Surgery Intern Preparatory Curriculum: A Step-Up Approach to Decrease Anxiety and Improve Performance?

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INTRODUCTION: The transition from medical school to surgical internship is a period of heightened anxiety. To ease this transition, over 50 medical schools have developed courses to prepare graduating students for intern responsibilities. This study aimed to demonstrate that a surgical intern preparatory course (S-IPC) decreases student anxiety regarding intern year and that orientation to a simulation experience improves clinical decision-making while lowering anxiety during the simulation.

METHODS: Nine graduating medical students who had matched into an ACGME-accredited general surgery internship participated in the two-week S-IPC. The curriculum was instructed in a step-up approach including lecture-based review sessions, hands-on technical skill instruction, and high-fidelity clinical decision-making simulations. The students’ anxiety levels were measured prior to the course and surrounding the simulations. Simulation confidence levels were also obtained after each session. For the first simulation, only half of the participants received an orientation to the simulation environment. An attending surgeon evaluated each participant’s performance using a standardized assessment tool. All students received the same orientation prior to the second simulation session which occurred at the end of the course. Following the course, students reassessed their anxiety levels pertaining to intern year.

RESULTS: Prior to each simulation, the entire cohort reported a heightened level of anxiety (M = 2.28 ± 0.62) when compared to trait scores (M = 1.64 ± 0.44, Z = –2.31, p = 0.021) with no difference between the control and oriented groups. Following the first simulation, the oriented group reported a higher level of confidence (M = 2.63 ± 0.78) than the control group (M = 1.63 ± 0.29, U = 0.00, p = 0.014). The oriented group significantly outperformed the control group (M = 4.57 ± 0.23 vs. M = 3.11 ± 0.53, U = 0.00, p = 0.014) during that simulation. A difference in performance was not observed during the second simulation session. After completion of the course, a significant decrease in anxiety pertaining to intern year was not observed (M = 3.00 ± 0.47 vs. M = 2.78 ± 0.42, Z = –1.414, p = 0.157).

CONCLUSION: There was not a significant change in participant anxiety pertaining to internship associated with this S-IPC. However, during the high-fidelity simulation scenario, the oriented group outperformed and reported higher confidence levels than the control group.
Is Compliance With American Thyroid Association Guidelines for Total Thyroidectomy in Graves’ Disease Necessary?

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BACKGROUND and OBJECTIVES: The American Thyroid Association (ATA) has issued specific pre-operative guidelines for patients undergoing thyroidectomy for treatment of their Graves’ disease. Our goal is to determine if compliance with ATA guidelines for thyroidectomy for Graves’ disease is associated with better outcomes. METHODS: A retrospective review of a prospectively maintained database was performed to identify 228 patients with Graves’ Disease who underwent a total thyroidectomy between August 2007 and May 2015. Patients were considered to be in compliance with the ATA guidelines if they were treated pre-operatively with SSKI and were either rendered euthyroid with methimazole (T4<1.5 ng/dl) or if that was not feasible were treated with a β-Blocker. Patient demographics, clinical characteristics, and treatment-related morbidity were compared using Stata v11 statistical software.

RESULTS: The mean age of all patients was 39 ± 1 years and 83% were female. Most patients were treated with methimazole (84%) and β-blockers (82%). All patients underwent a total thyroidectomy, and the mean OR time was 115 ± 3 minutes. 38% of patients had a complication following thyroidectomy. Transient hypocalcemia was the most common complication (28%). At the time of surgery, 52% of all patients were in compliance with ATA guidelines. Patients that were not prepped according to ATA guidelines had more intraoperative tachycardia (0.3 vs. 4.5, p = 0.04), but thankfully had no difference in peak SBP (p = 0.47) or in number of episodes of SBP >180 (p=0.76). ATA prepped and non-prepped patients had similar mean OR time (118.6 vs. 114.5 minutes, p = 0.77) and length of stay (0.6 vs. 0.7 days, p = 0.46). ATA prepped and non-prepped patients had similar complication rates, including transient hypocalcemia (30.4% vs. 25.5%, p = 0.45), prolonged hypoparathyroidism (0.98% vs. 4.3%, p = 0.15), hoarse voice (10.8% vs. 7.5%, p = 0.42), prolonged RLN paralysis (2.9% vs. 2.1%, p = 0.71), hematoma formation (2.9% vs. 0%, p = 0.09), or returning to the OR (2% vs. 1.1%, p = 0.60).

CONCLUSIONS: Our data suggests that compliance with ATA guidelines for thyroidectomy preparation is not a necessary prerequisite for a successful postoperative outcome. While preparation according to the guidelines decreased the frequency of intraoperative tachycardia, it did not impact intraoperative hypertension, OR time, or post-operative complications.
Growing a Relationship Between Northeast Clinic and Lake View Elementary: Collaborating on Food Insecurity

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BACKGROUND: UW Health Northeast Family Medical Center adopted Lake View Elementary School in 2012 and has been promoting wellness activities for children and their families. Notably, 77% of children at Lake View qualify for free or reduced lunch. OBJECTIVE: Recently, the clinic, school and Second Harvest Foodbank of Southern Wisconsin have partnered together to better understand concerns about food insecurity, which was identified by the school community as a top priority health concern. Dane County is rich in emergency food pantries and we wished to explore Lake View families’ understanding of available resources. METHODS: A five-question survey was distributed to children during an annual school Wellness Day to take home to their families. The survey assessed: presence of food insecurity; barriers to food access; knowledge and use of existing community resources; and comfort with school involvement in this issue. RESULTS: Fifteen total responses were collected (participation rate was 15%). Two-thirds of respondents met criteria as “food insecure.” Of these families, many revealed limited knowledge of available food resources, particularly in regard to three major food pantries within 1.5 miles of the school. As greater than 50% of food-insecure families who responded requested literature of existing community resources, a food pantry flier was created with information on each of the major pantries in the area. CONCLUSIONS: Future steps will include distribution of this flier to families of Lake View Elementary. To improve participation rate and foster development of future interventions, revision of the survey with face-to-face distribution of survey material at an upcoming school family night is anticipated.
Subretinal Injection of Kir7.1 shRNA Reduces Retinal Responses in Mouse Model of Leber Congenital Amaurosis (LCA16)

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BACKGROUND: Leber Congenital Amaurosis (LCA) is a group of complex congenital blindness diseases. The 16th gene associated with LCA (LCA16) is KCNJ13, which encodes the inwardly rectifying potassium channel Kir7.1. Kir7.1 is located in the retinal pigment epithelium (RPE) cells and plays a key role in photoreceptor-RPE communication. We previously characterized a nonsense mutation in this gene in a 10-year-old male and reproduced the phenotype in a mouse model using a RNA interference-mediated intravitreal injection. In preparation for gene therapy experiments, we sought to reproduce the LCA16 phenotype in the mouse model using a subretinal injection.

OBJECTIVE: We hypothesized that mouse eyes injected subretinally with short hairpin RNA (shRNA) for Kir7.1 would have reduced retinal responses, measured in comparison to the contralateral untreated eye, as compared to mice receiving saline injections.

METHODS: shRNA lentiviral particles were delivered by subretinal injection to one eye of each mouse in the experimental cohort, leaving the contralateral eye untreated for comparison. In control mice, saline was used for the injected eye. Electroretinogram (ERG) measurements were carried out at 2, 4, 7, and 14 days post-injection. A separate cohort of mice was injected with green fluorescent protein (GFP) -tagged shRNA lentiviral particles for use with optical coherence tomography (OCT) and fluorescence imaging to visualize retinal structures and localize shRNA expression. RESULTS: Experimentally treated eyes showed sustained decreases in ERG a-, b-, and c-wave amplitudes. Control injections had no lasting effect on retinal responses. The results were statistically significant. OCT confirmed post-injection integrity of retinal structures and fluorescence imaging showed expression of GFP in the targeted RPE layer of the retina.

CONCLUSIONS: In this study, we demonstrated the ability to induce a lasting LCA16 phenotype through shRNA silencing of Kir7.1, via subretinal injection. This result supports our previous findings that Kir7.1 is the disease source and thus, an ideal target for gene therapy. Our results also suggest proficiency in our vector delivery for use in future therapeutic development.
The Impact of a Flexible Care Area on Patient Experience

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BACKGROUND: The increase in emergency department (ED) patient visits and the effect of ED boarding have led to significant operational challenges. This has caused EDs to develop patient flow changes in an attempt to mitigate the resulting increased length of stay. Our ED has created a flexible care area (FCA) which combines elements of a fast track model with a physician in triage model allowing patients to be evaluated sooner. The effects of these changes on operational metrics have been described, but the effect on patient experience is unknown. OBJECTIVE: To evaluate the effect of FCA on Press-Ganey patient satisfaction scores. We hypothesized patients seen in FCA would show an overall increase in Press-Ganey satisfaction scores compared to patient that were not seen in the FCA. METHODS: In this IRB approved retrospective analysis, we reviewed the chart for the encounters corresponding to all returned Press-Ganey patient satisfaction surveys. The study was performed on a single site academic tertiary care emergency department from July 1, 2013 to June 30, 2014. The patient was considered an FCA patient if their attending physician, defined as the physician who completed the ED documentation, and the scheduled FCA attending were the same. All others were considered ‘non-FCA’. We compared the percentage of ‘very good’ responses between the FCA vs. Non-FCA groups using a z test of proportions. The overall rating of care and the physician domain survey questions were included in the analysis which was conducted using STATA version 14. RESULTS: The overall length of stay was lower in the FCA group. The overall rating of care for the FCA group was significantly lower than the non-FCA group. However, none of the physician domain questions were significantly different. CONCLUSIONS: Despite having shorter average length of stay, patients treated in the FCA rated their overall care worse than those in the non-FCA group suggesting that total length of care is not the only determinant of a positive patient experience. Interestingly, the perception of the physicians was unchanged. The effect of FCA on the perception of nursing is unknown. Additionally, the FCA treatment spaces are located within the ED waiting room which may be frustrating to patients leading to the decrease overall rating observed. This study is limited by the low sample size in the FCA cohort, low overall satisfaction scores and low % of returned surveys. The next steps for this research is to expand the data set and determine the driving factors for the lower Press-Ganey satisfaction in the FCA group.
Block of ROMK, the Putative Mitochondrial KATP Pore, Increases Infarct Size in Mice

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Mentor(s): Jonathan Makielski, MD; Jack Kyle, PhD

Support: UW Cardiovascular Research Center

BACKGROUND: The ATP-sensitive potassium channel (KATP) is an integral part of the cardiac stress response. There are two forms of KATP channels in cardiac myocytes: one found in the sarcolemma (sKATP) and one found in the mitochondrial membrane (mKATP). sKATP is well characterized and has a known cardioprotective role by decreasing calcium overload. mKATP is less studied but has been implicated in a more specific form of cardioprotection known as ischemic preconditioning (IPC), which involves smaller bouts of ischemia before a long ischemic attack. The components of mKATP are not characterized, but preliminary research has suggested that the renal outer medullary potassium (ROMK) channel comprises the mKATP pore. ROMK is primarily studied for its role in renal salt homeostasis, and its putative role in the heart is a relatively new proposal. As such, studies of its role in the heart are few and inconclusive.

OBJECTIVE: This study aims to elucidate the role of ROMK during ischemia in the heart.

METHODS: Hearts were excised from anesthetized mice and connected to an exogenous perfusion system containing Krebs-Henseleit buffer with or without the ROMK inhibitor VU591 (10 µM). After perfusion for a 30 min. washout period, hearts were subjected to ischemia-reperfusion (IR) or IR preceded by IPC. Left ventricular pressure data were obtained for hemodynamic analysis of systolic and diastolic function (dp/dT and –dP/dT, respectively). Infarction size was measured using TTC staining and ImageJ software.

RESULTS: Inhibition of ROMK led to increased infarct size in IR (32.2 ± 19.3% WT vs. 74.5 ± 13.8% VU591, n=4, p=0.028). Compared to WT, hemodynamic analysis showed a 36% decrease in left ventricle developed pressure, a 40% decrease in diastolic function, and a 34% decrease in systolic function (n=4, p<0.05).

