



WAYNE STATE

Eugene Applebaum College of
Pharmacy and Health Sciences



15th Annual College Research Forum

2018

Table of Contents

Organizing Committees	iii
Agenda	iv
Guest Speaker: Randy L. Jirtle, Ph.D.	v
Abstracts	1
Faculty.....	1
Postdoctoral Fellow	7
Health Care Sciences.....	16
Pharmaceutical Sciences.....	33
Pharmacy Practice.....	53

Organizing Committees

Research and Grants Committee

Diane Adamo, Chair
Kyle Burghardt
Kathleen Chardenet
Fei Chen
Malcolm Cutchin
Christine Davie
Aloke Dutta
Heather Fritz
Arun Iyer
Moh Malek
Anna Moszcynska (Assoc Chair)
Mary Jo Pilat
Michael J. Rybak
Timothy Stemmler (Assoc Dean of Research)

Research Forum Administrative Committee

Sonya Bell
Marissa Rossman
Daisy Wright

Agenda

- 8:00 a.m. Poster Setup
- 9:00 a.m. Student Poster Presentations
- 11:00 a.m. Welcome
Catherine Lysack, Interim Dean, College of Pharmacy and Health Sciences
Steve Lanier, Vice President for Research
- 11:05 a.m. Introduction of Keynote Speaker by Moh Malek, Ph.D.
Keynote Speaker
Randy Jirtle, Ph.D.
- 12:00 p.m. Presentation of Awards
Poster Awards
Diane Adamo, Ph.D., College Research Committee Chair
College Research Awards
Tim Stemmler, PhD., Assoc Dean of Research
- 12:30 p.m. Lunch
- 12:30–3:00 p.m. Poster Display and Presentation

Guest Speaker: Randy L. Jirtle, Ph.D.

Professor Randy L. Jirtle headed the epigenetics and imprinting laboratory at Duke University until 2012. He is now a Professor of Epigenetics in the Department of Biological Sciences at North Carolina State University, Raleigh, NC, and a Senior Scientist in the McArdle Laboratory for Cancer Research at the University of Wisconsin, Madison, WI. Jirtle's research interests are in epigenetics, genomic imprinting, and the fetal origins of disease susceptibility.



He has published over 200 peer-reviewed articles, and was a featured scientist on the *NOVA* television program on epigenetics entitled *Ghost in Your Genes*. He has delivered numerous endowed lectures, and was invited to speak at the 2004 Nobel Symposia on Epigenetics. He was honored in 2006 with the Distinguished Achievement Award from the College of Engineering at the University of Wisconsin-Madison. In 2007, Jirtle was nominated for *Time Magazine's* "Person of the Year." He was the inaugural recipient of the Epigenetic Medicine Award in 2008, and received the STARS Lecture Award in Nutrition and Cancer from the National Cancer Institute in 2009. Jirtle was invited in 2010 to participate in the Aspen Ideas Festival in Colorado, and the Nestlé's 7th International Nutrition Symposium in Switzerland. Jirtle organized the *Keystone Environmental Epigenomics and Disease Susceptibility* meeting, received the EHP Classic Paper of the Year Award, and was invited to speak again in the Nobel Forum at an epigenomics symposium sponsored by The Nobel Assembly at the Karolinska Institutet in Stockholm in 2011. Dr. Jirtle was invited in 2012 to present the NIH Director's WALSH lecture. Jirtle participated in the World Science Festival in New York, gave the Killam Lecture at Dalhousie University, and published two books on *Environmental Epigenomics in Health and Disease* in 2013. Dr. Jirtle received the Jean Andrews Centennial Faculty Fellowship in Human Nutrition from the University of Texas-Austin, delivered the Robert B. Church Lecture in Biotechnology at the University of Calgary, and received the Linus Pauling Award from the Institute of Functional Medicine in 2014. In 2016, Jirtle delivered the commencement address in the Department of Biological Sciences at North Carolina State University. ShortCutsTV did an English documentary in 2017, *Are You What Your Mother Ate? The Agouti Mouse Study*, which is based on Jirtle's epigenetic research. He received in 2018 the Northern Communities Health Foundation Visiting Professorship Award at University of Adelaide in Australia.

Abstracts

Faculty

ABSTRACT NO. 1	
Name	Azizeh Abusabha
Category	Faculty
Title	The Impact of Diabetes Knowledge and Distress on Diabetes Self-Management in Arab Americans.
Authors	Dana El Masri, PharmD; Azizeh Abusabha; Ashley Semma; Hanan Saleh; Amina Ammar; Linda Jaber, PharmD
Abstract	<p>Purpose: Fatigue is a prominent and debilitating symptom of multiple sclerosis (MS); up to 92% of individuals report fatigue that manifests as lack of energy, exhaustion or worsening of MS symptoms and ultimately contributes to increasing disability. Although exercise therapy is known to improve fatigue in persons with MS, access to these services is limited for many persons with MS. Telephone-delivered exercise interventions have the potential to increase participation in exercise and physical activity; however, no studies have investigated the feasibility and acceptability of telephone-delivered exercise interventions to target MS fatigue, nor have any studies compared the efficacy of telephone-delivered exercise therapy to traditional one- on-one, in-person delivered exercise therapy. The aims of this study were to determine the feasibility and acceptability of a telephone-delivered exercise intervention to target fatigue in persons with MS and to determine comparative effectiveness of a telephone-delivered vs. in-person delivered exercise therapy to target fatigue in persons with MS.</p> <p>Methodology: 20 individuals (mean (SD) age: 48.0 (7.8) years; symptom duration: 14.2 (10.0) years; 2 males; median [range] PDDS: 3 [0-5] with MS were randomized to receive either the in-person (n=10) or telephone-delivered (n=10) exercise for 8 weeks. Regardless of group allocation, all individuals received one in-person session where they were trained on the exercises, and prescribed 2x/week of aerobic exercise and 3x/week of leg strengthening exercises using elastic bands. Individuals in the in-person group worked with a trainer in-person 1x/week while those in the telephone group spoke with the trainer 1x/week on the phone. All participants received 1 hour of contact with the trainer/week in which the trainer progressed exercises and delivered educational content.</p> <p>Results: All individuals completed the intervention, but 1 participant was lost to follow-up. Our results indicate that telephone-delivered exercise is feasible, as evidenced by a 95% adherence rate (compared to 98% for in-person), and acceptable; 100% of participants reported that they were very satisfied with the intervention, with an average score of 31.1 (1.1) out of a possible 32 points on the Client Satisfaction Questionnaire. Both telephone-delivered and in-person exercise reduced fatigue in persons with MS; both interventions resulted in an average 14.5 point reduction in the Fatigue Severity Score. Similarly, both interventions resulted in vast improvements in physical activity, with the greatest improvement seen in time engaged in strenuous exercise. Conclusions: These results fill a significant gap in the literature by confirming the feasibility, acceptability and effectiveness of an alternative to traditional exercise therapy to target one of the most debilitating symptoms of MS, fatigue. Telephone-delivered exercise therapy target fatigue overcomes many of the barriers experienced by persons with MS, including transportation, finances and proximity to a major medical center.</p>

ABSTRACT NO. 2	
Name	Nora Fritz
Category	Faculty
Title	Feasibility, Acceptability and Effectiveness of Telephone-Delivered Exercise Therapy to Target Multiple Sclerosis Fatigue
Authors	Anna Kratz; PhD, Mareena Atalla, BS; Abigail Myles, BS; Taylor Thurston, BS; Nora Fritz, PhD, PT, DPT, NCS
Abstract	<p>Purpose: Diabetes self-management (DSM), a vital component of care for patients with diabetes, entails culturally-shaped health behaviors. Several culturally-specific barriers to selfmanagement have been identified in different ethnicities in the United States. Despite the increasing prevalence of diabetes in Arab Americans, there remains a lack of data on the effects of social and cultural factors on DSM in this population. The current study evaluated the effects of diabetes knowledge and diabetes distress on DSM activities in Arab American patients with type 2 diabetes.</p> <p>Methodology: Arab American patients with type 2 diabetes were recruited from the general public. Data was collected via face to face interviews using a general demographics questionnaire and three validated scales to assess diabetes knowledge and distress and self-care activities. The diabetes knowledge survey (DKT) consists of 14 questions related to general diabetes information and 9 additional questions related to insulin users. The diabetes distress scale (DDS) consists of 28 questions that are scored from 1 (not a problem) to 6 (a very serious problem). This scale assesses the participants' emotional distress associated with the experience of living with diabetes with 7 subscales (powerlessness, management distress, hypoglycemia distress, negative social perceptions, eating distress, physician distress, and friend/family distress). The Summary of Diabetes Self-Care Activities (SDSCA) scale consists of 11 questions and assesses general and specific diet, exercise, blood glucose monitoring, foot care, and smoking. Descriptive statistics were used for the analyses.</p> <p>Results: One hundred and eighty-one Arab Americans adults with type 2 diabetes completed the surveys. The mean age standard deviation (SD) was 62.12 years; 53% of participants were males and 51% were of Lebanese decent followed by Iraqis. Majority of participants were immigrants (96%). About one third reported no formal education. Majority were managed with oral diabetes agents; only 25% were maintained on insulin. Knowledge related to diabetes was generally poor; 26% of patients were able to identify proper treatment of hypoglycemia. The overall mean DDS score was 1.9 indicating generally low distress; however, approximately 25% of patient responses indicated high distress across all subscales. The mean scores varied across the 7 subscales: feeling of powerlessness, eating and management distress had higher mean scores of 2.4, 2.3, and 2.1, respectively indicating moderate distress. The overall mean SDSCA score was 3, which indicates that patients participated in DSM activities only 3 days per week. Patients scored the lowest on the exercise subscale, with a score of 2 days per week.</p> <p>Conclusions These findings emphasize the need for targeted patient-specific interventions aimed at improving diabetes knowledge and reducing sources of distress. These findings will inform the development of a culturally-specific DSM program for Arab American patients with diabetes.</p>

ABSTRACT NO. 3	
Name	Sean McConachie
Category	Faculty
Title	TNF Alpha Antagonist-Associated Infections in Inflammatory Bowel Diseases: A Case Series Analysis
Authors	Sean M. McConachie, Pharm.D., BCPS; Pramodini B. Kale-Pradhan, Pharm.D., FCCP; Julia Kulesza, Pharm.D.; Sheila M. Wilhelm, Pharm.D.
Abstract	<p>Introduction: Tumor necrosis factor-alpha (TNF-α) antagonists have been associated with an increased risk of opportunistic infections in cohort studies, case reports, and certain meta-analyses; however, data describing the specific infections reported and potential risk factors for infections is sparse.</p> <p>Objectives: The aim of this study was to consolidate available case report evidence linking TNF-α antagonists to infections to identify possible patterns that can guide future studies.</p> <p>Methods: A literature search was performed to identify all case reports of infections associated with TNF-α antagonists in patients with inflammatory bowel disease. Publications that did not include patient-level data were excluded.</p> <p>Results: A total of 101 cases of TNF-α antagonist-associated infections from 94 case reports were identified. The majority of cases were reported in infliximab patients (85%), in men (70%), and in patients with Crohn's disease (85%). Concomitant immunosuppressive therapy was common, with 73% of cases reporting at least one additional agent. Eleven cases resulted in patient mortality. The most common infections reported were Mycobacterium sp., Pneumocystis jiroveci, varicella zoster virus, and Legionella sp. The time from therapy initiation to manifestation of infection varied greatly; however, the majority of reported infections occurred within the first 6 months of therapy and within the first 3 doses of medication.</p> <p>Conclusions: A wide range of opportunistic infections have been reported in patients receiving TNF-α antagonist therapy. Knowledge of the types of infections associated with these agents may help improve clinical vigilance and adherence to preventive care guidelines.</p>

ABSTRACT NO. 4	
Name	Nora Fritz
Category	Faculty
Title	Feasibility, Acceptability and Effectiveness of Telephone-Delivered Exercise Therapy to Target Multiple Sclerosis Fatigue
Authors	Anna Kratz; PhD, Mareena Atalla, BS; Abigail Myles, BS; Taylor Thurston, BS; Nora Fritz, PhD, PT, DPT, NCS
Abstract	<p>Purpose: Diabetes self-management (DSM), a vital component of care for patients with diabetes, entails culturally-shaped health behaviors. Several culturally-specific barriers to selfmanagement have been identified in different ethnicities in the United States. Despite the increasing prevalence of diabetes in Arab Americans, there remains a lack of data on the effects of social and cultural factors on DSM in this population. The current study evaluated the effects of diabetes knowledge and diabetes distress on DSM activities in Arab American patients with type 2 diabetes.</p> <p>Methodology: Arab American patients with type 2 diabetes were recruited from the general public. Data was collected via face to face interviews using a general demographics questionnaire and three validated scales to assess diabetes knowledge and distress and self-care activities. The diabetes knowledge survey (DKT) consists of 14 questions related to general diabetes information and 9 additional questions related to insulin users. The diabetes distress scale (DDS) consists of 28 questions that are scored from 1 (not a problem) to 6 (a very serious problem). This scale assesses the participants' emotional distress associated with the experience of living with diabetes with 7 subscales (powerlessness, management distress, hypoglycemia distress, negative social perceptions, eating distress, physician distress, and friend/family distress). The Summary of Diabetes Self-Care Activities (SDSCA) scale consists of 11 questions and assesses general and specific diet, exercise, blood glucose monitoring, foot care, and smoking. Descriptive statistics were used for the analyses.</p> <p>Results: One hundred and eighty-one Arab Americans adults with type 2 diabetes completed the surveys. The mean age standard deviation (SD) was 62 12 years; 53% of participants were males and 51% were of Lebanese decent followed by Iraqis. Majority of participants were immigrants (96%). About one third reported no formal education. Majority were managed with oral diabetes agents; only 25% were maintained on insulin. Knowledge related to diabetes was generally poor; 26% of patients were able to identify proper treatment of hypoglycemia. The overall mean DDS score was 1.9 indicating generally low distress; however, approximately 25% of patient responses indicated high distress across all subscales. The mean scores varied across the 7 subscales: feeling of powerlessness, eating and management distress had higher mean scores of 2.4, 2.3, and 2.1, respectively indicating moderate distress. The overall mean SDSCA score was 3, which indicates that patients participated in DSM activities only 3 days per week. Patients scored the lowest on the exercise subscale, with a score of 2 days per week.</p> <p>Conclusions These findings emphasize the need for targeted patient-specific interventions aimed at improving diabetes knowledge and reducing sources of distress. These findings will inform the development of a culturally-specific DSM program for Arab American patients with diabetes.</p>

ABSTRACT NO. 5	
Name	Victoria Tutag Lehr
Category	Faculty
Title	Temporal Trends in Opioid Analgesic Claims: More information needed
Authors	Victoria Tutag Lehr, PharmD; Cynthia L. Arfken, PhD
Abstract	<p>Background: In 2016 drug overdose deaths exceeded 64,000 or more than deaths from motor vehicle accidents and gun violence. In response to the continuing increase in overdose deaths, multiple interventions at the national, state, and payer level have been implemented. For example, Michigan Medicaid implemented quantity limits for short-acting opioids in May 2014. Comparison of March and September claims showed 26.8% decline in number of claims. Comparison of 3 month claims 2014 post-implementation with same months in 2016 showed another decline (26.6%), suggesting impact of other interventions. Examining patients who received any opioid (either short acting or long acting) during a recent 6-month period, only 8.9% received them for 3 months or longer. These individuals may be at higher risk of overdose. However, it is not clear if those individuals were receiving palliative care, had malignant cancer diagnosis or resided in long-term nursing facilities, all of which are exempt from prescription limits. It is also not clear, if the trends occurred evenly across providers or if the number of providers prescribing opioids declined. We are funded by BCBSMF to examine these issues in Southeastern Michigan using community pharmacy claims.</p> <p>Purpose: To examine national, state and payer interventions using pharmacy claims for both scheduled and other prescribed medications using a local community pharmacy chain (January 2102- March 2018).</p> <p>Methods: The WSU-IRB approved this two-approach investigation: 1. A prospective review of Michigan DHHS regulations, formulary changes, legislative activity, and pharmacy benefit policies will document interventions with possible impact on opioid and controlled medication prescribing. 2. A longitudinal analysis of the de-identified pharmacy database to test if changes over time in type and number of prescriptions are temporarily related to specific policies.</p> <p>Results: Selected policies identified include: Conversion of opioids to MMED to assess opioid prescribing, dispensing, & guide interventions (2011); Payers limit opioid dosage to 90 MMED upon recommendation of American Society Interventional Pain Physicians (2012); Hydrocodone combinations rescheduled to CII; DHSS limits on immediate release opioids and some long acting opioids (2014) BCBSM implements opioid prescribing policies with other payers; MI Opioid Task Force (2015); CDC Guidelines on Opioid Prescribing Chronic Pain, MI Naloxone Standing Order; CMS requires MTM (2016); Opioid prescribing/MAPS/Consent Laws (2017).</p> <p>Conclusions: Multiple interventions are occurring at the national, state and payer level that could impact opioid prescribing. However, no one has examined if in response to these interventions, there are unintended consequences, such as providers refusing to prescribe opioids and patients experiencing suboptimal therapy. If this has occurred, it may restrict access to treatment and further stigmatize people with legitimate chronic pain.</p>

ABSTRACT NO. 6	
Name	Liping Xu
Category	Faculty
Title	AR affinity modulates cellular effects of enzalutamide-HDAC inhibitor hybrid drug 2-75 in AR+ prostate cancer cells
Authors	Liping Xu, Bailing Chen, PhD; Siyu Ou, MS; Zhihui Qin, PhD
Abstract	<p>Androgen receptor (AR) is the primary target for prostate cancer (PCa) treatment. We designed enzalutamide-histone deacetylase inhibitor (Enz-HDACi) hybrid drugs aimed to antagonize and downregulate AR in PCa cells. Here, we report the improved synthesis of 2-75, an Enz-HDACi hybrid, and its in vitro anti-PCa properties. 2-75 effectively suppressed androgen-stimulated AR transcriptional activity. Compared to pan-HDACi SAHA, 2-75 displayed significant cytoplasmic effects and relatively weaker impact on nuclear HDACs. 2-75 downregulated AR and AR-V7 expressions in multiple PCa cell lines and more specifically reduced the stability of full length AR, compared to HER2 and AR-V7. Mechanistic studies suggest that AR affinity retains hybrid drug in the cytoplasm of AR+ PCa cells and may further direct drug to AR-associated protein complex, resulting in higher impact on AR-associated Hsp90. The localized cytoplasmic effects could address the unfavorable resistance and toxicity mechanisms associated with classical AR antagonists, HDACis and Hsp90 inhibitors.</p>

ABSTRACT NO. 7	
Name	Xiangmin Zhang
Category	Faculty
Title	PLCG1 Regulates Insulin Signaling in Human Skeletal Muscle
Authors	Xiangmin Zhang PhD; Danjun Ma PhD; Aktham Mestareehi, MS; Berhane Seyoum, MD; Zhengping Yi, PhD.
Abstract	<p>Insulin resistance in skeletal muscle has been considered as among the primary contributors to the development of type 2 diabetes (T2D), though the underlying mechanisms remains incompletely understood. Phospholipase C, gamma 1 (PLCG1) is a signal transducer of tyrosine kinases and is activated in multiple receptor tyrosine kinase signaling pathways. PLCG1 interacts with the insulin receptor (IR) via its pleckstrin homology domain and plays a role in insulin-stimulated glucose uptake in adipocytes. Tyrosine phosphorylation of PLCG1 has been shown to regulate PLCG1 activity and plays a key role in various downstream signaling pathways. In human skeletal muscle tissue, we identified a site-specific PLCG1 tyrosine phosphorylation at 771 (pTyr771) which was positively correlated with insulin sensitivity. In this study we aim to determine whether PLCG1 plays an active regulatory role in insulin signaling in human skeletal muscle myotubes. Primary human skeletal muscle cells were cultured from muscle biopsy of a healthy insulin sensitive individual. The cells were differentiated into myotubes, followed by transduction with lentivirus encoding PLCG1 shRNA. Knockdown of PLCG1 reduced AKT pSer473 and AS160 pSer588, two well-known insulin-stimulated phosphorylation events, suggesting that PLCG1 knockdown impaired insulin signaling. Transduction of wild type PLCG1, but not PLCG1 mutant (Phe771), back into the PLCG1 knockdown cells rescued insulin stimulated AKT and AS160 phosphorylation. To determine how PLCG1 affects insulin signaling, we identified PLCG1 interaction partners through proteomic analysis of proteins bound to PLCG1 during co-immunoprecipitation. We found that multiple PLCG1 partners were reported to interact with various insulin signaling proteins. In vitro kinase assay was performed by incubating PLCG1 with the insulin receptor for 30 min with ATP provided. Proteomic analysis showed that insulin receptor preferentially phosphorylates Tyr771 of PLCG1. Western blot analysis showed dramatically elevated PLCG1 pTyr771 after incubation with insulin receptor. Our findings support PLCG1 as a new and important regulatory protein in insulin signaling.</p>

ABSTRACT NO. 98	
Name	Brittany Stewart
Category	Faculty
Title	Pharmacist-led blood pressure management for discharged urban emergency department patients with uncontrolled hypertension
Authors	Brittany Stewart, RD, PharmD; Liying Zhang, PhD; Revelle Gappy; Phillip D. Levy, MD, MPH, FACEP; Aaron Brody, MD, MPH
Abstract	<p>Purpose: More than 100 million adults in the US have hypertension (HTN) and despite effective treatment options, 50% of adults remain uncontrolled. Uncontrolled HTN leads to severe cardiovascular morbidity, and is highly prevalent in emergency department (ED) practice. Linkage to primary care is limited for many ED patients, specifically in underserved communities. Pharmacist-led HTN medication management has proven effective for patients with uncontrolled HTN. However, no studies to date have addressed the ability of pharmacists to manage HTN in ED patients post-discharge as an adjunct to primary care. The objective of this study is to assess the effectiveness of a pharmacist-led HTN management clinic in this population.</p> <p>Method: This a prospective, single arm trial of an innovative health care delivery system, a pharmacist-led HTN clinic. We recruited 89 patients with uncontrolled HTN and lack of access to primary care from our urban ED from May 24, 2017 to May 18, 2018. Per protocol, patients complete five follow up visits in an outpatient pharmacy clinic. The pharmacist initiates and titrates antihypertensive medications via a collaborative practice agreement with ED physicians. Descriptive statistics were used to analyze the data with graphic display of blood pressure change. These data represent an ad hoc, interim analysis of an ongoing study.</p> <p>Results: The mean age was 42.5 years old (SD=9.9); 51% were males; 94% were African American; 81% had 12th grade or more education; 53% reported full-time employment and 18% had no health insurance. The mean BMI was 34.5 and 51.2% were current smokers. The median BP at ED admission was 160/102 mmHg. Both systolic and diastolic BP declined throughout the follow up pharmacy clinic visits with the most impact on systolic BP (Figure), which showed a mean decrease of 48 mmHg (95% confidence interval 20-77). The pharmacist made 47 medication interventions (initiation or titration) during 95 follow-up visits, for a rate of 0.49 interventions/visit. At study completion, patients were prescribed an average of three antihypertensive medications.</p> <p>Conclusions: Preliminary results show pharmacist-led HTN management provided to ED patients post-discharge is effective at lowering BP in a clinically meaningful manner. The pharmacist was proactive in medication titration, and patients received evidence-based care. These data are encouraging, and provide the rationale for future larger scale studies. To assess the potential for clinical implementation, an exploration of factors influencing the effectiveness of treatment and a study with comparison to usual care are needed.</p>

Postdoctoral Scholars

ABSTRACT NO. 9	
Name	Hilary Marusak
Category	Postdoctoral Fellow
Title	Effects of early threat exposure and threat-related symptomology on fear extinction neural circuitry in children
Authors	Hilary Marusak, Ph.D.; Craig Peters, B.S.; Allesandra Iadipaolo, B.A.; Farrah Elrahal, B.A.; Christine Rabinak, Ph.D.
Abstract	<p>Purpose: Nearly 50% of individuals are exposed to childhood adversity and as a result these individuals are at increased risk for psychopathology, particularly anxiety disorders. However, the underlying neurobehavioral mechanisms through which childhood adversity confers heightened vulnerability to psychopathology are poorly understood. Given that anxiety disorders are characterized by a failure to appropriately inhibit or extinguish fear, the present study tests the effects of threat-related adversity on fear extinction and underlying neural circuitry in children.</p> <p>Methodology: 34 youth (6-11 yrs) completed a novel two-day virtual reality fear extinction task. 50% of youth endorsed previous histories of interpersonal violence or medical-related adversity. On day one, participants underwent fear conditioning and extinction. Twenty-four hours later, participants completed a test of extinction recall during functional magnetic resonance imaging. Behavioral (approach/avoidance), physiological (skin conductance), and subjective (fear/contingency ratings) measures of conditioned fear were collected during each session. Posttraumatic stress symptoms (PTSS) were also measured.</p> <p>Results: There were no group differences in measures of conditioned fear. However, relative to comparison children, adversity-exposed children demonstrated higher neural response in the dorsal anterior cingulate cortex, a region associated with the return of fear. Youth with more PTSS symptoms showed more avoidant (i.e., side-to-side) movement during fear and extinction learning, reported higher fear during extinction learning, and demonstrated higher neural response during extinction recall in the insula - patterns associated with fear renewal.</p> <p>Conclusions: Our data suggest that alterations in fear extinction neural circuitry may be a core mechanism through which adversity confers heightened vulnerability to psychopathology.</p>

ABSTRACT NO. 10	
Name	Samaresh Sau
Category	Postdoctoral Fellow
Title	Reprogramming malfunctioned tumor microenvironment to improve current therapeutic outcome of cancer.
Authors	Samaresh Sau, Ph.D.; Hashem Alsaab, Ph.D.; Rami Alzhrani, MS; Arun Rishi, Ph.D.; Arun K. Iyer, Ph.D.
Abstract	<p>Purpose: Tumor microenvironment is an extremely complex network associated with a various type of tumorigenic phenotypes, including tumor epithelial cells, tumor endothelial cells, tumor hypoxia, and stem cells, and tumor-associated immune cells. Despite the several approaches, conventional chemotherapy faced several challenges in the clinic and one of the major reasons is their poor tumor stroma penetration ability. The tumor stroma, comprised of the basement membrane, fibroblasts, and extracellular matrix has become a bottleneck barrier in penetration of chemotherapeutic drugs. Thus, there is an unmet need to develop a smart tumor stroma penetrating payload delivery system for inhibiting the major tumorigenic networks of the tumor microenvironment.</p> <p>Methodology: Nanomedicine is a promising therapy with more than 15-nanoparticles (NPs) have been used in the clinic to improve the therapeutic outcome. The lack of understanding of the interaction of NPs and tumor biomarkers is a major challenge. To overcome this, we developed various sized and shaped NPs that are efficient in tumor core penetration and reprogramming tumor-associated immune cells.</p> <p>Results: Toward this, we developed a library of nano-micelles and metallic NPs encapsulated with potent chemotherapeutic drugs and surface decorated with tumor multicomponent targeting ligands. These NPs showed significant tumor growth inhibition in non-small cell lung (NSCLC) and triple negative breast cancer (TNBC) patient-derived tumor xenograft (PDX) models. The uptake study of tumor hypoxia homing NPs showed superior tumor core penetration in 3D-spheroid culture compared to control. The dual tumor hypoxia and cancer stem cell (CSC) directed rod-shaped NPs demonstrated >8-fold higher tumor core penetration as compared to non-targeted NP in NSCLC Pdx tumor. Importantly, these NPs showed superior tumor uptake with low accumulation in liver and spleen, resulting reduction of non-specific toxicity. In therapy study, the NPs have demonstrated synergistic tumor growth inhibition compared to the individual drug in wild-type and drug-resistant tumor models, including TNBC, Everolimus-resistant kidney cancer. The combination of tumor hypoxia targeting NPs with FDA approved treatment, Sorafenib can significantly reverse the Everolimusresistanceof kidney cancer, associated with the complete wipeout of p-AKT kinase. This NP can significantly inhibit the function of tumor-promoting M-2 macrophage and upmodulate tumoricidal M1-macrophage markers, such as the CD86 and iNOS, warranting a multi-catered role in reeducation tumor promoting immune cells and eprogramming tumor microenvironment. The combination of hypoxia targeting NPs with sorafenib can induce tumoricidal macrophage-mediated apoptosis in cancer cells as revealed by caspase 3/7-Glo assay. The ultipronged smart nano-therapy approach has demonstrated a significant improvement of tumor stroma penetration with reduced safety, portending more promising potential for selective cancer treatment.</p>

ABSTRACT NO. 11	
Name	Samaresh Sau
Category	Postdoctoral Fellow
Title	Tumor Multicomponent Targeting Nanomicelles with Synergistic Combination to Overcome Drug Resistance and Reprogramming Macrophages in Renal Cell Carcinoma
Authors	Hashem Alsaab, Ph.D.; Samaresh Sau, Ph.D.; Vino T. Cheriyan, Ph.D.; Rami Alzhrani, M.S; Ulka Vaishampayan, MD; Arun K. Rishi, Ph.D.; Arun K. Iyer, Ph.D.
Abstract	<p>Renal Cell Carcinoma (RCC) contributes >90% of the most common form of kidney tumor and remains one of the ten leading causes of cancer death in the US. Current treatments for Renal Cell Carcinoma (RCC) include a combination of surgery, targeted therapy, and immunotherapy. The emergence of resistant RCCs contributes to the failure of drugs and poor prognosis, and thus warrants the development of new and improved treatment options for the disease. Tyrosine kinase inhibitors (TKIs), such as Cabozantinib, Axitinib, Sorafenib and Sunitinib, and mammalian target of rapamycin (mTOR) inhibitors Temsorlimus and Everolimus have increased therapeutic options of treating RCC. Although the impact on disease progression is encouraging, a substantial proportion of patients do not respond adequately, and therapy resistance almost inevitably occurs. Eventually, new strategies have emerged that include immunotherapy such as programmed death-1 inhibitor (Nivolumab), cytokines, and the combination of chemo-immune therapy. Possibly combination treatment aimed at different, non-related pathways may be advantageous. In this regard, we would like to come up with remarkable therapy strategies for nonresponsive, highly aggressive tumor types to tackle the current clinical challenges. We worked on different models of RCCs, with a poor prognosis due to a modest or non-response to systemic therapy. We also pursued different combination regimens, including drugs that work on the mTOR inhibition (everolimus), inhibit RTK-inhibitor or VEGFR (cabozantinib, axitinib sunitinib, or sorafenib). Also, since there is a critical need</p> <p>to develop safe and effective delivery vehicles that can carry the payload to the right target tissue and cell, different types of nanoparticles have been developed to deliver a variety of therapeutic agents to target tumor hypoxic microenvironment by using carbonic anhydrase-9 (CA9) for targeting hypoxic regions of the tumor; FR-b for targeting cancer epithelial cells; and FR-b for targeting tumor-associated macrophages (TAM) and combination delivery of RTK-inhibitor Cabozantinib (CB) and sorafenib with our own apoptosis inducer/CARP-1 protein activator CFM-4.16 (C4.16) for overcoming drug resistance and reprogramming TAM for RCC therapy. The current work also focused on multimodal approaches, including (a) Synthesis, characterization, and optimization of hypoxia marker conjugated targeted polymer-lipid nano-formulation (PLNP) using copper-free click chemistry; (b) In vitro and in vivo pre-clinical testing of targeted -PLNP loaded with multiple payloads in inhibiting RCCs; and (c) In vivo imaging and bio-distribution analyses of tumors using mice bearing resistant RCCs and patient-derived xenografts (PDX) administered with hypoxia-targeted-PLNPs conjugated with NIR dye to confirm the active targeting of the nano-formulation. The results of efficacy and biodistribution of targeted PLNPs (with the hypoxia-targeted ligand) in animals bearing RCC xenografts and PDX model showed higher accumulation of drugs at tumor sites with high tumor growth inhibition and that was achieved with the aid of hypoxia-targeted-PLNPs formulations. In addition, it showed high binding affinity and specific tumor uptake, faster normal tissue clearance and less non-target organ uptake. These findings portend promising therapeutic potential of hypoxia-targeted-PLNPs with anticancer combination in the treatment of RCCs.</p>

