diagnosis. We defined PTSD as having at least one ICD9 (309.81) or ICD10 (F43.10, F43.11, F43.12) code in the VHA EMR or in Medicare. We tested associations of PTSD and PD risk using a nested case-control design, matching 10 controls to each veteran with PD on age at diagnosis ("index date"), gender, race, and rank. We adjusted for Camp, duration in VA, smoking status and age in conditional logistic regression models and conducted a sensitivity analysis restricted to cases and controls with any VHA usage prior to PD index date.

CASE FINDING FOR VETERANS WITH A PARKINSON'S DISEASE (PD) DIAGNOSIS BY CAMP

	Camp Lejeune	Camp Pendleton	Total
Marines in ATSDR database (1975-1985)	172,128	168,361	340,489
Veterans with any VA or CMS use (2000-2021)	84,824	73,298	158,122 (46%)
Any diagnosis of Parkinson's disease (PD)	603	459	1,064
Chart review of cases to confirm PD	279	151	430 (40%)
Active VA use prior to PD diagnosis	181	95	276

CHARACTERISTICS OF VETERANS WITH/WITHOUT PD (1:10 MATCH)

	Confirmed PD diagnosis (N=430)	No PD diagnosis (N=4300)	Total (N=4730)
Sex-male female	413(96.1%) 17(3.9%)	4,130(96.1%) 170(3.9%)	4,543 187
Race – white black other	367(85.4%) 49 (11.4%) 14 (3.3%)	3,670 (85.34%) 490 (11.4%) 140 (3.23%)	4,037 539 154
Hispanic	27(6.3%)	342 (7.9%)	369
Military Rank – officer -enlisted	38 (8.8%) 392 (91.7%)	380 (8.8%) 3,290 (91.7%)	418 4,312
Smoking status – ever never missing	164 (38.2%) 164 (38.2%) 102 (23.7%)	2,020 (47.1%) 1,062 (24.78%) 1,218 (28.3%)	2,184 1,026 1,320
Age (at index date)	54.20 (std=7.4)	54.13 (std=7.5)	54.13 (std=7.4)
PTSD diagnosis (2 or more)	48 (11.2%)	419 (8.9%)	467 (9.9%)

COMPARISON OF PD+PTSD VS. PD CASES

	PD + PTSD (n=83)	PD only (n=347)	All PD (N=430)
Male	96.4%	95.6%	96%
Mean Age at index date	54.4 (std=7.7)	54.1 (std=7.3)	54.2 (std=4.4)
Race White Black Other	 85.5% 8.4% 6%	 85.3% 12.1% 2.3%	 85.4% 11.4% 6.3%
Hispanic	9.6%	5.5%	6.3%
Duration at Camp (mos)	25.2 (20.7)	25.8 (18)	25.7 (18.6)
Rank Enlisted Officer	 95.2% 4.8%	 90.2% 9.8%	 91.2% 8.8%
Toxin Exposure*	42.2%	41.5%	41.6%

*Toxin exposure only occurred at Camp Lejeune due to contaminated water. Approximately 2/3s of Camp Lejeune residents had exposure

PTSD is the most common reason for service-connected disability in the US Veteran population

The prevalence of PD is growing, and one possible reason is the association with toxins in our environment

Neuroinflammation is implicated in both PTSD and PD

PREDICTORS OF PD RISK*

	Estimate	Wald Chi-Square	P value	Point Estimate (CI)
Camp Lejeune	0.097 (0.06)	2.49	0.11	1.102 (0.97-1.24)
Attained Age^	0.34 (0.11)	8.41	0.004	1.41 (1.12-1.78)
PTSD#	0.38 (0.07)	29.30	<.0001	1.46 (1.27-1.68)
Duration (yrs)+	0.64	7.00	0.008	1.89 (1.18-3.04)
Ever Smoked	-0.57 (0.06)	79.0	<.0001	0.57 (0.50-0.64)
Missing smoking	-0.17 (0.10)	2.96	0.09	0.85 (0.70-1.02)

*N=2515 (257 PD cases with 10 matched controls – no PD) – this represents those who were active users of VA prior to PD diagnosis
^ attained age = age as of 2/17/21 (end of data collection) or death, whichever came first
+ Duration = duration of any VA health care use
# At least one PTSD diagnosis occurred prior to PD diagnosis