CONCLUSIONS: Previous research has shown that KATP activation protects the heart during IPC. We found that ROMK plays a significant role in cardioprotection of the heart during ischemia. Hemodynamic analysis suggests that ROMK may mediate ischemic cell survival by improving pressure development, systolic function, and diastolic function both during and after ischemia. These results support the idea that ROMK is the pore for mKATP. Further research is being performed to determine the effect of ROMK on mitochondrial membrane potential and the effect of ischemia on ROMK knockout mice.
Community Health Education and Referral System Assessment With Share the Health Free Gynecology Clinic

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Support: Prevention Innovations In Medical Education (PRIME) Madison Program; Share the Health Free Gynecology Clinic

BACKGROUND: Share the Health (STH) Clinic provides free specialized gynecologic care not offered by any other organizations to uninsured women of Dane County and the surrounding counties. STH also conducts community presentations and discussions to disseminate gynecologic health knowledge.

OBJECTIVE: This project aimed to accomplish the following: 1) assess barriers to appropriate referral to STH and 2) assess knowledge gaps related to gynecologic health within underserved populations of Dane and the surrounding counties. METHODS: An email survey of referring providers was conducted to identify the strengths, weaknesses, and barriers in the current referral system. Additionally, needs for educational programming was assessed through strategic connections and communication with community organizations and providers that serve uninsured women. RESULTS: The referring provider survey had a 26% (9 of 34) response rate. The majority of providers were mostly satisfied with the current referral system. However, 50% of the responders had never used the STH website, which provides current information about appropriate referrals. Relationships were established with organizations including MEDiC, Beloit Area Community Health Center and the Promotores de Salud. A common need among these organizations was knowledge about resources available for women and ways to connect women to these resources. DISCUSSION: Based on the survey, it was apparent that website usage should be encouraged. To address the need for knowledge of resources, several resource guides were developed and compiled. These guides included flyers summarizing services for uninsured women and algorithms to direct patients and providers to services that can address their need. The guides and updated referral forms were added the STH website to improve website utility and encourage use by referring providers.
Outcomes of Pediatric Supracondylar Humerus Fractures in Community

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Support: Shapiro Summer Research Program, Department of Orthopedics and Rehabilitation

BACKGROUND: Pediatric supracondylar humerus fractures are among the most common upper extremity fractures in children, involving 18% of all fractures in children. They often result from a fall on an extended hand, and are most common in children around 7 years of age. The objective of this study was to evaluate rate of clinical complications, malreductions, and postoperative loss of reduction in pediatric patients with supracondylar humerus fractures. Who were treated operatively at an academic center such as UW hospital with fellowship trained pediatric orthopedists vs. being treated at a community hospital such as St. Mary’s with non-pediatric orthopedists. Our central Hypothesis is that patient treated at either UW Hospital or St. Mary’s will have no difference in outcome. METHODS: A retrospective review of 815 patients ages 2-12 who presented with supracondylar humerus fractures to either UW hospital or St. Mary’s hospital between 2003 and 2013 was performed. Patients’ initial radiographs were reviewed and Gartland type recorded. The presence of any complications recorded along with the surgeon’s training and operative technique used. In addition, the Baumann angle and intersection of the anterior humeral line with the capitellum were also recorded from the final radiographs, so was the range of motion and coronal alignment at the final follow-up visit. The presence of any neurologic or vascular injury were also recorded at final follow-up visit. RESULT: Initial data collection was completed; however the date is currently being process. Upon completion of data processing the data will be analyzed. CONCLUSION: We will continue to process the data and once this is completed, the date will be promptly analyze. Once the data analysis is completed we hope to publish a paper.
Predictors of Childhood Anemia and Malnutrition in Imo State, Nigeria

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BACKGROUND: Childhood anemia and malnutrition are a significant global health issue. In Nigeria, acute malnutrition has a prevalence of up to 13%, leading to increased susceptibility to infectious diseases, developmental delays and anemia. Mezu International Foundation (MIF), conducts integrated medical missions to rural communities in South-Eastern Nigeria, and notes a high prevalence of childhood malnutrition and anemia in the community. OBJECTIVE: This study sought to determine modifiable risk factors for children with anemia and malnutrition in the community. METHODS: At the 2015 MIF medical mission, a survey addressing socio-demographics, health co-morbidities, and diet diversity was conducted on 96 children ages 1 to 7. Anemia was assessed clinically or by hemoglobin (Hgb) levels. Mid upper arm circumference (MUAC) was used to assess malnutrition status per WHO standards. RESULTS: 90 complete surveys were analyzed (49% male and 51% females). Anemia was the most prevalent clinical diagnosis (69%), followed by intestinal worm infection (53%), and malnutrition (29%). There was a significant association between Hgb level and clinical anemia (p=0.0457). Mean age (months) that breastfeeding was stopped was 11.8 (±2.2) in children with Hgb <11mg/dl (severe anemia), 10.5±2.8 in those with Hgb = 11-11.9mg/dl (mild anemia), and 9.4±3.9 in children with Hgb >12mg/dl (no anemia) (p=0.0445). Professionals were more likely to read to their children than skilled and non-skilled workers (p=0.0002), but their children had fewer medical visits compared to children of skilled or non-skilled workers (p=0.0139). There was no significant association between Hgb level and SES score (p=0.250) or diet diversity score (p=0.3933). A diagnosis of intestinal worms (p=0.7891) or anemia (p=0.8647) did not correlate with MUAC. CONCLUSION: Educated parents were more likely to read to their children, but less likely to take them to routine medical visits than less educated parents, likely a reflection of a poor economy affecting healthcare behaviors. Prolonged breast-feeding beyond 10.5 months old was associated with significant anemia, a reflection of poor maternal nutritional status. An integrated, family-centered intervention focused on preventive health care, diet diversity, and improved maternal nutrition would reduce child morbidity and mortality in the community.
Crossover: A Study of Frontal Plane Kinematics in Elite Runners

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BACKGROUND: Step width, or the mediolateral distance from each foot’s heel at initial contact, has been associated with increased risk for IT band syndrome and tibial stress fractures. However, its applicability to running may be limited because during running, only one foot is in contact with the ground at a given moment in time. Crossover, the mediolateral distance from the heel to center of mass during midstance, is a related variable that may provide more insight into running biomechanics and injury.

OBJECTIVE: To assess the relationship between crossover, limb, and speed. Secondary objectives were to describe the relationships between crossover, foot inclination angle, stride length, and cadence and determine if crossover varies by gender. METHODS: An 8-camera motion capture system recorded 19 healthy collegiate cross country athletes running at five different speeds (2.91, 3.20, 3.63, 4.12, 4.85 m/s). The motion tracking data was used to construct a 3D model from which all variables were calculated. 2x2 ANOVAs were used to assess possible interactions and correlations were calculated for relationships of interest. RESULTS: There was no significant interaction between limb and speed (p = 0.43) and no significant difference between limbs (p = 0.37). There was a significant speed effect (p < 0.01), with crossover increasing as speed increased. There was a significant difference in crossover between genders, with males crossing over more than females (mean difference = 1.7 cm; p = 0.01; 95% CI 0.4-2.9 cm). Crossover and foot inclination angle were not significantly correlated. There was a significant positive correlation between crossover and stride length across all speeds (p ≤ 0.02). There was a significant negative correlation between crossover and cadence across all speeds (p ≤ 0.024).

CONCLUSION: Crossover is a function of both speed and gender, and consequently both variables should be taken into account when evaluating if an individual’s crossover is excessive. Additionally, as stride length is a known risk factor for injury and is significantly correlated with crossover, evaluating crossover may help further assess injury risk in the running population. However, more research is required to assess if crossover is also related to kinetic running variables and how crossover may aid in determining injury risk.
17q21 Variation is Associated With Decreased Levels of GSDMB and ORMDL3

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**BACKGROUND:** Asthma, an increasingly prevalent, chronic lung disease, affected 18.7 million adults and 7 million children in the United States as of 2010. Its mechanisms are not completely clear and a there is currently no cure. Both genome wide association and candidate gene mapping studies have found several single nucleotide polymorphism (SNPs) at the locus 17q21 to be associated with asthma. One such association lies at the SNP rs7216389, where a TT genotype is more prevalent in asthmatics than the CC genotype. In comparison to 2 other SNPs associated with asthma in the 17q21 locus, rs7216389 confers the greatest risk for diagnosis of asthma following Human Rhinovirus wheezing illnesses in early childhood. We have previously observed that the TT genotype is associated with higher force exhaled nitric oxide (FeNO) levels and increased likelihood of blood eosinophil counts greater than 200/mm3. Recently, GSDMB, another gene at the 17q21 locus, showed decrease expression in a genotype dependent manner within the Severe Asthma Research Program (SARP) cohort, while ORMDL3 expression did not show genotype dependent expression. Functional relationships between ORMDL3/ GSDMB proteins and asthma pathophysiology remain unclear, as is the mechanism by which the rs7216389 TT genotype confers increased risk of asthma. **OBJECTIVE:** To investigate the relationship between ORMDL3 and GSDMB expression in eosinophils with the asthma associated SNP rs7216389. **METHODS:** Blood eosinophils were analyzed via QPCR and Western Blot for mRNA and protein levels. QPCR data were run in duplicate and normalized to no-template lanes. Protein samples were imaged and normalized to β-actin using an Odyssey Li-Core system. Antibodies for ORMDL3, GSDMB, and β-actin proteins were diluted at 1:1,000, 1:500, and 1:10,000 respectively. All statistical analysis was conducted in Sigma Plot. **RESULTS:** mRNA analysis of multiple immune cell types demonstrates that ORMDL3 and GSDMB expression is highest in Eosinophils. Baseline mRNA expression shows no significant change between rs7216389 genotypes. Baseline protein levels decrease in the TT genotype when compared to the CC genotype for both GSDMB and ORMDL3. **CONCLUSIONS:** The asthma associated rs7216389-TT genotype exhibits decreased levels of both ORMDL3 and GSDMB protein.
Use of a Wire-Guided Exchange Kit to Place Double Lumen Endotracheal Tubes for Lung Isolation

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Support: Shapiro Summer Research Program; Department of Anesthesiology

BACKGROUND: Lung isolation is frequently required for thoracic surgery procedures. Unfortunately, blind placement can oftentimes result in misplacement and inadequate lung isolation. In addition, airway anatomy or pathology can make double lumen endotracheal tube (DLT) difficult or impossible. Wire-guided airway exchange utilizing the Arndt Airway Exchange Catheter Kit (Cook Medical Inc., Bloomington, IN, USA) allows for the precise placement of DLTs. There is no literature reporting success utilizing this technique for lung isolation or potential complications associated with use of this technique.

OBJECTIVE: This retrospective chart review aimed to determine success, complications, and characteristics of patients who received wire-guided exchange kits for placement of double lumen endotracheal tubes. METHODS: Following IRB approval, the charts of patients who required DLT insertion placement and who had their DLT placed using the Arndt Airway Exchange Catheter set between 01/22/2010 and 03/26/2014 were reviewed. Demographic information (age, gender, BMI), American Society of Anesthesiologists (ASA) score, airway examination data, and airway management details (i.e. success or difficulties encountered) and complication information was collected. RESULTS: Forty-five patients underwent wire-guided DLT placement and were included in the analysis. Of the 45, there were no failures to secure the airway, two minor problems with the wire-guided exchange, and one minor complication that may have resulted from the wire-guided exchange. CONCLUSIONS: Wire-guided exchange may be a good tool to aid the correct placement of double lumen endotracheal tubes for cases that require lung isolation. Utilization of this technique resulted in 100% successful placement in the 45 cases reviewed. The risk of complications associated with this procedure is likely low and it may be useful to maintain ventilation while achieving lung isolation in patients with airway pathology or altered anatomy. Due to the limited sample size, further studies could be performed on a larger sample size to uncover other potential complications of this technique.
Establishing Learning Curves for a Simulated Surgical Task Using V-PITS

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Support: Department of Surgery T32 DC 9401-6 Training Grant

BACKGROUND: Traditional means of evaluating surgical resident performance, typically via assessment by a highly trained professional, can be subjective and labor intensive. Moreover, standardized learning curves for the evaluation of trainees’ phonomicrosurgical techniques have not been established. V-PITS (Video-Based Phonomicrosurgical Instrument Tracking System) provides 3D motion tracking of surgical instruments, and offers quantifiable, standardized, and objective descriptions of phonomicrosurgical technique. Preliminary investigation with V-PITS demonstrated significant improvements in motion metrics among novices over one week of practice. These measures significantly correlated with task outcome and supported V-PITS as a reliable quantification of performance. The Cumulative Summation (CUSUM) statistical analysis can be used to track trainees’ improvement as a function of cumulative experience. This method can be applied to V-PITS motion metrics to generate a learning curve for a phonomicrosurgical task.