ABSTRACT NO. 12	
Name	Jacinda Small Abdul
Category	Postdoctoral Fellow
Title	Daptomycin or Vancomycin Combined with Ampicillin Exhibits Synergistic Killing of Enterococcus faecium in Vancomycin Resistant and Daptomycin Non-Susceptible Patient Isolates
Authors	Jacinda Small Abdul, PharmD; Seth Rice, BS; Kyle Stamper, BS; Razieh Kabriaei, PhD
Abstract	<p>Background: Treating Multidrug resistant (MDR) enterococci, important healthcare pathogens, has become a clinical challenge, with enterococcus faecium (E. faecium) being named as the leading nosocomial resistant organism. Therapeutic options are often limited by the development of resistance to beta lactams, as well as to vancomycin (glycopeptide) and daptomycin (lipopeptide). Although Enterococcus faecium may be resistant to ampicillin (AMP), vancomycin (VAN), and daptomycin (DAP) when used as sole therapy; synergistic killing between glyco/ lipopetides when used with beta-lactam antibiotics has been demonstrated in vitro. The objective of this experiment was to evaluate the ability of combined DAP or VAN with AMP (B-lactam therapy) to eradicate E. faecium in 3 resistant patient strains.</p> <p>Methods: MIC values were determined by micro-broth dilution in duplicate for all strains according to CLSI guidelines. Time kill (TK) experiments were performed in MHB as growth media. The initial starting bacterial inoculum was 10⁶ CFU/ml. All antimicrobials were tested at 0.5 x MIC of the Peak (whichever was the lesser) for each organism. Ampicillin was analyzed alone and in combination with daptomycin and vancomycin. 0.1 aliquots were obtained from each well at 0, 4, 8, 24h. Samples were serially diluted and plated using automatic spiral plating. After 18-24h growth on TSA, bacterial colonies were counted using a laser colony counter.</p> <p>Results: There was at least a 4- fold decrease in the MIC of the 3 patient strains when combining DAP VAN with AMP, as observed in the microbroth dilution testing. Represented in the time kill experiment, synergy was observed the patient strains with a decrease of \geq to 2 log₁₀ CFU/ml over 24hrs.</p> <p>Conclusion: Combinations of DAP or VAN with ampicillin showed promise in successfully treating E. faecium amid the emergence of resistance in the patient strains. Similar regimens can potentially lead to optimizing treatment outcomes with DAP therapy, with minimal β-lactam exposures. Further in vitro research is warranted to determine the most optimized DAP or VAN+AMP dose-regimens for the continued eradication of Enterococcus faecium.</p>

ABSTRACT NO. 13	
Name	Vijayalakshmi Thamilselvan
Category	Postdoctoral Fellow
Title	LyGDI, a Rho guanosine diphosphate dissociation inhibitor, regulates islet function in health and metabolic stress
Authors	Vijayalakshmi Thamilselvan, Ph.D; Anjaneyulu Kowluru, Ph.D
Abstract	<p>Background: Diabetes mellitus is a metabolic disorder characterized by progressive loss or dysfunction of pancreatic insulin-producing beta-cells. Despite significant advancements in the field, cellular and molecular mechanisms involved in islet dysfunction remain poorly understood. Earlier evidence from our laboratory demonstrated novel regulatory roles for Rac1, a small G-protein, in the increased generation of intracellular oxidative stress and stress kinase activation culminating in islet β-cell dysfunction under metabolic stress. The functions of Rho GTPases are mediated by the cycling of small G-proteins (e.g., Rac1) between their inactive (GDP-bound) and active (GTP-bound) states and are firmly controlled by specific regulatory proteins. LyGDI belongs to the family of Rho guanosine diphosphate dissociation inhibitors (RhoGDIs) that regulate the cellular distribution of Rho GTPases and their interactions with regulatory guanine nucleotide exchange factors, GTPase-activating proteins, and effector targets. In the present study, we investigated the regulatory role of LyGDI in the sustained activation of Rac1 in pancreatic β-cells under metabolic stress.</p> <p>Methods: INS-1 832/13 cells, rat islets and human islets were cultured under basal (2.5 mM glucose) or metabolic stress (20 mM glucose; for 24h to 48h). Total lysates and subcellular fractions were analyzed for the protein expression and distribution of LyGDI by western blot analysis. LyGDI interaction with Rac1 was determined by co-immunoprecipitation followed by western blot analysis. Silencing of endogenous LyGDI protein expression was done by siRNA transfection. Rac1 activation and glucose stimulated insulin secretion (GSIS) were determined by Rac1 GLISA and secreted insulin level in the media by ELISA respectively.</p> <p>Results: Western blot analysis indicated that LyGDI is expressed in INS-1 832/13 cells, rat islets and human islets and distributed primarily in cytosolic and membrane fraction of pancreatic betacells. SiRNA-mediated knockdown of LyGDI markedly potentiated physiological insulin secretion. In addition, chronic exposure of isolated beta-cells to high glucose (metabolic stress) significantly increased the protein expression of LyGDI (1.5 fold; n=4). Furthermore, metabolic stress conditions significantly decreased its interaction of LyGDI with Rac1 leading to its sustained activation in INS-1 832/13 cells.</p> <p>Conclusions: Based on these findings we conclude that LyGDI plays novel regulatory roles in islet function. First, it contributes to physiological insulin secretion. Second, it is involved in sustained activation of Rac1, and potentially stress kinase activation under metabolic stress. This study for the first time provides evidence of LyGDI expression in pancreatic islet cells and its regulatory roles in islet function in health and metabolic stress.</p>

ABSTRACT NO. 14	
Name	Xiaokun Wang
Category	Postdoctoral Fellow
Title	Genetic and Developmental Variation of the Pharmacogenome in Children
Authors	Zhipeng Liu, Ph.D.; Xiaokun Wang, Ph.D.; Wanqing Liu, Ph.D.
Abstract	<p>Background: Dynamic changes happen in Drug-Metabolizing Enzymes and Transporters (DMET) function in children at the genome-wide level. However, how age and genetic factors together determine the variation of DMET function remains unclear. Purpose: Investigate the effects of age and genetic factors on DMET expression.</p> <p>Methodology: We collected a cohort of pediatric liver samples (n = 109) with different developmental stages. Whole-genome genotyping and RNA-seq were performed to obtain the genetic variations and mRNA profiling of each sample. ANOVA was used to identify genes whose expressions are significantly different among different age groups. The effect of the interaction between age and genetic factors on gene expression was evaluated by a linear regression model. Due to the drastic difference of gene expression patterns between prenatal and postnatal livers, we analyzed the two groups separately and compare the results afterwards.</p> <p>Results: We identified 177 genes that are significantly associated with age in prenatal livers (FDR < 0.05), among which 13 genes are key pharmacogenes and 94 are GWAS related genes. Significant age-genetics interactions were found to affect 2099 gene expressions (FDR < 0.05), among which 21 are pharmacogenes and 438 are GWAS genes. For the postnatal child livers, there are 236 genes found to be significantly correlated with age, among which 7 genes are pharmacogenes and 127 are GWAS genes. Similarly, we found 1695 significant Gene X Age eQTLs in the postnatal group (FDR < 0.05), among which 4 are pharmacogenes and 274 are GWAS genes.</p> <p>Conclusions: Age broadly affects gene expression, and many key pharmacogenes and disease-related genes are significantly affected by age.</p>

ABSTRACT NO. 15	
Name	Xiangmin Zhang
Category	Postdoctoral Fellow
Title	PLCG1 Regulates Insulin Signaling in Human Skeletal Muscle
Authors	Xiangmin Zhang, PhD; Danjun Ma, PhD; Aktham Mestareehi, MS; Berhane Seyoum, MD; Zhengping Yi, PhD.
Abstract	<p>Insulin resistance in skeletal muscle has been considered as among the primary contributors to the development of type 2 diabetes (T2D), though the underlying mechanisms remains incompletely understood. Phospholipase C, gamma 1 (PLCG1) is a signal transducer of tyrosine kinases and is activated in multiple receptor tyrosine kinase signaling pathways. PLCG1 interacts with the insulin receptor (IR) via its pleckstrin homology domain and plays a role in insulin-stimulated glucose uptake in adipocytes. Tyrosine phosphorylation of PLCG1 has been shown to regulate PLCG1 activity and plays a key role in various downstream signaling pathways. In human skeletal muscle tissue, we identified a site-specific PLCG1 tyrosine phosphorylation at 771 (pTyr771) which was positively correlated with insulin sensitivity. In this study we aim to determine whether PLCG1 plays an active regulatory role in insulin signaling in human skeletal muscle myotubes. Primary human skeletal muscle cells were cultured from muscle biopsy of a healthy insulin sensitive individual. The cells were differentiated into myotubes, followed by transduction with lentivirus encoding PLCG1 shRNA. Knockdown of PLCG1 reduced AKT pSer473 and AS160 pSer588, two well-known insulin-stimulated phosphorylation events, suggesting that PLCG1 knockdown impaired insulin signaling. Transduction of wild type PLCG1, but not PLCG1 mutant (Phe771), back into the PLCG1 knockdown cells rescued insulin stimulated AKT and AS160 phosphorylation. To determine how PLCG1 affects insulin signaling, we identified PLCG1 interaction partners through proteomic analysis of proteins bound to PLCG1 during co-immunoprecipitation. We found that multiple PLCG1 partners were reported to interact with various insulin signaling proteins. In vitro kinase assay was performed by incubating PLCG1 with the insulin receptor for 30 min with ATP provided. Proteomic analysis showed that insulin receptor preferentially phosphorylates Tyr771 of PLCG1. Western blot analysis showed dramatically elevated PLCG1 pTyr771 after incubation with insulin receptor. Our findings support PLCG1 as a new and important regulatory protein in insulin signaling.</p>

Health Care Science

ABSTRACT NO. 16	
Name	Candi Bennett
Category	Health Science
Title	Mixed Germ Cell Tumor Presenting as a Multifocal Mass within the Testis and Spermatic Cord
Authors	Candi Bennett
Abstract	<p>Introduction: Malignant testicular germ cell tumors are frequently seen in Caucasian males between the ages of 15-34 years old and account for 1% of all solid cancers. This case study follows a patient that is a 51-year old male with no previous significant medical history and no past significant surgical history, who presented to his primary care physician after noticing a fullness in his left inguinal area.</p> <p>Materials and Methods: The radical orchiectomy specimen was bivalved to reveal two separate distinct masses. Patient's slides were stained with H&E and immunohistochemical markers of clinical importance for this case include: CD117, CD 30, OCT 4, hCG, and CK. Results The tissue was stained with H&E and revealed two separate histological components consistent with seminoma and embryonal carcinoma. Immunohistochemical studies were done on formalin fixed, paraffin embedded tissues to confirm the diagnosis of a mixed germ cell tumor composed of seminoma and embryonal carcinoma. Overall, gross and histopathological findings were consistent with the diagnosis of a mixed germ cell tumor consisting of 95% seminoma and NSGCT with 5% embryonal carcinoma involvement.</p> <p>Discussion: The patient was staged as pT3, cN2, and M1. In mixed germ cell tumors if a nonseminomatous component is identified the patient will be treated as such due to their more aggressive nature when compared to seminomas.¹² The patients prognosis is good with about a 90% cure rate after being treated with chemotherapy.</p>

ABSTRACT NO. 17	
Name	Nate Bremer
Category	Health Science
Title	Repeated Incremental Workbouts Separated by 1 Hour Increases the Electromyographic Fatigue Threshold
Authors	Nate Bremer, SPT; Gavin Peoples, SPT; Brent Hasler, SPT; Robert Litzenburg, SPT; Andrew Johnson, SPT; Moh H. Malek, PhD
Abstract	<p>Studies examining the influence of priming, for continuous exercise, have mainly focused on improved exercise capacity related to oxygen uptake kinetics rather than on neuromuscular fatigue of the muscle. The purpose of this study, therefore, was to determine whether or not the electromyographic fatigue threshold (EMGFT) could be modulated by having subjects perform two incremental tests separated by 1 h. We hypothesized that the EMGFT determined from the second incremental test would be higher than the EMGFT determined from the first incremental test. Nine healthy college aged men [mean \pm SEM: age: 23.8 ± 0.6 y; weight: 79.5 ± 3.3 kg; height: 1.78 ± 0.02 m] were recruited from the university population. Each subject visited the laboratory on one occasion and performed two incremental single leg knee extensor ergometry to voluntary fatigue separated by 1 h. The EMGFT was determined for each trial and statistically compared using paired samples t-test. The results indicated significant mean differences between the EMGFT for the two trials (Trial 1: 27 ± 1 W vs. Trial 2: 34 ± 2 W; $p = 0.001$), whereas there were no significant mean differences for maximal power output (Trial 1: 53 ± 2 W vs. Trial 2: 57 ± 2; $p = 0.09$). These findings suggest that post-activation potentiation may, in part, explain the differences in EMGFT since the exercise mode used in the current study minimizes the cardiorespiratory responses to exercise.</p>

ABSTRACT NO. 18	
Name	Victoria Cassar
Category	Health Science
Title	Traditional Versus Nontraditional Anatomy Instruction Among Doctor of Physical Therapy Students: A Comparison Study
Authors	Victoria Cassar, SPT; Hannah Otto, SPT; Sarah Smith, SPT; Sara Maher, PT, DScPT, OMPT
Abstract	<p>Introduction: Alternative methods of anatomy instruction have increased in popularity, and cadaveric dissection was not supported as the most effective teaching tool. The purposes of this study were to: 1.) assess effectiveness of a nontraditional anatomy teaching model on doctor of physical therapy (DPT) students' retention of anatomical knowledge, 2.) determine if there is a preferred learning style among DPT students, 3.) determine if DPT students utilized a deep or surface approach to learning and maintained this style over one semester and 4.) assess if students spend time differently when using two different approaches to anatomy instruction.</p> <p>Methods: This study examined participants in two Midwestern DPT programs; an experimental group (EG) taught anatomy using prosected cadavers supported by other modalities, and a control group (CG) taught anatomy using traditional dissection supported with various bone models. A total of 208 students participated in the study (EG = 105, CG = 103). The dependent outcome measures consisted of an anatomy quiz, the Revised Two Factor Study Process Questionnaire (RSPQ-2F), a Learning Perception Inventory, and the Visual, Auditory, Read/Write, Kinesthetic Questionnaire (VARK). Data were collected at three points during the study: prior to anatomy class, at the conclusion of the anatomy class, and 6-months after the class had ended. Data were analyzed using SPSS 25.0 and included descriptive statistics, paired and independent t-tests, and Mann Whitney U-tests. Statistical significance was set a priori at $\leq .05$.</p> <p>Results: Quiz scores differed significantly between the two groups prior to the anatomy class ($p < .001$). Consequently, the changes in quiz scores were compared at 3 points in time previously discussed. The experimental group had significantly improved changes in scores for both pre and post quiz-to-6 months later ($p = .002$ and $p < .001$ respectively). Participants in both groups were primarily kinesthetic learners and utilized a deep learning approach at the start of anatomy instruction ($p = 0.001 - 0.042$). While both groups saw a decline in deep learning over the semester, the total deep learning score for the EG was significantly higher than the CG at the end of the semester ($p = .004$). The EG spent significantly more time in lab ($p < 0.001$), lecture ($p < 0.001$), with tutoring/supplemental instruction ($p = 0.011$), with plasticized models ($p < 0.001$), which increased the overall time spent on the class ($p < 0.001$). The CG spent significantly more time utilizing textbooks ($p < .001$).</p> <p>Discussion: DPT students preferred kinesthetic learning. While changes in anatomy quiz scores were statistically different between the groups, the mean quiz scores were similar both after the class and six months later, indicating that both types of instruction helped students learn. While significant differences were found in how the groups utilized time, both groups preferred a deep style of learning.</p> <p>Conclusion: Non-traditional methods for teaching human gross anatomy were found to be as effective as traditional anatomy instruction for DPT students, and may have the potential to reach a variety of learners, reduce costs, and facilitate a deep approach to learning.</p>

ABSTRACT NO. 19	
Name	Nicole DeMartino
Category	Health Science
Title	Do High Scores on a Critical Care Questionnaire Correlate with Acceptance into Nurse Anesthesia School? A Pilot Study
Authors	Drew Judge, SRNA; Michael McRorie, SRNA; Alyssa LoGrasso, SRNA; Nicole DeMartino, SRNA; Mary Walczyk, CRNA, DNP; Prudentia A. Worth, CRNA, PhD; George McKelvey, PhD
Abstract	<p>Introduction: Each year, Wayne State University's Nurse Anesthesia Program undergoes a difficult task selecting from a large pool of applicants the most qualified individuals for admission. Traditionally, applicants are selected based on their undergraduate and science grade point averages, CCRN composite score, number of years of critical care nursing experience, and a personal interview. Recently, studies have been conducted to assess supplemental interview tools, including high fidelity simulation and emotional intelligence assessment, in predicting future academic success of prospective students. Little research exists on specific tools for use during the interview and selection process of applicants and determination of potential academic success of the learner. A critical care assessment tool of 20 multiple-choice questions was developed with the aim to assist in predicting the most suitable applicants for admission and academic success. The purpose of this study was to determine a correlation between the interview selection of candidates by the Wayne State University's Nurse Anesthesia interviewing committee and the applicants who scored high on a specialized Critical Care Assessment tool.</p> <p>Method: A pilot study was completed with 88 nurse anesthesia applicants interviewing for the Wayne State University Class of 2020. After formal interview, each applicant was informed of the study by the student researchers. Applicants electing to participate in the study were given the Critical Care Assessment Tool consisting of 20 multiple-choice questions. The results were scored to generate a final percent score. All participants were informed that their score had no bearing on the acceptance into the program. The Critical Care Assessment Tool questions were selected from the American Association of Critical Care Nurses (AACN) Practice CCRN Questions Adult. Approval was obtained by AACN. Validity was tested by administering a 25-question tool to the WSU Nurse Anesthesia Class of 2018 and 2019. The five most missed questions (< 35% correct between both classes) were eliminated. Additional data was collected on all participants including CCRN score, months and type of ICU experience in an effort to compare variable across the accepted and denied groups.</p> <p>Results: Eighty-eight participants completed the study. No statistically significant differences were found between accepted candidates and total score on their Critical Care Assessment Tool (p=0.92). The accepted candidates' average score was 74.9% in comparison to the denied group of 73.9%. Average months of ICU experience for those accepted was 25.5 months compared to 27.6 months for those denied. Accepted candidates average CCRN score was 100.8 compared to 96.9 for those denied.</p> <p>Conclusion: Applicant selection into a nurse anesthesia program continues to be a multi-faceted process, with no one single factor being a determinant of admission or denial. The use of the Critical Care Assessment Tool as an adjunct to the current interview process provides an additional objective way to assess each applicants critical care knowledge. Further research is needed to determine if implementing the Critical Care Assessment Tool and CCRN score correlates with program acceptance and academic success.</p>

ABSTRACT NO. 20	
Name	Erin Edwards
Category	Health Science
Title	Backward Walking as a Clinical Tool to Detect Fall Risk in Multiple Sclerosis
Authors	Erin Edwards, BS; Mareena Atalla, BS; Nora Fritz, DPT, PhD
Abstract	<p>Purpose: Accidental falls are common among individuals with multiple sclerosis (MS). Better screening tools to identify future fallers are needed. Although differences in backward walking (BW) have been identified among healthy controls and individuals with MS, the relationship of BW to falls has not been explored.</p> <p>Subjects: Eighteen individuals with MS participated, including 16 females; average (SD) age 51.4 (9.7) years; symptom duration 17.1(10.2) years; 83% taking disease modifying therapies; and 39% utilized walking devices during testing.</p> <p>Methods: In a single session, we examined forward walking (FW) and BW performance over a GaitRite electronic walkway. Spatial and temporal gait parameters as well as coefficients of variation were calculated. Participants reported a 1-month fall and near-fall (i.e., trip or stumble) history. Participants then kept a fall diary for the subsequent 6 months. Relationships among FW, BW, and both retrospective and prospective falls were evaluated with Spearman correlations.</p> <p>Results: Both BW ($r=-0.681$; $p=0.005$) and FW ($r=-0.728$; $p=0.001$) velocity were related to retrospective reports of falls at 1 month. However, only BW velocity was related to retrospective reports of near-falls ($r=-0.540$; $p=0.038$). Similarly, only BW velocity was significantly related to both prospective falls ($r=-0.651$; $p=0.009$) and near-falls ($r=-0.651$; $p=0.009$) at 6 months. BW may better differentiate fallers from non-fallers.</p> <p>Conclusion: BW is strongly related to both retrospective and prospective fall reports, while forward walking was not. BW speed may be a more sensitive clinical tool to identify fall risk than FW speed in persons with MS.</p>

ABSTRACT NO. 21	
Name	Samantha Etters
Category	Health Science
Title	Breast Cancer Metastasis to the Colon Presenting After Fifteen Years
Authors	Samantha Etters, MS
Abstract	<p>The following is a case study of a female patient in her late 70s with a history of invasive ductal carcinoma, diagnosed in 2002. Fifteen years later, she was found to have metastases to the stomach and to the colon, both rare sites of spread from breast cancer. The metastasis to the colon is of particular note here as it was received as a surgical specimen and evaluated by a pathologists' assistant. Histologically, the cell morphology was compared between the primary breast cancer and colon metastasis and found to be strikingly similar. The purpose of this case study and literature review were to compare the characteristics of this rare case to other cases and analyses of similar breast cancer metastasis to the gastrointestinal tract published in the literature, and to share insights with pathologists' assistants and other health professionals diagnosing similar cases. Although rare, the possibility of gastrointestinal metastasis in a patient with a history of breast cancer should always be considered when diagnosing or grossing a gastrointestinal lesion.</p>

ABSTRACT NO. 22	
Name	Natalie Hardy
Category	Health Science
Title	Martial arts therapy reduces pain and distress among children with cancer, other serious health conditions, and their siblings
Authors	Natalie Hardy, Allesandra Iadipaolo, Cindy Cohen, Elimelech Goldberg, Jeffrey Taub, Felicity Harper, Kristopher Dulay, Rebecca Cramer, Autumm Heeter, Shelley Paulisin, Sajah Fakhoury, Hanan Rakine, Martin H. Bluth, Christine Rabinak, Ph.D; Hilary Marusak
Abstract	<p>Background: Treatment advances have drastically improved childhood cancer survival rates in recent years. However, children with cancer and other chronic and/or life-threatening diseases (e.g., sickle cell) are exposed to a high burden of pain and psychological distress. Kids Kicking Cancer (KKC) is a martial arts therapy program that incorporates breathing and meditative techniques to help children cope with pain and distress (negative emotions). A recent study demonstrated that KKC is an effective therapeutic modality for reducing pediatric cancer pain, with 85.3% reporting a reduction in pain with an average of 40% over the course of one session (Bluth et al., 2016). Purpose Building on this work, the present study tests self-reported pain and distress levels prior to and following a KKC class in children with cancer, other serious health conditions, and their siblings.</p> <p>Methodology: Sixty-one children, including children with cancer, other serious health conditions (e.g., sickle cell), and healthy siblings, reported on their pain and distress using Likert-style scales (ranges 0-10 and 1-6, respectively) before and after attending one-hour KKC classes. A total of 111 KKC classes were reported on, given that 46% of children completed multiple (up to 6) classes.</p> <p>Results: Thirty children reported pain (>0), and 21 children reported distress (>1) prior to class (39 and 31 classes, respectively). For those classes, 59% and 88% reported reductions (≥ 1 unit) in pain and distress, respectively, over the course of the class (28% and 55% reported no change, respectively). A subset of these children (n=13) reported both pain and distress prior to 15 classes. Across all classes, higher pre-class pain scores were associated with a greater reduction in pain, whereas higher pre-class distress was associated with greater reductions in both pain and distress. 94% of children endorsed the statement "I would recommend KKC to other kids".</p> <p>Conclusions: Results support the notion that KKC is an effective behavioral intervention for addressing pain and distress in pediatric populations, including pediatric oncology populations.</p>

ABSTRACT NO. 23	
Name	Kenneth Harlan
Category	Health Science
Title	Preexhaustion Exercise Differentially Influences Neuromuscular Fatigue Based on Habitual Physical Activity History
Authors	Kenneth G. Harlan, SPT; Roberto B. Merucci, SPT; Jalen J. Weaver, SPT; Thomas C. Windle, SPT; Moh H. Malek, PhD
Abstract	<p>While there is anecdotal evidence of a potential physiological benefit of preexhaustion exercise to enhance muscular recruitment few studies have systematically examined the effect on neuromuscular activity. Moreover, a subject's habitual physical activity history may, in part, contribute to the muscle's response on a subsequent workout following a single preexhaustion workout. To date, no studies have examined the effect of preexhaustion exercise on the electromyographic fatigue threshold (EMGFT). The purpose of this study, therefore, is to determine whether preexhaustion exercise influences the EMGFT. Specifically, we were interested in determining whether or not there is a dichotomous response to preexhaustion exercise based on the individual's habitual physical activity history. Thus, we hypothesized that healthy active subjects would have reduced EMGFT values, whereas elite runners would have increased EMGFT values as a result of the preexhaustion exercise. Eight healthy college-aged men [mean \pm SEM, age = 24.5 ± 0.3 yrs; weight = 83.1 ± 3.0kg; and height = 1.80 ± 0.02 m] and nine elite runners [mean \pm SEM, age = 23.4 ± 0.7 yrs; weight = 70.3 ± 2.7 kg; and height = 1.79 ± 0.03 m] participated in current study. Each subject visited the laboratory on two occasions separated by 7 days and performed the single leg knee extensor ergometry test. For one of the visits, the subjects performed the Thorstensson test (50 continuous, concentric knee-extensions) prior to the single leg knee extensor ergometry. The EMGFT was measured on both visits for all subjects. For healthy subjects, we found that the EMGFT was significantly reduced after performing the 50 isokinetic knee extensions (Control: 27 ± 6 W vs. Thorstensson: 21 ± 6.0 W; $p = 0.001$), whereas for elite runners there was no significant mean differences between the two visits (Control: 38 ± 3 W vs. Thorstensson: 39 ± 2 W; $p = 0.813$). These results suggest that 50 repetition of isokinetic muscle action, as a method of preexisting the quadriceps femoris muscles, may be influenced by the subject's habitual exercise history.</p>

ABSTRACT NO. 24	
Name	Jaclyn Johnson
Category	Health Science
Title	Minimally-Invasive Muscle Embedding (MIME)—A Novel Tool To Test Rehabilitative Interventions for Muscle Regeneration
Authors	Joseph Roche, BPT, PhD; Morium Begam, BS; Andrea, Eaton, BS; Collin, Elkins, BS; Jaclyn, Johnson, BS; Mattina, Rosinski, MA; Sujay Galen, PT, PhD
Abstract	<p>Introduction: Minimally-Invasive Muscle Embedding (MIME), is a novel technique developed in our laboratory, to facilitate the development of donor-cell-derived muscle fibers in a host muscle. MIME involves passing a sterile needle through the host muscle, and then embedding a segment of whole donor tissue along with its myogenic satellite cells, within the needle track in the host muscle.</p> <p>METHODS. We performed MIME on the left tibialis anterior (TA) muscle of immunodeficient host mice that ubiquitously express a green fluorescent protein (GFP; NSG-GFP mice, JAX Stk# 021937; N = 4). We implanted a single extensor digitorum longus (EDL) muscle from donor mice that ubiquitously express a red fluorescent protein (RFP; DsRed.T3 mice, JAX Stk# 006051; N = 2). After implanting the donor tissue, we sealed the needle wounds in host mice with veterinary tissue adhesive. As a SHAM procedure, we created a needle track in the right TA of the host mouse, but did not implant donor tissue. About 5 min after MIME (or SHAM), we injected barium chloride (BACL, myotoxin) into the left and right TA muscles, to induce concerted degeneration and regeneration of the host TA muscle and the embedded donor EDL muscle. At 14 days post-MIME, we euthanized the host mice, and collected their MIME- and SHAM-treated muscles. We weighed the muscles, snap-froze them in liquid nitrogen, and stored them at -80 °C. We made cross sections of MIME- and SHAM-treated muscles to quantify donor-cell-derived myogenesis, by counting the numbers of donor RFP+ and host GFP+ muscle fibers. On serial cross sections, we also performed immunofluorescent labeling of desmin (Z-disk protein, muscle marker) and dystrophin (sarcolemma-associated protein), and co-stained the sections with DAPI to visualize nuclei. We analyzed muscle weights, and GFP+ and RFP+ fiber counts, by Student’s t-tests; and analyzed the percentage of RFP+ fibers that were positive for desmin, dystrophin, and central nucleation (marker for myogenesis), by one-way ANOVA. P-values less than 0.05 were considered significant. All cell counts were performed by blinded evaluators.</p> <p>Results: There was no difference in muscle weight between MIME- and SHAM-treated muscles. In MIME-treated muscles, 22 ± 4 % and 78 ± 4 % muscle fibers were RFP+ and GFP+, respectively. There were no RFP+ fibers in SHAM-treated muscles. All RFP+ fibers were positive for desmin and dystrophin, and 65 ± 4 % fibers were centrally nucleated. Results are reported as Mean +/- S.E.M.</p> <p>Conclusion: MIME helps generate donor-cell-derived muscle fibers in host muscle. These donor-derived muscle fibers are viable since they express desmin and dystrophin. Central nucleation of the donor-cell-derived fibers, suggests that, they have originated from myogenesis rather than from muscle tissue engraftment. Future experiments will assess the morphology of donor-derived function in longitudinal sections, and also assess if MIME together with rehabilitative interventions, can promote regeneration in the context of volumetric muscle loss caused by muscle disease or trauma. In future studies, exercise will be used to stimulate controlled muscle degeneration and regeneration instead of BACL.</p> <p>Acknowledgements: Pilot Grant from the Alliance for Regenerative Rehabilitation Research and Training (AR3T, NIH-supported), NIH 1R03HD091648- 01 from NICHD, and a Faculty Startup Package from Wayne State University to JAR.</p>