DISCUSSION AND CONCLUSIONS

- Less than half (46%) of the Veterans in our cohort utilized VA healthcare services between 10/1999 and 2/2021
- Reliance on diagnostic codes only, particularly for diseases for which there are no definitive tests, results in overidentification (chart review validation resulted in only 40% of PD cases to be probable PD)
- Having a prior diagnosis of PTSD was a significant predictor of being diagnosed with PD [OR 1.46; (1.27-1.68)]
- PD diagnosis was also associated with increased age, longer duration of VA health care use, and negatively associated with ever or missing smoking status
- Although not statistically significant, closer examination of the role of toxin exposure during residence at Camp Lejeune is warranted as both PTSD and PD are associated with neuroinflammation

ACKNOWLEDGEMENTS AND DISCLAIMER

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Antibiotic utilization trends in Veterans Affairs patients with Stenotrophomonas maltophilia bloodstream infections

Clara H. Lee, Ursula C. Patel, Amanda Vivo, Lishan Cao, Charlesnika T. Evans

Background: Stenotrophomonas maltophilia is a multidrug resistant gram-negative bacillus that has the potential to cause serious infections in vulnerable hosts. Historically, trimethoprim-sulfamethoxazole (TMP-SMX) has been the preferred agent for S. maltophilia infections, but there is limited clinical data to support its use over alternative therapies. The goal of this study is to establish trends in treatment of S. maltophilia bloodstream infections (BSI) using national Veterans Affairs (VA) data.

Methods: This is a national VA, retrospective cohort study within a 10-year timeframe from 2012 to 2021. All veterans ages ≥18 years with ≥1 positive blood culture for S. maltophilia within the VA Health System during the specified time frame were included. The VA national microbiology, pharmacy, and encounter data sources were utilized to collect culture data and antibiotics administered. Chart reviews were conducted to verify microbiologic results and obtain additional patient data. Treatment strategies were categorized by antibiotic agents selected. Descriptive and bivariate statistics were used to summarize patient demographics, facility characteristics, microbiologic data, and treatment trends.

Results: A total of 374 blood cultures positive for S. maltophilia were identified across 75 VA facilities. The frequency of S. maltophilia blood cultures decreased over time, with 14.4% of the cultures in 2012 and 3.5% in 2021. Out of the 282 unique BSI cases, most patients were male (93.6%), white (67.4%), and the mean age was 64 ± 13.1 years. Of those patients, 5.3% had a documented sulfa allergy, 12.8% had polymicrobial blood cultures, 25.5% were diagnosed with end-stage renal disease, and 78% received treatment for S. maltophilia BSI. The most commonly tested agents for susceptibility were TMP-SMX, levofloxacin, and ceftazidime with 4.5%, 4.3%, and 44.4% resistant isolates, respectively. The antibiotics that were most utilized were TMP-SMX (41.5%) and levofloxacin (39.4%), followed by ciprofloxacin (13.8%) and ceftazidime (12.4%). Combination therapy, with ≥2 active agents, was given in 32.6% of the cases. No significant trends were found with TMP-SMX and fluoroquinolone prescribing over time.

Conclusions: TMP-SMX and levofloxacin were the most commonly used antibiotics for the treatment of S. maltophilia BSI in veterans during 2012-2021. Despite TMP-SMX being the preferred agent historically, its use was comparable to fluoroquinolones. These trends could partly be explained by the high risk of adverse effects associated with TMP-SMX especially in the presence of renal dysfunction, which was common in our patient population.

Survey on the Impact of VA Medication Copayment Restructuring on Veteran cost of medications and use of non-VA pharmacies

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Objectives: In February 2017, VA restructured their outpatient medication copayment system. Previously, VA charged non-exempt Veterans either $8 or $9 for each 30-day or less supply of medication. Under the restructured system, VA created 3 medication tiers similar to the private sector distinguished, in part, by whether the medications are available from multiple or single sources. Restructured copayments per 30-day supply are based on their medication tier classification: $5, $8, and $11 per 30-day supply for tier 1-3 medications, respectively. VA also lowered the cap on annual medication copayments for Veterans from $960 to $700. This study utilized a survey to assess the impact of the copayment restructuring on Veterans' medication costs and use of non-VA pharmacies.

Methods: We conducted a national cross-sectional survey of Veterans in 2018 to understand their perspectives about the VA's copayment restructuring. We invited a random sample of 10,000 Veterans with chronic conditions treated with medications (i.e., diabetes, hypertension, hyperlipidemia, depression, benign prostatic hyperplasia, or rheumatoid arthritis) who utilized VA services between 2/1/2015-1/31/2017 to complete the survey by mail. We received responses from 2,884 Veterans (29% response rate). We compared survey responses between Veterans with (vs. without) VA medication copayments using Chi-square tests. Analyses were weighted to account for sample design and non-response.