OBJECTIVE: To establish a continuum of performance ability (a learning curve) as a function of practice trials.

METHODS: This was a longitudinal prospective study of 20 participants who did not have any prior laparoscopic or endoscopic surgical experience. Participants completed 15 sessions over 3 weeks. At each session, the participant performed a surgical simulation task twice on each hemifold. The paper lesion task, adapted with permission from Contag, et al, involves the bimanual dissection of an ovoid lesion from the superficial epithelial level of simulated vocal folds. V-PITS recorded microsurgical instrument movements throughout task completion. For each trial, the following three-dimensional motion metrics were computed from the video data: time, path length, depth perception, motion smoothness and task accuracy. These metrics will be plotted as a function of total number of trials completed using a CUSUM analysis.

RESULTS: Data analysis is ongoing. Thus far, motion metrics have been computed for subject C001. Accuracy data have been computed for subjects C001-C003.

CONCLUSION: We will continue to extract motion metrics from each subject’s video data. Upon completion of data analysis, the number of trials required to reach specified levels of competence and skill level plateau will be defined. These findings will be applied to the evaluation of phonomicrosurgical trainees.
Current Use of Telemedicine for Post-Discharge Surgical Care: A Systematic Review

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BACKGROUND: Telemedicine (TM) is defined by the Institute of Medicine (IOM) as “the use of electronic information and communications technologies to provide and support health care when distance separates the participants.” Its wide array of clinical applications has been used to overcome service barriers. Existing reviews of TM describe its uses in surgical subspecialties or a particular mode of technology; however, none focus on its potential to bridge care gaps in the post-operative transitional care period. OBJECTIVE: Examine telemedicine’s current uses in facilitating post-discharge surgical care transitions. METHODS: Systematic review of original research articles conducted in the United States, published in English, from 2010-2015. The 21 articles that apply TM post-operatively, in a way that fit the IOM definition of TM, were included. RESULTS: Post operatively, TM is used for scheduled follow up, routine and on-going monitoring, issue management, videoconferencing, text messaging and smartphone digital photography. Most studies reported significant travel time (77.5-317 minutes), distance (79.6 – 367.2 miles), and cost ($36.74-$183.60) savings to patients, with high patient willingness to participate (77-100%), and without compromise of clinical outcomes (0-4.8% higher complication rate), patient satisfaction (90-98.8%), or provider satisfaction. Other benefits include improved access to surgical services, decreased wait times (110 clinic openings over 10 months), and eliminating unnecessary transfers (64% transfer rate reduced to 39%). Existing limitations to TM include its medico-legal pitfalls, as well as concerns about compensation and provider credentialing. Limitations to existing research include small sample sizes and selection bias for participants who already have access to and experience with technology. Additionally, none of the studies invoked a conceptual framework for transitional care. CONCLUSIONS: Telemedicine is safe, patients and providers are willing to use it, and it saves patients and the health care system time and money. Further work is needed to determine which patient populations and procedures are appropriate, and address the regulatory barriers to widen implementation. Future work would benefit from invoking a conceptual framework for transitional care to inform measures of transitional care, establish cost effectiveness, and broaden understanding of patient-centered care transitions.
Quantitative Evaluation of the Ellipsoid Zone in Eyes With Retinal Vein Occlusion: A SCORE2 Ancillary Study

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Support: Shapiro Summer Research Program; Dan and Ellie Albert Student Vision Research Award

BACKGROUND: Central retinal vein occlusion (CRVO) is a common retinal vascular disorder, and one of its main complications is macular edema (ME). Treatment of ME secondary to CRVO with anti-VEGF intravitreal injection often does not lead to a concurrent increase in visual acuity (VA). In previous studies, loss of visibility on spectral-domain optical coherence tomography (SD-OCT) of the ellipsoid zone (EZ) in the fovea has been correlated with poor visual outcomes, and retinal thickness has been found to be inversely correlated with VA. In this study we hope to quantify the role the EZ in vision loss by investigating whether the thickness of the EZ correlates with VA. OBJECTIVE: To compare thickness of the EZ with VA in eyes of patients with ME secondary to CRVO enrolled in Studies of COmparative Treatments for REtinal Vein Occlusion 2 (SCORE2).

METHODS: Volume SD-OCT scans were obtained from 75 study participants at baseline and every month for 12 months as part of the SCORE2 randomized clinical trial. Scans from 6 screening visits and 42 Month 1 visits met inclusionary criteria and were segmented using a semi-automated method for the inner limiting membrane (ILM), the top of the EZ, and the top of the retinal pigment epithelium complex (RPE). Thickness maps were generated to obtain central retinal thickness, EZ thickness, and EZ volume. Central retinal thickness was measured as the distance in microns between the ILM and the top of the EZ. EZ thickness was measured as the distance in microns between the top of the EZ to the top of the RPE. RESULTS: For the screening visits, average EZ thickness was 22.57 microns, average EZ volume was 0.77 cubic mm, average retinal thickness was 478.57 microns, and average retinal volume was 9.15 cubic mm. For the Month 1 visits, average EZ thickness was 24 microns, average EZ volume was 0.801 cubic mm, average retinal thickness was 300.07 microns, and average retinal volume was 8.37 cubic mm.

CONCLUSIONS: These results show that EZ thickness and volume increase on average after one treatment, while retinal thickness and volume decrease on average. These trends are expected with decreasing ME and increasing VA after treatment. In future studies, we will take measurements from Month 3 and Month 6 visits to determine if these trends continue. Area maps in an en face view will also be generated to obtain the area of ellipsoid zone defect. Finally, associations between these data and visual acuity will be investigated.
Increasing Extent of Treatment For Differentiated Thyroid Cancers

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Support: Department of Surgery NIH T35 Training Grant

INTRODUCTION: The incidence of differentiated thyroid cancer (DTC) has increased exponentially over the last 25 years. Small, low risk tumors account for most of this increase. During this same period, the U.S. population continues to age with the average life expectancy of 79 years. In this study, we explored trends in the extent of treatment for DTC over the last 25 years, with a focus on the elderly. METHODS: This study is a retrospective analysis using the Survey Epidemiology and End Results (SEER) database. Patients 20 years and older with thyroid cancer who underwent surgery from 1988 to 2012 were included. Cases were considered low risk if they were either classical papillary or follicular carcinoma, T1 (a or b) N0 M0 by TNM classification, and without extrathyroidal extension. Larger tumors, with unfavorable histology, nodal or distant metastases or extrathyroidal extension were considered high risk. We defined elderly as ≥ 70 years old. Trends in rates of total thyroidectomy (TT), radioactive iodine treatment (RAI) and lymph node dissection (LND)(removal of at least three lymph nodes) were analyzed and compared using chi square test, student's t-test, weighted least square linear regression and multivariate logistic regression where appropriate. RESULTS: 131,590 cases of DTC met our inclusion criteria and 11.3% were elderly. Overall, rates of TT have increased since 1988 by an average of 0.4% annually. The rate of increase was greater in the elderly compared to the younger cohort (0.58 vs. 0.38%/year, p=0.02). This disparity between the elderly and younger was most pronounced within the low risk group alone (0.66 vs 0.3%/year p=0.03). Through the entire study period, the elderly remained less likely to receive a TT than those under 70 when controlling for all patient and tumor features (OR = 0.66 p < .001). Rates of RAI increased between 1988 and 2012 by 0.19%/year. Annual rates of RAI treatment averaged 12.4 % lower in the elderly than the younger cohort (p =0.063). The elderly and younger patients experienced similar rates of increasing RAI treatment (p = 0.99). Annual rates of LND rose by 0.88%/year. Considering year of diagnosis alone, patients were much more likely to receive a LND in the most recent five years (2008 - 2012) compared to early years (OR 2.33 p < 0.01). Overall, elderly patients were half as likely to receive LND as younger patients in our model (OR 0.52, p < 0.01). CONCLUSIONS: Treatment for DTC has become more aggressive over the last 20 years with increasing use of TT and LND. The elderly experienced this trend, but older age alone was not independently associated with more aggressive treatments. The overall increase in more extensive treatment for low risk tumors warrants improved risk adjusted treatment decisions.
Next-Gen Sequencing of Steroid Hormone Receptor Biomarkers in Patients With ER+ MBC Treated With Endocrine Therapy

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Mentor(s): Amy M. Fowler, MD, PhD; Aparna Mahajan, MD

Support: University of Wisconsin Paul P. Carbone Young Investigator Award (AMF); Department of Radiology and Shapiro Summer Research Program (MD)

BACKGROUND: Breast cancer is the most prevalent cancer in women. About 70% of these cases are estrogen receptor (ER) positive. Blocking ER function with endocrine therapies is a key treatment approach and although these treatments can be effective, many metastatic tumors develop resistance to endocrine therapy over time. In many of these cases the tumor ESR1 gene develops an activating mutation that occurs most commonly in the ER ligand binding domain. The frequency of these mutations is unclear as exclusion criteria differ between studies and eligible patient populations are generally small.

OBJECTIVE: The study aims to 1) perform genotyping of ESR1 and determine the mutational frequency in ER+ metastatic breast cancers of patients treated with endocrine therapy, 2) identify previously uncharacterized ESR1 mutations, and 3) perform genotyping of PGR, the gene encoding the progesterone receptor.

METHODS: This is an IRB-approved, HIPAA-compliant retrospective study. Potentially eligible patients were identified from a search of the University of Wisconsin Carbone Cancer Center registry of patients with ER+ metastatic breast cancer. Eligible patients must have received at least 6 months of endocrine therapy after biopsy-proven diagnosis of metastatic or locally recurrent disease and have sufficient tissue remaining in the archived pathology specimen for further processing. Review of histology slides and formalin-fixed paraffin embedded tissue blocks for areas of tumor with >50% cellularity was performed. Genomic DNA was extracted from tumor and normal tissue and next-generation sequencing of the coding regions of ESR1 and PGR was performed.

RESULTS: A total of 75 genomic DNA extractions (from 42 tumor and 33 normal tissues) were performed for 49 female patients (35-88 years old). Sites of metastatic tissue samples included bone, liver, lung, brain, and lymph node. Next-generation sequencing is currently in progress. These results will be analyzed with demographic and treatment information to determine if different patient factors and therapeutic regimens are associated with specific mutations.