ABSTRACT NO. 25	
Name	Kimberly Krusinski
Category	Health Science
Title	The Effects of Verbal Texting on Gait Parameters
Authors	Kimberly Krusinski; Sean Murray; Jennika Myers; Sujay Galen, PT, PhD, FHEA; Nora Fritz, PhD, PT, DPT, NCS
Abstract	<p>Introduction: An important aspect of texting and walking is the ability to dual-task, or perform two tasks simultaneously. Young adults are able to perform dual-tasks similarly in high and low distraction environments; however, older adults may not be able to shift or divide their attention as effectively, particularly as other age-related declines may impact their performance. With an increase in voice recognition software, it is crucial that we gain a better understanding of the impact of the concurrent-use of these technologies on gait speed, spatiotemporal gait parameters, and propensity for falls. We hypothesize that verbal texting and walking (VTW) will have a greater negative impact on gait speed and quality than manual texting and walking (MTW) in both open and closed environments, and that VTW will have a greater negative impact than MTW on gait parameters in older adults compared to younger adults.</p> <p>Methods: This study was non-experimental and a cross-sectional design. Two age groups were recruited with 17 participants in the younger (Age: 25+2.7), and 6 participants in the older (Age:62.2+2.4). A stopwatch was used to measure gait speed over a set 15-meter distance, WI-GAT sensors were used to measure spatiotemporal gait parameters and foot contact asymmetries. The Stroop test was used to measure executive function as the interference condition can be related to dual-task ability. A one-way ANOVA was performed to determine differences between MTW and VTW, open and closed, and younger compared to older adults. Spearman correlations were used to determine relationships among walking conditions and cognitive performance.</p> <p>Results: Older adults performed significantly worse on the Stroop interference test ($p=.001$), and spent more time in double limb support in open baseline ($p=.022$), open VTW ($p=.042$), and the closed VTW ($p=.022$) conditions compared to younger adults. While there was no relationship between the walking conditions and Stroop performance in the younger group, strong correlations were observed in the older adult group, with poorer Stroop performance related to more time spent in double support ($r=.754$, $p=.084$) in the baseline condition. Poorer Stroop performance was also related to slower walking speed in both open ($r=.812$, $p=.050$) and closed ($r=.829$, $p=.042$) environments, as well as and greater asymmetry ($r=.700$, $p=.188$) in open environments. Strong correlations were also found between the following within the closed environment.</p> <p>Discussion: The findings of this study demonstrate that VTW has a more negative effect on gait parameters in the older population than MTW. This negative effect on gait parameters could lead to a higher risk of falls in the older adult population, having a negative impact on the quality of life of these individuals. CONCLUSION: Older adults had more difficulty with the dual-tasking conditions; the environment and the type of dual-task differentially affected walking performance. Clinicians should examine performance on VTW and MTW in both open and closed environments to provide more information on an individuals' fall risk. Given the common usage of voice applications while walking and driving, recommendations to avoid dual-tasking may be necessary for safety in some patients.</p>

ABSTRACT NO. 26	
Name	Jordan Lawal
Category	Health Science
Title	Revisiting the Single Visit Protocol for Determining the Electromyographic Fatigue Threshold
Authors	Fatin L. Khan, SPT; Jordan M. Lawal, SPT; Drew O. Kapture, SPT; Joseph D. Swingle, SPT; Moh H. Malek, PhD
Abstract	<p>The electromyographic fatigue threshold (EMGFT) has been shown to demarcate between non-fatiguing and fatiguing exercise workloads. One potential limitation of incorporating the single EMGFT test in a clinical setting is the 2 min stage increment inherent to the protocol. In most rehabilitation clinics time with the client is limited and any testing procedures need to consider this factor. The purpose of this study, therefore, was to determine whether or not the estimation of the EMGFT is influenced by reducing the incremental stage to 1-min intervals. We hypothesized that 1-min incremental protocol would provide similar estimates of the EMGFT as the traditional 2-min incremental protocol. Nine college-aged men performed the single leg knee extensor ergometry at 1 min (3 Watts) and 2 min (6 Watts) stages in random order separated by 7 days. The exercise indices as well as EMGFT were determined from the two protocols and analyzed using a paired samples t test. The EMG amplitude was assessed from the rectus femoris muscle. The results indicated significant differences between protocols for maximal power output (1-min: 31.7 ± 2.2 W vs. 2-min: 38.0 ± 3.3 W, $p = 0.016$) and heart rate at end-exercise (1-min: 137 ± 5 b/min vs. 2-min: 148 ± 5 b/min, $p = 0.024$). There was, however, no significant mean differences for EMGFT (1-min: 19.8 ± 1.8 vs. 2-min: 20.3 ± 1.9 W, $p = 0.63$) and rating of perceived exertion for the exercised leg (1-min: 9 ± 0 vs. 2-min: 9 ± 1, $p = 0.68$). These results indicate that reducing the exercise protocol by 50% did not change the estimated EMGFT. The practical application of this finding resides in the potential use in sports or rehabilitative settings in which there is limited time with the client and no objective measures of determine neuromuscular fatigue for aerobic exercise.</p>

ABSTRACT NO. 27	
Name	Jamie Maurice
Category	Health Science
Title	Acquired Cystic Disease-Associated Renal Cell Carcinoma Arising in a Patient After Fifteen Years of Hemodialysis
Authors	Jamie L. Maurice, MLS(ASCP)CM, BS
Abstract	<p>Acquired cystic disease-associated renal cell carcinoma (ACD-RCC) is a recently recognized subtype of renal cell carcinoma (RCC) occurring exclusively in individuals with acquired cystic kidney disease (ACKD).¹ Before being described in the literature in 2005 as a distinct entity, ACD-RCC was commonly diagnosed as renal cell carcinoma-unclassified (RCC-unclassified) or papillary renal cell carcinoma (PRCC).¹ ACD-RCC is the most common subtype of RCC developing in patients with ACKD, predominantly occurring at a younger age and in the male sex. ACKD occurs in 80% of patients with end stage renal disease (ESRD) that have undergone long-term hemodialysis, typically 10 to 20 years. Despite several existing hypotheses, the etiology and pathogenesis of ACKD and ACD-RCC remain largely unknown. The patient presented in this case study is a 71 year-old male with a history of 15 years of hemodialysis as a result of ESRD due to hypertension. A literature review of the macroscopic morphology, microscopic morphology, ancillary testing, staging, and treatment of ACD-RCC is discussed in the context of the patient case study.</p> <p>Reference List</p> <ol style="list-style-type: none"> 1. Foshat M, Eyzaguirre E. Acquired Cystic Disease-Associated Renal Cell Carcinoma. Arch Pathol Lab Med. 2017;141:600-606. doi: 10.5858/arpa.2016-0123-RS. 2. Mehra R, Smith SC, Divatia M, Amin MB. Emerging Entities in Renal Neoplasia. Surg Pathol Clin. 2015; 8(4): 623-656. doi: http://dx.doi.org/10.1016/j.path.2015.08.004. 3. Sule N, Yakupoglu U, Shen SS, et al. Calcium Oxalate Deposition in Renal Cell Carcinoma Associated With Acquired Cystic Kidney Disease. Am J Surg Pathol. 2005; 29(4):443-451. doi: http://dx.doi.org/10.1097/01.pas.0000152131.58492.97. 4. Rahbari-Oskoui F, O'Neill WC. Diagnosis and Management of Acquired Cystic Kidney Disease and Renal Tumors in ESRD Patients. Semin Dial. 2017; 30(4): 373-379. doi: 10.1111/sdi.12605. 5. Alpers CE, Chang A. The Kidney. In: Kumar V, Abbas Ak, Aster JC, Perkins JA, eds. Robbins and Cotran Pathologic Basis of Disease, 9th Edition. Philadelphia, PA: Elsevier Inc.; 2015: 897-957. 6. Scovell J, Hernandez J, Hollander A, Link R. Transposon mutagenesis drives renal cyst formation in vivo when combined with C-Met hyperactivation: implications for acquired renal cystic disease. J Urol. 2017; 197 (4S):e494-e495. doi: https://doi.org/10.1016/j.juro.2017.02.1179.

ABSTRACT NO. 28	
Name	Stephanie Mehmed-Bialowicz
Category	Health Science
Title	Effect of Using a Foot Strap on Muscle Activation During Recumbent Stepping in Healthy Individuals
Authors	Ann Brahier, SPT; Amelia, Crandall, SPT; Alexzanda, Johnson, SPT; Stephanie Mehmed-Bialowicz, SPT; Victoria Pardo, PT, DHS; Sujay Galen, PT, PhD.
Abstract	<p>Introduction/Clinical Relevance: NuStep is a recumbent stepper that is used in a variety of clinical settings as an exercise modality. To date there are no investigations to our knowledge that have studied the effect of using a foot strap on lower extremity(LE) muscle activation, while exercising using the NuStep. Therefore, the purpose of this study was to determine the effects of using a foot strap during recumbent stepping on LE muscle activation. This study also aimed to determine if recumbent stepping with a foot strap would have an immediate effect on distal LE muscle activation during rhythmic weight shifting.</p> <p>Methods: Twenty-five participants (17 female, mean age male: 24.3 ± 3.2 years, female: 26.1+ 4.6 years) were recruited. An initial 10 minute stepping protocol on the NuStep was performed to determine the self-selected cadence. EMG surface electrodes were then applied to the rectus femoris (RF), vastus medialis (VMO), semitendinosus (ST), soleus (SO), medial gastrocnemius (MG), and tibialis anterior (TA) muscles bilaterally. The force and EMG output during maximal voluntary contraction (MVC) of each muscle were measured simultaneously using surface EMG and a hand-held dynamometer. The participants then performed 4 bouts of 5 minutes of stepping with a 5 minute rest in between each experimental condition: no foot straps (NFS), right foot strap (RFS), left foot strap (LFS), all foot straps (AFS). EMG data were recorded at 10 second intervals during the 2nd, 3rd and 4th minutes of each experimental condition and were normalized to MVC. After each condition, participants completed the rhythmic weight shifting program on the Balance Master (medio-lateral and anterior-posterior at slow, medium and fast speeds), while simultaneous EMG data were recorded. A descriptive analysis was performed followed by a repeated measures ANOVA to examine differences in muscle activation between experimental conditions, and muscle groups.</p> <p>Results: The repeated measures ANOVA revealed significant differences in muscle activation between the four experimental conditions in both LE (p<0.001). A post-hoc analysis revealed that the TA and VMO had significantly greater activation compared to the RF across all experimental conditions (p<0.05), except when the LE was resting while the opposite LE was exercised as part of the single leg foot strap condition (LFS/RFS).</p> <p>Discussion: Muscle activation in the LE while stepping using the NuStep appears to generally increase when individuals used just a single LE to perform stepping. Some low level LE muscle activation was seen in the resting LE. TA and VMO activation were significantly increased when subjects used a single leg to performing stepping (LFS/RFS). Muscle activation in the LE muscles remained the same with or without the foot straps. Conclusions: This study has demonstrated that the foot strap did not have an effect on LE muscle activation. However key muscles that are activated during walking such as VMO and TA were referentially recruited across all experimental conditions, and were significantly greater during single leg stepping. This finding may have clinical relevance in various orthopedic and neurological conditions where VMO and/or TA may need to be strengthened.</p>

ABSTRACT NO. 29	
Name	Abigail Myles
Category	Health Science
Title	Physical Markers of Functional Fitness in Persons with Dementia and Their Family Care Partners
Authors	Abigail Myles, SPT; Kristin Brown, SPT; Madiso, VanAntwerp, SPT; Lauren Bollinger, SPT; Fredrick D. Pociask, PhD, PT; Rosanne DiZazzo-Miller, PhD, OTRL; Diane E. Adamo, PhD, OT
Abstract	<p>Introduction: Six million individuals are currently living with an Alzheimer's dementia diagnosis in the U.S., which is expected to grow as the population over the age of 65 rises. The number of family care partners (FCPs) will also increase to meet the caregiving needs of persons with dementia (PWD). The potential risk for declines in physical function and subsequent loss of functional independence exists in both groups. This study investigated the relationship between physical markers of functional fitness using the Senior Fitness Test (SFT), and cognition using the Mini Mental State Exam (MMSE) scores for FCPs and PWD.</p> <p>Method: Using an exploratory cross-sectional research design, group differences for measures of SFT performance, grip strength, and memory impairment were compared between 15 FCPs (mean age \pm SD = 60.4 \pm 13.7 years) and 15 PWD (mean age \pm SD = 76.9 \pm 8.3 years). SFT components included the following tests: chair stand, arm curl, 6-minute walk (6MWT), chair sit and reach, back scratch, and 8-foot up and go (8FU&G) tests. Independent t tests and correlations were used to report associations and differences for groups. The percentage of individuals at risk for loss of functional independence was reported.</p> <p>Results: Significant group differences were found for the sit and reach test [mean (SD) in. = FCPs: 1.01 (4.40), PWD: -2.49 (2.98)], the 6MWT [mean (SD) yds. = FCPs: 430.29 (116.43), PWD: 284.51 (119.14)], the 8FU&G test [mean (SD) s. = FCPs: 6.78 (1.80), PWD: 13.48 (6.42)], and average grip strength bilaterally [mean R/L (SD) kg. = FCPs: 31.73 (11.29)/28.73 (8.37), PWD: 18.92 (6.48)/18.33 (7.50)]. MMSE scores were associated with the 6MWT for the PWD group ($r = .672, p < .01$). MMSE scores were associated with the 8FU&G test for all participants ($r = -.652, p < .01$). The percentage of participants in each group who performed below the level for loss of functional independence for each SFT task are as follows: chair stand; FCPs (0%), PWD (46.7%), arm curl; FCPs (20%), PWD (40%), back scratch; FCPs (33.3%), PWD (53.3%), sit and reach; FCPs (6.7%), PWD (40%), 6MWT; FCPs (26.7%), PWD (80%), 8FU&G; FCPs (13.3%), PWD (73.3%).</p> <p>Discussion & Conclusion: At least 40% of PWD performed below the threshold for loss of functional independence in every SFT measure. At least 6.7% of FCPs performed below the threshold for loss of functional independence in five of the six SFT measures. The age range of the FCPs group included participants under the age of 60. When the FCPs sample was adjusted for age, only including participants who were over 60 years old, differences between groups were noted for grip strength, chair stand, 8FU&G, and the 6MWT. Despite being younger than 60 years old, FCPs still showed a risk for loss of functional independence based on the thresholds for the 60+ group. Results suggest that interventions should be developed for both FCPs and PWD to minimize potential loss of functional independence.</p> <p>ACKNOWLEDGMENTS: We would like to thank the Alzheimer's Association for supporting this study.</p>

ABSTRACT NO. 30	
Name	Jenna Page
Category	Health Science
Title	Effect of Using a Nunstep Footstrap on Muscle Activation in Patients with Chronic Stroke
Authors	Page J; Popescu-Alexa V; Thurston T; Galen S; Pardo V
Abstract	<p>Intro: The NuStep recumbent stepper is widely used by clinicians to improve cardiovascular health and physical performance. There is currently no evidence on the effects of using a foot strap during recumbent stepping, and whether this has an immediate effect on distal muscle activation during rhythmic weight shifting. This study investigates changes in electromyographic (EMG) activation and force production while exercising with and without the foot strap(s) in subjects with chronic stroke, and any carryover effect it may have on muscle activation during rhythmic weight shifting.</p> <p>Methods: Eleven participants (8 female, 8 right hemiparesis, and mean age 62.5 ± 15.9 years) with chronic stroke were recruited. Participants completed a 10 minute trial of stepping on the NuStep to determine self-selected speed (SS). EMG surface electrodes were then applied to the rectus femoris (RF), vastus medialis (VMO), semitendinosus (ST), soleus, medial gastrocnemius, and tibialis anterior (TA) muscles bilaterally. The force and EMG output during maximal voluntary contraction (MVC) of each muscle were measured simultaneously using surface EMG and a hand-held dynamometer. The participants then performed 5 minutes of stepping with a 5 minute rest in between each experimental condition: no foot strap (NFS), right foot strap (RFS), left foot strap (LFS) and both straps (AFS). During the LFS and RFS conditions, the resting leg was placed on a footstool and not involved in the stepping motion. EMG data were recorded at 10 second intervals during the 2nd, 3rd and 4th minutes of each experimental condition and were normalized to MVC. After each condition, participants completed the rhythmic weight shifting program on the Balance Master (medio-lateral and anteriorposterior at slow, medium and fast speeds), while simultaneous EMG data were recorded. A descriptive analysis was performed followed by a repeated measures ANOVA to examine differences in muscle activation between experimental conditions, hemiparetic side, and muscle groups.</p> <p>Results: There were significant differences between muscle activity within the same experimental conditions ($p < 0.001$). There were significant differences between muscle activity across experimental conditions for the left leg ($p = 0.003$), but not for the right leg ($p = 0.115$). Significant TA activation was seen compared to other muscles within the LFS and RFS conditions on the right, and when compared to several muscles in all 4 conditions on the left. The VMO showed significantly greater activation ($p < 0.001$) than RF in the NFS, AFS and LFS conditions on the left side. There were no significant differences in velocity or directional control of rhythmic weight shifting across the 4 conditions.</p> <p>Discussion: Stepping on the NuStep with the foot strap (on the right) and in all 4 conditions on the left causes TA to be activated preferentially. In the left leg VMO showed increased activity compared to RF ($p < 0.05$) during most conditions except RFS. There was also increased muscle activation in resting leg.</p> <p>Conclusions: This preliminary study has demonstrated that TA was preferentially activated on during RFS and LFS conditions. VMO can be preferentially activated compared to the RF when stepping on the NuStep both with and without the use of foot straps. It is also clinically relevant that the resting leg had increased muscle activation, possibly allowing PTs to activate muscles in individuals who are unable to move their affected leg. The TA and VMO are muscles that are difficult to recruit in many patient populations, making the NuStep a potentially useful tool in targeted neuro reeducation.</p>

ABSTRACT NO. 31	
Name	Hanan Rakine
Category	Health Science
Title	Effects of prior trauma exposure on emotion reappraisal among student police officers: an EEG study
Authors	Hanan Rakine, BS; Hilary Marusak, Ph.D; Craig Peters, BS; Christine Rabinak, Ph.D
Abstract	<p>Background Trauma exposure is extremely common, yet only a subset of individuals develops posttraumatic stress disorder (PTSD). Recent studies have shown that patients with PTSD display deficits in the regulation of negative affect and exaggerated emotion-related brain activity; as measured by the late positive potential (LPP), an electroencephalography (EEG) event-related potential that responds to emotional stimuli and regulation of emotion. Moreover, these effects persist over time. However, studies have not delineated whether trauma-exposure without the subsequent development of PTSD is related to an altered LPP signal during emotion regulation. Purpose Examining the effects of prior trauma exposure on cognitive reappraisal in psychiatrically-healthy individuals. Methodology This study reports on 24 psychiatrically-healthy individuals (ages 20-33, 21M/3F) recruited from the Detroit Police Academy and Lansing Police Academy. Lifetime exposure to traumatic events was quantified using the Life Events Checklist, while participants were still students in the police academy and prior to active police duty in the field, in which officers would be chronically exposed to traumatic events. Participants also completed an emotion regulation task (ERT), which uses cognitive reappraisal, an emotion technique to actively reinterpret a negative stimulus to make it less negative. In this study, participants viewed neutral and unpleasant images and were instructed to either “maintain” or “reappraise” their negative affect (e.g., “This image is not real - it’s from a movie”). Following each trial, participants rated their negative affect. EEG was used to record LPP amplitude during emotion regulation. Results 92% of participants reported exposure to one or more traumas (range=0-8, median=2.6).</p> <p>Overall, individuals reported less negative affect following neutral images compared to negative images during the ERT ($p's < 0.05$). LPP response was greatest during negative images compared to neutral images, but LPP response did not differ significantly during reappraise or maintain instructions for negative images. A greater number of traumatic events experienced and witnessed was correlated with lower negative affective ratings and lower LPP response, respectively, during reappraisal of negative images. Conclusion Our results suggest that prior trauma exposure is associated with better emotion reappraisal ability. Given that better reappraisal ability is associated with lower risk of PTSD, these data suggest that better emotion reappraisal may be protective against negative psychological outcomes following trauma exposure.</p>

ABSTRACT NO. 32	
Name	Kelsey VanAmberg
Category	Health Science
Title	Age related differences in grip strength and cognitive performance
Authors	Kelsey VanAmberg, SPT; Tara Anderson, SPT; Mahtab Koochaki, SPT; Diane Adamo, PhD; Nora Fritz, PhD, PT, DPT, NCS
Abstract	<p>Introduction: With declining cognitive capacity, the ability to monitor changes in motor and cognitive function is crucial to identifying specific interventions that may intercede and reduce potential loss. Declining grip strength has been shown to be an early biomarker of cognitive decline for individuals with mild cognitive impairment, dementia, and declines in mental state, but has not been explored in individuals younger than 65 years old. Therefore, the purpose of this study was to investigate the relationship between grip strength and cognitive function in young and middle-aged adults. Early examination of physical and cognitive performance may provide evidence that these changes occur earlier than previously reported. The results of this study may inform future work, including longitudinal designs to establish a predictive relationship between cognitive performance and grip strength.</p> <p>Methods: This research study was a cross sectional with a within-subjects design. All subjects were right handed (Edinburgh Handedness Inventory score of >0.7), had a Montreal Cognitive Assessment (MoCA) score of >26/30, were young (20-30 years old) or middle-aged (45-65 years old), had no orthopedic or neurological conditions, were able to grip without difficulty, were able to follow simple instructions, and had normal/corrected vision and hearing. All subjects performed right and left grip strength measures and five cognitive tests: 1. Stroop, 2. California Verbal Learning Test, 3. Symbol Digit Modalities Test, 4. Trail Making Tests, and 5. Controlled Oral Word Association Test (COWAT). Data was assessed for normality and a descriptive analysis was completed on all outcome measures to determine means and standard deviations. Pearson's correlations were used to examine the relationship between grip strength and each individual cognitive test. Independent t-tests determined group differences between middle-age and young-age.</p> <p>Results: Forty-six subjects were recruited from the young (n = 25) and middle-age group (n = 21). Independent t-tests revealed no significant differences between the young-age and middle-age groups for handedness, MoCA, education, height, and weight. However, middle-aged adults performed significantly worse on right and left grip strength and the Stroop test (p<0.05). There was no significant relationships among grip strength and cognitive performance at the whole-group level or within the young-age group; however, worse grip strength was significantly associated with poorer COWAT (R=0.440; p = 0.045) and Stroop (R=0.438; p = 0.047) performance in the middle-aged group.</p> <p>Discussion: Simple clinical tests of strength and cognitive function can distinguish between young and middle-aged adults. Poorer grip strength was significantly associated with poorer cognitive function in the middle-age group, suggesting that some domains of cognition appear to be particularly sensitive to age-related changes, specifically semantic categorization and executive function.</p> <p>Conclusion: Cognitive changes may occur earlier than previously thought (i.e., prior to age 65). Grip strength has the potential to serve as a biomarker for early cognitive changes. Clinicians should consider monitoring both grip strength and cognition in both middle age and older adults.</p>

Pharmaceutical Sciences

ABSTRACT NO. 33	
Name	Kawthat A. Alali
Category	Pharmaceutical Sciences
Title	Crash Risk and Crash Avoidance Studies in a Driving Simulator: A Method for Studying the Effects of Drugs on Driving
Authors	Kawthar A. Alali, BS Kijana S. Malone MaryAnne J. Stewart, MS Hanna Omar, BS Anese Yaffai, BS Rimzim Taneja, BS, MS Brandon Buchanan Edison Nwobi Julian Ezell Doreen Head, MS, PhD Randall L. Commissaris, PhD
Abstract	<p>One goal of our research group is to develop a research tool (procedure) that will be useful in studying/quantifying driving impairments associated with alcohol, marijuana and other drugs (legal and illegal). Using a fixed based driving simulator (2001 Chevy Impala), we developed a procedure (Avoidance Reaction Time Involving Collisions; ARTIC) to demonstrate and measure a driver's accident avoidance skills and reaction times. In this procedure, a stationary 'entity' (in this case, a stalled car) appears in the roadway 35 meters ahead of the simulator car, and the driver's task is to quickly steer around the stalled car to avoid crashing. In this study, subjects 'drove' our car on three straight roadways at 55 mph. On one roadway (Control), the subjects were not distracted; on a second roadway (Mild Distraction), the subjects were instructed to avoid stalled cars and also count the number of occasions when an ambulance randomly appeared on the side of the road. On the third roadway (Cell Phone Browsing Distraction), the subjects were instructed to actively browse on their cell phone (e.g., Instagram, Facebook, Snapchat, Twitter) while driving and avoiding 'stalled' cars. Ten 'stalled' cars were presented on each roadway. For all roadways, we measured the number of crashes and the severity of the crashes (14 scale; 1 = safe avoidance; 4 = squared up rear end crash). We also measured avoidance reaction times, defined as the time from onset/appearance of the 'stalled' car on the screen to the time when the driver exhibited a steering wheel turn of greater than 10 degrees. In addition, we used synchronized dual camera videos (face camera and road camera) to separate the data into categories based upon whether the drivers' eyes were or were not directed toward the road when each 'stalled' car initially appeared. (We also identified a few 'ties' where the drivers' eyes moved to or from the road at virtually the same moment that the 'stalled' car appeared). In the Control roadway (i.e., no distractions), a 35meter lead time resulted in approximately 5% crashes (7.5%), with a mean Avoidance Reaction Time (ART) of 538 + 70 msec; (Mean + SD). Mild Distraction (i.e., counting ambulances) increased these values slightly (10% crashes; ART: 543 + 76 msec) and Cell Phone Browsing Distraction increased these values even more dramatically (50% crashes; ART: 751 + 73 msec). Analysis of the videos revealed that the primary cause of the increase in crash frequency was eye glances away from the road at the moment the 'stalled' car appeared on the distraction roadways. These data suggest that our ARTIC testing procedure will be useful for quantifying the effects of alcohol, marijuana and other drugs on driving performance and Avoidance Reaction Times. (WSU IRB #066717BE).</p>

ABSTRACT NO. 34	
Name	Rami Alzhrani
Category	Pharmaceutical Sciences
Title	Cancer Stem Cells and Tyrosine Kinase Receptors Directed Macromolecules for Pancreatic Ductal Adenocarcinoma Imaging
Authors	Rami Alzhrani; Samaresh Sau; Amro Aboukameel; Hashem O. Alsaab; Asfar S. Azmi; Arun K. Iyer*
Abstract	<p>Pancreatic ductal adenocarcinoma (PDAC) is the third highest cause of cancer-related death in the United States. PDAC represents one of the most challenging cancer due to its pathological characteristics, such as dense desmoplastic tissue with >90 % tumor stroma. Tumor stroma consists of several agents including extracellular matrix proteins and tumor immune cells that induce drug resistance to therapy. Among all epithelial tumors, PDAC has the densest stroma that contributes to chemotherapy resistance and reduces drug delivery to the core of the solid tumor. Accumulated evidence found that pancreatic cancer cells are overexpressing multiple surface biomarkers such as CD24+, CD44+, ESA+, and c-Met that contribute to forming PDAC stroma. CD44+ along with CD24+ and ESA+ cells, which are a subset of cells that belong to ATP binding cassette transporter (ABC), play a significant role in increasing both multidrug resistance (MDR) and tumorigenicity of PDAC. Beside CD44+ biomarker, c-Met, which is a member of tyrosine kinase family, is another surface biomarker that plays a pivotal role in pancreatic cancer development, tumorigenesis, regeneration, cells invasion and metastasis. Taking together, positive CD44+ and c-Met receptors are novel targeting biomarkers that can be utilized in enhancing drug delivery and efficacy. In this regard, we developed a dual-targeted macromolecule (DTMM) that can target the overexpressed CD44+ and c-Met. The macromolecule was designed to penetrate the pancreatic cancer stromal barrier and deliver the imaging agent deep to the core of the tumor. So far, we successfully synthesized, characterized the dual-targeted macromolecule using copper free-click chemistry. The chemical conjugation between the macromolecule and the dual-targeted ligands was confirmed using FTIR and MALDI-TOF MS. The characterized construct was tested on orthotopic PDAC model for evaluating the imaging agent efficiency. The biodistribution of DTMM using near Infrared (NIR) dye showed the vast majority accumulated in the tumor site. To confirm the bio-distribution results, the tumor/liver uptake ratio study was carried out. The result of this study revealed that DTMM is seven folds higher than non-targeted macromolecule (NTMM). On the tumor tissue level, the co-localization study was carried out to evaluate the DTMM localization with both CD44 and c-Met receptors using immunohistochemistry study (IHC). IHC was showed that the intensity of DTMM is higher than NTMM. Overall, the obtained results indicated that the dual-targeted MM would open avenues for imaging-guided diagnosis in PDAC tumor.</p>

ABSTRACT NO. 35	
Name	Sharon Batelu
Category	Pharmaceutical Sciences
Title	Molecular characterization and interactions of the Ferredoxin protein involved in the mitochondrial iron sulfur cluster assembly
Authors	Sharon Batelu, Ph.D Candidate; Timothy Stemmler, Ph.D
Abstract	<p>Molecular characterization and interactions of the ferredoxin protein involved in the mitochondrial iron sulfur cluster assembly. Sharon Batelu, Timothy Stemmler. Abstract Iron, absorbed by the body is destined for potential use in several different biochemical pathways. Once inside, iron is either stored in the ferritin protein complex, utilized in metallo-biomolecules, or targeted to the mitochondria. Mitochondria are a major controller of cellular iron metabolism. Both heme and Fe-S cluster biosynthesis is accomplished within the mitochondria, and since Fe-S clusters are used in almost every biochemical pathway, proteins containing these Fe cofactors are not surprisingly, essential. These Fe containing cofactors are structurally and chemically suited to carry out redox reactions and also serve as electron conduits, so their appearance in so many essential biochemical pathways is not surprising. Their prevalence in biology only highlights the vital importance of their controlled biogenesis and many of the proteins involved in the Fe-S cluster biogenesis and maturation are essential for cell viability¹. The iron sulfur cluster (ISC) assembly machinery, found within the mitochondria of eukaryotes, provides the clusters required for most of the cell. The ISC assembly complex in yeast consists of several proteins, each with a targeted role including a ferredoxin (Yah1), which itself contains a Fe-S cluster, that regulates the reducing environment for cluster assembly. The human mitochondria contain two isoforms of the protein ferredoxin that perform similar redox functions despite being only 33% similar in protein sequence². While the first ferredoxin (FDX1) participates in many pathways including the steroid biogenesis and vitamin D biosynthesis, the second ferredoxin (FDX2) is exclusive to the ISC assembly pathway³. Our lab works with the yeast equivalent of the FDX2 protein called Yah1. As this protein is a vital for cluster assembly, a thorough study of its molecular characteristics and interactions with other proteins within the system is important. Here we show and insights into the Fe-S cluster of this protein and some of its binding interactions and affinities for the other proteins of the ISC pathway. The importance and necessity for such studies can be appreciated as disruption in the activity of any of these proteins would cause a breakdown in the overall activity of the ISC machinery which would lead not only to a decrease in cluster biogenesis, but also hinder the controlled utilization of redox active iron, leading to uncontrolled chemistry by the metal and reactive oxygen species generation that can kill the cell and kill the organism. References: 1. Dutkiewicz R; Nowak M (2017) Molecular chaperones involved in mitochondrial iron–sulfur protein biogenesis. <i>J Bio Inorg Chem</i> 23(4) 569-579 2. Sheftel A. D.; Stehling O.; Pierik A. J.; Elsasser H. P.; Muhlenhoff U.; Webert H.; Hobler A.; Hannemann F.; Bernhardt R.; Lill R. (2010) Humans possess two mitochondrial ferredoxins, Fdx1 and Fdx2, with distinct roles in steroidogenesis, heme, and Fe/S cluster biosynthesis. <i>Proc. Natl. Acad. Sci. U. S. A.</i> 107, 11775–11780.10.1073/pnas.1004250107. 3. Ewen K. M.; Ringle M.; Bernhardt R. (2012) Adrenodoxin--a versatile ferredoxin. <i>IUBMB Life</i> 64, 506–512.10.1002/iub.1029.</p>