Results: After weighting, the sample was 8% female, 17% Black, and 58% married with a mean age of 66 years. Over 71% had an annual household income of <=$35,000, and 23% had a bachelor's degree or higher. Just under half of our sample (42%) had VA copayments for at least 1 medication, and 39% received medications from non-VA pharmacies in 2018. A larger portion of Veterans with (vs. without) VA copayments who obtained non-VA medications reported obtaining them to save money (39% vs. 12%, $p<0.001$). Regarding medication use in 2018, a larger portion of Veterans with (vs. without) VA copayments reported that due to the copayment restructuring they obtained medications from VA they previously obtained outside VA (10% vs. 8%, $p<0.001$) or obtained medications outside VA they previously obtained from VA (8% vs. 3%, $p<0.001$). Veterans with (vs. without) VA copayments reported that the copayment restructuring helped control prescription costs (29% vs. 15%, $p<0.001$) and that monthly medication costs were much lower after the copayment restructuring (20% vs. 9%, $p<0.001$). However, even with the copayment restructuring, a larger portion of Veterans with (vs. without) VA copayments reported that medication costs are still a significant burden (19% vs. 4%, $p<0.001$); they worried about being able to pay for prescriptions (31% vs. 12%, $p<0.001$); and they spent less on utilities and other basic needs to have enough money for prescriptions (18% vs. 5%, $p<0.001$).

Conclusions: A substantial portion of Veterans (20-30%) with medically treated chronic conditions reported that the VA copayment restructuring decreased their medication financial burden. However, even with the copayment restructuring, a portion of Veterans continue to worry about the costs of medications and make tradeoffs between medications and other needs.

Impact: VA could consider additional copayment reforms targeting those facing the greatest burden from medication costs.

Developing and Validating a Decision Support Tool to Prevent Community Acquired Pressure Injuries in SCI

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Background: Pressure injuries (PrI) are the second leading cause of hospitalization in people with spinal cord injury (SCI). The majority of PrIs occur in the community, but there is little specific guidance available on community-acquired PrI (CAPrI) prevention. Current PrI prevention clinical guidelines are based on institutional care, and do not directly address risk factors in the community. To date, there are no instruments to guide CAPrI preventive care for persons with SCI. This presentation describes the development and evaluation of a decision support tool to prevent CAPrIs in individuals with SCI for use in the SCI clinic that is grounded in current guidelines and qualitative research.

Research Design: Concept mapping to draft the tool and Delphi method to validate the tool.

Methods: Concept mapping with literature review, current guidelines and qualitative research was used to develop 14 Veteran checklist items (Items) along with 11 associated healthcare provider actions (Actions) on the tool. Delphi surveys were used to validate Items and Actions with a panel of interprofessional SCI provider experts in PrIs (n = 15), Veterans with SCI (n = 4) and caregivers (n = 3). Two Delphi surveys measured agreement on a 4-point Likert scale (strongly agree – strongly disagree) for each Item and Action in terms of: research and existing evidence, measurement framework, item format, level of language, and overall agreement of appropriateness along with open comments. Agreement was set a priori at 75% of responses rated as strongly agree or agree.

Results: Panelists were 60% female, 65% Black, 30% wound care certified with a mean age of 59 years. Two survey rounds were required. Response rate was 95% for Round 1 and 100% for Round 2. Round 1 showed all 14 Items and 11 Actions affirmed for agreement above 75%. Open comments guided Item and Action revisions with Item comments most related to 'language' with suggested revisions and Action comments related to 'completeness' with suggestions additional referrals. Delphi Round 2 included 6 revisions, 3 Items and 3 Actions, all affirmed for agreement above 83%. The final tool includes a 14-item Veteran survey to be programed on an iPad app and a Provider report of recommended actions based on Veteran responses.

Conclusions: A decision support tool was affirmed for face and content validity for usability and acceptability by both patients and providers.

Learning Objectives (3) measurable learning objectives using action verbs; the learner will describe, explain, discuss, etc.

1. Describe how qualitative results and clinical practice guidelines were mapped to Veteran survey items and associated provider actions. 2. Describe the Delphi process and how the Delphi method can be used to determine content validity. 3. Discuss how the Delphi results supported the development of a Veteran survey and provider report. 4. Describe the actionable steps that can be implemented using the final tool.

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Variations in Implementation of Antimicrobial Stewardship via Telehealth at Select VA Medical Centers

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Background: Antimicrobial stewardship programs (ASPs) seek to reduce the prevalence of antimicrobial-resistant and healthcare-associated infections. There are limited infectious disease (ID) physicians and pharmacists to support these ASPs, particularly in rural areas. The Veteran Health Administration has a robust telehealth program in place. Our previous work has demonstrated the feasibility of using telehealth modalities to support ASPs at rural Veterans Affairs medical centers (VAMCs) by pairing them with an ID expert from a larger, geographically distant, VAMC. This program, dubbed the Videoconference Antimicrobial Stewardship Team (VAST), emphasizes on discussion of patients undergoing treatment for an active infection and additional relevant clinical topics with a multidisciplinary team at the rural VA. VAST dissemination is ongoing at VAMCs. To understand and compare the qualitative differences in implementation, we used process maps to describe the VAST at 3 VAMC dyads.