CONCLUSIONS: Identification of ESR1 and PGR mutations in endocrine therapy resistant metastatic breast cancer patients may improve treatment options. Future studies will focus on how the presence of steroid receptor biomarker gene mutations can be predicted through conventional anatomic imaging and targeted molecular imaging studies.
Location, Location, Location... Site of Rib Fracture Predicts Outcomes in Trauma Patients

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Mentor(s): Suresh K. Agarwal Jr., MD, FACS, FCCM, FCCP

Support: Shapiro Summer Research Program; Department of Surgery

INTRODUCTION: The number of rib fractures an individual suffers has long been considered an independent predictor of morbidity and mortality; however, in previous studies all rib fractures were considered to be the same. OBJECTIVE: We hypothesized that not only total number of ribs fractured, but also location of fracture is a strong predictor of patient outcomes in terms of mortality, length of stay, and discharge disposition. METHODS: An IRB-approved retrospective chart review was performed at an academic, level one trauma center. Patients who suffered traumatic rib fractures between January 2013 and April 2015 were identified by CPT codes for possible inclusion in the study. Individual computer tomography scans of the chest were reviewed and validated by staff radiology reads. The location of the rib fractures were characterized in terms of anterior, posterior, lateral, upper, middle, lower, and right versus left. SAS statistical software, logistic regression curves and ANOVA data analysis examined the data for relationships between rib fracture location and patient outcomes in terms of length of stay, ICU length of stay, discharge disposition and overall mortality. RESULTS: 929 patients were initially reviewed for possible inclusion in the study and 248 excluded. A total of 3,864 fractures were identified in the patient population. Statistically significant positive correlation coefficients were identified between length of stay and number of rib fractures in all locations with the strongest relationships seen in the upper (0.191, p=<0.0001), middle (0.185, p=<0.0001) and lateral (0.189, p=<0.0001) locations. Similarly, statistically significant correlations were seen between all rib fracture locations and ICU days with the strongest relationships seen in patients with upper (0.184, p=<0.0001), middle (0.189, p=<0.0001) and lateral (0.205, p=<0.0001) fractures. In addition, there was a statistically significant association between in hospital mortality and lateral rib fractures, with the non-survivors having on average 2 more lateral rib fractures than survivors (p=.0192), and left-sided rib fractures, with the non-survivors also having on average 2 more left-sided rib fractures than survivors (p=.0287). A statistically significant association was seen between discharge disposition and left-sided fractures (p=0.0160) as well as lateral rib fractures (p=0.0002). There was a linear relationship between type of discharge, in terms of increasing need for support, and number of lateral rib fractures. CONCLUSION: Rib fracture location, particularly left sidedness and lateral location, help predict outcomes in terms of mortality and discharge disposition. This may assist in discussing care and planning resources for traumatically injured patients. A larger validation trial is needed to confirm these results.
Improved Surgeon First Case On Time Starts Enhance Operating Room Efficiency and Cost Savings

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Mentor(s): Charles Heise, MD

Support: Shapiro Summer Research Program; Department of Surgery

INTRODUCTION: Decreasing under-utilized time in the operating room (OR) has been suggested as a means of achieving meaningful cost reductions for hospitals. One proposed method is to improve on time first case starts in the OR, though related financial analysis is lacking. The purpose of this study is to determine the downstream effect and financial impact of improving on-time starts for the first case of the day in the outpatient operating room at an academic teaching institution. OBJECTIVE: The purpose of our study is to determine the financial impact of improving on-time starts for the first case of the day in the outpatient operating room at an academic hospital. Specifically, we will analyze the impact of such improvements on over-utilized time and overtime operating room costs. METHODS: The Department of Surgery set a goal to decrease first case delays, specifically those attributable to surgeons. On time starts were defined as those beginning within 10 minutes of the scheduled start time. Beginning in fiscal year (FY) 2014, major efforts were made to improve surgeon related first start delays. On-time start percentage and over-utilized time were measured in the outpatient surgery setting and cost was estimated using a per-minute OR direct cost value. Fisher’s exact chi square test was used to assess proportional differences in first case delay percentage between FY 2013 and 2014. An independent samples t-test was performed to analyze pre-post changes in mean monthly over-utilized time.

RESULTS: At baseline, the rate of first-case delays in the Department of Surgery was 7.5%. Post improvement efforts, this rate improved to 4.8% (p < 0.05). The Department of Surgery saw a 51% drop in over-utilized time, corresponding to 998 fewer minutes that ORs ran past 5 pm. The monthly average over-utilized time in the Department of Surgery decreased by 84 minutes per month (p < 0.05, 95% CI [22,146]). These improvements were estimated to translate into an average direct cost savings of $1,300.00 per month. CONCLUSION: Improving on-time first case starts by promoting surgeon timeliness is associated with decreases in over-utilized time at the end of the OR day. While direct cost-savings in the outpatient surgery setting may be minimal, decreasing over-utilized time does have some financial benefit and likely improves the work environment by avoiding overtime staffing issues.
How Do Patients, Physicians, Staff Identify Their Patient Care Team?

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Mentor(s): Valerie Gilchrist, MD; Marlon Mundt, PhD; Matthew Swedlund, MD

Support: Department of Family Medicine and Community Health Student Summer Research and Clinical Assistantship Program

BACKGROUND: Teams are a core concept of the Patient Centered Medical Home (PCMH) and the Patient Protection and Affordable Care Act (PPACA); however, there is little understanding of how primary care patients view their care team. **OBJECTIVE:** This study describes and compares membership of care teams identified by patients and by faculty/staff in family medicine clinics.

**METHODS:** Surveys with the care team definitions, member pictures and team relationship were distributed to patients and to faculty/staff at 7 University of Wisconsin Department of Family Medicine and Community Health clinics. Descriptive statistics, multivariate regression analyses and social network analyses, were conducted. **RESULTS:** 1319 patients (RR 37%) and 254 faculty/staff members (RR 75%) completed a survey. Patients identified an average of 5.6 individuals on their care team and faculty/staff identified an average of 25.0 individuals on their team. Patients who were younger, female, spent more years at a practice, and indicated more clinic visits identified more care team members. Patients with perceived worse health status were more likely to include behavioral health specialists as part of their care team. Care team size and composition varied widely by clinic. Faculty and staff identified instrumental support (helped with a task) as provided most often by clinical support (registered nurse and medical assistant), office support (receptionist and administration), and lab/x-ray personnel. Informational (gave information) and emotional support (expressed care) was provided most often by clinical support personnel. **CONCLUSIONS:** Membership of care teams identified by patients varied according to multiple demographic and clinic variables. Staff identified a larger care team size than did patients. Perceived support offered by staff varied according to job type and clinic. Further analyses will include analysis of statistically significant differences among clinics, correlations of patient characteristics with size and composition of care teams, and the comparison of care team membership by patients and faculty/staff.
Big Data in Surgery: Modeling How Post-Operative Complications Increase Risks for Further Complications

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Support: Department of Surgery NIH T35 Training Grant

BACKGROUND: Patients who suffer from post-operative complications have longer hospital stays, higher rates of readmission and mortality, and higher cost of care. Many studies have evaluated predictors of complication development. However, little is known about sequences of multiple complication development over time. OBJECTIVE: The goal of this study was to assess the temporal relationships among post-operative complications. Knowledge of these relationships will improve our ability to select targeted interventions to prevent cascades of these complications. METHODS: The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database includes preoperative risk factors, intraoperative variables and 30-day postoperative outcomes for patients who underwent major inpatient and outpatient surgical procedures. This study includes cases from this database from 2005 – 2013. Data included all ACS NSQIP-defined complications within 30 days post operation. Machine learning methods were used to model the temporal dependencies between complications. A Markov chain model was developed to model the development of subsequent complications given knowledge of the complications a patient has experienced. RESULTS: The model was best at predicting death, coma longer than a day, cardiac arrest, septic shock, renal failure, pneumonia, unplanned re-intubation, longer than 2 days on a ventilator and bleeding transfusion (greater than 75% sensitivity at the 75% specificity threshold). We found some complications to be more likely to occur in isolation while others are likely to be associated with a second. The risk for later complications depends on the complications a patient has experienced. Complications such as cardiac arrest or MI, renal insufficiency or failure, stroke, intubation, septic shock and coma contributed to complication cascades to a much greater extent than other complications. For example, a patient who has a coma has an odds ratio of >2 of dying within 30 days of the operation while the odds ratio for death following a diagnosis of pneumonia is <0.5. CONCLUSIONS: A Markov Chain Model combining information about prior complications and time to occurrence after surgery can inform the likelihood of future complications. The present study utilized a novel method to determine several associations among post-operative complications which will contribute to our ability to better target interventions for high-risk post-operative patients.
mTOR1/2 Inhibition as a Treatment Strategy for Subtypes of Colon Cancer

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Mentor(s): Dustin Deming, MD

Support: Shapiro Summer Research Program; Department of Medicine; Carbone Cancer Center; Wisconsin Alumni Research Foundation; University of Wisconsin School of Medicine and Public Health; Funk Out Cancer - in honor of Kate Gates Falaschi

BACKGROUND: Colorectal cancer (CRC) is the third most common cancer in the United States. Here we aim to improve treatment options for patients with subtypes of CRC. Several key mutations are important in the biology of CRC, including APC (80%), TP53 (50%), and PIK3CA (20-30%). Abnormalities in the PI3K signaling pathway play an integral role in the development of cancers due to its involvement in cell growth, proliferation, and apoptosis. Mutations in the PIK3CA gene, resulting in a constitutively active PI3K, often occur concomitantly with loss of the APC gene in human CRCs. Our lab has developed a murine model system where a constitutively active PI3K and loss of APC occur simultaneously in the colon (AK3K). Concomitant loss of p53 is also expressed (AK3KTO) in a separate model. Colon tumors from these models are then cultured as three-dimensional spheroids and treatment studies are performed on mutation profiles of interest. OBJECTIVE: We are investigating the use of mTOR1/2 inhibition as a treatment strategy for subtypes of colon cancer. METHODS: AK3K and AK3KTO spheroids were treated with a dual PI3K/mTOR inhibitor, NVP-BEZ235, or a novel mTOR inhibitor, MLN0128, and compared to vehicle only controls. Images were taken both pre- and post-treatment and changes in spheroid diameter were measured. Parallel treatment studies were performed on an adherent cell line from a primary human colon cancer tumor, SW48, which carries a mutant FBXW7 and on a cell line with an additional PIK3CA mutation (SW48PK). (FBXW7 targets mTOR for degradation.) Immunoblotting was performed on each cell line to examine for effects between the treatment groups on the PI3K/mTOR signaling pathway. RESULTS: Treatment with NVP-BEZ235 and MLN0128 resulted in a significant treatment response. In the AK3K spheroids, MLN0128 was a more effective drug. Comparing across cell lines, AK3KTO spheroids were more sensitive to treatment. MLN0128 was more effective in SW48 and SW48PK cells as well and SW48PK cells were more sensitive to treatment. CONCLUSIONS: mTOR1/2 inhibition is sufficient to induce responses in PIK3CA and APC mutated CRCs. Additionally, concomitant loss of TP53 does not lead to resistance and potentially increases sensitivity. In a cell line predisposed to PI3K/mTOR signaling sensitivity, mTOR1/2 inhibition remains sufficient as a treatment strategy and the addition of a PIK3CA mutation further increases sensitivity. In conclusion, mTOR1/2 inhibition is at least equally effective as dual PI3K/mTOR inhibition and should be investigated further as a treatment strategy for patients with PIK3CA mutant CRC.
External Surrogates for Liver Tumor Motion During Radiation Therapy

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Support: Shapiro Summer Student Program; Department of Human Oncology; UW Carbone Cancer Center