ABSTRACT NO. 36	
Name	Ketki Bhise
Category	Pharmaceutical Sciences
Title	Lipid Formulations for Combination of Antibiotics in Methicillin-resistant Staphylococcus aureus Infection: A Promising Approach
Authors	Ketki Bhise, M.Tech; Samaresh Sau, PhD; Seth Rice, BS; Kyle Stamper, BS; Razie Kebriaei, PhD; Michael J. Rybak, PhD; Arun K. Iyer, PhD
Abstract	<p>Purpose: Vancomycin (VAN) is a common drug used for treating Methicillin-resistant Staphylococcus aureus (MRSA) infections. However, vancomycin causes nephrotoxicity at doses that approach 4g/day. In addition, resistant bacterial strains are continuously emerging with limited to no treatment options. The combination of VAN with cefazolin (CFZ) has proven effective against both MRSA and Methicillin-sensitive Staphylococcus aureus (MSSA). In this study, we engineered long circulating liposomal formulations of VAN and CFZ with high drug loading and tested their efficacy against MRSA and MSSA strains by minimum inhibitory concentration (MIC) and biofilm disruption studies. We further tested the extent of liposomal uptake in the kidneys to see whether there is reduction in kidney uptake which formed the preliminary data to assess possible safety.</p> <p>Methods: Liposomal VAN and CFZ (abbreviated Lipo-VAN and Lipo-CFZ, respectively) were prepared by a modified reverse phase evaporation method. The particle size of liposomes was measured by transmission electron microscopy (TEM) and dynamic light scattering (DLS). Drug loading was determined by HPLC and UV. MICs were determined by incubating Lipo-VAN and Lipo-CFZ for 24 h at 35°C with SA 494 (MRSA) and ATCC 29213 (MSSA) strains. For kidney uptake studies, liposomes loaded with NIR dye S0456 (Lipo-VAN-S0456) were injected intravenously (i.v.) at 20 nM dose in athymic nu/nu mice and euthanized after 4h, followed by ex-vivo imaging of liver and kidneys. Biofilm disruption by liposomal formulations was studied by pin lid assay.</p> <p>RESULTS: Liposomes of sizes between 170-198 nm were obtained by modified reverse phase evaporation method that resulted in high drug loading of 53% and 26% (wt/wt) for VAN and CFZ, respectively. The combination of Lipo-VAN and Lipo-CFZ demonstrated 4-fold lower MICs with respect to the free drug combination. Using the biofilm pin lid assay we observed that the liposomal formulations caused remarkable bacterial growth inhibition in the tested MRSA strains in comparison to commercial product VAN and CFZ controls, possibly due to efficient biofilm penetration by the liposomes. The NIR imaging of mouse injected i.v. with Lipo-VAN-S0456 clearly indicated that the liposomes had limited accumulation in the kidneys with slightly higher accumulation in the liver, suggesting that the long circulating anocarriers could enhance its delivery efficacy in treating superbug infections while reducing the nephrotoxicity associated with antibiotics such as VAN in the clinical setting.</p> <p>CONCLUSION: The combination of Lipo-VAN and Lipo-CFZ provides a rational approach for combating MRSA infection and are likely to be translated clinically on successful demonstration of reduced animal toxicity.</p>

ABSTRACT NO. 37	
Name	Caitlin Bolick
Category	Pharmaceutical Sciences
Title	Clinical Outcomes with Cephalosporins vs. Penicillins in Combination with Vancomycin for the Treatment of Methicillin-Resistant Staphylococcus aureus Bloodstream Infections
Authors	Caitlin Bolick, M.P.H., Pharm. D. Candidate; Sarah C.J. Jorgensen, Pharm. D., BCPS; Michael J. Rybak, Pharm. D., M.P.H., Ph.D.
Abstract	<p>Background: Methicillin-resistant Staphylococcus aureus (MRSA) bloodstream infection (BSI) is associated with significant morbidity and mortality. Vancomycin (VAN) monotherapy is the standard treatment for MRSA BSI. Unfortunately, treatment failure can occur due to decreased VAN susceptibility and poor penetration in deep seated infections. In addition, cross resistance to alternative therapy such as daptomycin has been reported, further limiting therapeutic options. It has been demonstrated that VAN in combination with beta-lactam antibiotics results in a reduction in VAN MICs, improved bactericidal activity, and prevents of the emergence of VAN non-susceptibility. While the combination with either cephalosporins or penicillins have demonstrated potential synergy with VAN, the combination of VAN + penicillin class antibiotics appear to be more nephrotoxic. In addition, cephalosporins may be associated with lower rates of other adverse events. Objective: To determine if patients with MRSA BSI treated with VAN + cephalosporins vs. VAN + penicillins have a lower risk of clinical failure, defined as a composite of 30-day all-cause mortality, persistent BSI (≥ 7 days), 60-day recurrence, and/or nephrotoxicity.</p> <p>Methods: This was a retrospective, observational study conducted at the Detroit Medical Center between 2010 and 2018. Adult patients (18+) who were diagnosed with MRSA BSI and received intravenous VAN + a beta-lactam within 48 hours of blood culture collection and continued together for ≥ 48 hours were included. Patients with polymicrobial BSI, acute kidney injury, or end-stage renal disease prior to initiation of VAN were excluded. Nephrotoxicity was defined as an increase in serum creatinine $\geq 50\%$ and 0.5 mg/dL over two consecutive measurements. Multivariable analysis was conducted to determine independent predictors of clinical failure.</p> <p>Results: A total of 137 patients were included (117 VAN + cephalosporin and 20 VAN + penicillin). The median age was 56 (47 –67) years, 68% were African American, the median Charlson Comorbidity Index was 1 (1 – 3), and the median APACHE II score was 13 (8 – 21). The predominant sources of infection were lower respiratory tract (23%), skin/soft tissue (17%), bone/joint (9%), and infective endocarditis (6%). Clinical and infection characteristics were similar in the two groups. Clinical failure occurred in 22% vs. 40% of patients in the VAN + cephalosporin vs. VAN + penicillin group, respectively ($P = 0.09$). Overall, 6 (4%) patients developed nephrotoxicity: 4 (3%) in the VAN + cephalosporin group and 2 (10%) in the VAN + penicillin group (OR 0.32, 95% CI 0.05-1.85). The median time to nephrotoxic event was 7.5 days in the VAN + cephalosporin group vs. 4 days in the VAN + penicillin group ($P = 0.057$). On multivariable analysis, infective endocarditis (aOR, 95% CI, 11.74, 3.76-36.67), lower respiratory tract BSI source (aOR 4.02, 95% CI 1.56–10.35) and treatment with VAN + penicillins (aOR 3.43, 95% CI 1.13 – 10.40) were independently associated with clinical failure. Conclusions: Our findings suggest VAN + penicillins may be associated with a higher risk of clinical failure vs. VAN + cephalosporins. Larger studies are needed to confirm these preliminary results.</p>

ABSTRACT NO. 38	
Name	Amanda Fawaz
Category	Pharmaceutical Sciences
Title	Clinical outcomes of vancomycin therapy in the presence of hypoalbuminemia compared to normoalbuminemia
Authors	Amanda Fawaz, PharmD Candidate; Lama Hsaiky, PharmD BCPS
Abstract	<p>Purpose: Vancomycin is the mainstream therapy for MRSA infections. Vancomycin pharmacokinetics is dependent on certain baseline patient characteristics. One well known and wellstudied parameter which dictates vancomycin efficacy is renal function. Another parameter, however not well studied, is albumin deficiency. Vancomycin acts in its non-protein bound state, hence having hypoalbuminemia can potentially cause an increase in vancomycin concentrations, placing the patient at increased risk for toxicities. To establish an association between albumin levels and vancomycin treatment outcomes, this study will examine toxicity and dosing outcomes of patients with normoalbuminemia compared to hypoalbuminemia, who are treated with vancomycin.</p> <p>Methods: The institutional review board approved this retrospective, open-label, cohort study within Beaumont Hospital Dearborn. Patients were included if they were more than or equal to 18 years of age, admitted between January and September 2017, received at least 4 doses of vancomycin and had a documented albumin level. Patients were grouped into: Group one (normoalbuminemia, albumin more than 2.5 mg/dl) and group two (hypoalbuminemia, albumin less or equal to 2.5 mg/dl). The following data was collected: baseline demographic characteristics (age, gender, weight, serum creatinine, creatinine clearance, albumin level, length of stay, comorbidities (diabetes mellitus, cancer, renal insufficiency, hypertension, heart failure, and peripheral vascular disease), concomitant nephrotoxic medications and empiric vancomycin dosing regimen and the two proceeding regimens along with kinetic parameters [dose (mg), frequency, extrapolated levels ($\mu\text{g}/\text{mL}$), half-life, elimination rate and volume of distribution]. Data is expressed as means and standard deviations with a T-test for the statistical analyses. The primary study outcome is achieved vancomycin trough levels at steady state as well as the presence of nephrotoxicity [serum creatinine increase 2 to 3 times above baseline or more than 50% decrease in glomerular filtration rate (GFR)]. The secondary outcome of this study is length of hospital stay.</p> <p>Results: One hundred and seventeen patients were included in the study, 58 (49.5%) in Group one and 59 (50.5%) in Group two. There were no statistically significant differences in age, gender, race, history of diabetes, peripheral vascular disease, hypertension, body mass index, and baseline creatinine clearance. Congestive heart failure patients were 22 percent in group one versus (vs) 7 percent; P equal 0.016. Malignancy was significantly higher in group two, 34 versus 7 percent in group one, P equals 0.0002. Compared to group two, no significant difference we observed for average doses of empiric Vancomycin load (mg) [1723 plus or minus 469 vs 1597.5 plus or minus 434; P equals 0.138], empiric first dose (mg) [2672.5 plus or minus 1229.3 vs 2923.7 plus or minus 1249.8; P equals 0.279] and extrapolated first steady state level ($\mu\text{g}/\text{mL}$) [14.5 plus or minus 6.1 vs 15.9 plus or minus 7.8; P equals 0.246] in group one vs group two. All pharmacokinetic parameters, proceeding doses, and trough levels were not statistically different. Acute kidney injury (AKI) developed in 26% (group one) vs. 27% (group two); P equals 0.878. Hospital length of stay was significantly longer in hypoalbuminemia group 20.1 vs 12.8 days; P equals 0.0007.</p> <p>Conclusion: Vancomycin use in the presence of hypoalbuminemia did not affect the rate at which nephrotoxicity occurred. In addition, the vancomycin trough levels were very comparable in both groups throughout the treatment and levels were within acceptable therapeutic ranges regardless of albumin status. However, the length of stay was observed to be longer among patients presenting with hypoalbuminemia. Further prospective controlled studies with well-matched groups, might be able to determine if the degree of hypoalbuminemia has any impact on AKI and vancomycin trough levels and prolonged length of stay due to unachievable therapeutic level early in the treatment.</p>

ABSTRACT NO. 39	
Name	Suhadinie Gamage
Category	Pharmaceutical Sciences
Title	PREX1, a guanine nucleotide exchange factor for Rac1, mediates physiological insulin secretion in pancreatic beta-cells
Authors	Suhadinie Gamage, MS; Anjaneyulu Kowluru Ph.D.
Abstract	<p>Purpose: Pancreatic beta cells secrete insulin following a stimulus of glucose via a complex metabolic event known as glucose stimulated insulin secretion (GSIS). Previous work from our laboratory demonstrated that Rac1, a member of the Rho GTPase subfamily, is involved in GSIS. Rho GTPases are important for remodeling of the cytoskeleton, trafficking and recruitment of insulin laden vesicles onto the plasma membrane to facilitate insulin secretion from pancreatic beta cells. GDP bound Rac1 (inactive) must be converted to GTP bound Rac1 for activation. This process is aided by GDP/GTP exchange factors. PREX1 (phosphatidylinositol-3,4,5-trisphosphate-dependent Rac exchange factor 1) is a Rac1 guanine nucleotide exchange factor (GEF), the role of which is not examined in the islet beta-cell function, specifically in GSIS. The aim of this study is to investigate the role of PREX1 as a novel regulator for Rac1 activation and GSIS in the beta cells of pancreatic islet beta-cells.</p> <p>Methods: Expression of PREX1 in beta cells was confirmed by Western blot. Short interfering RNA (siRNA) was used to suppress the expression of PREX1. Rac1 activation was determined by Rac1 pull down assay. Enzyme-linked immunosorbent assay (ELISA) was used to assess GSIS.</p> <p>Results: Western blotting showed that PREX1 is expressed in INS-1 832/13 beta cells, normal rat islets and human islets. siRNA mediated knockdown of PREX1, consistently reduced glucose-induced activation of Rac1 and insulin secretion in INS-1 832/13 cells.</p> <p>Conclusion: We provide the first evidence for the regulation of glucose-induced activation of Rac1 and insulin secretion by PREX1 in pancreatic beta-cells.</p>

ABSTRACT NO. 40	
Name	Tiffanie Hargraves
Category	Pharmaceutical Sciences
Title	A novel metformin-methylglyoxal imidazolinone metabolite (IMZ) sensitizes cells to insulin; a potential role in alleviating T2DM complications
Authors	Tiffanie Hargraves, PhD Candidate; Nicholas Mastrandrea, PhD; Serrine Lau, PhD; Terrence, Monks, PhD
Abstract	<p>Reactive dicarbonyls, such as methylglyoxal (MG), are elevated in type-two diabetes mellitus (T2DM) patients. These endogenous electrophiles covalently modify proteins, which may contribute to diabetic complications. The T2DM first-line therapy, metformin (MF), significantly reduces adverse diabetic endpoints and mortality more effectively than other antihyperglycemic agents, the mechanism(s) of which remain unclear. We previously identified and characterized the product of the MF and MG reaction as a novel five-membered imidazolinone (IMZ) metabolite. IMZ was detected via LC/MS in all MF-treated T2DM patients, and increased MF urinary levels directly correlated with elevations in urinary IMZ. Scavenging of MG by MF represents a possible alternative mechanism of MF drug efficacy, in addition to its antigluconeogenesis properties. Imidazolinone receptor subtypes (I1R, I2R, and I3R) are novel targets for drug development in disorders associated with T2DM because they are involved in insulin sensitization, insulin secretion, and glucose homeostasis. Thus, we examined the ability of IMZ to modulate insulin-mediated cell signaling pathways via western blot in PC12 cells, which express high levels of I1R and lack the α2-adrenergic receptor, which many I1R agonists also activate. Combination treatment of insulin and IMZ at physiologically relevant concentrations increased AKT and ERK1/2 phosphorylation above levels seen with insulin treatment alone. This potentiation was not observed in the presence of I1R antagonists. Moreover, IMZ restores insulin sensitivity in an insulin resistant HEPG2 cell model. The results revealed that IMZ may enhance insulin action in the insulin-dependent AKT and ERK1/2 pathways through I1R activation. Preliminary in vivo pharmacokinetic studies show that IMZ (IP; 10mg/kg and 20mg/kg) is rapidly absorbed, with an elimination half-life of 12-16.5 minutes. In addition, IMZ enhanced hepatic pAKT 40 minutes after the 10mg/kg dose. In summary, the formation of IMZ in T2DM patients provides evidence that MF scavenges MG, potentially reducing detrimental protein modifications. This property of MF may play a role in the reduction of diabetic complications and represent a potential alternative mechanism of MF drug efficacy. Further, IMZ itself may have the ability to enhance insulin action, suggesting possible clinical utility in the treatment of T2DM.</p>

ABSTRACT NO. 41	
Name	Argel Islas Robles
Category	Pharmaceutical Sciences
Title	Determination of the role of PAR-associated proteins in ROS-mediated cell death
Authors	Argel Islas-Robles; Serrine S. Lau; Terrence J. Monks
Abstract	<p>2,3,5-Tris-(glutathion-S-yl)hydroquinone (TGHQ) is a nephrotoxic and nephrocarcinogenic metabolite of hydroquinone. TGHQ can redox cycle, generating ROS which cause DNA strand breaks, hyperactivation of poly(ADP-ribose) polymerase-1 (PARP-1), increases in intracellular calcium concentration ($i[Ca^{2+}]$), and cell death. PARP-1 is a nuclear protein involved in DNA repair, transcriptional regulation and intracellular trafficking, and catalyzes the attachment of a posttranscriptional modification, consisting of multi branched ADP-ribose polymers (PAR) on target proteins. ROS stress promotes PARP-1 hyperactivation and elevations in $i[Ca^{2+}]$ which are reciprocally coupled, resulting in cell death. The molecular mechanism of this interaction is unclear. The aim of the present study was to identify TGHQ-induced PAR-associated proteins and their potential role in cell death. Human kidney proximal tubule cells (HK-2) were treated with 400 μM TGHQ to induce ROS-stress leading to PARP-1 hyperactivation. PAR-associated proteins were immunoprecipitated, followed by subsequent separation by SDS PAGE and proteomic analysis. A relative protein abundance analysis by spectral counts allowed us to obtain fold-changes in protein abundance relative to control. 361 PAR-associated proteins were significantly identified as modified by TGHQ treatment. From this cohort, 276 proteins showed an increased PAR association while 85 were decreased. Additionally, 13 targets had Gene Ontology annotations related to calcium. Of these, neuroblast differentiation-associated protein (AHNAK), calcium homeostasis endoplasmic reticulum protein (CHERP) and general transcription factor II-I (TFII-I) are directly involved in modulation of $i[Ca^{2+}]$. TFII-I is a transcription factor that regulates $i[Ca^{2+}]$ by sequestering phospholipase C (PLC) in the cytosol. Under basal conditions free PLC binds and promotes the translocation of the transient receptor potential channel (TRPC3) to the plasma membrane leading to increases in $i[Ca^{2+}]$. TFII-I increased PAR-association might therefore lead to calcium influx via TRPC3. Using co-immunoprecipitation and immunodetection against TFII-I, we confirmed increased TFII-I PAR-association. The effect of a TRPC3 inhibitor on TGHQ-dependent modulation of $i[Ca^{2+}]$ was determined by live imaging of HK-2 cells with the calcium sensitive dye fluo-8 AM. Inhibition of TRPC3 promoted a delayed but higher increase in $i[Ca^{2+}]$. Cellular compartmentalization of TFII-I under TGHQ treatment was determined by cellular fractionation. TGHQ induced TFII-I translocation from the nucleus to the cytosol as well as decreased tyrosine phosphorylation, which might have a functional effect on the transactivation potential of TFII-I. In summary, LC-MS/MS identified proteins with altered PARylation under ROS stress. TFII-I is a novel PAR interacting protein which participates in signaling pathways with potential importance in TGHQ-mediated cell death. Currently we are investigating the transcriptional and DNA repair effects of PAR-associated TFII-I that might be relevant to the mechanism of ROS-dependent toxicity.</p>

ABSTRACT NO. 42	
Name	Marisa Kujawa
Category	Pharmaceutical Sciences
Title	MicroRNA-200 and microRNA-466 contribute to endothelial cell dysfunction by increasing endothelial cell permeability
Authors	Marisa Kujawa, Jiemei Wang
Abstract	<p>Introduction: Endothelial cell permeability is an important aspect of vascular repair in diabetes. MicroRNAs (miRs) are a group of non-coding RNAs that have been shown to regulate gene expression. The role of miRs in regulating EC permeability has yet to be elucidated. We hypothesized that miR-200 and miR-466 play important roles in endothelial cell permeability. The purpose of this experiment was to test endothelial cell permeability as a result of upregulation of miR-200 and miR-466 in human aortic endothelial cells (HAECs).</p> <p>Methods: HAECs from healthy subjects (H-HAECs) and type 2 diabetic patients (D-HAECs) (both purchased from Lonza) were transfected with miR-200 mimic or miR-466 mimics (Dharmacon). H-HAEC and D-HAEC cells were grown on the upper chambers of Transwell filter plates (Corning). Isothiocyanate-Dextran Fluorescent dye was added to each transwell filter plate well. Permeability was measured by amount of dye that leaked through the transwell filter. Fluorescence was recorded using GloMax Explorer fluorescent reader (excitation 475nm, emission 495-505). RNA was recovered from H-HAECs and D-HAECs (miRNAeasy kit; Qiagen). A real time PCR was used to determine levels of micro-RNA using primers synthesized by Exiqon. Results Results from the real time PCR showed higher expression of miR-200 and miR-466 in D-HAECs compared to H-HAECs. However there was no difference in expression of miR-200 and miR-466 in H-HAEC transfected with these mimics compared to H-HAECs that were not. Results from the fluorescent testing showed an increase in permeability of sothiocyanate-Dextran between H-HAEC transfected with miR-200 and miR-466 mimic as well as D-HAEC compared to H-HAEC not transfected with mi- RNA (n=3 per each group; P=0.15)).</p> <p>Conclusion: Functional tests showed there was a difference between H-HAECs and D-HAECs miR-200 and miR-466 levels which resulted in an increase in endothelial cell permeability in D-HAECs. Additional tests are needed to discover the inflammatory role these miRNA play that may lead to endothelial cell dysfunction and permeability.</p>

ABSTRACT NO. 43	
Name	Brianne Lewis
Category	Pharmaceutical Sciences
Title	Understanding the unique roles of Fe and Zn binding to the yeast Fe-S cluster scaffold assembly protein "Isu1"
Authors	Brianne E. Lewis; Zachary Mason; Gregory Holmes-Hampton; Manunya Nuth; Eric Dizin; Jimmy Cowan, PhD; Paul Lindahl, PhD; Andrew Dancis, MD,PhD; Timothy L. Stemmler, PhD
Abstract	<p>Fe-S clusters are prosthetic groups that are essential for life and utilized in nearly every biochemical pathway. Their structural and redox versatility allows them to participate in a wide range of functions, including control of ROS production, energy metabolism and targeted redox chemistry that cannot be performed under a strictly organic medium. A breakdown in the cluster production pathway results in a diseased state, as shown in Friedreich's Ataxia (FRDA). Uncovering the molecular mechanisms of Fe-S cluster biogenesis is the first step towards identification of potential new therapeutic strategies that can be used to treat disorders like FRDA. The goal of our laboratory is to characterize, at the molecular and atomic level, key factors that promote Fe-S cluster biogenesis in mitochondria. This work is focused on identifying the molecular process for yeast mitochondrial Fe-S cluster biosynthesis, specifically with regards to the function of the yeast scaffold protein, Isu1 which assembles Fe-S clusters. Isu1 is a dynamic protein whose function is to coordinate delivery and the utilization of iron and persulfide during the transfer of these substrates for cluster synthesis. Markley's lab has shown that in order to accommodate this function, the scaffold protein exists in two distinct states; these states are directly apparent in the presence and absence of zinc. Here, we have characterized both the Fe and Zn binding properties of the yeast scaffold protein. Our objective was to provide molecular details for both Fe and Zn binding to Isu1 to clarify iron-binding events related to Fe-S cluster assembly and understand the role Zn may play in impacting Isu1 molecular structure and cofactor biogenesis. Details regarding Isu1 Zn-binding certainly impact the resting in vitro structure and reactivity of the scaffold, and binding of this metal can help clarify Fe binding. In addition, we compare Fe-binding sites across scaffold protein orthologs to determine common underlying characteristics of all the scaffold proteins. Combined, these analyses provide a unique understanding of how divalent metal binding can impact the structure, substrate binding and activity properties of the ISC scaffold protein family, and provide the molecular details to exploit this protein as a drug target.</p>

ABSTRACT NO. 44	
Name	Aktham Mestareehi
Category	Pharmaceutical Sciences
Title	Global phosphorylation profiles of primary human skeletal muscle cells
Authors	Aktham Mestareehi; Berhane Seyoum; Xiangmin Zhang; Zhengping Yi
Abstract	<p>Global phosphorylation profiles of primary human skeletal muscle cells Aktham Mestareehi, Berhane Seyoum, Xiangmin Zhang, and Zhengping Yi Diabetes is a group of metabolic diseases characterized by hyperglycemia caused by defects in insulin secretion, insulin action, or both. Diabetes is associated with damage, dysfunction, and failure of various organs, such as eyes, heart, kidneys, and brain. Diabetes affect more than 30 million people in the USA (about 1 in 10) and more than 90% of diabetic patients have type 2 diabetes (T2D). Insulin resistance is a main characteristic feature of type 2 diabetes. Skeletal muscle insulin resistance is considered to be the primary defect that is evident decades before β-cell failure and overt T2D. Skeletal muscle is the major site of insulin-stimulated glucose uptake (>70%) in the postprandial state in humans. Protein phosphorylation regulates many key cell signaling events, including insulin signaling. Abnormal protein phosphorylation has been implicated in the development of skeletal muscle insulin resistance and T2D. However, most studies on phosphorylation-mediated signaling in skeletal muscle insulin resistance focused on a few known targets. Emerging as a key technology in exploring signal-transduction, phosphoproteomics has mapped many differential phosphorylation events in signaling networks and cascades. Nonetheless, no large-scale phosphoproteome studies on primary skeletal muscle cells derived from lean healthy insulin sensitive participants have been reported. In the present study, human skeletal muscle biopsy was obtained from a lean insulin sensitive participant. The biopsy was washed and minced into small pieces with 0.05% Trypsin-EDTA added. The minced tissues were centrifuged and filtered through a nylon mesh. The resulting human skeletal muscle cells were cultured in growth media, lysed, and subjected to in-solution trypsin digestion. The resulting peptides were analyzed by HPLC-ESI-MS/MS using an Orbitrap Fusion Lumos. We have identified >12,000 phosphorylation sites in 3,700 proteins, which is one of the largest catalog of experimentally determined phosphorylation sites in primary human skeletal muscle cells. Among all phosphorylation sites identified, >9,000 were specifically localized and these localized phosphorylation sites are assigned to 3,000 proteins. We identified phosphorylation sites in 180 kinases/kinases subunits (e.g., AKT, AMPK) and 29 phosphatases subunits of protein phosphatase 2A (e.g., PPP2R1B, PPP2R2B, PPP2R3A, PPP2R5A, PPP2R5D, and PPP2R5E). In addition, DAVID bioinformatics tool was used to identify biological processes, molecular functions, and pathways that are significantly enriched in the phosphoproteins we identified as compared to the whole human proteome. The results indicated that multiple biological processes (e.g., protein phosphorylation, mRNA splicing, intracellular signal transduction, positive regulation of GTPase activity, and signal transduction), molecular functions (e.g., protein binding, poly (A) RNA binding, ATP binding, protein serine/threonine kinase activity, protein phosphatase binding) as well as KEGG pathway (e.g., insulin signaling pathway, HTLV-I infection, endocytosis, ErbB signaling pathway, AMPK signaling pathway, and mTOR signal pathway) were enriched. In summary, we have characterized the largest phosphoproteome of primary skeletal muscle cells derived from a lean healthy insulin sensitive participant, and identified multiple biological processes, molecular functions, and pathways that are significantly enriched in the phosphoproteins we identified. These results provide potential new targets for mechanistic studies on skeletal muscle insulin resistance in humans.</p>

ABSTRACT NO. 45	
Name	Huong (Rachel) Nguyen
Category	Pharmaceutical Sciences
Title	Metformin scavenges methylglyoxal to form a product that improves endothelial cell function: potential novel mechanism of metformin action.
Authors	Huong Nguyen, BS; Serrine Lau, Ph.D.; Terrence Monks, Ph.D.
Abstract	<p>Reactive dicarbonyls, such as methylglyoxal (MG), are highly elevated in type-two diabetes mellitus (T2DM) patients. These endogenous electrophiles covalently react with lysine and arginine residues on proteins to form non-enzymatic advanced glycation end products (AGEs). AGEs are widely recognized as a major cause of cellular damage and dysfunction during diabetic cardiovascular complications. The T2DM first-line drug therapy, metformin (MF), significantly reduces adverse diabetic endpoints and mortality more effectively than other antihyperglycemic agents. The exact mechanism(s) by which metformin protects diabetic patients against cardiovascular complications is far from well characterized. We previously discovered that metformin scavenges MG to form a novel imidazoline (IMZ) metabolite, thus reducing MG-related AGEs. Many compounds that possess an imidazoline group act as ligands for imidazoline receptors (IR) and the alpha-2 adrenergic receptor. Activation of these receptors initiates a cascade of processes, including vasodilation. We therefore hypothesize that IMZ improves endothelial cell function and contributes to the beneficial therapeutic effects of MF. In the current studies we examined the in-vitro effects of IMZ on endothelial cell function using primary human umbilical vein endothelial cells (HUVECs) and characterized potential signaling pathways. We show that IMZ at physiological relevant concentrations induces the production of the endothelial derived relaxation factor, nitric oxide (NO), concomitant with an increase in the activation of endothelial nitric oxide synthase (eNOS) via phosphorylation of serine 1177. IMZ-induced NO production was blunted by pretreatment with imidazoline 1 receptor (I1R) and alpha-2 receptor (α2R) antagonists, suggesting that IMZ action is receptor mediated. We also observed that IMZ cause the activation of Akt and ERK1/2, in both a concentration and time-dependent manner; maximum activation occurred at 10 and 20 minutes. IMZ-induced activation of Akt, ERK1/2, eNOS was inhibited in the presence of a PI3K inhibitor. Interestingly, ERK1/2 phosphorylation mediated by IMZ was also reduced in the presence of Akt1/2 specific inhibitors, suggesting that ERK1/2 might lie downstream of Akt during IMZ-initiated activation. The effects of IMZ on angiogenesis function was examined by a tube-formation assay. IMZ treatment significantly increased tube length compared to untreated controls. Collectively, the data demonstrate that IMZ might contribute to the protective effects of metformin on endothelial cell function by activating I1R and/or α2R-Akt-ERK1/2-eNOS-NO pathway. Studies are ongoing to further elucidate and confirm the effects of IMZ in in-vivo models.</p>

ABSTRACT NO. 46	
Name	Megan O'Meara
Category	Pharmaceutical Sciences
Title	The role of G Protein Coupled Receptor 39 in regulation of endothelial cell function
Authors	Megan O'Meara; Hainan Li, MS; Jiemei Wang, MD, PhD
Abstract	<p>Introduction and Purpose: Endothelial Cells (ECs) play active roles in maintaining vascular homeostasis and initiating angiogenesis. Endothelial dysfunction contributes to the onset and progression of atherosclerosis. Many factors can cause damage to ECs, including hyperglycemia, hypertension, smoking, and aging. Reactive oxygen species (ROS) are formed from a byproduct of energy metabolism. During times of environmental stress, ROS can increase drastically causing mitochondria to swell and break down. G protein coupled receptor 39 (GPR39) is an orphan receptor whose physiological role is still unknown. GPR39 has been implicated in cardiovascular disorders but the mechanisms are not clear. The purpose of this study is to determine GPR39's role in regulating endothelial cellular function, specifically in the mitochondria.</p> <p>Methods and Results: Primary mouse aortic ECs were isolated and cultured from the aorta of GPR39^{+/+} and GPR39^{-/-} mice. Changes in mitochondrial transmembrane potential were determined as differences in the tetramethylrhodamine methyl ester (TMRM) versus Mito-Tracker Green signal ratio. Mitochondrial derived ROS was determined by fluorescent staining of MitoSOX. Cell functional tests, such a proliferation and tube formation, were completed on the ECs. Quantitative real-time PCRs were performed on various genes using β-actin as the internal control. Our results indicated that under both normal (5mM) and high glucose (25mM) conditions GPR39^{-/-} ECs showed upregulation in the mitochondrial membrane potential and reduced ROS formation, with significant upregulation of Sod2 and Ucp-2 mRNA expression, compared to the GPR39^{+/+} ECs. Functional tests showed an increase in proliferation and tube formation in the GPR39^{-/-} ECs.</p> <p>Conclusions: Our data suggest that GPR39 deletion improved mitochondrial function and angiogenic activities such as proliferation and tube formation in endothelial cells in vitro. Specifically, Sod2 and Ucp-2 are two mitochondria antioxidant enzymes that are inhibited by GPR39. We believe that our data will provide useful information for developing novel therapeutic approaches to rescue endothelial dysfunction and improve angiogenesis in the future.</p>