Methods: Team members from each dyad participated in interviews at 3, 6, and 9 months after beginning their VAST sessions. Questions addressed several aspects of VAST implementation and included identifying cases and topics to discuss; advance preparation for meetings; the frequency and general structure of VAST meetings; along with the documentation including workload capture. The research team used the responses to develop process maps to permit visual display and comparison of VAST implementation.

Results: The first dyad began in January 2022 and the third in March 2022. The sessions had three phases: preparation, team meeting, and documentation of experts' recommendations, with tasks shared between VAST champions at the rural VAMC and the ID experts. The preparation phase evidenced the most variation among the 3 dyads. In general, champions at the rural VA identified cases and topics for discussion that were sent to the ID expert for review. The approach used to find cases and the type of preparatory work by the ID expert differed. Team meetings differed in both frequency and participation by professionals from the rural site. Documentation of expert recommendations processes appeared similar among the dyads.

Discussion: Each of the 3 dyads implemented VAST differently. These results suggest that the overall structure of the VAST is readily adaptable, and that each site tailored VAST to suit the clinical needs, workflow, and culture of their partner facility. Future work will seek to determine which aspects in the preparation, team meeting, or documentation phases are associated with successful ASPs, including assessment of quantitative and qualitative outcomes.

The Impact of Including Medicare Data in Research on Veterans with COVID-19

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Objectives: Many Veterans who test positive for COVID-19 in the VA also receive healthcare outside the VA that is paid for by Medicare. The purpose of this study is to assess Medicare utilization for these Veterans and to identify which groups are most likely to utilize Medicare in the 2-month period following COVID-19 diagnosis (post-COVID period). We will also determine the benefit of adding Medicare data to ascertain additional comorbidities for Veterans with COVID-19.

Methods: Veterans who tested positive for COVID-19 in a VA facility prior to 8/1/22 were identified from the VA's COVID-19 Shared Data Resource. Medicare fee-for-service (FFS) claims data were examined during the 60 days following a Veterans' first positive test in a VA facility (post COVID period). Due to the lag in Medicare data availability, the cohort was limited to Veterans who tested positive prior to 8/1/22 to include 60 days of follow-up. Logistic regression was used to examine predictors of Medicare utilization. Two variations of the Charlson Comorbidity Index (CCI) were calculated with 12 months of pre-COVID-19 data, one using only VA data and one using combined VA and Medicare data.

Results: Among 772,735 Veterans who tested positive for COVID-19 in a VA facility, 11% of Veterans under 65 and 97% of Veterans 65 and older were enrolled in Medicare. Overall, 71% of Medicare enrollees were in fee for service (FFS), as opposed to Medicare Advantage. Because data are currently available only for FFS enrollees, further results are limited to FFS enrollees (n=224,776). During the post-COVID period, 4.7% of Veterans had an ER visit, 7.5% had an inpatient stay, and 4.8% had a SNF stay. 41.3% of Veterans had any Medicare utilization during the post COVID period. Medicare utilization increased with age. We identified almost 21,000 inpatient stays, the majority of which (78%) included a diagnosis code for COVID-19. Predictors of use: The odds of any Medicare utilization in the post-COVID period increased with age and number of comorbidities, while odds of Medicare use was lower among Veterans who had used VHA in FY19. Comorbidities: When using only VA data, 10% of Veterans had a CCI score of 3 or higher, whereas using combined VA and Medicare data, 20% had a score of 3 or higher. For all conditions contained within the CCI, the number of patients identified with each condition increased significantly, often doubling, when adding Medicare data.

Conclusions: Many Veterans who tested positive for COVID-19 in VA received care in the post-COVID period outside of VA paid for by Medicare, including inpatient care related to their COVID-19 infection. Veterans most likely to use Medicare after testing positive in VA were older and had more comorbidities. Including Medicare data allowed for the identification of significantly more comorbidities as compared to using VA data only.

Impact Statement: Researchers should add Medicare data to their analyses to obtain a more complete picture of healthcare utilization post COVID-19 infection. Comorbidities identified utilizing only VA data should be considered incomplete for Veterans who receive healthcare outside the VA. In the future, as the data become available, other sources of non-VA healthcare should also be considered for inclusion, such as Medicaid and Medicare Advantage.