BACKGROUND: Stereotactic body radiation therapy (SBRT) has become increasingly used to treat well-defined tumors, including both primary and metastatic liver tumors. This treatment modality allows for delivery of high doses of radiation to tumors while minimizing exposure to healthy tissue. Motion management is a critical component of delivering accurate treatment due to respiratory tumor motion. Chest wall motion has been shown to correlate with tumor motion in controlled studies; however, this has not been assessed during radiation therapy. OBJECTIVE: To determine if chest wall motion correlates with liver tumor motion in patients during delivery of radiation therapy. METHODS: Five patients with either primary or metastatic liver tumor were treated with five fractions of SBRT using real-time MRI-guided Coblat-60 radiation treatment. Cinematic MR images (cineMRI) were recorded during each treatment for subsequent motion analysis. For each fraction, four chest wall points and a tumor centroid were delineated on sagittal view MRI files using OsiriX imaging software. Twenty cineMRI frames were analyzed per fraction, 3 fractions per patient. Chest wall motion along the anterior-posterior (AP) axis was correlated with tumor centroid motion along the A-P and Cranio-Caudal axes using linear regression statistics. RESULTS: Data for five liver SBRT patients was collected, three fractions per patient. Linear regression correlation coefficients ranged from $R^2=0.0011$ to $R^2=0.95$. For patients 1 and 3 the initial surface point, near the xiphoid process, provided the best correlation with tumor motion ($R^2>0.8$). For patients 4 and 5 tumor motion correlated better with more inferior surface points. Patient 2 had poor correlation at all points analyzed ($R^2<0.4$). Motion correlation showed little variation within subjects over the five-fraction course. CONCLUSIONS: Correlation between chest wall motion and liver tumor motion can vary greatly among patients. This may depend on the chest wall location tracked, body habitus, and variation in breathing technique during treatment. A larger study population is needed to determine which factors predict positive tumor-chest wall motion correlation. Patients whose chest wall motion correlates poorly with tumor location are at risk of geometric miss during radiation treatment and may benefit from real-time MRI-guided therapy.
**Effects of Isoflurane on Descending Connections in Cortex**

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**Mentor(s):** Matthew Banks, PhD

**Support:** Shapiro Summer Research Program; Department of Anesthesiology

**BACKGROUND:** Though anesthetics are widely used, their underlying mechanisms of loss and recovery of consciousness are unknown. Sensory awareness depends critically on integration of information; anesthetics are postulated to specifically impair top-down pathways while leaving bottom-up pathways intact. **OBJECTIVE:** We hypothesize that regardless of molecular targets and pharmacological profile, anesthetic agents will selectively suppress top-down pathways at just-hypnotic doses, while leaving bottom-up pathways intact. **METHODS:** Rats were implanted with bipolar stimulating/recording electrodes in the primary auditory cortex (A1) and posterior auditory field (PAF) (to activate top-down pathways). A1 and PAF were electrically stimulated in four pulse trains as isoflurane was given at sub-hypnotic and just-hypnotic (indicated through loss of righting reflex) doses. The resulting waveforms were analyzed and the ratio of intensity of the fourth pulse to the first pulse was calculated for each drug condition. **RESULTS:** Three female rats were implanted and recorded, but one rat was removed due to improper implant location. There was no consistent response pattern in the ratio of fourth pulse to first pulse intensity, and both increased and decreased ratios in response to isoflurane anesthesia were seen. **CONCLUSIONS:** There was no consistent change in the ratio of fourth pulse to first pulse intensity of response to electrical stimulation under isoflurane anesthetic. These results may indicate the electrical stimulation of inhibitory neurons in one implant and excitatory neurons in the other. This study demonstrates that bipolar electrode implantation is useful for both electrical stimulation and recording in rat cortex in vivo.
Novel HDAC Inhibitor AB3 Regulates NF-κB and Notch Signaling in Medullary Thyroid Cancer Cell Lines

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Support: Department of Surgery NIH T35 Training Grant

BACKGROUND: To date, no effective systemic therapies for medullary thyroid cancer (MTC) have been established. AB3 is a promising new histone deacetylase inhibitor (HDACi) that has been shown to diminish MTC cell line proliferation. OBJECTIVE: Preliminary studies have suggested that phenotypic regulation by AB3 may be mediated by Notch3 signaling; however, AB3’s broader effects on gene expression and its mode of Notch3 activation are not well understood. METHODS: The effects of AB3 treatment on transcription were investigated using a DNA microarray. MTC cell lines (MZ-CRC-1 and TT) were treated with 2 μM AB3 or DMSO vehicle control. The microarray results were filtered to remove non-coding genes, unnamed genes, and genes with an absolute fold change <1.5 or ANOVA p-value >0.05 in either cell line. Selected DNA microarray results were then validated by qRT-PCR. Lastly, a luciferase reporter construct harboring deletion fragments of the Notch3 upstream region was used to map AB3 responsive elements within the Notch3 promoter. Luciferase activity of the constructs and a promoter-less backbone were measured following treatment with AB3 or vehicle control. RESULTS: 67,528 genes were assessed by DNA microarray after AB3 treatment. Of these, 2,243 showed differential expression after filtering. Genes affected by AB3 treatment included members of the nuclear factor-κB (NF-κB) pathway and its targets: NFKB1, ATM, PARP1, XIAP, IκBα, cyclin D1, and BCL2 (down-regulated), as well as SENP2 (up-regulated). These results were consistent with NF-κB pathway down-regulation and were validated by qRT-PCR. Interestingly, qRT-PCR showed substantial increases in Notch 1-3 transcription, including a 33 fold increase in Notch3. Deletion mapping identified the potential AB3-responsive elements within the human Notch3 promoter as a 31-bp fragment located 109 to 140 nucleotides upstream of the Notch3 start codon. CONCLUSIONS: Down-regulation of the NF-κB pathway by AB3 was demonstrated by DNA microarray and validated by qRT-PCR. NF-κB is a major stress-responsive transcription factor whose activation is associated with intrinsic cancer cell resistance to chemo- and radiation therapy. Understanding the mechanism by which AB3 down-regulates NF-κB could provide insight into improving HDACi-based therapies. Furthermore, we describe for the first time the potential HDACi binding site within the Notch3 promoter, which could determine the mechanism(s) of HDACi regulation of Notch signaling.
The Impact of Emergency Department Census on the Decision to Admit

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Mentor(s): Brian Patterson, MD, MPH

Support: Shapiro Summer Research Program; BerbeeWalsh Department of Emergency Medicine

BACKGROUND: The Emergency Department (ED) serves as a “gatekeeper” for inpatient services. ED physicians’ decisions to admit or discharge patients are responsible for significant variance in treatment costs. Admissions to the hospital are not only costly, but result in increased lengths of stay for patients in the ED, contributing to crowding. OBJECTIVE: We evaluated the effect of Emergency Department (ED) occupancy on disposition decisions made by ED physicians. METHODS: We performed a retrospective analysis using 18 months of ED adult patient encounters at a Level 1 trauma center. ED patient census information was calculated at the time of physician assignment for each individual patient, and included the number of patients in the waiting room (waiting room census), number of patients being treated in the ED (roomed patient census), and number of patients being managed by the patient’s attending (physician load census). A multiple logistic regression model was created to assess the association between these census variables and the disposition decision, controlling for potential confounders including acuity level, patient demographics, arrival hour, and chief complaint. RESULTS: We included 49,496 patients in this analysis. All three census measures showed a statistically significant positive association with admission when examined with univariable logistic regression. The adjusted odds ratio (aOR) per patient increase for waiting room census was 1.058 (95% CI=1.051-1.066), the aOR for roomed patient census was 1.015 (95% CI=1.012-1.017), and the aOR for physician load census was 1.024 (CI 1.017-1.030). When all three measures were included in a single multiple logistic regression only two variables, waiting room census (aOR=1.012, 95% CI=1.001-1.023) and attending physician load (aOR=1.010, 95% CI=1.001-1.020), were shown to significantly impact the disposition decision. CONCLUSION: Waiting room census and physician load census at time of physician assignment were positively associated with the probability that a patient would be admitted, even after controlling for potential confounders. Our data suggests that disposition decisions in the ED are influenced not only by objective measures of a patient’s disease state, but also by occupancy levels and physicians’ workloads. Further study is needed to capture the impact of physicians’ environments on disposition decisions.
Screening for Iron Deficiency (ID) and Iron Deficiency Anemia (IDA), More Than a Hematological Disease

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Mentor(s): Pamela J. Kling, MD

Support: Shapiro Summer Research Program; UW Cardiovascular Research Center

BACKGROUND: Iron deficiency (ID) and ID anemia (IDA) among infants constitutes a serious public health problem worldwide. In the US, routine screening using hemoglobin for ID is recommended by the American Academy of Pediatrics but not by the US Preventive Services Task Force. Lack of uniformity among providers for screening infants results in practice and outcome variation.

OBJECTIVE: To explore: (1) recommendation compliance after implementing an electronic best practice alert (BPA); (2) practice variation; and (3) the efficacy of using combined dual biomarkers for detecting ID in infants. METHODS: Hemoglobin (Hb), mean corpuscular volume (MCV), and ferritin (Fer) levels of infants between 8 and 12 mo of age seen at UW Family Medicine (FM) or Pediatric clinics from 1/1/14 to 4/8/15 were analyzed. Means and fail rates were compared for different individual and combined biomarkers.

RESULTS: 2545 children pre-BPA and 4068 children post-BPA were studied. The BPA increased screening rates from 48% (n=1127) to 72% (n=2921), with pediatricians more compliant with the BPA than FM. Among ID screening tests ordered, 96% were completed, with more being for an initial test than for follow-up. Single biomarker screens included CBC (n=1707), Hb (n=443), and Fer (n=378). For infants with values for >=1 biomarker, dual combined biomarker screens were constructed and assessed, including Hb+Fer (n=376), Hb+MCV (n=1840), and Fer+MCV (n=368). 90% of infants received their initial iron screen at 12 mo, 6% at 9 mo, 4% at 9 to 12 mo, and <1% at 8 to 9 mo. For initial screen, Fer alone (<12 g/L) found 15% of infants as ID and Hb alone (<11 g/dL) found 13% of infants as ID. Among infants with values for Hb+Fer, 8% had low Hb only, 11% low Fer only, 4% low Hb+Fer, and 77% normal. For Hb+MCV, 11% had low Hb only, 5% low MCV only, 2% low Hb+MCV, and 82% normal. For Fer+MCV, 4% had low MCV only, 4% low Fer+MCV, and 80% normal.

CONCLUSIONS: Hb, a measure of anemia, was most commonly used. Less commonly used, Fer is an important pre-anemic screen for ID and, in this analysis, identified an important high-risk cohort – those with normal Hb but low Fer. Thus, a combined screening test with both Hb and Fer can signal providers to intervene before the disease progresses to IDA, and this should be further studied. Research is also needed to assess follow-up measures taken in infants with low Hb and/or Fer for insight on how to optimize provider follow-up and quality of care.
Neurocognitive Performance and Increased Risk of Lower Extremity Musculoskeletal Injury After Concussion

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Department: University of Wisconsin Orthopedics and Rehabilitation; Badger Athletic Performance

Mentor(s): Alison Brooks, MD, MPH; Jennifer L. Sanfilippo, ATC, MS

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: Recent studies have demonstrated increased risk of musculoskeletal injury for athletes returning to play after a concussion. It is possible that subtle deficits in neurocognition and neuromuscular control, such as inhibited concentration, balance, or prolonged reaction times, could increase risk of subsequent injury following concussion. However, there is little understanding of the variables that may help characterize risk during this time of vulnerability. OBJECTIVE: Our goal was to determine if concussed collegiate athletes with worse neurocognitive or balance performance are at increased risk of acute lower extremity musculoskeletal injury (LEI) following return-to-play (RTP) from concussion.