ABSTRACT NO. 47	
Name	Shelley Paulisin
Category	Pharmaceutical Sciences
Title	Links between a common variant in the cannabinoid receptor 1 gene and fear extinction in adversity-exposed children
Authors	Huong Nguyen, BS; Serrine Lau, Ph.D.; Terrence Monks, Ph.D.
Abstract	<p>Background: Deficits in fear extinction are implicated in the pathophysiology of anxiety disorders such as posttraumatic stress disorder. Recent studies suggest that signaling via the cannabinoid receptor 1 (CB1R) is essential for fear extinction. A common variant in the gene encoding the CB1R (CNR1) has been linked to poor extinction learning in adults. However, anxiety disorders typically begin in childhood.</p> <p>Objective: Examine the effect of CNR1 on fear extinction learning and its later recall in children. Method: 37 children (6-11 years) underwent a novel two-day fear extinction learning and memory recall experiment in virtual reality. Skin conductance responses (SCRs) were collected and genotyping was performed for CNR1 (rs2180619). Of note, a subset of children reported previous exposure to adversity (e.g., violence, intensive medical treatments). Results: Overall, there were no group differences in extinction learning or subsequent memory recall. However, within the adversity-exposed group, children with the AA genotype showed poorer extinction learning and extinction recall compared to C allele carriers, evidenced by higher SCRs to an extinguished cue.</p> <p>Conclusion: Genetic differences in the endocannabinoid system may contribute to a reduced ability of to extinguish learned fear among adversity-exposed children. Failure to extinguish may increase risk of anxiety.</p>

ABSTRACT NO. 48	
Name	Alex Petrovici
Category	Pharmaceutical Sciences
Title	PDL1 Antibody Drug Conjugate for Selective Chemo-guided Immune Modulation of Cancer
Authors	Huong Nguyen, BS; Serrine Lau, Ph.D.; Terrence Monks, Ph.D.
Abstract	<p>Immune checkpoint molecules, such as programmed death-1 (PD1) and its ligand (PDL1), have become promising therapeutic targets for cancer therapy. These are expressed on the surface of immune cells (monocytes, T cells, B cells) and cancer cells, respectively. While their interaction with each other is important for healthy cells to appropriately reduce inflammation, the mechanism is abused by tumors to inhibit T-cell mediated cancer cell destruction. To prevent this immunosuppression and restore anti-cancer ability of T-cells, immune checkpoint inhibitors have been designed to block the interaction between PD1 and PDL1. The discovery and development of these immune checkpoint inhibitors, which are now critical to treatment of several advanced cancers, have recently been recognized by the 2018 Nobel Prize in Physiology and Medicine. PDL1 is overexpressed in various tumors and targeting it has been successful as evidenced by clinical approval of anti-PDL1 antibodies for metastatic urothelial carcinoma, non-small cell lung cancer, and other cancers. Furthermore, these antibodies are wisely being investigated for the treatment of triple negative breast cancer (TNBC) which lacks estrogen, progesterone, and HER-2 receptors while overexpressing PDL1. However, the utility of anti-PDL1 therapy has been limited to few cancer types, attributed to the transient expression of PDL1 and the difficulty in tumor stroma penetration to gain access to PDL1. To overcome these limitations, we report creating a conjugate between the clinically approved PDL1 antibody Atezolizumab (ATB) with potent chemotherapeutic, Doxorubicin (Dox), termed ATB-Dox. This ATB-Dox is conjugated through a tumor acidic pH responsive hydrazone linker containing a polyethylene glycol (PEG2000) spacer to allow dissociation of Dox in tumor milieu with reduced accumulation in healthy tissue. This targeted strategy does not only reduce the non-specific cardiotoxicity of Dox but also help in selective delivery of the drug to tumor tissues overexpressing PDL1 receptors, including the tumor stroma. Dox can disrupt the tumor stroma so that ATB can further penetrate the tumor core, resulting in pronounced antitumor response. We verified the formation of ATB-Dox after synthesis by using MALDI-TOF and UV analysis. ATB-Dox demonstrated significant cell killing in MTT assays, disruption of tumor spheroid model, and induction of apoptosis in TNBC cell line MDA-MB-231. The fluorescence imaging of ATB conjugated near infrared (NIR) dye in patient derived tumor xenograft (PDX) models supports the selective tumor targeting ability, and core penetration of the construct. The significant increase of IFN-γ compared to Dox treatment alone suggests that ATB-Dox can upmodulate T cell activation. As IFN-γ is one of the cytokines inhibited by PD1/PDL1 interaction, its increase in production is evidence that the conjugate blocks PDL1 so that it cannot interact with PD1. Overall, our first approach in developing immune checkpoint antibody drug conjugate and imaging agent demonstrates a rational platform for chemo-guided immunotherapy that can be further tested for evaluating in vivo tumor therapeutic outcome in humanized NSG (immunodeficient) mice.</p>

ABSTRACT NO. 49	
Name	Nicolette Santilli
Category	Pharmaceutical Sciences
Title	Evaluation of the impact of PrsA on synergy between Beta-Lactam combinations with Vancomycin
Authors	Nicolette Santilli; Razieh Kebriaei; Andrew Berti; Adriana Renzoni; Michael J. Rybak
Abstract	<p>Background: Glycopeptide antibiotics like vancomycin (VAN) have been considered the mainstay of methicillin-resistant Staphylococcus aureus (MRSA) treatment. Decades of selective pressures have led to the emergence of vancomycin intermediate resistance (hVISA and VISA). The synergistic effect of combination beta-lactam (BL) and VAN is not well understood; however, a specific protein of interest, PrsA, is believed to play a major role in this synergy. PrsA is an oligomeric chaperon lipoprotein localized in distinct regions on the outer face of the cytoplasmic membrane and assists in post-translocational folding. Penicillin Binding Proteins (PBPs) were previously suggested as candidates for PrsA-dependent translocation and are membrane bound transglycosylase and transpeptidase enzymes utilizing precursors to synthesize peptidoglycan. PBPs play a role in cell wall growth, cell division, and lateral wall development with an activity and folding believed to be influenced by sodium. The objective of this investigation was to evaluate the impact of PrsA on synergy between a variety of BLs and VAN, while simultaneously evaluating the potential impact of sodium ions (present in sodium chloride enriched Mueller Hinton Broth) on PBP folding.</p> <p>Methods: MRSA COL with PrsA knockout (KO) [COLdelprsA (AJ728), Mu3delprsA (AJ457), and MW2delprsA (AJ724)] were selected for evaluation against the parent strains. MICs by broth microdilution were performed on each strain using VAN, oxacillin (OX), cefazolin (CFZ), ceftaroline (CPT), cefepime (FEP), ceftriaxone (CRO), cefaclor (CEC), ceftiofloxacin (FOX), and ertapenem (ERT). To evaluate the potential for synergistic combinations, MICs were performed on these organisms using VAN in the presence of the BLs. To further evaluate for the presence of synergy, time-kill analysis was performed in Mueller Hinton broth (with and without sodium chloride) to understand the role of salt in PBP folding.</p> <p>Results: VAN MICs for COL, COL KO, Mu3, Mu3 KO were 2mg/L and MW2 and MW2 KO were 0.5 mg/L. Except for CPT (MIC range 1-2 mg/L), COL, Mu3 and MW2 were highly resistant to the BLs (MIC range 128->2048 mg/L). The BL MICs for COL and Mu3 KOs decreased by 1-2-fold. However, the MIC for the MW2 KO decreased from 4-256-fold. Regarding combination MIC testing, in the presence of BLs the VAN MIC decreased from 1-66-fold for both the parent and KO for COL, Mu3 and MW2 with no distinctive differences in MIC noted between the parent and KOs. The combination of VAN+CFZ demonstrated synergy for all parent and KO strains while VAN+OXA demonstrated synergy for KO strains only. The addition of NaCl appeared to inhibit the combination of VAN + OXA. Conclusions: The disruption of PrsA lowered the MIC for eight different BL antibiotics and dramatically for the MW2 KO further documenting the influence of PrsA on BL susceptibility. In addition, the MIC for VAN was consistently lower in the presence of BLs documenting the potential for VAN synergy across a wide range of BL antibiotics. Additional experiments evaluating the impact of NaCl on the potential synergy of these compounds is needed. Further research exploring the influence of PrsA on BL susceptibility in relation to vancomycin is warranted.</p>

ABSTRACT NO. 50	
Name	Marcella Sharma
Category	Pharmaceutical Sciences
Title	Detecting Inhibitors of N5-CAIR Mutase using High-Throughput Screening
Authors	Marcella Sharma; Shiv Sharma, PhD; Steven Firestine, PhD
Abstract	<p>The discovery of antibiotics is one of the major breakthroughs in medicine, yet the rise of antibiotic-resistant infections threaten this advance. In the United States, at least 2 million people acquire resistant infections each year indicating the strong need for new antimicrobial agents that function against novel drug targets. One interesting target is purine biosynthesis pathway where studies have shown a divergence in the pathway between microbes and humans. In humans, aminoimidazole ribonucleotide (AIR) is converted to carboxyaminoimidazole ribonucleotide (CAIR) by the enzyme, AIR carboxylase. In microbes, two separate enzymes, N5-CAIR synthetase (PurK) and N5-CAIR mutase (PurE) are needed to do the same conversion. Unfortunately, there are no selective inhibitors of N5-CAIR mutase. To address this problem, the Firestine lab conducted a high-throughput screen of 48,000 compounds at the University of Michigan's Center for Chemical Genomics. The campaign was unsuccessful, but utilized an assay conducted at 260 nm where interference from compounds was prevalent. Recently, we have developed a novel fluorescence-based assay. In this poster, we will outline the use of this assay and our initial screening of a small fragment library as well as a 2,400 compound library. This work is done in collaboration with the Fribley Lab in the Department of Pediatrics and</p> <p>Otolaryngology. We will outline the screening approach and our follow-up studies on the hits identified from these libraries. We will discuss the challenges with the fluorescence assay and methods to identify true binders from false positives.</p>

ABSTRACT NO. 51	
Name	Zoha Siddiqua
Category	Pharmaceutical Sciences
Title	Emerging and Endocrine Disrupting Chemicals in Detroit Drinking Water
Authors	Zoha Siddiqua; Tracie Baker; Manahil Monshi; Laxshmi Neha Alla Reddy; Jeremiah Shields; Karim Alame; Andrea Wahls; Danielle Meyer; Emily Crofts; Camille Akemann; Fadie Saad; Judy El-Nachef; Merna Antoon; Raquel Nakhle; Nemer Hijazi; Maha Hamid; David K. Pitts
Abstract	<p>Detroit, Michigan a post-industrial city, situated on the banks of the Detroit river receives contaminants from wastewater treatment plants, runoff from urban gardens and agriculture, landfill leachate, abandoned and demolished infrastructure and storm water from impervious surfaces. Contaminants in water include contaminants of emerging concern (CECs) which are not regulated and/or monitored by the governing agencies. Some CECs can disrupt the normal endocrine function of humans and wildlife and hence this subset is called endocrine disrupting chemicals (EDCs). There are reports of EDCs present in local sediment and surface water and evidence of endocrine disruption such as intersex male white perch in Lake Saint Clair with elevated vitellogenin (an ecomarker for estrogenic activity), and testicular oocytes and elevated vitellogenin in small and largemouth bass in the Detroit river. Potential EDC effects on humans have been reported locally as a significant decrease in the male birth rate for residents living in Sarnia, Ontario where there is a heavy presence of petrochemical industry. However, very little is known about the presence, transport and fate of these CECs/EDCs or their effects on environmental or human health. Our hypothesis is that model aquatic organisms can be used to develop a molecular identification model capable of detecting estrogenic and anti-androgenic activity using behavioral, morphologic, and genomic data. Using <i>Daphnia pulex</i> (invertebrate) and <i>Danio rerio</i> (vertebrate) we have evaluated the toxicity of 8 known or suspected CECs/EDCs in behavioral, morphological, and genomic assay systems. Significant differences in behavioral responses were found: (1) across chemicals within a species, (2) across species for a given chemical, and (3) in chemical sensitivity across species. A significant concentration-dependent inhibition of swim bladder development by the pesticide, dieldrin, was detected at relatively low concentrations (10 nM, 5 days). Changes in gene expression are currently being evaluated using QuantSeq analysis. After completion of the genomic analysis we plan to develop a customizable q-PCR plate that can differentiate the estrogenic and anti-androgenic properties of water samples from the field.</p>

ABSTRACT NO. 53	
Name	Qian Zhang
Category	Pharmaceutical Sciences
Title	Mdig acts as an antagonist for the inhibitory histone methylation markers
Authors	Qian Zhang Chitra Thakur, PhD; Yao Fu, MS; Zhuoyue Bi, MS; Priya Wadgaonkar; Zhipeng Liu; Wanqing Liu, PhD; Li Wang, PhD; Fei Chen, PhD
Abstract	<p>Mineral dust-induced gene (mdig) has been implicated as an environmentally induced oncogene for some types of human cancer. Unlike other JmjC-domain containing protein, the debate on whether mdig is involved in histone protein demethylation is unsettled yet. To provide direct evidence suggesting the contribution of mdig to the demethylation of lysines on histone proteins, we recently knocked out mdig gene by CRISPR-cas9 technique in bronchial epithelial cells followed by examining the profiles of histone methylation and gene expression through ChIP-seq and RNA-seq approaches, respectively. Global histone methylation analysis revealed a pronounced increase of trimethylation of lysines 9, 27 on histone H3 (H3K9me3, H3K27me3) and H4K20me3 in the cells with depletion of mdig. ChIP-seq and RNA-seq data suggested that enrichment of H3K9me3, H3K27me3, or H4K20me3 at gene loci is associated with a significant inhibition of gene expression. Gene ontology analysis unraveled that mdig controls the expression of genes in the pathways of cell growth, self-renewal, inflammatory lung fibrosis, and cell motility. Taken together, our data suggest that mdig is an antagonist for the inhibitory histone methylation markers. Knockout of mdig, thus, results in an elevation of H3K9me3, H3K27me3 and H4K20me3, followed by a decreased expression of genes in cell growth regulation and inflammation.</p>

Pharmacy Practice

ABSTRACT NO. 8	
Name	Somitra Dey
Category	Postdoctoral Fellow
Title	Daptomycin resistance via cooperative disruption of ion translocation and electron transport
Authors	Somrita Dey, Ph.D; Paula Smolenski, MS; Christopher Miller, BS; Ajay Pradhan, Undergrad; Andrew D Berti, Pharm D, Ph.D
Abstract	<p>Background: Daptomycin is a bacterial membrane-targeting antibiotic effective against invasive staphylococcal infections including methicillin-resistant <i>Staphylococcus aureus</i> (MRSA). The development of daptomycin resistance is rare and involves modification of the cell envelope to antagonize daptomycin binding. Following in vitro exposure to daptomycin, we recovered highly daptomycin-resistant <i>S. aureus</i> containing mutations in novel genes. Individually, mutation in <i>snoF</i> or <i>octB</i> did not result in daptomycin resistance but simultaneous disruption in both loci resulted in high-level daptomycin resistance. Neither <i>snoF</i> nor <i>octB</i> is predicted to be involved in cell envelope modification.</p> <p>Methods: Regions with variant sequences identified via comparative whole genome sequencing were aligned using the Basic Local Alignment Search Tool (BLAST). Homology was determined using Needleman- Wunsch methodology. Daptomycin susceptibility was assessed via Etest on different media types. Menaquinones were recovered from whole cells via sequential organic extraction and solid phase chromatography.</p> <p>Results: The <i>sno</i> cluster is predicted to encode a monovalent cation translocation complex. A second cluster (<i>mnh</i>) was identified at a distal site on the chromosome homologous and syntenic to the internal six genes from the predicted eight-gene operon. Disruption in <i>octB</i> resulted in the recovery of immature menaquinones lacking octaprenylation. Growth of an <i>octB</i> mutant, but not a <i>snoF</i> mutant or wild type, on a non-fermentable carbon source (succinate) resulted in a marked increase in daptomycin resistance. A <i>snoF octB</i> double-mutant demonstrated daptomycin resistance regardless of carbon source. The daptomycin resistance phenotype in a <i>snoF octB</i> double-mutant is reversed when media are supplemented with exogenous menaquinone.</p> <p>Conclusion: Growth on nonfermentable substrates results in daptomycin resistance if and only if <i>S. aureus</i> lacks mature menaquinones. Simultaneous disruption of the <i>sno</i> system and menaquinone results in daptomycin resistance regardless of carbon source and susceptibility can be restored by addition of exogenous menaquinone. These findings suggest that the <i>sno</i> may be involved in fermentation energy generation processes. Ongoing studies will examine: (i.) the effect of disruption in the <i>mnh</i> cluster on daptomycin resistance, (ii.) the effect of disruption in additional <i>sno</i> cluster elements on daptomycin resistance and (iii.) the effect of monovalent cation ionic strength on daptomycin resistance. These basic metabolic studies will expand our knowledge about daptomycin's complex mechanism of action and additional pathways resulting in resistance.</p>

ABSTRACT NO. 54	
Name	Nour Baalbaki
Category	Pharmacy Practice
Title	Community-Based Survey for Shingles and Shingles Vaccines
Authors	Nour Baalbaki, PharmD Candidate; Ezinwanne Okorafor, BS; Melanie Ng, PharmD Candidate; Asad Nawaz, BS Candidate; Wesley Chiu, PharmD Candidate; Joseph Fava, PharmD; Abdulbaset Salim, M.B.Ch.B., M.P.H.; Paul E. Kilgore, M.P.H., M.D
Abstract	<p>Background: An estimated one-third of all Americans will experience Herpes Zoster (HZ) in their lifetime. Of those, ~13% will experience post-herpetic neuralgia (PHN)-a painful sequelae of HZ that may be long-lasting and result in reduced quality-of-life. Although the first vaccine against HZ was FDA-approved in 2006, it is only about 50% effective. In October 2017, the FDA approved a new vaccine that is ~97% effective in preventing HZ. Despite the availability of an effective vaccine, the proportion of patients vaccinated against HZ remains low at 17- 20% nationwide and ~8% in Detroit, Michigan. The purpose of this study is to investigate current knowledge, attitudes, beliefs, and practices relative to HZ and HZ vaccines in a representative sample of Detroit residents.</p> <p>Methods: This survey was conducted among 381 participants aged 50 years and older at four venues in the city of Detroit (Joseph Walker Williams Recreation Center, Tabernacle Missionary Baptist Church, Meijer store #286, and Meijer store #268). Visitors, members, and/or customers of these establishments were recruited via posted flyers, informational tables and personal invitation from study personnel. After agreeing to participate, each resident received a study information sheet. Study personnel conducted face-to-face interviews using a standardized, paper-based survey instrument. Survey items collected specific information on respondents' HZ knowledge, attitudes, beliefs and practices for HZ treatment and prevention. Upon completion of the interview, participants received educational handouts for HZ and HZ vaccines and a \$10 Meijer gift card. The Wayne State University Institutional Review Board approved this study (#043918B3X).</p> <p>Results: A majority of respondents were female (64.6%) and 60 years of age or older (69.0%). Also, while 68.8% of respondents reported knowing an individual who had experienced HZ, a substantial proportion of respondents were not aware (34.9%) or did not believe (18.9%) that HZ can result in sequelae or adverse events. Our data further suggest that an individual's awareness of someone who had experienced HZ is associated with a higher level of knowledge about HZ and the vaccine, as well as more favorable attitudes towards HZ vaccination ($P < 0.05$). Receiving a recommendation from a healthcare provider (38.3%), followed by gaining a better understanding of the vaccine (37.3%) and of HZ disease (30.4%) were leading factors that appear to influence participants' decision to receive the HZ vaccine.</p> <p>Conclusion: Our study suggests that a lack of awareness related to HZ disease and its complications are significant factors associated with hesitancy to receive HZ vaccine. In contrast, knowing someone who has experienced HZ and receiving a healthcare provider recommendation for HZ vaccination are significantly associated with a willingness to receive HZ vaccine. Our findings underscore the need to educate patients about HZ illness and sequelae as well as new HZ vaccine recommendations in order to improve vaccination rates and reduce the incidence of HZ and sequelae in the United States.</p>

ABSTRACT NO. 55	
Name	Brad Berak
Category	Pharmacy Practice
Title	Oral ribavirin for Respiratory Syncytial Virus (RSV) treatment in lung transplant recipients. The impact of policy implementation on cost and appropriate use.
Authors	Brad Berak, PharmD Candidate; Susan Davis, PharmD; Bryant Summers, PharmD, BCPS
Abstract	<p>Background: RSV is a leading cause of viral infections in lung transplant recipients and is associated with significant morbidity and mortality. While the role of inhaled and oral ribavirin as the primary treatment of RSV infections in this patient population is still unclear, the cost of inhaled ribavirin therapy is significantly higher than a comparable oral regimen. In June 2016 the Henry Ford Health System Antimicrobial Stewardship Program guidelines were updated in order to provide recommendations for the appropriate use of inhaled and oral ribavirin. The purpose of this study is to evaluate the economic impact of oral ribavirin therapy in RSV treatment for lung transplant recipients.</p> <p>Methods: This was a two-phase, retrospective, quasi-experimental study including lung transplant recipients whom were treated with inhaled or oral ribavirin for RSV infections, from 2013 to Quarter 3 of 2018. Patients were excluded if less than 18 years of age, allergic to ribavirin, pregnant, or receiving didanosine concomitantly. The primary endpoint evaluated the economic impact of oral ribavirin compared to inhaled ribavirin. Additional data points were collected to evaluate appropriate ribavirin utilization and clinical outcomes. Descriptive variables were described using measures of central tendency and variability. Categorical outcome variables, baseline characteristics, and clinical characteristics were compared between patient groups using Pearson’s Chi-squared test or Fisher’s exact test. Continuous variables such as length of stay, pulmonary function tests, and cost of therapy were compared using Mann-Whitney U test.</p> <p>Results: [RESEARCH IN PROGRESS]</p> <p>Conclusion: [RESEARCH IN PROGRESS]</p>

ABSTRACT NO. 56	
Name	Ashley Blanchette
Category	Pharmacy Practice
Title	Effects of $\Delta 9$ -tetrahydrocannabinol on cortico-limbic responses to threat in trauma-exposed and trauma-naïve individuals
Authors	Ashley Blanchette, BS; Craig Peters, BS; Hilary A. Marusak, PhD; Christine A. Rabinak, PhD
Abstract	<p>In healthy adults, we have previously demonstrated that pharmacological enhancement of endocannabinoid signaling, via administration of an acute dose of $\Delta 9$-tetrahydrocannabinol (THC), modulates cortico-limbic neural processing. For example, relative to placebo (PBO), healthy adults who received THC showed reduced threat-related amygdala activation and increased connectivity between the amygdala and the rostral anterior cingulate cortex/medial prefrontal cortex (rACC/mPFC), fitting with the notion that interventions that target the endocannabinoid system may be effective for reducing fear and anxiety. However, pharmacological studies also demonstrate that THC can have either anxiolytic or anxiogenic effects, depending on various factors (e.g., dosage, patient population). Here, we tested the effects of an acute dose of THC on threat-related amygdala activation in three groups: healthy controls (HC), trauma exposed controls (TEC), and patients with posttraumatic stress disorder (PTSD). Using a randomized, double-blind, placebo-controlled, between-subjects design, 56 adults (22-46 years of age) were randomly assigned to receive either THC (oral, 7.5mg; n=25) or PBO (matching capsule; n=31). Administration of THC or PBO was equal across groups. Participants subsequently completed a well-established threat processing paradigm that robustly elicits cortico-limbic activation during functional magnetic resonance (fMRI). Across all groups (HC, TEC, PTSD), we found higher activation in both amygdala and rACC/mPFC to threatening (i.e., angry) faces for participants who received THC relative to PBO. There were no significant effects of patient group (HC, TEC, PTSD) or group x drug interactions on cortico-limbic activation. Results were significant within the basolateral subdivision of the amygdala, consistent with a previous study. These data suggest that THC increases the activity of a known emotion regulation circuitry.</p>

ABSTRACT NO. 57	
Name	Ashley Blanchette
Category	Pharmacy Practice
Title	Marijuana use and treatment adherence among adults with chronic diseases
Authors	Ashley Blanchette, BS; Craig Peters, BS; Hilary A. Marusak, PhD; Christine A. Rabinak, PhD
Abstract	<p>Despite remaining illegal under federal law, more states are voting to legalize medical marijuana use (MMU). Marijuana and other endocannabinoid-targeting drugs appear to have an emerging therapeutic role in the management of chronic diseases (i.e. epilepsy, pain, HIV/AIDS). Patients with chronic diseases have approximately 50% adherence rate to prescribed therapies resulting in an estimated \$100-\$300 billion annual cost burden. Previous studies have demonstrated conflicting evidence on MMU and adherence among varying disease states. Research is needed to elucidate the impact of MMU on adherence to prescribed therapies. In the current study the authors conducted a literature review to characterize the association of MMU on prescribed medication adherence in adults with chronic diseases.</p>

ABSTRACT NO. 58	
Name	Anna Boik
Category	Pharmacy Practice
Title	Evaluation of intravenous versus oral opiates in the management of post-operative pain in orthopedic surgery patients
Authors	Anna Boik
Abstract	<p>Purpose: Typically, providers prefer using intravenous (IV) opiate therapy post-operatively due to the rapid onset of action. Currently, a nationwide shortage of injectable opiates exists. Owing to this shortage, a shift in the use of oral (PO) opiates postoperatively has been seen. To address this shortage, Henry Ford Macomb Pharmacy implemented an IV to PO policy, in March 2018, allowing pharmacists to change IV pain medications to the PO equivalents. The purpose of this study is to evaluate the effect of using PO opiates versus IV opiates in post-operative orthopedic patients after the IV to PO policy was implemented.</p> <p>Methods: Patients were included if they were 18 years or older, underwent an elective total hip or knee arthroplasty, and received opiates post-operatively between March 16, 2017 to June 16, 2018. Patients were excluded if they were pregnant, admitted to the intensive care unit, or used opiates within seven days of surgery. Pain scores before the IV to PO policy implementation were compared to patient's pain scores after policy implementation. The primary outcome was to compare post-operative pain scores of orthopedic surgery patients who received IV opiates to those who received PO opiates. Secondary endpoints included the incidence of breakthrough pain medication administration and documented nausea and vomiting. The institutional review board approved this retrospective, observational study.</p> <p>Results: N/A still awaiting IRB approval</p> <p>Conclusion: N/A still awaiting IRB approval</p>

ABSTRACT NO. 59	
Name	Renee Bookal
Category	Pharmacy Practice
Title	Chronic Medication Optimization Pharmacist's (CMOP) Intervention in the Management of Patients with Uncontrolled Diabetes
Authors	Amber Lanae Martirosov, PharmD, BCPS, BCACP
Abstract	<p>Background: Patients with uncontrolled diabetes may find managing their health to be overwhelming without continued guidance. Although most patients with diabetes utilize the services of a primary care physician (PCP), patients with uncontrolled diabetes may require further assistance in optimizing their therapy to maintain long term success. Furthermore, the complications that can arise from uncontrolled diabetes may lead to an increase in physician office visits and hospitalizations. The utilization of a Chronic Medication Optimization</p> <p>Pharmacist (CMOP) could be pivotal in making treatment interventions in patients with diabetes. The CMOPs serve a vital function in managing patients with chronic diseases by individualizing their medication therapy regimens to be most efficacious, safe and affordable. The purpose of this study is to assess the impact of CMOPs on outcomes related to medication therapy in patients with uncontrolled diabetes in an outpatient clinic setting.</p> <p>Methods: This was a retrospective cohort study conducted at Henry Ford Health System (HFHS) in six outpatient clinics and approved by the Henry Ford Hospital (HFH) Investigational Review Board. Patients were referred from other HFHS providers or identified through an artificial intelligence tool created by the pharmacy department that identified patients with uncontrolled diabetes. Patients were included in this study if they had type 2 diabetes, an HbA1C of 8% or greater, and were managed by a CMOP in one of the designated clinics. Patients were excluded from the study if they had an HbA1C less than 8%, were over 80 years old, had type 1 diabetes, were in hospice or had their diabetes managed by an endocrinologist. The primary objective was to observe a change in HbA1C after the CMOP's intervention period. Data points collected included baseline characteristics, baseline and repeat HbA1cs, and interventions by the pharmacists. Descriptive statistics were used to describe pharmacist interventions. The primary endpoint was evaluated using a paired t-test. Results - Interim: A total of 72 patients were analyzed. Fifty eight patients (80%) were identified through the artificial intelligence tool and fourteen patients (20%) were referred to the CMOP by their PCP. The majority of the population was African American (67%) and female (53%). The average age was 57.3 ± 12.2 years. The mean baseline HbA1c was 9.9% before CMOP intervention. The median time between baseline and first HbA1c recheck was 105 days (IQR 88- 168 days). After CMOP intervention, the mean HbA1c for the population was 8.6%, resulting in a mean difference in HbA1c of 1.3% (P < 0.0001).</p> <p>Conclusion: Based on these preliminary results, the implementation of CMOP demonstrated an improvement in diabetes control through a reduction in A1c. Patients with diabetes require thorough education, treatment, and follow-up to manage their condition, all of which may be fulfilled by a CMOP.</p>

ABSTRACT NO. 60	
Name	Sara Bugamelli
Category	Pharmacy Practice
Title	Comparative Analysis of Daptomycin Combination Therapies for MRSA Bloodstream Infections
Authors	Sara Bugamelli, PharmD Candidate; Sarah Jorgensen, PharmD, BCPS; Kimberly C. Claeys, PharmD, BCPS; Michael J. Rybak, PharmD, MPH, PhD
Abstract	<p>Background: Methicillin-resistant Staphylococcus aureus (MRSA) bloodstream infections (BSI) are serious, life-threatening infections that are challenging to manage and often lead to high rates of treatment failure. In the event of treatment failure, several combination therapies have demonstrated efficacy in eradicating infection in this patient population. Two strategies that have been shown to be effective are daptomycin (DAP) with a β-lactam antibiotic and DAP with trimethoprim/sulfamethoxazole (SXT). Objective: To compare the effectiveness of DAP + SXT to DAP + a β-lactam. Methods: This was a retrospective, comparative cohort study of adults with MRSA bacteremia at the Detroit Medical Center from March 2008 to July 2018. Inclusion criteria: age \geq 18 years, \geq 1 MRSA positive blood culture, received DAP + SXT or DAP + β-lactam for $>$ 72 hours. Exclusion criteria: polymicrobial bacteremia, pneumonia as primary source of infection, DAP + both SXT and a β-lactam concurrently. The primary outcome was treatment failure, defined as a composite of: (1) bacteremia duration \geq 7 days after starting combination therapy, (2) 30-day mortality, (3) worsening or failure to resolve abnormal WBC count and/or temperature while receiving combination therapy, (4) 30-day MRSA bacteremia recurrence and (5) need to escalate or change antibiotic therapy due to worsening, no response, or adverse effects. Independent predictors of clinical failure were sought through multivariable logistic regression analysis. Results: A total of 60 patients were included in the study (DAP + β-lactam = 42, DAP + SXT = 18). The treatment groups had similar clinical characteristics except there was a higher incidence of infective endocarditis in the β-lactam group (43.9% vs. 27.8%, $p = 0.11$) and a higher incidence of deep abscess in the SXT group (38.9% vs. 2.4%, $p = 0.001$). In multivariable analysis, infective endocarditis was the only independent predictor of treatment failure. (Table) Variable Unadjusted Odds Ratio p-value Adjusted Odds Ratio p-value Age 1.0 (0.96 – 1.04) 0.29 0.99 (0.94 – 1.04) 0.63 IVDU 0.52 (0.17 – 1.67) 0.27 0.48 (0.10 – 2.23) 0.35 Infective Endocarditis 7.2 (2.20 – 23.57) 0.001 5.75 (1.50 – 22.04) 0.01 Admission from skilled nursing facility 3.00 (0.67 – 13.40) 0.14 1.69 (0.27 – 10.42) 0.57 APACHE II Score 1.06 (1.00 – 1.13) 0.11 1.02 (0.96 – 1.10) 0.49 Time from index culture to start of combination therapy (days) 1.07 (0.98 – 1.18) 0.48 1.07 (0.96 – 1.20) 0.24 Study Group 0.25 (0.07 – 0.88) 0.03 0.28 (0.06 – 1.46) 0.13 Conclusion: The complex nature of the patients examined in this study shows the continued need for new data to improve treatment strategies for MRSA BSI. In this study, we observed an interesting prescribing behavior whereby patients with infective endocarditis were far more likely to be treated with DAP + β-lactam while those with a skin source were more likely to receive DAP + SXT. Further studies are needed to uncover the underlying reasons for this differential prescribing and to determine which patient populations benefit more from one regimen over the other.</p>

ABSTRACT NO. 61	
Name	Dana Chammaa
Category	Pharmacy Practice
Title	Monitoring Vancomycin in Children: When Should the Initial Trough be Measured?
Authors	Dana Chammaa, B.S., PharmD Candidate 2019; Leah Molloy, Pharm.D.; Amanda Dowker, B.S., PharmD Candidate
Abstract	<p>Purpose: The optimal time to check an initial vancomycin serum trough concentration (Vt) has not been established in children. Different approaches were compared to assess impact on Vt attainment, acute kidney injury (AKI), and pharmacy workflow.</p> <p>Methodology: 3 approaches to initial Vt monitoring were compared. In Phase 1, initial Vt was ordered per pharmacist discretion. In Phase 2, initial Vt was ordered before the 4th dose of every regimen. In Phase 3, initial Vt was drawn before the 4th or 5th dose of every regimen for selected patients only, and per pharmacist discretion for others. Criteria for early Vt during Phase 3 were: PICU admission, renal impairment, concomitant nephrotoxins, burn, ECMO, recent cardiovascular surgery, empiric doses >60 mg/kg/day or ≥4 gm/day, and premature infants <4 weeks old. Patients were excluded if they were dosed by levels, admitted to NICU, or received <4 doses.</p> <p>Results: 290 patients were included: 72 in Phase 1, 127 in Phase 2, and 91 in Phase 3. More patients in Phase 2 had a Vt drawn than in Phase 1 (96% vs. 63%, p<0.001). This was reduced to 82% in Phase 3 (p=0.001 compared to Phase 2), but still greater than in Phase 1 (p=0.013). Of patients with at least one Vt, attainment of Vt ≥10 mg/dL was more common in Phase 1 (69%) than Phase 2 (44%, p<0.01) or Phase 3 (44%, p=0.08), possibly owing to a smaller proportion of patients getting a Vt in Phase 1. AKI was infrequent and similar between phases. More patients in Phase 2 had a Vt checked during courses lasting <48h (89%) than in Phases 1 (54%), p<0.001) or 3 (52%, p=0.001). More Vts were ordered during afternoon and midnight shifts during Phase 2 (45%) than Phase 1 (22%), p<0.001. In Phase 3, initial Vt was drawn significantly earlier for patients meeting criteria for early Vt than those who did not (24h vs. 37h, p=0.041; after 3 doses vs. 5 doses, p=0.024). These patients were numerically more likely to have a dose reduction after the first level but this was not statistically significant (12% vs. 0, p=0.08).</p> <p>Conclusions: A targeted approach to early Vt monitoring provided early monitoring for patients potentially at higher risk for AKI while limiting extraneous monitoring pharmacy workload.</p>

ABSTRACT NO. 62	
Name	Max Charron
Category	Pharmacy Practice
Title	Evaluation of a Modified Patient Intervention Capture Survey in an Interprofessional Student Clinic for Underserved Populations
Authors	Charron M; Smith J; Gortney JS; Mendez J.
Abstract	<p>Purpose: A patient intervention capture survey (PICS) was developed based on the types of education and services provided to patients at an interprofessional, student-run free clinic. Patient records were evaluated retrospectively to determine interventions made by students and to uncover gaps in documentation. Modifications were then made to the PICS and to patient assessment forms the clinic uses to enhance capture of patient interventions made. This study was designed to determine the impact of the modification of the PICS and patient assessment forms in helping the clinic more accurately capture interventions.</p> <p>Methods: The initial PICS was developed to capture services offered including: medical and medication-related education, social assistance, written prescription or free over-the-counter medications, therapy, and referrals made to other providers. Services were aligned with the student disciplines in the clinic including medical, pharmacy, social work, and physical therapy programs. The PICS was used to retrospectively to evaluate patient records of 2016 to determine how to quantify patient interventions made at the clinic. Based on this data, common themes of education and services provided were identified. Modifications were made to the PICS including combining medical and medication-related education provided, expanding counseling aspects social work students were providing, and referrals. Patient assessment forms for each discipline were updated to encourage students to more accurately describe services and interventions provided. The modified PICS and forms were implemented in August 2017, and the PICS was utilized in a prospective manner to get “real time” information. To do this, students were asked to complete the PICS upon completion of the patient encounters to reflect the interventions that were done the clinic. A quantitative analysis was done to compare differences between the retrospective PICS and the modified PICS used prospectively.</p> <p>Results: From August 2017 to May 2018, a total of 85 patients were seen at the CHIP clinic. A total of 160 interventions were provided by medical, pharmacy, social work, and physical therapy students. Using the modified PICS for prospective data capture, 91% of patients seen at the clinic were provided with medical, drug, or another type of education compared to 58% retrospectively. Interventions captured per month with modified PICS was 17.7 versus 6.9 retrospectively. Medication counseling was documented in 15% using modified PICS versus 18% retrospectively. Prospective use showed that 11% of patients received a prescription from a physician, and 9% received an OTC medication compared to 8% and 32% with retrospective PICS.</p> <p>Conclusion: Modifications made to the survey and patient evaluation forms have increased documentation of patient education and increased students’ awareness and attention to detail. We believe the modifications made to the clinic assessment forms as well as the PICS survey has provided additional education to the rotating student volunteers as to what is expected during clinic and as a result has enhanced their skills and patient interactions. Continuing to use PICS in “real time” should continue to provide more accurate capture of the interventions made at the clinic in the future and result in better provision of patient care.</p>

ABSTRACT NO. 63	
Name	Patricia Choi
Category	Pharmacy Practice
Title	Characterization of gram-variable organisms and impact on antimicrobial management
Authors	Patricia Choi, Student Pharmacist; Nicholas Mercurio, PharmD; Susan Davis, PharmD
Abstract	<p>Background & Purpose: The gram stain is a powerful and commonly used tool in healthcare for the preliminary identification of bacteria. Gram stain results are either positive or negative, based on the bacteria's taxonomic characteristic. This information allows clinicians to initiate an appropriate empiric antibiotic regimen while the microbiology laboratory verifies the organism from specimen cultures. However, gram stain results are sometimes 'variable' and the mechanisms why are not well understood. It is also unknown how clinicians react to these results or how they attempt to optimize the antibiotic regimen when this rare instance occurs. Without the clear positive or negative gram stain result, the time to change from empiric to targeted antimicrobial therapy may be delayed. This delay may lead to prolonged exposure to broad-spectrum antibiotics, and thus pose an increased risk to adverse effects for patients with suspected infections. Gaining a clinical picture of antibiotic utilization at Henry Ford Hospital (HFH) for gram variable organisms may be useful to help guide clinicians approach these cases in the future.</p> <p>Methods: This is a retrospective, cross-sectional study that included all patients with gram variable organisms from May 2014 to July 2018 at HFH. The primary endpoints include: type of infection or indication for treatment, source of specimen, final species identification, and antibiotic utilization defined as de-escalation, escalation, initiation, and/or discontinuation. Additional data collected include development of acute kidney injury upon receiving antimicrobials, development of a multi-drug resistant organism, and development of C. difficile infection. Statistical analysis used is standard descriptive statistics via measures of central tendency and variability.</p> <p>Results & Conclusions: Research currently in progress. Results and conclusions will be presented at Research Day on November 7th, 2018.</p>

ABSTRACT NO. 64	
Name	Sara Denton
Category	Pharmacy Practice
Title	Impact of the Career Pathway Self-Assessment Tool on Student Career Planning
Authors	Sara Denton, BS Psychology, BS Health Sciences, PharmD Candidate; Jason Cormier, BA English, BA Chemistry, PharmD Candidate
Abstract	<p>Background/Objectives: The study objective was to assess the impact of the Career Pathway Assessment Tool (CPAT) on student career planning. CPAT is part of the American Pharmacists Association’s Career Pathway Evaluation Program. The tool suggests possible pharmacy career paths based on 48 critical factors. The program also describes various pharmacy careers. CPAT usefulness to student pharmacists has been minimally assessed. First-year student pharmacists completed the CPAT before attending a career fair as part of a required winter social and administrative sciences course.</p> <p>Methods: Immediately after the career fair, student pharmacists answered two reflection questions about CPAT’s impact on career planning and career fair presentation selection. The answers were analyzed using grounded theory, a qualitative research technique. Two investigators independently assigned initial codes, and then adjudicated codes to develop categories and themes. From these themes, a 31-item survey was devised incorporating Likert scale assessments and numerical boxes to assess personal impact (13 items), career fair influence (6 items), tool usability (5 items), and demographics (7 items). The survey was administered via Qualtrics 5 months after using the CPAT. Responses were anonymous and analyzed using descriptive statistics (SPSS v25). Research was institutional review board exempt.</p> <p>Results: Student age was 23.7 + 3.2 years. Response rate for the reflection questions was 99% (N=111; 71 women, 40 men) and for the survey was 54% (N=60; 42 women, 18 men). Most respondents felt the CPAT was user-friendly (92%), helped with career planning (82%), increased enthusiasm towards pharmacy (82%), and identified careers in which they were not interested (88%). Respondents felt the CPAT accurately reflected their needs - i.e. innovation and fulfillment (82%), relationships (82%), clinical practice (77%), workload factors (77%), non-salary compensation (77%), and freedom (77%). Many respondents (78%) felt the CPAT influenced their career fair selections. Almost all respondents (98%) learned about one or more new pharmacy careers (3.4 + 1.3). The respondents described how the CPAT expanded their knowledge of possible careers (69 codes); helped focused their career interests (47 codes); matched accurately to their personality characteristics, wants and needs (28 codes); was valuable (18 codes); and motivated them to learn more (10 codes). A few students felt the CPAT was moderately or not accurate (9 codes), not useful (9 codes) or not easy to use (3 codes). Some respondents (23%) used the CPAT 1 to 6 times after the career fair. Almost all respondents stated they would (58%) or possibly would (32%) recommend the CPAT to other student pharmacists. The only difference between genders was the female respondents reviewed more career descriptions prior to the career fair than the male respondents. Implications/Conclusions The CPAT helped student pharmacists discover employment characteristics important to them, identify new pharmacy career options, and select career fair presentations. Almost all student pharmacists found the tool easy to use and accurate. Incorporating the CPAT into the pharmacy curriculum facilitates student pharmacist reflection on their future career, educates them about non-traditional pharmacy careers, and stimulates students to research careers further on their own.</p>

ABSTRACT NO. 65	
Name	Amir Emamdjomeh
Category	Pharmacy Practice
Title	Evaluation of day two hydration and electrolyte protocol for high-dose cisplatin therapy
Authors	Nicole Elkhoury, BS; Amir Emamdjomeh, BS; Jean Doh, PharmD; Diana Kostoff, PharmD, BCPS, BCOP; Angela Michael, PharmD, BCOP; Vishnuprabha Vogel, PharmD, BCPS, BCOP
Abstract	<p>Purpose: Nephrotoxicity and electrolyte wasting are two major adverse effects of cisplatin therapy, especially at high doses. There is limited data on hydration and electrolyte replacement strategies, and protocols vary greatly by institution. The current protocol at Henry Ford Health System is a standardized day two hydration and intravenous (IV) electrolyte replacement for all patients receiving high-dose cisplatin. The purpose of this project was to evaluate the appropriateness of the existing replacement protocol after highdose cisplatin in the ambulatory infusion center setting.</p> <p>Methods: This was a retrospective study evaluating the appropriateness of high-dose cisplating hydration and IV electrolyte replacement protocol. Administration events where patients received cisplatin doses greater than or equal to 60 mg/m² between January 1, 2018 and April 30, 2018 were included in this evaluation. Patients were excluded if potassium and magnesium levels were not drawn the day after high-dose cisplatin was administered or if the patient was participating in an investigational study that included cisplatin. Data collected included the proportion of patients receiving unnecessary hydration and IV electrolytes, cisplatin dosing, serum potassium and magnesium levels pre- and post-cisplatin infusion, and the number of emergency department/urgent care visits, or hospital admissions. Descriptive statistics were used to analyze the data.</p> <p>Results and Conclusion: Final results and conclusion will be presented at Eugene Applebaum College of Pharmacy and Health Sciences Annual College Research Day.</p>

ABSTRACT NO. 66	
Name	Michael Farrah
Category	Pharmacy Practice
Title	Minimizing time to optimal therapy for Enterobacteriaceae bloodstream infections: Is organism identification enough?
Authors	Jessica J. Mourani, PharmD; Michael Farah, PharmD Candidate; Ryan P. Mynatt, PharmD, BCPS-ID; Tristan T. Timbrook, PharmD, MBA, BCPS; Jason Pogue, PharmD, BCPS-ID
Abstract	<p>Background: Bloodstream infections (BSIs) due to ceftriaxone (CRO) resistant Enterobacteriaceae (ENT) are increasing in frequency and are associated with delays in time to appropriate therapy. However, treating all patients at risk for CRO-resistant organisms with empiric carbapenem (CARB) therapy risks over exposure. Strategies are needed to appropriately balance these competing interests. Current scoring tools have been established in patient populations with low extended spectrum beta-lactamase (ESBL) burden, making it difficult to rely on these methods. There is a need to create a strategy that accurately identifies patients with ESBL Enterobacteriaceae bacteremia rapidly so that empiric treatment can be initiated promptly with a carbapenem. The purpose of this study was to create a novel scoring tool for detection of CRO-ENT in order to appropriately initiate carbapenem therapy.</p> <p>Methods: Retrospective observational study of patients at the Detroit Medical Center with ENT BSI from July 1, 2016 to August 1, 2018. Patients with E. coli, K. oxytoca, K. pneumoniae, or P. mirabilis bacteremia will be included. Patients are excluded if CARB resistance was detected via genetic markers. A case control study will be performed to identify predictors of ceftriaxone-resistant Enterobacteriaceae. Cases will consist of patients with ceftriaxone-resistant isolates and controls will consist of cases with ceftriaxonesusceptible isolates. Logistic regression will be used to identify risk factors for ceftriaxone-resistant Enterobacteriaceae BSI. Variables associated with ceftriaxone resistance in bivariate analyses ($p < 0.10$) will be eligible for inclusion in a multivariate logistic regression. Risk factors will be included in the final model if they were independently associated with a ceftriaxone-resistant Enterobacteriaceae BSI. Points for each independent risk factor will be weighted by the corresponding regression coefficients. A receiver operating characteristics curve (ROC or C-curve) will be used to quantify a cutoff point for prediction of a ceftriaxone-resistant Enterobacteriaceae and empiric use of a carbapenem. Lastly, a Hosmer-Lemeshow test will be used to calibrate and internally validate the proposed scoring tool that best fits this population. Similar curves will be created with the scoring tools from Augustine and Lee to allow comparison of the three scoring methodologies in a high burden ESBL population.</p> <p>Results: pending</p> <p>Conclusions: pending</p>

ABSTRACT NO. 67	
Name	Brian Feldpausch
Category	Pharmacy Practice
Title	A Pharmacist-Managed Diabetes Clinic Demonstrates Sustained A1c Reduction in Active Patients and Creates a Mechanism to Identify Barriers for Inactive Patients
Authors	Brian Feldpausch; Shelby Koppinger; Hannah Scharboneau; Amina Ammar; Linda Jaber, Pharm.D.; Dana El Masri Pharm.D.; Helen Berlie BHS, Pharm.D., BCACP
Abstract	<p>Purpose: Health Centers Detroit Medical Group (HCDMG) is a primary care clinic with 13 physicians, ancillary healthcare professionals and a pharmacist. The pharmacist pharmacistmanaged diabetes clinic (PMDC) functions independently under a collaborative practice agreement to provide care for patients with diabetes, referred by their primary care physician. Pharmacy interventions at HCDMG have previously demonstrated significant A1c lowering and related cost savings. However, appointment no-shows have also been observed, which can lead to reduced revenue. The purpose of this study was to assess sustained A1c lowering in active patients and create a mechanism to identify barriers to care for inactive patients.</p> <p>Methods: This was a retrospective chart review conducted at HCDMG and included patients seen at the PMDC between August 1, 2017 and July 31, 2018. HCDGM uses the electronic health record program "EHRYOURWAY", which was used for the chart review. Data collected included: vital signs, lab values, medication therapy, and interventions. Data collected from the current time period was compared to data from the patients' initial visit to the PMDC as well as 2 other data collection periods. Paired t tests and descriptive statistics were used for analysis. Patients were deemed "active" if they were seen by the PMDC in during the data collection period. Stable patients are usually seen every 3 months. No-show visits were also assessed by retrieving the last recorded date the patient was seen by the PMDC (as recorded in the electronic health record). A patient survey was created to identify barriers to keeping appointments.</p> <p>Results: A total of 101 patient records were reviewed between August 1, 2017 and July 31, 2018. From the records reviewed, 43 patients had been seen by the PMDC during that timeframe and were considered "active". Average A1c for these patients during that timeframe was 7.65% (SD +/- 1.82). The average baseline A1C upon initial referral was 9.98% (SD +/- 2.61). When compared to the initial referral, difference in A1c was -2.33% (95% CI: 1.10 - 2.40, p<0.001). This A1c reduction was similar to previous findings with the PMDC at HCDMG. A total of 58 patients were deemed "inactive" during the data collection period. A telephone survey was created in an effort to identify barriers and reduce the number of "inactive" patients. The survey included 4 questions. The last question pertains to the reason that patients have not returned to the PMDC and includes the following categories: physical barrier, cognitive barrier, and issues with facility, time conflicts, financial barrier, disease related, care related, and indirect reasons.</p> <p>Conclusion: The PMDC demonstrated sustained A1c reduction from initial referral for active patients. However, there was a high number of patients that were no longer active. In order to identify barriers to clinic visits of inactive patients, a phone script and survey was developed. Future studies will determine barriers and identify potential solutions in an effort to increase visit adherence.</p>

ABSTRACT NO. 68	
Name	Stephanie Fern
Category	Pharmacy Practice
Title	Comparison of Pre and Post-ExamSoft Use Perceptions of First Year Pharmacy Students
Authors	Stephanie Fern; Benjamin August; Justine Gortney, Pharm.D., BCPS; Minakshi Lahiri, Ph.D.
Abstract	<p>Purpose: To evaluate both P1 student perceptions of online testing before and after implementation of ExamSoft®, an exam management system, in the first year Pharm.D. curriculum.</p> <p>Methods: Based on previous literature and administrative experience, a pre-ExamSoft use survey was developed to assess the perceptions of students in the P1 curriculum. Pre-use survey content related to users' perceptions of past online testing experiences, potential benefits and challenges of using ExamSoft, and its potential impact on learning or teaching. A post-use survey was developed to be administered after one semester of use and included similar pre-use survey content with both scaled and open-ended, reflective questions on the user's experiences. Responses were collected using 5 point Likert scale, ranging from strongly agree to strongly disagree. Respondents were asked to enter a 4 digit code of their birth month/date, enabling matching of pre and post-use surveys. Students were sent an email with a Qualtrics link to the survey. This study was determined to be exempt by the IRB. Post-use survey data was also evaluated to determine overall student experience with ExamSoft. Data was analyzed using the Wilcoxon Signed-Rank Test to compare the matched samples of the pre and post-use survey results.</p> <p>Results: A total of 110 pre-surveys and 67 post-surveys were completed. There were 48 validated pre-post matches. Among pre-post matches, no statistically significant difference was observed among age and gender categories. A majority of post-use respondents were neutral or in agreement with ExamSoft's interface being flexible to interact with. Although a greater frequency of favorable attitudes towards ExamSoft was noted, there was no statistically significant difference observed. More students disagreed that ExamSoft enhanced effectiveness in learning ($P < 0.001$) and improved course performance and learning compared to pencil and paper ($P = 0.047$) after ExamSoft use. A total of 67.15% of post-survey respondents agreed that having used ExamSoft will help them prepare for future exams (e.g. PCOA, NAPLEX, MJPE, BCPS).</p> <p>Conclusions: Among P1 pharmacy students in the first year of the Pharm.D. curriculum, general attitudes regarding ExamSoft use were relatively neutral, with no significant difference of favorable versus unfavorable attitudes. Given that 55% of respondents had previously used electronic testing and potentially possessed preformed opinions, it may have been difficult to detect changes in perception in this population. The finding that more students disagreed with ExamSoft enhancing their effectiveness in learning could relate to several factors. ExamSoft has been newly introduced at our institution and its feedback capabilities have not been fully maximized. Early and more effective distribution of reports may change the way students understand the utility of an assessment management system. Further, this finding may be influenced by technical difficulties in electronic upload, a frustration that could have overshadowed other perceptions of students. Among those new to electronic assessment, test anxiety may have been contributory in our finding that students did not feel optimization of performance and learning when compared to pencil and paper testing.</p>

ABSTRACT NO. 69	
Name	Souheila Hachem
Category	Pharmacy Practice
Title	Assessing Vancomycin Dosing Requirements in Patients with Right-Ventricular Dysfunction
Authors	Souheila Hachem, B.S., PharmD Candidate 2019; Laura Hencken, PharmD, BCCCP, Long To, PharmD, BCPS; Zachary Smith, PharmD, BCPS, BCCCP
Abstract	<p>Background: Left-ventricular (LV) dysfunction has previously been associated with reduced vancomycin clearance. Patients with severe pulmonary hypertension or heart failure with reduced ejection fraction (HFrEF) can experience right ventricular (RV) dysfunction. There is currently no literature describing the impact of RV dysfunction on vancomycin clearance. The purpose of this investigation is to describe the vancomycin dosing requirements in patients with RV dysfunction.</p> <p>Methods: This was a retrospective study conducted in patients admitted to cardiac or medical intensive care unit at a large, academic institution between November 1, 2016 and July 31, 2018. Patients were included if they were greater than 18 years old, had a transthoracic echocardiogram (TTE) indicating RV dysfunction, received a pulmonary vasodilator, and received vancomycin with an evaluable trough level. RV dysfunction was defined as having two of the following: right atrial pressure >15 mmHg, TAPSE 1.6 cm, a description of RV dysfunction on TTE, or as diagnosed by physician in the medical record. Included patients were further categorized to biventricular failure if the LV ejection fraction is ≤ 40 or RV dysfunction if the LV ejection fraction is $>40\%$. Pulmonary vasodilators were defined as milrinone or any medication FDA approved for pulmonary arterial hypertension. Patients were excluded if they received dialysis or developed acute kidney injury (AKI) prior to the first vancomycin trough level. The primary endpoint was to evaluate the actual vancomycin regimen mg/kg dosing and interval requirements compared to institutional vancomycin dosing guideline recommendations. Secondary endpoints include goal trough attainment and frequency of AKI. Data will be described using descriptive statistics.</p> <p>Results/Conclusion: Data collection and analysis are ongoing. Results and conclusions will be presented at the WSU Research Day.</p>

ABSTRACT NO. 70	
Name	Andrew Hanna
Category	Pharmacy Practice
Title	Student led initiative to improve staff knowledge of medication synchronization and impact on proportion of days covered in a community pharmacy setting
Authors	Hanna, Andrew, Pharm.D. Candidate; Tayar, Tony Pharm.D. Candidate; Kolc, Sara Pharm.D. Candidate; Fava, Joseph Pharm.D.; Hegeman-Dingle, Rozelle Pharm.D., BCPS,CPHIMS
Abstract	<p>Background/Objective: Objective: To improve utilization of a medication synchronization program, SyncScript, and improve the knowledge of staff members with the goal of improving patient adherence through increased proportion of days covered (PDC). The Centers for Medicare and Medicaid Services (CMS) utilizes a "pay-for-performance" model. Insurance plans and pharmacies are issued a Star Rating that ranges from 1-5 (one being the lowest and five being the best) based on performance. Star Rating criteria are directly related to medication adherence, with emphasis on certain classes of drugs including statins, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), and non-insulin antidiabetic medications. Non-adherence to these medications and the disease states are associated with increased morbidity, mortality, and health care costs. The most cost effective, nonmedical intervention that leads to improved outcomes is increased patient adherence. Medication synchronization has been shown to increase patient adherence, which decreases health care costs. There is literature regarding medication synchronization and its impact on healthcare, however, there is no known research that focuses on the effective utilization and implementation of a medication synchronization program.</p> <p>Methods: The pharmacy staff (technicians, interns, and pharmacists) at three pilot Meijer pharmacies will be provided a medication synchronization program knowledge assessment survey at baseline, as well as at project conclusion. The project team that head the teaching of this program consists of a community-based pharmacy resident and two fourth year pharmacy students. This team will conduct in-person training for pharmacy staff members using a standardized training module developed by the project team. Pharmacy staff members will receive one-on-one training from the project team. This training includes reviewing the training module, as well as opportunities for the staff members to demonstrate knowledge and use the project team to aid in filling knowledge gaps. The project is conducted over six months, October 2018 to April 2019. The project team will contact participating patients by telephone or in person to provide education and assess adherence using the Merck Adherence Estimator® at baseline and at six months.</p> <p>Results (pending): Pre and post-pharmacy staff education data regarding SyncScript metrics will be analyzed, as well as data regarding patient adherence indicators such as proportion of days covered (PDC) and responses from the Adherence Estimator®. Outcomes will be analyzed using descriptive statistical methods.</p> <p>Conclusion (pending): We hypothesize that implementation of this program will improve pharmacy staff knowledge, abilities, and comfort levels with the SyncScript program, as well as increase the number of prescriptions being filled using SyncScript. We also hypothesize that PDC will increase for medications that factor into CMS Star Ratings.</p>

ABSTRACT NO. 71	
Name	Tiffanie Hargraves
Category	Pharmacy Practice
Title	Lead (Pb) inhibits insulin-activated AKT signaling and reduces glycogen in rat liver
Authors	Tiffanie Hargraves, PhD Candidate; Nicholas Mastrandrea, PhD; Kyle Burghardt, PharmD; Todd Leff, PhD; Terrence Monks, PhD; Victoria Tutag Lehr, PharmD
Abstract	<p>Introduction: Lead (Pb) exposure disrupts insulin signaling which may contribute to insulin resistance and diabetes in humans. As Pb exposure increases from aging urban water infrastructure, it is imperative to investigate the specific disruptive mechanisms of Pb to develop interventions for exposed populations.</p> <p>Hypothesis: To determine whether Pb exposure affects hepatic glycogen content, insulin signaling, and gene expression changes in rat liver and cultured hepatocytes. Study Design: Prospective cohort, quantitative study using ex-vivo liver from Zucker diabetic fatty (ZDF) rats and isolated primary cultured rat hepatocytes (PCH) from Sprague Dawley rats. Methods: ZDF rats, PCH, and HEPG2 cells were exposed to various concentrations of Pb. Changes in glycogen content were measured via glycogen assay and histological analysis. Changes in the AKT signaling pathway were determined via immunoblot analysis. Gene expression changes were identified via microarray, followed by Ingenuity Pathway Analysis. One-way analysis of variance, followed by Tukey-Kramer multiple comparison analysis was used to compare differences between groups. Significance was $p < 0.05$</p> <p>Results: Glycogen concentrations were significantly reduced in ZDF rat liver and PCH following Pb exposure ($p < 0.05$). In addition, dose-dependent decreases in pAKT and pGSK, and increases in pGS, were found ($p < 0.05$). Finally, microarray and gene pathway analyses identified significant changes in the expression of genes involved in glycogen synthesis. Exposure of PCH to Pb caused enrichment of genes related to the canonical pathways of pregnane X receptor (PXR)/retinoid X receptor (RXR) activation, caveolar-mediated endocytosis signaling, and hepatic fibrosis/hepatic stellate cell activation ($p < 0.01$).</p> <p>Conclusion: Pb exposure causes insulin resistance in rat liver, in part, via AKT inhibition and changes in gene expression, both of which are involved in glycogenesis. This is associated with decreased hepatic glycogen levels. These data represent possible mechanisms behind Pb and insulin resistance. Human hepatocyte validation may support routine diabetic screening of Pb exposed populations.</p>

ABSTRACT NO. 72	
Name	Autumn Heeter
Category	Pharmacy Practice
Title	Skin Conductance Responses as an Index of Fear: Excluding “Non-Responders” May Exclude a Relevant Phenotype
Authors	Autumm Heeter, Craig Peters, Farrah Elrahal, Joshua Hatfield, Brian Silverstein, Jeremy DeLor, Miranda Rippin, Hilary A. Marusak, Christine Rabinak
Abstract	<p>Purpose: Pavlovian fear conditioning is widely used to understand fear-related learning and the pathogenesis of anxiety and posttraumatic stress disorder (PTSD). Common outcome measures of conditioned fear responding include physiological recordings, i.e. skin conductance responses (SCRs). However, participants are routinely excluded because they have low SCRs or are ‘non-responders’, which may compromise generalizability of results and preclude the full characterization of pathology. Further, because SCRs are typically recorded from the non-dominant hand (commonly left), it is unclear if participants would be characterized as ‘responders’ if SCRs were instead recorded from the dominant side. To address this, we tested for lateralization of SCRs. We examined the effects of demographic factors (e.g., gender, age, race), as well as patient groups in which SCRs are commonly recorded: PTSD, trauma-exposed control (TEC), or healthy control (HC). Methodology: Ninety-eight right-handed participants (ages 21-55; 49 female; 16 PTSD, 37 TEC, 45 HC) completed this study. SCRs in response to a series of novel sounds were recorded from each hand (order counterbalanced across participants). Results: About 40% of participants were symmetric responders. No difference in laterality was found between groups, genders, or across races. Older individuals displayed more bilateral SCRs compared to younger individuals. Mean SCR did not differ by group, gender, or age. Conclusions: Our results indicate that many individuals show symmetric SCRs. For those who show lateralization of SCRs, our data suggest that patient group, gender, and race are not contributing factors. Future studies will combine functional magnetic resonance imaging to explore brain-based correlates of SCR lateralization.</p>