METHODS: This retrospective cohort study examined male (n=70) and female (n=14) athletes participating in NCAA Division I football, ice hockey, soccer, wrestling, and basketball, who sustained a concussion between June 2011- May 2015. All student-athletes completed symptom score, computerized neurocognitive (ImPACT - Immediate Post-concussion Assessment and Cognitive Testing) and balance (BESS – Balance Error Scoring System) testing at baseline and post-injury time points (0-4, 5-11, 12-18, >30 days). The remaining academic school year following RTP from concussion was reviewed for acute, non-contact LEI, and athletes were divided into two groups (LEI, No LEI) for comparison. Differences in total symptom, ImPACT composite, and BESS scores over time were compared between groups using repeated measures ANOVA. RESULTS: 152 cases of concussion were identified during this time period. Following strict exclusion criteria, 104 cases in 84 athletes were used for analysis. 31 athletes sustained 32 LEI between RTP from concussion and the end of the academic school year. There were no significant changes in total symptom, ImPACT composite, or BESS scores from baseline to any post-injury time point between injured (LEI) and uninjured (No LEI) groups. CONCLUSIONS: There was no significant difference in neurocognitive or balance performance in concussed athletes who sustained a LEI after RTP compared to concussed athletes who did not sustain a LEI. ImPACT and BESS testing may not be sensitive enough to detect athletes with subtle impairments who may be at increased risk of LEI following concussion. Future studies may utilize different testing methods, such as the Sensory Organization Test, vestibular-oculomotor deficit testing, or other measures of reaction time.
Use of the Health Belief Model to Study Patient Perceptions of Antimicrobial Stewardship in the Acute Care Setting

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Mentor(s): Nasia Safdar, MD, PhD

Support: Shapiro Summer Research Program; Department of Medicine

BACKGROUND: Antibiotic resistant infections are a public health crisis and overuse of antibiotics is a main driver of resistance. Recent data suggest that 30-50% of antibiotic use in hospitals is unnecessary or inappropriate. Optimizing inpatient antibiotic prescribing through antimicrobial stewardship programs has therefore been identified as a major focus for curtailing the spread of antibiotic resistance. However, these programs currently target interventions at the hospital or individual prescriber level, and little research has been done to determine how patients may be able to contribute to stewardship efforts in the hospital setting. OBJECTIVE: To identify key themes associated with patient perceptions surrounding antibiotic use and the patients' role in antimicrobial stewardship using the Health Belief Model.

METHODS: We conducted semi-structured interviews with 30 general medicine inpatients taking anti-infectives at UW Hospital. Interviews followed a question guide consisting of open ended questions and discretionary follow-up probes. Interviews were audio recorded, transcribed and coded. Data were analyzed using the constructs of the Health Belief Model. RESULTS: Participants expressed low perceived personal susceptibility to being affected by antibiotic resistance although they identified antibiotic resistance as a serious public health threat. Views of susceptibility were influenced by a high degree of trust in physicians and misperceptions about the mechanisms underlying resistance. Participants expressed high self-efficacy and a desire to be involved in their healthcare. Perceived roles for patients in preventing the inappropriate use of antibiotics ranged from voicing concerns to active involvement in choosing between antibiotic treatments. Despite these beliefs, few participants reported being offered the opportunity to engage in such shared decision making while in the hospital.

CONCLUSIONS: Until now, patients have been left out of the focus of antimicrobial stewardship programs. This study proposes that patients may in fact serve an important role in improving antibiotic use in hospitals. However, likelihood of patient engagement in stewardship practices is currently limited by low perceived susceptibility and lack of cues to action. Further investigation into how patients may be engaged to facilitate the aims of antimicrobial stewardship programs may reveal new ways to improve antibiotic prescribing practices in the inpatient setting.
Role of Prolactin Receptor Signaling in the Regulation of FoxM1 Gene Expression

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Department: Department of Medicine, Division of Endocrinology, Diabetes, and Metabolism

Mentor(s): Dawn Davis, MD, PhD; Mieke Baan, DVM, DACVIM

Support: Shapiro Summer Research Program; Wisconsin Academy for Rural Medicine (WARM) Program; Department of Medicine

BACKGROUND: Diabetes mellitus (DM), projected to affect an estimated 552 million people worldwide by 2030, is characterized by a reduced number of functional beta cells in the pancreas. Finding ways to increase the number of beta cells, and thus increase insulin production in DM patients, is important for the development of new therapies to treat type-2 diabetes. The transcription factor Forkhead box M1 (FoxM1) is known to enhance beta cell proliferation when up-regulated in mouse and human pancreatic islets ex vivo. Yet, the pathways that drive FoxM1 expression are not entirely known. **OBJECTIVE:** Clarify the role of prolactin receptor signaling in the regulation of FoxM1 expression in the pancreatic beta cell.

METHODS: Placental lactogen (PL) and human growth hormone (hGH) signal through the murine prolactin receptor, and PL increases FoxM1 expression in mouse pancreatic islets. Min6 cells were culture in FBS (fetal bovine serum)-free DMEM media at 37° C and 5% CO2. Cells were left untreated (no Tx) or were treated with PL 500 ng/mL, hGH 500 ng/mL, or vehicle control (NaHCO3) for 8 and 24 hours. Total RNA was extracted using the RNeasy Mini Kit (Qiagen), and cDNA was prepared. FoxM1, beta actin, TPH1, TPH2, and Bcl-xl mRNA expression were assessed with quantitative PCR. Furthermore, FOxM1 promoter activity was investigated using a luciferase reporter-assay, after transfection with a pGL4 17[luc2/Neo] vector (Promega) containing the FoxM1 promoter sequence using lipofectamine 2000. **RESULTS:** There was an 8-hour treatment fold reduction (ΔΔCT) for the no treatment group (ΔΔCT = - 0.035) and human growth hormone (ΔΔCT = - 0.404). There was a slight, but not significant, fold up-regulation for PL (ΔΔCT = 0.047). There was a 24-hour treatment fold reduction for the no treatment group (ΔΔCT = - 0.027), and a slight, but not significant, fold up-regulation for PL (ΔΔCT = 0.029) and hGH (ΔΔCT = 0.156). **CONCLUSIONS:** 500 ng/mL PL or hGH treatment did not up-regulate FoxM1 mRNA expression in Min6 cells. Without establishment of positive controls, the luciferase–assay could not be done. The high baseline FoxM1 mRNA expression in the Min6 cell line may have attenuated further up-regulation of mRNA expression. Min6 cells were serum starved for 24 hours prior to treatment, but FoxM1 expression still remained high. Future research should repeat the experiment in a different cell line with lower FoxM1 baseline expression.
Survey of Physician Attitudes as a Barrier to Opioid Prescription

Authors: Lauren Hintz; James Cleary

Department: Department of Medicine, University of Wisconsin School of Medicine and Public Health

Mentor(s): James Cleary, MD

Support: Shapiro Summer Research Program; Department of Medicine

BACKGROUND: According to the World Health Organization’s (WHO) World Cancer Report, there was an estimated cancer incidence of 12.4 million individuals, and 7.6 million deaths from cancer. Opioid analgesics have been recommended by the WHO as the method of treatment for cancer pain, but many developing countries show inadequate opioid consumption levels, suggesting poor pain management of terminally ill cancer and HIV/AIDS patients. Among those countries with low opioid consumption are countries in Latin American and the Caribbean. OBJECTIVE: This study seeks to understand the major barriers to opioid consumption in the member countries of the Caribbean Palliative Care Association using a survey tool developed and previously implemented by Joranson here at the UW Carbone Cancer Center. METHODS: The survey tool is designed to assess physician practices and attitudes concerning the prescription of opioids for the use of cancer and HIV/AIDS related pain. The survey was distributed to licensed physicians in the five member countries of the Caribbean Palliative Care Association (Jamaica, Trinidad and Tobago; Grenada; Barbados and Cayman Islands. RESULTS and CONCLUSION: Results of the survey are forthcoming and will be presented.
Implementation of a Hand Hygiene Improvement Campaign in a Non-Referral Hospital in Rural Rwanda

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Mentor(s): Nasia Safdar, MD, PhD

Support: Farrell Public Health Scholars Program; Health-PACT

BACKGROUND: Healthcare-associated infections remain a significant risk for hospitalized patients around the world. Hand hygiene is known to be a critical action in ensuring patient safety. OBJECTIVE: To promote improvement of hand hygiene compliance amongst doctors and nurses in a rural hospital in Rwanda using the World Health Organization’s (WHO) “Five moments for hand hygiene” and modified hand hygiene educational tools. METHODS: The study was a cross-sectional, quasi-experimental design divided into four phases: (1) Preparedness and hospital administration commitment, (2) baseline evaluation, (3) intervention, and (4) follow-up evaluation. The intervention involved education, introduction of personal hand rub, and hand hygiene reminders. Hand hygiene evaluations were done using WHO’s direct observation technique. RESULTS: Overall hand hygiene compliance improved from 34.1% at baseline to 68.9% post intervention ($X^2 = 127.2$, $p<0.0001$). There was one sink for 29 patient rooms, and 100% of hand hygiene opportunities used alcohol based hand rub. Hand hygiene was significantly higher amongst doctors (69.3%) compared to nurses (31.3%) ($X^2 = 151.1$, $p<0.0001$). The only measure of hand hygiene compliance that did not improve was “after body fluid exposure,” which as 51.7% before intervention and 52.8% after intervention ($X^2 = 0.009$, $p=0.924$). CONCLUSIONS: Hand hygiene campaigns using WHO methods in sub-Saharan Africa have almost exclusively been implemented in large, referral hospitals. This study shows that slightly modified WHO tools for improving hand hygiene can also be successfully executed in low-income, rural hospitals in sub-Saharan Africa.
Improving Adherence to Clinical Practice Guidelines in a Low-Resource Primary Care Setting in Kenya

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Mentor(s): James H. Conway, MD

Support: Shapiro Summer Research Program; Department of Pediatrics

BACKGROUND: Penda Health is a community-based private healthcare organization located in Kenya. In Kenya, and at Penda Health, non-physician healthcare providers called Clinical Officers (COs) often deliver outpatient clinical services. Due to the substantial responsibility placed on mid-level care providers in Kenya, interventions to increase and evaluate their adherence to clinical quality guidelines may lead to substantial improvements in the quality of primary care. Our project focused on provider-level educational interventions to increase adherence to clinical practice guidelines and build skills related to patient-centered care. OBJECTIVE: First, to standardize Penda Health’s clinical training modules for childhood diarrhea, respiratory tract infections, tonsillitis, urinary tract infections, vaginal discharge, and family planning, in accordance with Penda Health’s Clinical Quality Guidelines (CQMs) and internationally-recognized standards. Second, to incorporate education related to patient-centered care within the training modules. Third, to develop an online training platform for Penda Health. METHODS and RESULTS: The relevant training modules were reviewed for consistency and formatted to emphasize evidence-based clinical quality guidelines to be used at all Penda Clinics. Penda Health’s “Patient-Provider Interaction” training module and expectations were incorporated into each clinical training module to better emphasize the importance of both evidence-based and patient-centered primary care. Finally, after considering multiple online training programs, we chose the SkyPrep system and uploaded a prototype training module and quiz for COs to complete. CONCLUSIONS: This project had concrete results through which Penda Health is able to improve upon existing provider training methods. The integration of evidence-based clinical practices with guidelines for patient-centered care is a novel approach for Penda Health, through which both clinical outcomes and patient satisfaction may be improved. Next steps include incorporating all Penda Health trainings into the online system, improving the assessment of COs who have gone through the trainings, garnering feedback from COs about the efficacy and functionality of the online trainings, collecting data from charts to compare with prior CQM adherence, and collecting data from patients to evaluate any improvements in patient satisfaction.
BACKGROUND: With HIV seroprevalence as high as 1.5% among incarcerated individuals, HIV care continuity upon release from prison is essential in maintaining T cell counts and reduced viral load. Reintegration presents many barriers to HIV care, such as mental health concerns, substance use relapse, access issues, and status disclosure concerns related to HIV stigma. HIV stigma exists in multiple forms, including internalized, perceived, and enacted stigma. In general, high levels of HIV stigma have been linked to poor HIV care outcomes. OBJECTIVE: Through data from semi-structured interviews of people living with HIV who were recently released from Wisconsin correctional facilities, we hope to better understand of HIV stigma and its influence on HIV care continuity during reintegration back into the community. METHODS: Eligible participants for a qualitative study on HIV care adherence during reintegration were recruited through a convenience sampling of incarcerated individuals with an upcoming release date who were receiving care from the UW HIV Comprehensive Care Clinic. Participants completed two semi-structured, in-depth interviews guided by the situated information-motivation-behavioral skills (sIMB) framework. The first interview was completed within a week prior to release, with the second completed six-months after release. Interview data was transcribed into NVivo Versions 9 and 10 and coded for stigma measures, based on a codebook drafted by the research team. Codes were verified using consensus coding completed by at least two coders. RESULTS: Internalized stigma was most commonly presented as HIV status disclosure concerns and adverse mental health outcomes. It was the most prevalent form of stigma reported and had a direct influence on participants' reported willingness to seek HIV care. Perceived stigma included social reactions and interpersonal experiences surrounding HIV status, which demonstrated social acceptance as a protective factor for continuity of care. Enacted stigma was less commonly reported, but it was often linked to participants' internalization of stigma and the subsequent adverse mental health outcomes that discouraged care-seeking behavior. The data was consistent with findings that high internalized stigma was linked to adverse mental health outcomes and subsequently poor adherence to care. However, in spite of high levels of reported stigma, as many as 95% of participants were able to keep their viral loads undetectable and attended at least one appointment with an HIV care provider in the six months since release. Majority of participants also reported high levels of social support, either from family, friends, partners, or professional contacts, to help them navigate barriers to reintegration, beyond managing their HIV care. CONCLUSIONS: Assistance from objective, professional sources, such as the linkage-to-care specialists and counselors, provides essential social support that is protective against stigma. To most effectively support HIV care continuity, personal and professional social support should holistically address the broad array of barriers to HIV care inherent in the reintegration process.
Identification of Predictors of Post-Operative Complications in Renal Cell Carcinoma Thermoablation Patients