ABSTRACT NO. 73	
Name	Aneesh Hehr
Category	Pharmacy Practice
Title	Sleep duration is associated with altered activation of fear extinction neural circuitry in children
Authors	Aneesh Hehr, BS Candidate; Hilary A. Marusak, PhD; Craig Peters, BS; Christine A. Rabinak, PhD
Abstract	<p>Purpose: The transition from childhood to adolescence is marked by a sharp increase in the incidence of anxiety disorders, and also a rise in sleep problems. Shorter sleep duration is associated with deficits in emotion regulation and increased cortico-limbic responses to emotional stimuli in children. These neurobehavioral changes may underlie the link between sleep problems and the emergence of anxiety. Given that anxiety disorders are characterized by disruptions in the ability to appropriately inhibit or extinguish fear, the present study examines the relationship between sleep duration and fear extinction and underlying neural circuitry in children.</p> <p>Methods: 43 children (6-11 years, 22 females) participated in a two-day virtual reality fear extinction paradigm. Participants underwent fear and extinction learning on the first day. Twenty-four hours later, a test of extinction recall was performed during functional magnetic resonance imaging (fMRI) scanning. Skin conductance responses (SCRs) were recorded during all sessions as a measure of conditioned fear. Sleep duration was estimated using an overnight sleep journal. We compared sleep with SCRs and activation in cortico-limbic regions.</p> <p>Results: Children with poorer extinction learning, evidenced by higher SCRs at the end of extinction learning, subsequently slept fewer hours. Less sleep was, in turn, associated with poorer extinction recall, evidenced by higher SCRs to the previous extinguished cue. Less sleep was also associated with higher neural response to the previously extinguished cue in the amygdala, a region associated with fear expression.</p> <p>Conclusion: Links between shorter sleep duration, poorer fear extinction, and altered functioning of fear extinction neural circuitry should be considered in the etiology and treatment of pediatric anxiety disorders.</p>

ABSTRACT NO. 74	
Name	Mariam Hijazi
Category	Pharmacy Practice
Title	Effects of Calcium Replacement on Ionized Calcium Levels in Surgical Intensive Care Unit Patients
Authors	Vitaliy Perets, PharmD; Christopher Giuliano, PharmD, MPH; Joseph Buck, MD; R. David Hayward, PhD; Mariam Hijazi, Renee Paxton, PharmD, BCPS, BCCCP
Abstract	<p>Purpose: Hypocalcemia in the surgical intensive care units (SICU) has been associated with increased mortality and longer intensive care unit (ICU) stay. There is a paucity of literature to guide calcium replacement in hypocalcemic patients. The purpose of this study is to evaluate the association between IV calcium dose(s) and the corresponding ionized calcium (iCa) levels.</p> <p>Methods: This is a single center, retrospective cohort study in adult patients with hypocalcemia admitted to the SICU between January 2010 and May 2018. Patients were included if they had an iCa \leq 1.12 mmol/L and received IV calcium therapy. Patients were excluded if they were pregnant, had hypo or hyperthyroidism, of if they were receiving total parenteral nutrition therapy, renal replacement therapy or plasmapheresis. The primary objective of this study was to evaluate the association between IV calcium dose and changes in iCa levels. The secondary objectives were to determine the average IV calcium dose required to normalize iCa levels, determine time to normalization of iCa levels, compare the SICU length of stay between those patients who did and did not normalize iCa levels and to assess the safety of IV calcium replacement. Descriptive statistics was used to describe the cohort. Linear regression was used for the analysis of the primary objective.</p> <p>Results: 194 patients were included in the final study analysis. Majority of patients in the study were followed by general, neurological, and trauma surgery. The average iCa level was 0.97 ± 0.15 mmol/L. We found the association between iCa level and Ca dose for our cohort of patients to be explained by the following regression equation: change in iCa level = $0.367 + 0.038 \times [\text{Ca dose}] + 0.002 \times [\text{Blood products}] + 0.014 \times [\text{LR}] - 0.001 \times [\text{Age}] - 0.229 \times [\text{Initial iCa}] - 0.052 \times [\text{initial iCa} \times \text{Ca dose}]$. Normalization of Ca levels was observed in 32.5% of patients, with mean calcium dose to be 1.81 gram, and mean time to normalization of 16.8 hours. There was no difference observed in other secondary objectives.</p> <p>Conclusion: There is a positive association between calcium dose and iCa levels, however there are other factors that are associated with change in iCa levels not explained by our model. We found no difference in secondary outcomes between those who normalized and did not normalize ionized calcium levels.</p>

ABSTRACT NO. 75	
Name	Kevin Marck Intig
Category	Pharmacy Practice
Title	Direct Oral Anticoagulant (DOAC) Use versus Warfarin in Morbidly Obese Patients for Prevention of Recurrent Venous Thromboembolic Events (VTE)
Authors	Kevin Marck Intig, PharmD Candidate; Samer Matti, PharmD Candidate; Allison Golom, PharmD; Sin-Ling Jennings, PharmD; David Wilpula, PharmD
Abstract	<p>Background: Anticoagulants have been the therapy of choice for the prevention and treatment of venous thromboembolic events. Currently, there are four FDA approved Direct-acting Oral Anticoagulants (DOAC) for clinical use: Apixaban (Eliquis), Rivaroxaban (Xarelto), Dabigatran (Pradaxa), and Edoxaban (Savaysa). The 2016 International Society on Thrombosis and Haemostasis (ISTH) guidelines recommend against the use of DOACs in morbidly obese patients (>120 kg or BMI > 40 kg/m²) due to the scarcity of clinical data in this population. Recent studies evaluating pharmacokinetic data of DOACs suggest that adequate drug levels are achieved in obese patients and no dose adjustments are necessary. However, there are no large randomized controlled trials specifically evaluating the efficacy and safety of DOACs for the use in the morbidly obese population. Thus, it is uncertain whether or not DOACs can be safely and effectively used in the morbidly obese.</p> <p>Purpose: Evaluate the safety and efficacy on the use of Direct Oral Anticoagulants vs Warfarin in morbidly obese (>120 kg or BMI > 40 kg/m²) patients for the prevention of recurrent venous thromboembolic events.</p> <p>Methods: The incidence of recurrent VTEs, clinically relevant non-major, and major bleeding events were analyzed via a multicenter retrospective-case control study at Beaumont Health Systems October 2016 through October 2017.</p> <p>Results: Pending</p> <p>Conclusion: Pending</p>

ABSTRACT NO. 76	
Name	Ritika Jain
Category	Pharmacy Practice
Title	Evaluation of sub-dissociative dose ketamine (SDDK) for treatment of acute pain at Beaumont Hospital – Royal Oak
Authors	Ritika Jain; Andrea Haugtvedt, PharmD; Sheena Merwine, PharmD, BCPS; Levi Hall, PharmD, BCPS
Abstract	<p>Purpose: Ketamine is used in numerous healthcare scenarios, such as rapid sequence intubation (RSI), procedural sedation, and anesthesia. It is well-known for its sedative and dissociative properties, but also possesses analgesic properties. At Beaumont Hospital-Royal Oak, low-dose ketamine, which is also known as sub-dissociative dose ketamine (SDDK), is one of many therapeutic options available to providers to treat acute pain. The purpose of this study is to evaluate the use of SDDK at Beaumont Hospital-Royal Oak since the approval of a guideline for its use in the Emergency Center on May 4th, 2017.</p> <p>Methods: This study will be submitted to the Institutional Review Board (IRB) for approval. The electronic medical record (EMR) system will identify patients who received ketamine up to 50 mg total [intravenously (IV), intramuscularly (IM), or intranasally (IN)] at Beaumont Hospital-Royal Oak from May 4th, 2017 to September 7th, 2018. Through chart review, investigators will determine if the dose of ketamine being evaluated was intended to be a sub-dissociative dose versus a dose for other indications, such as procedural sedation. The following data will be collected: age, gender, body weight, location of patient, dose of ketamine, documentation of other pain medications given, pain scores, candidacy for SDDK, administration instructions and adverse reactions. The primary outcome will be the number of patients who received SDDK at Beaumont Hospital – Royal Oak. Secondary outcomes will include incidence of adverse events attributable to SDDK, evaluation of opioid use before and after ketamine administration, and adherence to guideline dosing and monitoring recommendations.</p> <p>Results: N/A</p> <p>Conclusion: N/A</p>

ABSTRACT NO. 77	
Name	Tyler Jedinak
Category	Pharmacy Practice
Title	Appropriateness and Safety of Intravenous Trimethoprim-sulfamethoxazole in comparison to Oral Trimethoprim-sulfamethoxazole for Similar Indications and Doses
Authors	Kristen Zofchak; Tyler Jedinak; Susan Davis, PharmD
Abstract	<p>Background: Trimethoprim-sulfamethoxazole (TMS) is a commonly used antimicrobial in clinical practice nationwide for the treatment of infectious diseases with a wide array of indications. TMS is not typically considered to be a high-profile antimicrobial: it is low cost, has no current criteria for monitored use, and there are no restrictions placed on how, when, or to whom it is prescribed. However, TMS is associated with significant toxicities including: electrolyte disturbances, acute kidney injury, hematologic disturbances, skin changes, and volume overload. Inappropriate use and monitoring of IV TMS, long treatment durations, or high doses, have the potential to cause a large impact on patient safety outcomes and antimicrobial resistance. This impact may even be greater in patients with additional risk factors for harm secondary to IV TMS use. There is a need to examine the appropriateness and safety of IV TMS use in order to curb these unintended consequences.</p> <p>Methods: This was a matched cohort study, including patients who received IV TMS therapy for greater than 72 hours in the Henry Ford Health System from August 2015 to August 2018. Patients were excluded if they were <18 years old, pregnant, or received IV TMS for a prophylactic indication. The primary endpoint of interest is selected TMS-associated adverse effects. Adverse effects included were: 1. Hyponatremia (Na <135 mmol/L) 2. Hyperkalemia (K>5.0 mmol/L) 3. Acute kidney injury (increase in serum creatinine of at least ≥ 0.3mg/dL, or 1.5-1.9 times from baseline value) 4. Neutropenia (ANC<1000 cells/ mm³) 5. Thrombocytopenia (a platelet count of less than 100,000 cells/mm³ or a decrease in platelet cell count by 50% from baseline values) 6. Hypoglycemia (blood glucose <72 mg/dL) 7. Volume overload (documented edema on physical exam, documented pulmonary edema on chest imaging which may or may not require diuresis, or an increased dose of an existing diuretic) 8. Skin changes (documented erythema, urticaria, blistering, or pustular eruptions that may or may not be accompanied by fever, defined as body temperature of $\geq 38^{\circ}\text{C}/100.4^{\circ}\text{F}$) The secondary endpoint was appropriateness of use defined by indication, duration, and dose. Additional data collection included length of hospital stay, concomitant medications, and 30-day readmission. Data was collected via a retrospective chart review of selected IV TMS patients. Identical data was collected for the indication-matched, oral TMS (PO TMS) comparator group. Patient characteristics and outcomes were compared between IV and PO TMS groups using standard bivariate statistics including X², Mann Whitney U, and student's t-test. Alpha of 0.05 is considered significant. Analyses were completed using SPSS. These analyses are considered exploratory in nature, due to the limitations of establishing causality with retrospective medical record review data of adverse effects. Descriptive analyses including proportions, measures of central tendency and variability were used to examine prescribing patterns and adverse effects of TMS.</p> <p>Results: [Research in Progress]</p> <p>Conclusions: [Research in Progress]</p>

ABSTRACT NO. 78	
Name	Sarah Jorgensen
Category	Pharmacy Practice
Title	Sequential Intravenous-to-Oral Therapy for Methicillin-Resistant Staphylococcus aureus Bacteremia: One Step Closer
Authors	Sarah C.J. Jorgensen, PharmD; Aldalhamid M. Lagnf, MPH; Sahil Bhatia, MPH; Muhammad-Daniayl Shamim; Michael J. Rybak, PharmD, MPH, PhD
Abstract	<p>Published guidelines call for prolonged courses of intravenous (IV) antibiotics for the treatment of methicillin-resistant Staphylococcus aureus (MRSA) bloodstream infection (BSI) to ensure eradication of deep foci and decrease relapse risk. Sequential IV-to-oral antibiotic therapy has been successfully applied to other serious infections but has not been evaluated for MRSA BSI. The primary objective of this single-center, retrospective, cohort study was to compare 90-day clinical failure (MRSA BSI recurrence, deep-seated MRSA infection, or all-cause mortality) in adult patients completing therapy with oral versus parenteral antibiotics in the outpatient setting (OOAT versus OPAT) for MRSA BSI between 2008 and 2018. Analyses were adjusted for confounding using inverse probability of treatment weighting (IPTW). A total of 492 patients were included (70 OOAT, 422 OPAT). In general, OOAT patients had characteristics consistent with a lower risk of poor outcomes, however after IPTW, balance was achieved in key prognostic factors. In IPTW-adjusted analysis, there was non-significant reduction in the rate of 90-day clinical failure in the OOAT group compared to the OPAT group (aHR 0.379, 95% CI 0.131, 1.101). In analyses restricted to pre-specified subgroups defined by index infection complexity and comorbidity burden, findings were consistent with the main analysis. Furthermore, OOAT patients had a significantly reduced rate of 90-day hospital readmission (aHR 0.603, 95% CI 0.388, 0.937). We provide preliminary evidence that select patients with MRSA BSI may have at least equivalent clinical outcomes with OOAT versus OPAT and provide support to ongoing and future studies evaluating oral antibiotics for MRSA BSI.</p>

ABSTRACT NO. 79	
Name	Jamie George
Category	Pharmacy Practice
Title	Impact of Antibiotic Duration on Clinical Outcomes Following Positive Procalcitonin Levels
Authors	Jamie George, Pharm.D. Candidate; Pramodini B. Kale-Pradhan, Pharm.D; and Leonard B. Johnson, MD
Abstract	<p>Background: Procalcitonin (PCT) is a biomarker that is used to direct continued use of antibiotic therapy in patients with sepsis and community acquired pneumonia. There is a lack of data on patients with a positive PCT who do not receive continued antibiotics. We compared outcomes in patients with positive PCT levels who received antibiotics <24 hours to those who received >24 hours.</p> <p>Methods: A single-center, retrospective study to compare outcomes of adult patients with positive PCT (> 0.25 µg/L) levels based on antibiotic duration. A report of hospitalized patients from January to June 2018 was generated and screened for inclusion criteria. Demographics, microbiologic data, Charlson Weighted Index of Comorbidity (CWIC), ICU admission, length of stay (LOS), and discharge disposition data was collected. Continuous and categorical variables were analyzed using student's t-test and chi-square, respectively.</p> <p>Results: 454 of 998 patients met the inclusion criteria. 123 patients received <24 hours of antibiotics, and 331 patients received > 24 hours. ICU admissions and LOS were not found to be different between the groups (p = 0.442 and 0.076, respectively). The mortality rate was 25.2% in those that received antibiotics for <24 hours compared to 11.8% in the group that received antibiotics for >24 hours (p = <0.001). Antibiotics <24 hours Antibiotics >24 hours p-value (n = 123) (n = 331) Mean Age 64.6 +/- 14.9 65.5 +/- 16.9 0.607 Males (%) 56.1 50.5 0.285 Mean CWIC +/- SD 1.71 +/- 1.16 1.69 +/- 1.22 0.875 Mean PCT +/- SD 5.11 +/- 20.2 11.7 +/- 35.6 0.053 Positive Cultures (n) Blood 7 (5.6%) 53 (16.0%) 0.004* Urine 5 (4.1%) 40 (12.1%) 0.011* Sputum 3 (2.4%) 20 (6.0%) 0.120 Sterile site 0 (0%) 6 (1.8%) 0.438 Other sites 2 (1.6%) 14 (4.2%) 0.181 ICU Admission (%) 34.1 38.1 0.442 LOS (Days) 5.6 7.9 0.076 Discharge Disposition (%) In-Hospital Mortality 25.2 11.8 < 0.001* Home 44.7 50.2 0.303 ECF 12.2 26.3 0.001* Transfer 3.3 1.5 0.237 Hospice 3.3 1.8 0.353 AMA 4.1 0.3 0.002* Rehabilitation 7.3 8.2 0.768 * p-value significant</p> <p>Conclusion: ICU admission and hospital LOS did not differ; however, mortality was significantly higher in those that did not receive continued antibiotics. Further studies need to be performed to confirm this finding.</p>

ABSTRACT NO. 80	
Name	Ali Khalil
Category	Pharmacy Practice
Title	Amiodarone-Induced Cirrhosis: A Well-Known Entity, But Yet Underappreciated and Under-recognized Complication.
Authors	Ali Khalil, BS; Farzad Daneshvar, PharmD, BCPS
Abstract	<p>We present an overlooked, rare and fatal case of amiodarone-induced cirrhosis (AIC). A 77-year-old male with a history of heart failure with preserved ejection fraction, atrial fibrillation status post ablation, on warfarin and amiodarone 200 mg daily since 2015, presented with a two-month history of progressive abdominal pain, predominantly right upper quadrant (RUQ) and fatigue. He was routinely seen by his healthcare providers. One week prior to admission, amiodarone was discontinued due to transaminase AST 186U/L and ALT 125 U/L, an increase from one year ago AST 82 U/L, ALT 112 U/L. Of note, his LFTs in 2015 were normal. He denied alcohol abuse or liver disease. On presentation, vital signs were normal. On exam, he had abdominal ascites and diffused tenderness, especially in the RUQ, with no rebound or guarding. Initial blood work showed a leukocytosis, mild macrocytic anemia, hypoalbuminemia, elevated total bilirubin 1.9 mg/dL, elevated alkaline phosphatase 258 U/L and transaminase with AST 203U/L and ALT 133U/L. Further blood work showed, an INR of 5.1, prolonged PT/PTT in the setting of warfarin. In the ER, an abdominal ultrasound revealed acute cholecystitis, ascites, and cirrhosis. The patient received vitamin K and Fresh Frozen Plasma (FFP). Afterwards, he underwent a laparoscopic cholecystectomy, liver needle biopsies and paracentesis. A hepatitis panel was negative. Liver biopsy showed ballooned hepatocytes and Mallory-Denk bodies with very minimal macrovesicular steatosis, a known pattern of amiodarone toxicity, confirming our diagnosis of amiodarone-induced cirrhosis (AIC). His AST/ALT continued to worsen. Concerned for a possible biloma, an Endoscopic Retrograde Cholangio-Pancreatography (ERCP) was scheduled. However, the patient deteriorated, developing oliguric renal failure requiring Continuous Renal Replacement Therapy (CRRT), septic shock secondary to klebsiella pneumonia, which ultimately lead to his death. AIC is a rare and fatal complication with an incidence of ~1%/annually. Once AIC develops, the clinical prognosis is very poor with a 5-months mortality rate of 60%. Amiodarone toxicity is attributed to its high lipophilic composition accumulating in lipid-laden organelles resulting in a large volume of distribution combined with a long half-life (mean 52 days). Current recommendation includes, baseline LFTs to rule out any pre-existing hepatic impairment, repeat LFTs every 6 months, and discontinuation of amiodarone if persistent elevation of AST/ALT are two times the upper limit of normal. However, amiodarone toxicity often causes asymptomatic liver injury, thus LFTs are often unattended and unchecked by clinicians. Interestingly, a literature search revealed only 35% of clinicians adhere to these recommendations. Although rare, AIC has a high mortality rate, but it is preventable; thus requiring a high clinical suspicion and increase awareness by monitoring LFTs every 6 months and prompt discontinuation with persistent elevation of LFTs.</p>

ABSTRACT NO. 81	
Name	Abadalhamid Lagnf
Category	Pharmacy Practice
Title	Predictors of Vancomycin Switch or Escalation in Patients with Methicillin-Resistant Staphylococcus aureus Bloodstream Infection
Authors	Abdalhamid M. Lagnf, M.B.Ch.B., MPH; Sarah Jorgensen, PharmD, BCPS, AAHIVP; Evan J. Zasowski, PharmD, MPH; Trang D. Trinh, PharmD, MPH; Sail Bhatia, B.S., MPH; Susan L Davis, PharmD; Michael J. Rybak, PharmD, MPH, PhD
Abstract	<p>Background: Vancomycin (VAN) is the primary agent for the treatment methicillin-resistant Staphylococcus aureus (MRSA) bloodstream infections (BSI). VAN is frequently combined with or switched to a second anti-MRSA agent for the treatment of serious BSI because VAN monotherapy has been linked to treatment failures. We aimed to determine the potential risk factors for patients with MRSA BSI who switched or had therapy escalated.</p> <p>Methods: This was a multicenter, retrospective cohort study of adults (≥ 18 years) initially treated with VAN (>24 hours) for MRSA BSI between 2006 and 2018. Patients with a respiratory source were excluded. Baseline clinical and infection characteristics were compared between patients who received VAN as the sole anti-MRSA agent and continued on VAN until discharge and patients who switched or had a second anti-MRSA agent added during their admission (switch/escalate group). Multivariable logistic regression was performed to identify independent predictors of therapy switch or escalation.</p> <p>Results: A total of 195 patients were included (66 VAN and 129 switch/escalate). The mean (SD) age of the study population was 56 (15.5) years, 68.2% were male, and 81.0% were African-American. Most (80%) of patient had community-onset BSI. The median (IQR) Charlson Comorbidity index and Acute Physiology and Chronic Health Evaluation (APACHE) II scores were 3 (1-5) and 14 (8-20), respectively. The major sources of BSI were skin/soft tissue (24.6%), infective endocarditis (24.1%), and bone/joint (23.1%). Median (IQR) time to switch/escalation was 67 (44- 97) hours. In multivariable logistic regression analysis, infective endocarditis (aOR 6.2, 95% CI 2.2-16), hospitalization in the past 90 days (aOR 2.0, 95% CI 1.0-4.0), and APACHE II (aOR 1.07, 95% CI 1.01-1.12) were independently associated with switch/escalation.</p> <p>Conclusion: We have identified a number of baseline clinical and infection characteristics that should be taken into account for clinicians to predict the likelihood of switch or escalation in vancomycin treated patients with MRSA BSI. Further studies evaluating the impact of up front alternative therapies in these higher risk patients are needed.</p>

ABSTRACT NO. 82	
Name	Samantha Langell
Category	Pharmacy Practice
Title	Study Design Considerations for Evaluating Point-of-Care Testing in Community Pharmacies
Authors	Samantha M. Langell; Dr. Paul E. Kilgore M.D. M.P.H.; Dr. Joseph P. Fava PharmD; Abdulbaset Salim, MBChB, MPH
Abstract	<p>Background: In the United States, pharmacists are often the first healthcare provider that patients turn to even before visiting their primary care physician or emergency department. Over the past few years, community pharmacists are offering an increasing array of services including medication therapy management and immunizations. This places pharmacists in a unique position to offer additional services such as point-of-care testing (POCT). The use of POCT in community pharmacies represents a practical approach that brings diagnostic testing closer to the patient where testing is most urgently needed. Rationale In urban settings such as those in Detroit, patients have limited access to healthcare facilities and diagnostic testing for acute and chronic disease states. Such limited access may delay diagnosis and treatment of common health conditions. At the same time, there are few studies that have evaluated the practical implementation and effectiveness of POCT in communities.</p> <p>Objectives: The overarching goal of our research is to improve the timeliness of diagnostic testing and help improve access to appropriate drug therapy for individuals that suffer from common medical conditions found among urban community residents such as those living in Detroit, Michigan. As a first step to introducing and evaluating POCTs, we considered study design methods that would provide high-quality evidence of POCT utility in urban settings.</p> <p>Approach: Mixed methods research designs provide an efficient strategy to gather both qualitative and quantitative data in a study population. Convergent, explanatory sequential and exploratory sequential designs offer unique approaches for community-based studies. In this study, we will focus our research activities among urban community pharmacies. The first phase of our project will conduct a knowledge, attitudes and practices (KAP) survey to understand how best to implement POCTs among a sample of community pharmacies located in Metropolitan Detroit. Pharmacists will be provided with an unboxing video that demonstrates use of POCTs. Prior to and after viewing the video, pharmacists will complete a KAP survey. This data will be analyzed to help us understand the KAPs related to point-of-care tests of community pharmacists. In addition, we will also gather data about the helpfulness of the video to see if the video was the proper platform to inform community pharmacists about point-of-care testing. Results of the KAP survey will be used to inform the community pharmacy-based trial of POCTs. In the second phase of this project, we will conduct a quantitative evaluation of POCTs used in a representative sample of pharmacies from three groups: large chain (e.g., Meijer), small chains (e.g. SavMor) and independent pharmacies. In the second phase, data will be collected to evaluate number and types of POCT utilized, time to test result, timeliness of reporting results to healthcare providers and sustainability of test offering by community pharmacists. Additional data will be collected to evaluate the economic viability of offering new POCT services at the community pharmacy level in Metropolitan Detroit.</p>

ABSTRACT NO. 83	
Name	Mona Mawari
Category	Pharmacy Practice
Title	Improved Adherence to a Controlled Substance Agreement Policy: An Interprofessional Approach
Authors	Mona Mawari, Mohamad El Abdallah MD, Ruaa Elteriefi MD, Insaf Mohammad, PharmD
Abstract	<p>Introduction: Overuse of controlled substances has created a public health crisis that requires efforts to prevent misuse, abuse, diversion, and death. Although guidelines recommend measures such as controlled substance agreements (CSAs) to attenuate risks, adherence to these practices remains inadequately evaluated. Furthermore, best practices to promote use of and adherence to CSAs are undefined.</p> <p>Research Question or Hypothesis: Can an interprofessional team-based approach to quality improvement (QI) impact adherence to a CSA policy in a resident-run internal medicine clinic with a newly embedded clinic pharmacist?</p> <p>Study Design: Quasi-experimental pre-post study Methods: In January 2018, interprofessional QI initiatives were implemented to improve adherence to the clinic CSA policy. The clinic pharmacist identified patients meeting policy criteria and educated medical residents, providers, and staff to ensure CSAs were discussed and signed during patient visits. We evaluated the following parameters pre- and post- implementation of the interventions: The percentage of patients on long-term controlled substances (>3 continuous months or recurrent use >6 months) with (a) signed CSA in the electronic medical record, (b) ICD-10 code utilization noting "controlled substance agreement signed" (not required by the policy, but a parameter used to track signed CSAs), and (c) completed urine drug screens (UDS). We also evaluated clinic visits every 3 months since the CSA policy was introduced in April 2017. MedCalc® was used for statistical analysis. Results: A total of 127 patients were included in this analysis. Prior to QI initiatives, 12% of eligible patients had a CSA signed, which increased to 83% post-QI (OR 36, 95% CI 18-72, p<0.0001 versus preintervention). ICD-10 code utilization increased from 2% pre-QI vs. 80% post-QI (OR 169, 95% CI 50-574, p<0.0001 versus pre-intervention). Completed UDS increased from 14% pre- QI to 64% post-QI (OR 11, 95% CI 6-20, p<0.0001 versus pre-intervention). Since implementation of the CSA policy, 64% of patients attended a clinic visit every 3 months. Conclusion: This study showed improved adherence to the clinic CSA policy, demonstrating the benefit of an interprofessional team-based approach with a clinic pharmacist.</p>

ABSTRACT NO. 84	
Name	Christopher Miller
Category	Pharmacy Practice
Title	Distinct, segregated daptomycin-susceptible and daptomycin-resistant Staphylococcus aureus populations associated with tricuspid-valve infective endocarditis
Authors	Christopher Miller, BS Andrew Berti, PharmD, PhD Somrita Dey, PhD Paula Smolenski, MS Pushkar Kulkarni, MS
Abstract	<p>Patient Case: A 46 year old female with a history of IV drug abuse presented July 2018 at a Detroit-area hospital with MRSA (methicillin-resistant Staphylococcus aureus) bacteremia susceptible to both vancomycin and daptomycin. Tricuspid valve infective endocarditis was diagnosed by transesophageal echocardiogram. The patient initially refused valve replacement surgery and was managed medically with vancomycin for 6 days before deciding to leave against medical advice. Prior to leaving, blood cultures had cleared and the patient was switched to daptomycin as an outpatient treatment for her bacteremia. The patient was readmitted to hospital in August 2018 claiming she was now ready for heart valve surgery. Blood cultures on readmission were positive for MRSA, again susceptible to both vancomycin and daptomycin. Intra-operative cultures were taken from each leaflet of the removed tricuspid valve. One leaflet was sterile, the second leaflet contained daptomycin-susceptible S. aureus, and the last leaflet contained S. aureus cultures that were daptomycin-resistant (MIC=4). Background: Daptomycin resistance, although rare, is often associated with the presence of sequestered infection including osteomyelitis or infective endocarditis. Anatomical site susceptibilities are not routinely performed and the susceptibility of blood cultures is used as a surrogate. Development of two bacterial populations with different susceptibilities at a single anatomical site is not necessarily surprising; however, the exclusive recovery of only daptomycin-resistant populations from one leaflet and exclusive recovery of only daptomycin-susceptible populations from another leaflet of the same valve is surprising and to our knowledge has not been reported elsewhere.</p> <p>Methods: Both isolates have been submitted for comparative whole genome sequencing. The presence of heterogeneous daptomycin-resistant subpopulations was assessed by dilution plating and population analysis profiling.</p> <p>Results: The daptomycin-susceptible isolate does not demonstrate heteroresistance while the daptomycin-resistant population is uniformly daptomycin resistant. Additional analyses are ongoing.</p> <p>Conclusion: This patient case represents a unique opportunity to observe evolution of antibiotic resistance at a single anatomical site. Ongoing studies will examine (i.) the comparative fitness of the two isolates via co-culture modeling with and without antibiotics and (ii.) comparative genomics to identify the genetic mediators of the resistance phenotype. These studies will identify features of distinct bacterial populations that can promote differing patterns of ecological succession during infection at a sequestered anatomical site.</p>

ABSTRACT NO. 85	
Name	Namitha Nair
Category	Pharmacy Practice
Title	Evaluation of clinical outcomes in ST-segment elevation myocardial infarction (STEMI) patients on ticagrelor.
Authors	Namitha Nair, B.S, PharmD Candidate 2019; Christine Jiang, PharmD; Long To, PharmD, BCPS; Jona Lekura, PharmD, BCPS; Michael Hudson, MD; Akshay Khandelwal, MD; Henry Kim, MD.
Abstract	<p>Purpose: Positive clinical outcomes of STEMI patients depends on continuing dual antiplatelet therapy post-discharge. Our institution has recently replaced clopidogrel with ticagrelor as the P2Y12 inhibitor of choice for STEMI patients prior to percutaneous coronary intervention. However, ticagrelor may be discontinued or switched to another antiplatelet agent post-PCI due to variability in third-party coverage or adverse effects. This study aims to evaluate the appropriateness of transitioning from ticagrelor to prasugrel or clopidogrel during the patient's index hospitalization, as well as the outcomes related to antiplatelet switch up to 12 months following index discharge.</p> <p>Methods: The project was designed as a retrospective medication use evaluation of STEMI patients that received ticagrelor. Patients included in the study had to meet the following criteria: age > 18 years who presented with STEMI and received a loading dose of ticagrelor and were continued on dual antiplatelet therapy (DAPT) post index discharge between January 1, 2016, and December 31, 2017. Patients that were lost to follow up before 30 days post index discharge and non- Henry Ford patients were excluded from the study. The outcomes of interest include appropriateness of dosage and timing of antiplatelet transition during index hospitalization, bleeding events, stent thrombosis, and readmission data for 12 months post-STEMI. Data was analyzed using measures of central tendency. Normally distributed data was analyzed using mean plus or minus standard deviation. The non-normally distributed data was analyzed using the median (interquartile range).</p> <p>Results: Data analysis is currently in progress and final results will be presented at Wayne State research day.</p> <p>Conclusions: Data analysis is currently in progress and conclusion will be presented at Wayne State research day.</p>