Authors: Saira Khanna; E. Jason Abel; Timothy Ziemlewicz; Shane Wells; Marki Klapperich; Tyler Wittman; Sara Best

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Mentor(s): Sara Best, MD

Support: Shapiro Summer Research Program; Department of Urology

BACKGROUND: Thermoablation techniques to treat renal cell carcinomas (RCC) have become increasingly popular and effective, due to the reduced complications and invasiveness. The reported major complication rate for cryoablation is 4.9%; similar to the complication rates for radiofrequency ablation, open partial nephrectomy and open radical nephrectomy, but far lower than for laparoscopic partial nephrectomy. Ablation could potentially be performed on an outpatient basis, thus saving considerable cost, but predictors of immediate complications are lacking. OBJECTIVE: The goal was to identify patient and tumor characteristics predictive of post-operative complications, specifically bleeding complications, in patients undergoing percutaneous thermoablation to treat small RCCs. METHODS: An IRB-approved retrospective chart review was completed on 313 patients who underwent a thermoablation for RCC from 2001-2015. We excluded patients who underwent laparoscopic approach or had ablation of metastases, leaving a total of 235 patients. A patient was defined as having a bleeding complication if he had a symptomatic hematoma, a related blood transfusion within 30 days of the ablation, readmission for bleeding or a hematoma, or a hospital stay greater than one day due to bleeding. Wilcoxon rank sum and Fisher's exact tests were used to determine which factors are associated with complications in these patients. RESULTS: 6 (2.5%) patients had a bleeding complication and these patients had a higher BMI (39.4 vs 31.3, p=0.047), larger tumors (median 4.0 vs 2.6cm, p=0.04), higher RENAL nephrometry score (9 vs 7, p=0.056) and were more likely to have a hematoma seen on the immediate post-procedure CT (67% vs 12%, p=0.004). Only one tumor <3cm bled. High grade complications were rare (3.4%) and no patient factors associated with these were identified, possibly because 5/8 complications occurred more than a week after surgery. CONCLUSION: In this patient population, bleeding complications were rare, as were early post-operative serious complications. Seeing a hematoma on the post-op CT scan, larger/more complex tumors, and high BMI may help identify patients who may benefit from inpatient observation after ablation. Otherwise, most percutaneous ablation patients could experience cost savings through early discharge and it could be performed as an outpatient procedure.
Anesthetic Management of Patients Presenting for Surgical Management of Substernal Goiters

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Mentor(s): Richard E. Galgon, MD, MS

Support: Shapiro Summer Research Program; Department of Anesthesiology

BACKGROUND: Anesthesiologists maintain a high suspicion for airway management difficulties in patients with substernal goiters who present for partial or total thyroidectomy. However, the current literature suggests that this heightened regard may be unwarranted. OBJECTIVE: Is the presence of a substernal goiter associated with an increased risk for perioperative airway management complications? METHODS: After IRB approval, charts of patients who presented primarily for a partial or total thyroidectomy between February 2014 and June 2015 were identified using departmental billing records and reviewed. Patients presenting for other procedures were excluded. Patient characteristics, procedure data, and recovery data were extracted and analyzed. Intergroup (with vs. without substernal goiter) comparisons were performed using unpaired t, chi-squared, and Fisher's exact tests. RESULTS: From 438 encounters, 434 were analyzed after exclusions. Twenty-five (6%) patients had a substernal goiter. Patient characteristics were generally similar between patients with and without a substernal goiter. Exceptions to well-balanced characteristics included age, ASA score, Mallampati score, and the presenting symptom of dyspnea (all higher or worse in the substernal group). Substernal goiter patients more often were managed in the main operating room (48% vs. 14%, p = 0.0001), were fiberoptically intubated (32% vs. 1%, p < 0.0001), remained intubated at procedure end (8% vs. 1%, p = 0.042), and had larger goiters (101.5 ± 79.4 g vs. 27.0 ± 35.2 g, p < 0.0001). However, no statistically significant differences in the incidence of difficult intubation (4% vs. 1%, p = 0.303), intraoperative complications (4% vs. 3%, p = 0.57), post-operative acute complications, recurrent laryngeal nerve injury, surgical site infection, 30-day re-hospitalization, or 30-day all-cause mortality were found between the two groups. In addition, no statistically significant differences in Phase I, Phase II, or overall recovery times (regardless of disposition) were found between the two groups. CONCLUSIONS: From this retrospective study, the presence of a substernal goiter does not appear to result in an increased risk for perioperative airway management complications, and some patients with a substernal goiter may be safely managed in an outpatient surgical environment. However, the study sample size remains limited, and further study is necessary to help delineate these patients.
Percutaneous MW Ablation of 100 T1a Renal Cell Carcinoma: Tumor Complexity and Technique Effect on Complication Rate

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Mentor(s): Fred T. Lee, Jr., MD; Shane A. Wells, MD; Christopher L. Brace, PhD

Support: Shapiro Summer Research Program; Department of Radiology

PURPOSE: To examine the safety and early oncologic efficacy of percutaneous microwave (MW) ablation for the treatment of 100 cases of biopsy-proven T1a renal cell carcinoma (RCC). METHODS: A retrospective single center review of 96 consecutive patients with 100 T1a N0M0 biopsy-proven RCC (68 M/28 F, mean age 66±9.4; tumor diameter 2.6±0.8) treated with percutaneous MW ablation between March 2011 and June 2015. Patient and procedural data were collected including BMI, comorbidities, tumor size, histology and grade, RENAL scores, number of antennas, generator power and duration of ablation. Mean patient BMI was 32.2 (SD=8.6) and mean Charlson comorbidity index was 6 (SD=1.8). Mean RENAL nephrometry was 6.6 (SD=1.6). Technical success, presence of local tumor progression (LTP), and presence of complications were assessed at immediate and serial follow-up imaging.

RESULTS: Technical success was achieved for 100 tumors (100%) including 52 moderate to highly complex RCC. Mean clinical and imaging follow-up was 14 months (range 0-42) and 12 months (range 0-38) respectively. One treatment failure (1%) was identified 25 months post-procedure. Local progression-free survival (PFS), cancer specific survival (CSS) and overall survival (OS) were 95/96 (99%), 96/96 (100%) and 93/96 (97%), respectively. No change in eGFR was noted post-procedure (p=0.49). There were 11 (11%) early (0 – 30 days) complications with three directly related to the ablation procedure and 6 (6%) delayed complications, all urinomas. CONCLUSION: Percutaneous MW ablation is an effective treatment option for low, moderate and highly complex T1a RCC with a low rate of procedure-related complications. Long-term follow-up is needed to establish durable oncologic efficacy and survival relative to competing ablation modalities and surgery.
Examination of White Matter Tract Abnormalities in Pediatric PTSD

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Mentor(s): Ryan J. Herringa, MD, PhD

Support: Shapiro Summer Research Program; American Academy of Child and Adolescent Psychiatry Summer Medical Student Fellowship Award

BACKGROUND: Pediatric post-traumatic stress disorder (PTSD) is a disabling condition that manifests through symptoms of re-experiencing, avoidance, negative cognitions, and hyperarousal. PTSD prevalence doubles from 3.7% at age 14 to 7.0% by age 18, underscoring the importance of achieving a clearer understanding of its pathophysiology. OBJECTIVE: To date, fear-circuit (FC) white matter (WM) tract integrity has not been examined in pediatric PTSD. Accordingly, the current study analyzed structural properties of the uncinate fasciculus (UF) and the cingulum bundle (CB) in a sample of pediatric PTSD and healthy youth. Non-FC tracts were also assessed, namely, the superior and inferior longitudinal fasciculi (SLF and ILF), without the expectation of group differences. METHODS: Participants included 35 healthy youth and 33 youth with PTSD ages 8-18. PTSD diagnosis, severity, and symptom cluster scores (re-experiencing, avoidance, and hyperarousal) were assessed along with depression and anxiety scores. WM properties were assessed via extracting four Diffusion Tensor Imaging-generated weighted scalar means (WSMs): Fractional Anisotropy (FA), Mean Diffusivity (MD), Axial Diffusivity (AD), and Radial Diffusivity (RD). Multivariate general linear models interrogated the characteristics of each tract. RESULTS: No group differences were found for UF or CB. However, in PTSD youth, CB Right AD was inversely correlated with total PTSD, avoidance, and negative cognition symptoms. No group differences were found for SLF. However, in PTSD youth, SLF Bilateral RD was positively correlated with re-experiencing and inversely correlated with depressive symptoms. A significant group difference was present for ILF, revealing reduced ILF FA bilaterally in PTSD youth. Moreover, ILF Bilateral FA was inversely correlated with general anxiety and depressive symptoms in PTSD youth. CONCLUSIONS: The ILF group difference, coupled with its relationship to symptom severity, suggests a causal relationship between ILF abnormalities and trauma-related illness. Furthermore, symptom correlations for the CB and SLF suggest that abnormalities in these tracts may influence the expression of PTSD, depression, and anxiety symptomatology. Future work with this sample will employ whole-brain voxel-wise analyses to provide enhanced localization of tract abnormalities in the greater effort to explore WM abnormalities in pediatric PTSD.
The Impact of Previous Ankle Injury on the Health of Young Athletes

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Mentor(s): Timothy A. McGuine, PhD, ATC