ABSTRACT NO. 86	
Name	Nicholas Peters
Category	Pharmacy Practice
Title	What effect does student attendance in class have on course performance?
Authors	Nicholas Peters, B. S.; Zachary Mueller, B. S.; Ryan Caputo, B. S.; Saif Findakly, MPH; Sheila Wilhelm, PharmD, FCCP, BCPS
Abstract	<p>Introduction: In the fall 2017 semester, a Wayne State University Doctor of Pharmacy Program curricular decision to require second-year Pharm.D. Student (P2) attendance in all class sessions was made. In the winter 2018 semester, it was determined that an assessment of the effects of P2 student attendance in all class sessions on performance should be undertaken. To that end, course coordinators in the winter 2018 P2 courses lifted the mandatory attendance requirement to allow for this assessment to occur.</p> <p>Objective: To determine whether class attendance correlates with student performance as assessed by course grades in the winter P2 courses and grade point average (GPA).</p> <p>Methods: Students enrolled in the P2 class during the winter 2018 semester devised an online spreadsheet system for collecting student attendance data. Following course coordinators' submission of course grades and the completion of any grade appeals, P2 student grades from each course, GPA reports, and attendance data was compiled and de-identified. Descriptive statistics and evaluations for correlation were completed to evaluate the relationship between attendance and performance.</p> <p>Results: Attendance and performance data were gathered and deidentified for 99 P2 students for 60 class sessions during the winter 2018 semester. Team-Based Learning, Pharmacotherapeutic Problems Solving, and Patient Care Laboratory class sessions which have required attendance were not collected. Average attendance during the 60 class sessions was 66.8% (range, 13.3%-100%). Overall attendance had a weak correlation with both semester GPA ($r=0.089$, $p=0.38$) and overall GPA ($r=0.188$, $p=0.064$). Attendance and final grades in courses were weakly to moderately correlated, with one course's correlation, Applied Pharmacokinetics and Pharmacogenomics, reaching statistical significance.</p> <p>Correlation R p-value Cumulative GPA vs % attendance overall 0.186862 0.064 Semester GPA vs % attendance overall 0.08869 0.382 Infectious Disease (ID) Module Grade vs Module attendance 0.031008 0.76 Neurology, Psychology Module Grade vs Module Attendance 0.002125 0.98 Medication Use Process – Pharmacist Responsibility (SAS) grade vs SAS attendance 0.134441 0.184 Applied Pharmacokinetics and Pharmacogenomics grade vs course attendance 0.358162 0.0003</p> <p>Conclusion: Overall, the correlation between individual course attendance and individual course grade showed a weak to moderate positive correlation across the four courses. This finding suggests that class attendance is not a strong indicator of student performance within the P2 winter curriculum. Further research is planned to capture factors that may affect student motivation to attend class and additional student factors that may affect performance.</p>

ABSTRACT NO. 87	
Name	Craig Peters
Category	Pharmacy Practice
Title	Association between heart rate and resting-state neural connectivity in children and adolescents
Authors	Hilary A. Marusak; Craig A. Peters; Shelley Paulisin; Aneesh Hehr; Patrick Mueller; Christine A. Rabinak
Abstract	<p>Background: Emerging data show a widespread network of cortical and subcortical regions involved in the regulation of cardiovascular (CV) functioning, including the insula and amygdala. Altered functioning in these brain areas is reported in several common mental disorders (e.g., depression, posttraumatic stress disorder), which are also hallmarked by CV dysfunction (e.g., changes in heart rate [HR]). These brain regions undergo dramatic changes throughout brain development, which may underlie age-related changes in CV regulation. However, links between CV regulation and neural connectivity have not been examined in a pediatric sample.</p> <p>Objective: To identify a brain signature (i.e., patterns of connectivity between brain regions) of CV regulation in children and adolescents. Methods: 37 children and adolescents (ages 6-17) completed a 10-minute eyes-closed resting-state scan. Average HR was recorded during the scan, using a pulse-oximeter attached to the fourth digit of the non-dominant hand. Average HR was compared with resting-state connectivity of the insula and the amygdala with the rest of the brain. The insula and amygdala were selected as seed regions given that prior meta-analyses have shown these to be critical regions for CV regulation in adults.</p> <p>Results: Consistent with previous studies, HR was faster in younger compared to older youth. Faster HR was associated with higher connectivity between the amygdala and dorsal anterior cingulate cortex (dACC), lower connectivity between the amygdala and caudate, and lower connectivity between the insula and brainstem.</p> <p>Conclusion: To our knowledge, this is the first study to examine the neural correlates of CV regulation in a pediatric sample. Given that the dACC is implicated in the brain's generalized response during CV arousal, increased connectivity between the dACC and the amygdala, a region critical for emotional arousal, in youth with faster HR suggests that amygdala-dACC connectivity may reflect heightened arousal. Faster HR was also associated with lower amygdala-caudate functional connectivity, which may reflect poorer integration between limbic and motor systems during heightened arousal. Lower insula-brainstem connectivity in youth with faster heart rate may reflect lower top-down insula control on CV functioning. The insula has baroreceptors and the brainstem is a key relay station for CV functioning, with direct reciprocal linkages with the insula. Taken together, these data implicate both subcortical and cortical areas in CV regulation in children and adolescents.</p>

ABSTRACT NO. 88	
Name	Pia-Allison Roa
Category	Pharmacy Practice
Title	Assessing DISCharge patients with chronic ObstructiVe pulmonary disease with pharmacy Education protocol to Reduce readmission (The Discover Trial) – Interim Analysis
Authors	Pia-Allison Roa, Pharmacy Student; Melanie Dalton, MD; Daniel Ouellette, MD; Amber Lanae Martirosov, PharmD, BCPS, BCACP
Abstract	<p>Background: Chronic obstructive pulmonary disease (COPD) is a chronic lung disease that results in breathing complications that affect more than 16 million people in the United States. COPD is the third leading cause of death in the United States and the yearly cost for treatment is estimated to be 32 billion dollars. This number is projected to continue to rise and reach 49 billion dollars by 2020. This mounting economic burden is largely in part due to the staggering number of preventable acute COPD exacerbations which lead to costly emergency department visits and hospitalizations. Approximately 10-20% of these patients will also be readmitted within 30 days of discharge. COPD treatment involves the use of inhalers that patients often use multiple times per day. Furthermore, each inhaler has precise techniques that are vital for obtaining optimal efficacy. Selection of proper inhaler devices that are therapeutically indicated and that patients are able to use correctly is crucial for patient management that reduces exacerbations and emergency room visits. Current standard of care protocols lack optimization of patient-specific therapy upon discharge in the inpatient setting as well as effective transition for outpatient care for exacerbation prevention. Current evidence also shows that patients who receive education concerning appropriate inhaled therapy technique have improved efficacy and compliance. Pharmacists are knowledgeable in the therapeutic treatment choices for COPD as well as educated in assessing and educating patients on inhaler technique, making them ideal to lead the optimization of patient-specific therapy. The objective of this study is to assess the effect of inpatient inhaler assessment and education provided by pharmacist to patients admitted for acute exacerbation of chronic obstructive pulmonary disease on 30-day readmission rates.</p> <p>Methods: This was a quasi-experimental cohort study conducted at Henry Ford Hospital (HFH), an 802-bed tertiary care facility located in downtown Detroit, MI. The study was approved by the HFH Institutional Review Board. Patients were included in the study if they were admitted to the F2 floor with a primary diagnosis and treatment of acute exacerbation of COPD at HFH and discharged with inhaled therapy starting in May 2018. Patients were excluded from data analysis if they did not have a primary diagnosis of acute exacerbation of COPD or they were not being discharged on inhaled therapy. The specific aims were: (1) determine the role of a pharmacist in identifying inhaler device at discharge (2) determine the impact of the new multidisciplinary bundle on 30-day readmissions, outpatient exacerbations and symptom control; and (3) determine the frequency and timeliness of outpatient follow-up visits. The primary outcome is pharmacist recommendation at discharge and acceptance of recommendation. Secondary outcomes include patient inhaler technique prior to discharge, barriers to optimizing inhaled medications, and patient outcomes following pharmacist intervention. Descriptive statistics will be used to summarize outcomes. Continuous data will be analyzed using Mann-Whitney U-tests or T-test. Categorical data will be analyzed using Chi-square test or Fischer's exact test. Multivariable analysis will be used as appropriate.</p> <p>Results/Conclusion: Data collection and analysis are ongoing. An interim analysis will be presented at the WSU Research Day.</p>

ABSTRACT NO. 89	
Name	Richa Shah
Category	Pharmacy Practice
Title	Adverse effects of dexmedetomidine in liver dysfunction: a medication use evaluation
Authors	Richa Shah; Zachary Smith, PharmD; Michael Peters, RPh
Abstract	<p>Background: Dexmedetomidine (DEX) is a sedative used for continuous sedation in critically ill patients that has analgesic effects with minimal effects on respiratory drive. DEX is predominantly hepatically metabolized. Dose reductions are recommended in patients with hepatic impairment, but no formal recommendations exist. Common adverse effects of DEX include hypotension and bradycardia. It is unknown if liver dysfunction increases the risk of these adverse effects. The purpose of this study is to assess the prevalence of cardiovascular adverse effects of DEX in patients with liver dysfunction in the intensive care unit (ICU).</p> <p>Methods: This was a retrospective chart review of patients receiving DEX in the medical ICU at a large, academic medical center admitted between January 1st, 2015 and June 30th, 2018. Patients 18 years or older receiving a continuous infusion of DEX were included if they had acute or chronic liver dysfunction. Acute liver dysfunction was defined as AST/ALT greater than 10 times the upper limits of normal and chronic liver dysfunction was defined as MELD score greater than 11. Patients were excluded if they were on vasopressors prior to DEX. The primary endpoint was the prevalence of hypotension and/or bradycardia. Hypotension was defined as MAP less than 60 or less than 55 mmHg if the baseline MAP was greater than 65 or less than 65 mmHg, respectively. Bradycardia was defined as heart rate less than 50 beats per minute. Secondary endpoints included initial, minimum, and maximum DEX doses before and after each adverse drug event as well as escalations of care as a result of the event. Adverse events were analyzed using the Naranjo Adverse Drug Reaction Probability Scale. Categorical variables were presented as proportion n (%); continuous variables were reported as mean (range) or median (IQR) as appropriate.</p> <p>Results: N/A</p> <p>Conclusion: N/A</p>

ABSTRACT NO. 90	
Name	Noor Shammout
Category	Pharmacy Practice
Title	Relationship Between Metformin Induced Vitamin B12 Deficiency and Comorbid Peripheral Neuropathy and/or Anemia
Authors	Noor Shammout; Amar Patel; Laila Shammout; Amber Lanae Martirosov, PharmD, BCPS, BCACP; and Nada Farhat, PharmD, BCPS, BCACP
Abstract	<p>Background: Metformin is currently the cornerstone of treatment for patients with type 2 diabetes mellitus (T2DM). Long-term metformin therapy has been linked to a decrease in vitamin B12 levels. However, controversy exists regarding this effect and its impact on the development of the other comorbid conditions. B12 deficiency causes neuronal damage through axon demyelination, degeneration, and death.(1) Thus, vitamin B12 deficiency can cause a clinical presentation of neuropathy. Clinically, this neuropathy is indiscernible from T2DM and may be misinterpreted as diabetic peripheral neuropathy.(1) Vitamin B12 is an important micronutrient required in DNA synthesis, cellular repair and the formation of blood cellular components.(2)Vitamin B12 deficiency can lead to hematological consequences such as anemia.(2) The purpose of this study is to assess if metformin-induced vitamin B12 deficiency is associated with peripheral neuropathy (PN) and/or anemia.</p> <p>Methods: This retrospective cohort analysis investigated the relationship between metformin induced vitamin B12 deficiency and peripheral neuropathy and anemia in patients treated at Henry Ford Health System (HFHS) between January 2013 and June 2018. Patients were included if they were > 18 years old, had a formal diagnosis of T2DM and were currently taking Metformin for > 6 months. Patients were excluded if they met a diagnosis of alcoholism, had pancreatic insufficiency, malabsorption syndromes, chronic giardiasis, HIV infection, surgery involving the small intestine, had an estimated Glomerular Filtration Rate (e-GFR) < 30 mL/min/ 1.73 m² based on Cockcroft-Gault formula, underwent a gastrectomy/gastric bypass surgery and had co-morbid disease states that indicate short life expectancy (Cancer, ESRD/dialysis, chronic liver disease, hospice, etc.). The study objectives were to: (1) Quantify the number of patients with diabetes on long-term metformin therapy who develop peripheral neuropathy or anemia (2) determine if there is a correlation between low vitamin B12 levels and the development of PN or anemia in patients with diabetes on long-term metformin therapy and (3) identify areas for improvement in the management of patients with diabetes on long-term metformin therapy. Patients were stratified based on whether they were diagnosed with PN or anemia, and then additional data was collected in relation to vitamin B12 levels and potential B12 supplementation. The HFHS Institutional Review Board approved this study. Data was collected using the Henry Ford electronic medical records (Epic and CPNG) along with a standardized data collection form. Each patient's first metformin prescription (Rx) date was collected first. Relevant labs and medications within a year of the first metformin Rx were then collected. The B12 level collected was the first level available after the first metformin Rx date. Descriptive statistics will be used to summarize outcomes.</p> <p>Results/Conclusion: Data collection and analysis ongoing. Results will be presented at the Wayne State Research Day.</p>

ABSTRACT NO. 91	
Name	Zied Shammout
Category	Pharmacy Practice
Title	Infective Endocarditis Outcomes in Immunosuppressed vs. Non-immunosuppressed patients
Authors	Zied Shammout
Abstract	<p>Background: MRSA infective endocarditis is associated with increased morbidity and mortality. Due to medical advances, many once fatal diseases can be managed as chronic conditions. However, immunosuppressed patients with multidrug resistant infections are vulnerable to a poor prognosis. Several studies have compared outcomes in endocarditis patients with single or varying forms of immunosuppression. We sought to evaluate the epidemiology and outcomes of MRSA IE in immunosuppressed compared to non- immunosuppressed patients at the Detroit Medical Center.</p> <p>Methods: This was a retrospective, observational cohort study of adult patients diagnosed with MRSA IE between 2008 and 2018 at the Detroit Medical Center. The inclusion criteria were age \geq 18 years, at least one positive MRSA blood culture, and definite or possible IE according to the modified DUKE criteria. In this study, immunosuppression was defined as having one or more of the following: neutropenia, AIDS, splenectomy, solid organ or bone marrow transplant in preceding 90 days, cytotoxic chemotherapy in preceding 90 days, or high-dose corticosteroids. The primary outcome was composite treatment failure defined as persistent bacteremia (\geq 7 days), 30-day mortality, and 60-day infection recurrence. Secondary outcomes included individual components of the composite outcome. Nominal variables were compared between treatment groups using the Chi-square test and Fisher’s exact test. Ordinal and continuous variables were compared using the Mann-Whitney-U test and student’s t-test as appropriate. Multivariable logistic regression was conducted in order to determine the independent impact of immunosuppression after controlling for confounding variables. Results: There were 179 patients included in this study (immunosuppressed IE=51; non-immunosuppressed IE= 128). Notable differences in baseline characteristics included history of MRSA infection within 1 year of index blood culture (immunocompromised 5.9% vs. non-immunosuppressed 20.3%; $P<0.023$); acute kidney injury (immunosuppressed 19.6% vs. non-immunosuppressed 39.1%; $P<0.013$); IV drug use (immunosuppressed 27.5% vs. non-immunosuppressed 43.8%; $P<0.044$); myocardial infarction immunosuppressed 13.7% vs. non-immunosuppressed 3.9%; $P<0.006$); cerebrovascular disease immunosuppressed 27.5% vs. non-immunosuppressed 9.4%; $P<0.002$); pulmonary septic emboli immunosuppressed 17.6% vs. non-immunosuppressed 35.2%; $P<0.021$); age, mean (immunosuppressed 59.67 vs 53.74; $P<0.021$).</p> <p>The outcomes of the study are presented below: Immunocompromised N=51 Non-immunocompromised N=128 P-value Composite treatment failure 26 (51.0%) 60 (46.9%) 0.624 BSI duration \geq 7 days, n (%) 16 (31.4%) 42 (33.6%) 0.775 30-day mortality, n (%) 9 (17.6%) 21 (16.4%) 0.841 60-day recurrence of MRSA BSI, n (%) 4 (7.8%) 15 (12%) 0.420 In multivariate analysis, African American race (aOR 2.457, 95% CI 1.052-5.736) and the APACHE II Score (aOR 1.042, 95% CI 1.007-1.078) were independently associated with treatment failure. Immunosuppression was not independently associated with treatment failure (aOR 1.125, 95% CI 0.557- 2.272).</p> <p>Conclusion: Immunosuppression was not found to be an independent predictor of treatment failure in this study. The high failure rates regardless of immune status underscore the need for improved treatment strategies.</p>

ABSTRACT NO. 92	
Name	Limi Sharif
Category	Pharmacy Practice
Title	Anxiogenic Effects of Acute THC Exposure on Fear Extinction
Authors	Limi Sharif; Craig Peters, B.S.; Hilary, Marusak, Ph.D.; Christine Rabinak, Ph.D.
Abstract	<p>Background: Posttraumatic stress disorder (PTSD) is characterized by an inability to suppress inappropriate fear responses. Patients with PTSD report using cannabis to alleviate these negative affective responses. However, Δ9-tetrahydrocannabinol (THC), the psychoactive ingredient in cannabis, can either be anxiolytic or anxiogenic potentially limiting the therapeutic potential of cannabis for treating anxiety and fear-based disorders. In this study, we investigated whether an acute dose of THC effect self-reported state anxiety in traumaexposed individuals with and without PTSD during a task of fear inhibition.</p> <p>Methods: We conducted a randomized, double-blind, between-subjects design to compare drug (i.e., THC vs. Placebo) and group (PTSD vs. control) effects on inhibition of conditioned fear responses in adults. Volunteers were randomly assigned to THC (7.5 mg, n = 31) or placebo (PBO, n = 33) groups and both were administered prior to extinction learning. Participants subsequently completed a fear conditioning-extinction task and reported their level of anxiety using a Subjective Units of Distress Scale (SUDS; scale from 0-100, where 0 = no anxiety and 100 = worst anxiety experienced) at three time points during the task.</p> <p>Results: During a recall test for extinction learning, individuals with PTSD self-reported significantly higher anxiety than control participants (Mean SUDS\pmSD: PTSD = 18.8\pm21.6; Control = 11.5\pm 17.8 ; p <0.05). Across all time points, THC significantly increased self-reported anxiety ratings compared to PBO (Mean SUDS\pmSD: THC = 30.5\pm20.7; PBO = 21.0\pm 19.8 ; p < 0.05) during extinction learning. However, there was no significant group-by-drug interaction at any of the time points during the task.</p> <p>Conclusions: These results indicate that acute THC exposure is associated with increased anxiety during extinction learning which suggests that THC may have anxiogenic effects in the acute phase, irrespective of PTSD symptoms. Together, these findings provide new evidence on the effects of acute THC on state anxiety levels during fear conditioning in individuals with PTSD and provide further insights into the limiting effects of acute cannabis exposure on potential anxiety and fear-based disorder therapies</p>

ABSTRACT NO. 93	
Name	Andrew Stone
Category	Pharmacy Practice
Title	Weighing the effect: Time and safety impact of gravimetric technology on an ambulatory oncology compounding workflow
Authors	Andrew Stone, PharmD Candidate 2019; Amanda Sirisaengtaksin, PharmD; Brooke Hoff, PharmD; Theresa Mazurek, RPh; Angela Michael, PharmD, BCOP
Abstract	<p>Purpose: Chemotherapy agents are widely known as narrow therapeutic index drugs, requiring precision in compounding to ensure the best balance between safety and efficacy. Gravimetric technology is a newer process that can be implemented into intravenous (IV) compounding preparation workflows to assist with accuracy in the compounding process. However, there is limited data on the impact of the implementation of this technology. The purpose of this study was to describe the impact of implementation of gravimetric technology on the workflow of ambulatory care oncology IV compound preparation.</p> <p>Methods: This study was a retrospective, descriptive analysis of the impact of implementation of gravimetric technology on an ambulatory care oncology IV compounding workflow. Preparations compounded using gravimetric technology, post-implementation in July 2016, from August 1, 2017 through October 31, 2017 were analyzed for safety and time impact. Safety was evaluated by number of errors and overall error rate. An error was defined as either variance of final product weight outside 5 percent, cancellation of preparation during compounding, or correction of the preparation during compounding. Time points were collected at the start of compounding, completion of compounding, and pharmacist verification of the compound, as recorded within the compounding technology. Time and safety data were stratified based on the difficulty of the preparation. Difficulty of each preparation was determined by need for drug reconstitution, number of vials needed for preparation, and volume of drug required. Descriptive statistics via measures of central tendency and variability were used to characterize the data.</p> <p>Results/Conclusions: Research in progress. To be presented at research forum.</p>

ABSTRACT NO. 94	
Name	Natkrita Turner
Category	Pharmacy Practice
Title	Evaluation of clozapine use in the outpatient behavioral health setting
Authors	My Tran, PharmD Candidate1; Natkrita Turner, PharmD Candidate1; Opal Bacon, PharmD, BCPS, BCPP1,2
Abstract	<p>Background: Approximately 30% of patient with schizophrenia are treatment-resistant, which is often defined as schizophrenia that has not responded to at least two antipsychotics at therapeutic doses for 6 or more weeks. Despite clozapine being the only FDA-approved treatment for treatment-resistant schizophrenia (TRS), it is likely under prescribed due to adverse drug effects and the need for frequent blood monitoring. The goal of this study was to examine antipsychotic prescribing patterns in a health system.</p> <p>Methods: The study design was a retrospective cohort of adult patients who visited a Henry Ford Health System behavioral health outpatient location and were prescribed clozapine or 2 or more antipsychotic medications between January 1st, 2015 and July 26th, 2018 . Data was collected from an electronic medical record and included: age, sex, comorbidities, smoking status, suicidality, the duration and dose of prescribed medications, medication monitoring, and psychiatric diagnosis.</p> <p>Results: There were 986 patients prescribed 2 or more antipsychotic medications during the study period. Of these, 330 were diagnosed with either schizophrenia or schizoaffective disorder. During the same time period 94 patients were prescribed clozapine. Of the 94 prescribed clozapine, 76 were diagnosed with either schizophrenia or schizoaffective disorder.</p> <p>Discussion: Many of the 986 patients who are on 2 or more antipsychotics likely qualify for treatment with clozapine. Clozapine is being under-utilized at this health-system and a pharmacist intervention to identify patients who are appropriate for clozapine therapy would be beneficial.</p>

ABSTRACT NO. 95	
Name	Mary Whitney
Category	Pharmacy Practice
Title	Impact of Second-Year Pharmacy Student Assessment of Calcium and Vitamin D Intake in Older Adults: A Retrospective Analysis
Authors	Mary Whitney, BS; Joseph Fava, PharmD; Mary Beth O'Connell, PharmD
Abstract	<p>Purpose: Calcium and vitamin D intake through the diet or supplements is a continuous issue for older adults which can lead to complications including osteoporosis and increased fracture risk. Many older adults live with a high Fracture Risk Assessment Tool (FRAX) score and do not take enough calcium and/or vitamin D. Simple assessments exist to quickly determine individual calcium and vitamin D intake as well as individualized fracture risk, and these assessments can be adequately performed by health professional trainees. It is crucial to identify potential gaps in knowledge for geriatric patients in order to empower these patients to reduce their risk for fractures and optimize dietary and supplemental intake of calcium and vitamin D. This study was designed to determine whether second-year student pharmacists could adequately assess FRAX scores as well as dietary and supplemental calcium and vitamin D intake in a representative sample of older adults residing in Detroit and the surrounding Metropolitan areas.</p> <p>Methods: This study implemented the skills of Wayne State University (WSU) second-year student pharmacists in an interprofessional team visit (IPTV) setting to assess FRAX scores and dietary and supplemental intake of calcium and vitamin D in older adults to then provide recommendations that were adjusted and approved by a licensed pharmacist and WSU faculty member. Survey data was obtained from older adults who participated in the WSU IPTV program in September and October 2017 and retrospectively reviewed. Data collected included patient demographics, pertinent medical history, and dietary and supplemental intake of calcium and vitamin D. Descriptive statistics were utilized to analyze the data. This study was approved by the WSU Institutional Review Board (IRB) under medical exemption (IRB #067918M1X).</p> <p>Results: A total of 97 patients were included in the analysis. The average age was 76.8 years (range: 64-94 years), and 81.4% of participants were female. We found that 51.5% of patients reported taking less than the recommended daily allowance (RDA) of calcium (from both diet and supplements) per the National Institutes of Health (NIH). In addition, 27.8% of patients reported taking less than the RDA of vitamin D. Interestingly, 54.6% were taking too much vitamin D based on assessment of their diet and supplementation. Regarding calcium intake, 64.3% of patients required adjustments recommended by the student through either changes in diet, supplementation, or both. 42.9% of patients required adjustments in their vitamin D intake as recommended by the student pharmacist. All recommendations were adjusted and/or deemed appropriate by the course coordinator prior to communication to the patient.</p> <p>Conclusion: In a sample population of older adults residing in an urban setting, we found that over half of these patients were not receiving their appropriate RDA of calcium based on their age and gender; however, most were receiving adequate vitamin D based on established RDAs. Through this model, the assessment of calcium and vitamin D intake was able to be adequately performed by second-year student pharmacists on an IPTV with minimal preceptor oversight.</p>

ABSTRACT NO. 96	
Name	Ramiz Yousif
Category	Pharmacy Practice
Title	Evaluation of Perioperative Anticoagulant Bridging in Atrial Fibrillation Patients
Authors	Ramiz Yousif; Norm Buss, Pharm.D., BCPS; Marilen Martinez, Pharm.D., BCPS
Abstract	<p>Purpose: Anticoagulant bridging with parenteral anticoagulants is utilized in practice to prevent thrombus formation in patients undergoing procedures requiring interruption of warfarin or direct oral anticoagulant (DOAC) therapy. According to American College of Cardiology/American Heart Association (ACC/AHA) guidelines, the decision to use bridge therapy in atrial fibrillation is based on the presence of risk factors as determined by the CHA2DS2-VASc score. The purpose of this study is to evaluate the use of heparin or low molecular weight heparin (LMWH) perioperative bridging in patients with atrial fibrillation who underwent interruption of warfarin or DOAC therapy prior to a procedure.</p> <p>Methods: This evaluation is a retrospective chart review at Henry Ford Macomb Hospital. Patients included were those admitted from June 2017 to June 2018 who were 18 years of age or older, had a diagnosis of atrial fibrillation, required interruption of warfarin or DOAC therapy prior to a procedure, and received heparin or LMWH for perioperative bridging. Patients were excluded if they received anticoagulant bridging for conditions other than atrial fibrillation such as pulmonary embolism (PE) or deep vein thrombosis (DVT). Patients were also excluded if they had prosthetic valves. To determine the appropriateness of bridge therapy, CHA2DS2-VASc scores were calculated and evaluated based on recommendations from ACC/AHA guidelines. Risk for bleeding was also assessed by calculation of HAS-BLED scores.</p> <p>Results: Five hundred patient charts were reviewed, and thirty patients were ultimately included in the study. Fifteen (50%) patients had a CHA2DS2-VASc score less than or equal to 4. Nine (33%) patients had a CHA2DS2-VASc score of either 5-6. Of those patients, three patients had a history of prior stroke or transient ischemic attack (TIA). Six (22%) patients had a CHA2DS2-VASc score greater than or equal to 7. Nine (33%) patients were appropriately bridged according to ACC guidelines while twenty one (70%) patients were inappropriately bridged. Twenty three (77%) patients had a HAS-BLED score of 3 or more, indicating a high risk for bleeding events, while seven (23%) patients had a score less than 3.</p> <p>Conclusion: Compliance with ACC/AHA guidelines at Henry Ford Macomb Hospital could be improved as many patients were unnecessarily bridged prior to a procedure, increasing risk for bleeding events. The risk for bleeding was high in the majority of patients, further indicating that bridge therapy may not always be appropriate. Clinicians should always calculate a CHA2DS2-VASc score and take into account patient specific factors when determining if perioperative bridge therapy is appropriate.</p>

ABSTRACT NO. 97	
Name	Nicole Zabik
Category	Pharmacy Practice
Title	Depressive Symptoms Reduce Default Mode Network Activity Following Fear Extinction
Authors	Nicole Zabik, B.S.; Allesandra Iadipaolo, B.A.; Farrah Elrahal B.A.; Craig Peters, B.A.; Hilary A. Marusak, PhD; Christine A. Rabinak, PhD
Abstract	<p>Background/Purpose: Positive affect has been associated with enhanced ability to suppress conditioned fear responses in safe environments and prevent reemergence of extinguished fears. Depression, in contrast, is a condition of low positive affect which may interfere with fear extinction. Impairments in fear extinction and dysfunction of the underlying neural circuitry are a hallmark of fear-based disorders, conditions that are often comorbid with depression. However, no study has investigated the effects of depressive symptomology on fear extinction.</p> <p>Methods: Sixty-two adults (ages 18-45) completed a novel adaptation of an established Pavlovian fear conditioning and extinction paradigm, involving immersive reality. During acquisition: one conditioned stimulus (CS+) was paired with an aversive unconditioned stimulus (US) during acquisition, while a second conditioned stimulus (CS-) was never paired with the US, serving as the safety cue. Following fear acquisition conditioned fear response to the CS+ were extinguished (extinction learning), by presenting the CS+ alone in a new environment ('safe' context). Twenty-four hours later, recall of extinction learning was measured by presenting the CS+ in the absence of the US in the 'safe' context. In addition, we also presented the CS+ (in the absence of the US) in the fear acquisition environment ('danger' context) to measure renewal of conditioned fear responses (fear renewal). Depressive symptoms were measured using the Beck Depression Inventory (BDI-II). Functional magnetic resonance imaging (fMRI) data were collected during recall and renewal.</p> <p>Results: During extinction recall, individuals with a greater number of depressive symptoms exhibited lower activation of the right hippocampus and precuneus to the previously extinguished CS+. Similarly, during the fear renewal test individuals with greater number of depressive symptoms show lower activation in the precuneus to the previously extinguished CS+.</p> <p>Conclusions: Depressive symptoms reduce activation of core regions of the default mode network (DMN) during fear recall and renewal. The DMN is engaged during safety learning in healthy individuals and reduced activation during recall highlights a lack of safety contextualization and memory engagement. Lowered activation of a core DMN structure during renewal expresses the disengagement seen in depressed individuals and reflects reduced activation of this structure during fear-learning. Consistent with recent evidence, alterations in activation of DMN regions have been reported in individuals with depression; blunting of the DMN due to increased number of depressive symptoms may interfere with appropriate fear contextualization.</p>