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: Ankle sprains are the most common injury in high school sports. Small clinical studies have suggested that ankle sprains in adolescence can lead to long term disablement by causing chronic instability, which can lead to osteoarthritis and lower quality of life. Ankle impairment thus poses a significant public health concern. However, data on disablement and health related quality-of-life (HRQL) in the active adolescent athletes who have sustained an ankle sprain is limited. Collecting data with validated self-report measures of disablement will allow providers to quantify ankle disablement post ankle sprain injury. OBJECTIVE: The goal of this study is to describe the impact that previous ankle injuries have on the self-reported ankle function, ankle instability, HRQL, and activity level in a cohort of adolescent athletes. METHODS: Cross-sectional survey study. Approximately one thousand (male and female, age 13-18) basketball, football, soccer, and volleyball players were recruited at local high schools and club sports venues to serve as subjects. Preliminary data analysis was carried out using 2 tailed independent t tests for independent samples to determine if the scores on the self-report measures were different for athletes who had and had not sustained a previous ankle sprain. RESULTS: Four hundred and ninety-nine male and 503 female athletes completed the study. Two hundred and ninety-seven (29.64%) of the subjects reported sustaining a sprain on one, or both ankles within the previous 36 months. Subjects who had sustained an ankle sprain had significantly lower self-reported physical health (<0.001), lower ankle function (p = <0.001), and overall HRQL (p = 0.001) than subjects who did not sustain an ankle sprain. CONCLUSIONS: Previous ankle injuries are correlated with increased ankle disablement and reduced HRQL. These results could be used to justify the funding of a large longitudinal population based study on the long term repercussions of adolescent ankle injuries. These results also provide the rationale to coaches and trainers to utilize ankle sprain prevention strategies, as well as encourage the funding of future research on sprain prevention.
BACKGROUND: Mastery of motor skills necessary to perform orthopedic surgery requires years of practice. Recent shifts in the education of technical skills requires surgical trainees to gain competency before operating on patients. With the increasing availability of inexpensive additive manufacturing (3D printing) devices, there is a growing interest in 3D printed anatomical models for use in surgical training. 3D printing from Digital Imaging and Communications in Medicine (DICOM) files offers the possibility of patient-specific, high fidelity anatomical models that students, residents, and surgeons may use to practice surgical technique. OBJECTIVE: The aim of our study was to identify 3D printable materials that have haptic fidelity to bone and thus can be used for surgery simulation. Based on mechanical properties we identified seven potential candidates and tested for haptic fidelity to bone during manipulation with common orthopedic surgical instruments. METHODS: Seven 3D printed materials were individually presented to a group of orthopedic surgeons (n=7), orthopedic spine fellows (n=3), and orthopedic resident surgeons (n=6). After viewing a tutorial video, participants performed eight common orthopedic surgical tasks using the following instruments, power drill, tap, screw, burr, power saw, and osteotome. After performing each task, participants were asked to rate on an 11-point likert scale fidelity to bone (0 being very dissimilar to bone, 10 being indistinguishable from bone). In addition to rating machining actions, participants rated the overall educational value of each material. RESULTS: Overall educational value was chosen as the primary assessment of each polymer. Acrylonitrile Styrene Acrylate (ASA) from Stratasys received the highest average rating of 6.69; additionally ASA was ranked the highest in each individual machining category. Other potential candidates included ABS-M30 (average rating of 6.00) and PPSF (average rating of 6.19). CONCLUSIONS: We identified a list of likely candidates for simulation; however, limitations exist regarding cost. The majority of the polymers chosen were printed on machines that most orthopedic departments could not financially manage. In addition, our study focused primarily on polymers supplied by one printing company, Stratasys, it is important to note that other companies with a range of other polymers and printing techniques exist and thus could be investigated in the future for use in simulation training.
Effectiveness of Hexaminolevulinate Fluorescence Cystoscopy for the Diagnosis of NMIBC in Daily Clinical Practice

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Department: Department of Urology, University of Wisconsin School of Medicine and Public Health

Mentor(s): Tracy Downs, MD

Support: Shapiro Summer Research Program; Wisconsin Academy for Rural Medicine (WARM) Program; Department of Urology

BACKGROUND: Transurethral Resection of Bladder Tumors (TURBT) is a relatively non-invasive procedure used by urologists to visualize the internal surface of the bladder and allow resection of tumors. The current standard of care involves White Light Cystoscopy (WLC), which allows the urologist to map and resect all visible lesions. Blue light Cystoscopy (BLC) involves the administration (intravesically) of a photosensitizing agent one hour prior to TURBT, and when using BLC, lesions become fluorescent, aiding the urologist’s ability to remove all cancerous lesions. OBJECTIVE: The primary objective of this Shapiro sponsored summer research project is to retrospectively analyze a single institution’s experience with Blue Light Cystoscopy (BLC) for patients who have undergone TURBT and/or Cystoscopic biopsy at UWHC from 2002-2015. We aim to determine if the use of BLC leads to increased tumor detection (especially for Carcinoma in situ (CIS)) compared with WLC. We also want to see if BLC leads to a significant reduction in overall bladder cancer recurrence rates and lower recurrence rates of high-risk tumors compared with WLC. METHODS: Using the electronic medical records database, EPIC, pathological and surgical information for patients who underwent a TURBT between 2002-2015 was recorded. Excel and the statistical analysis program REDCap (Research Electronic Data Capture) was used to analyze and store the information in the IRB approved Superficial Bladder Cancer database. This information was stratified according to a number of categories including patient date of birth, stage of cancer resected, grade of cancer resected, WLC only, patient gender, time to recurrence BLC vs WLC, time and date of surgery, whether patient uses tobacco, tumor size (cm), whether or not CIS was present, and whether or not prior treatment had been performed. RESULTS: A total of 512 patients are in the database. There were 73 procedures performed with BLC and 496 with WLC only. There was improved CIS detection with BLC, with 30% of BLC procedures showing CIS vs. 15% in WLC procedures (P val = .0014). We have not yet determined recurrence-free survival rates for WLC vs BLC. CONCLUSIONS: BLC can lead to improved detection of bladder tumors that are harder to visualize in surgery, such as CIS. We hope to find that increased detection using BLC of these types of tumors and tumor margins will lead to an increase in recurrence free survival for patients with bladder cancer.
The Effect of Topical JAG1, a Notch Activator, on Wound Closure Rates in Diabetic Mice

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Mentor(s): Timothy King, MD, PhD, FACS, FAAP

Support: Department of Surgery NIH T35 Training Grant; UW Medical School Start up Fund; NIGMS KO8GM101361

INTRODUCTION: Decreased rates of wound healing affect millions of diabetic patients annually. We are interested in discovering novel strategies to enhance the wound healing process in diabetic patients. We have previously shown that inhibiting Notch inhibits wound healing, thus we propose that up-regulation of Notch would increase rates of wound healing. JAG1 is a known activator of Notch. OBJECTIVE: We hypothesized that applying topical JAG1 to stented excisional wounds on the backs of diabetic and wild-type mice would result in increased Notch activity, and thus an increased wound healing rate as compared to untreated wounds. METHODS: 8-week old, healthy male diabetic mice (db/db, n=44), or heterozygous mice exhibiting wild-type phenotype (WT/db, n=44) were anesthetized and after depilation, two 1cm2 full-thickness wounds were placed on their backs extending through the panniculus carnosus. A 12 mm diameter silicone stent was secured around each wound with cyanoacrylate glue and interrupted 5-0 nylon suture to prevent healing by contraction. Treatment application began postoperative day 3. Dressings were changed and treatments of JAG1 (10 nM) or vehicle (PBS) were topically reapplied and digital photographs were taken daily thereafter for 14 days. To conclude, the mice were sacrificed and wounds were harvested for histological and protein analysis. Wounds are being analyzed using ImageJ software and are expressed as a ratio of wound area to stent area. Wound area will be calculated as a percent area of the original wound size. Statistical significance will be defined as p<0.05 using the students’ t-test. RESULTS: Partial to complete re-epithelialization was seen in the wounded tissues over the experimental period in both the control & JAG1 treated groups. Data is currently being analyzed and both diabetic and wild-type mice treated with topical JAG1 are expected to have an increased rate of wound closure when compared to wounds treated with PBS. No significant local side effects such as increased edema or allergic reaction were noted in the JAG1-treated mice. CONCLUSIONS: JAG1 is expected to increase the rate of re-epithelialization of cutaneous wounds in the in vivo diabetic murine stented wound-healing model. These findings would indicate that Notch signaling plays a crucial role in wound healing in mice. Further study of Notch in diabetic wound healing should be conducted which may lead to better therapeutics for the wound healing process in patients.
**Study and Production of Procedural Videos For Neurosurgical GME Quality Improvement**

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**Mentor(s):** Joshua Medow, MD

**Support:** Shapiro Summer Research Program; Department of Neurological Surgery

**BACKGROUND:** The Accreditation Counsel for GME provides general guidelines for neurosurgical NS training that allow for a high degree of variability in the educational structure across institutions. Surgical videos have been shown to increase resident competency as measured by objective assessments. Only 30% of surveyed residents claim to use surgical videos for learning procedures. This may be due to the uncertainty of the quality associated with using online videos. **OBJECTIVE:** Develop a video quality assessment template VQAT to investigate the quality of online videos for basic NS procedures and similarly complex procedures. Survey NS residents regarding the current use of videos. Use data to produce optimal instructional videos for NS GME. **METHODS:** The VQAT was developed to measure technical and educational aspects of online videos. Two independent researchers reviewed the videos to validate the inter-rater reliability. 14 UW NS residents were surveyed regarding their current use of online videos and the sources of videos. The results of the aforementioned methods were used with the VQAT criteria to produce a high quality, novel first person perspective, instructional video demonstrating proper external ventricular drain placement. **RESULTS:** External ventricular drain n=2, average technical aspect score 19.5/23 SD=0.7; average educational aspect score 13.5/20 SD=2.1; average total score 33/43 SD=1.4)(Lumbar drain n=3, 19.3/23 SD=2.1; 11.7/20 SD=5.9; 31/43 SD=7.8)(Endotracheal intubation n=9, 20/23 SD=1.0; 10.9/20 SD=6.2; 31/43 SD=6.8)(Venous central line via the jugular vein n=9, 20.9/23 SD=0.3; 14.7/20 SD=4.4; 35.6/43 SD=4.4). VQAT inter-rater reliability (Pearson Correlation, n=15 videos, technical aspect score = 0.94, educational aspect score = 0.87, and total score = 0.91). Video length and VQAT score were proportional for endotracheal intubation and central line videos (0.87, R2 =0.75 and 0.62, R2 = 0.38 respectively). All respondents (7/14) expressed a strong desire to formally incorporate videos into their education. **CONCLUSIONS:** Video resources for basic NS procedures are limited. Available videos omit critical nuances of technique, instruments, and patient care bringing into question the comprehensiveness of these videos as educational tools. Videos are highly desired by residents to fill this void in the NS GME curriculum. The VQAT is a valid quality assurance tool, and template for producing high quality videos as demonstrated by our EVD video.
The Effect of Methotrexate on Sperm Quality in Men With Inflammatory Bowel Disease

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Mentor(s): Sumona Saha, MD, MS

Support: Shapiro Summer Research Program; Department of Medicine, Division of Gastroenterology

BACKGROUND: The inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn’s disease (CD), are chronic inflammatory conditions of the gastrointestinal tract which peak in incidence during the reproductive years. Methotrexate (MTX), an immunomodulator used to treat IBD, is a teratogen known to induce abortion in women. It is contraindicated for use in women who may become pregnant. Few data, however, are available on the effects of MTX on male reproductive capacity. Currently the literature on MTX and male fertility range from several case reports and series reporting no effect on sperm quality to others reporting reversible sterility. Given its therapeutic benefits, more information is needed with regard to MTX’s effect on male fertility in patients with IBD. OBJECTIVE: The purpose of this project was: 1) to perform a literature review to evaluate the impact of MTX on male fertility and male fertility in patients with IBD and 2) to create a protocol to determine whether the treatment of IBD patients with MTX is associated with an increased risk for decreased sperm quality using multiple methods for assessing male fertility. METHODS: A literature search was conducted with findings summarized in a review paper. A protocol was written to study men aged 18 to 40 years with a confirmed diagnosis of UC or CD who will be recruited from the gastroenterology clinic at UW Health. Seventy-five patients who have taken MTX for at least 3 months and 75 age-matched controls with IBD who are not on the drug will be recruited. Subjects will undergo semen collection at the UW Health Generations Fertility Clinic. Specimens will undergo conventional microscopic analysis using World Health Organization criteria, molecular testing using a sperm DNA fragmentation assay and oxidative stress adduct testing, and sperm morphologic analysis using Fourier Harmonic Amplitudes. RESULTS: A review paper was written. Source documents and a data collection spreadsheet have been created. The protocol was revised to include molecular testing of specimens, and IRB approval is currently pending. We anticipate recruitment will begin in fall 2015. CONCLUSIONS: After a thorough literature search, no data on MTX and its effect on male fertility in IBD patients could be found. Because MTX is widely available and may have a favorable side effect profile compared to other immunosuppressants used to treat IBD, determining its impact on male fertility is important.
Complications of Baclofen Pumps in Scoliosis Surgery for Cerebral Palsy Patients

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Mentor(s): Kenneth Noonan, MD

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: Cerebral palsy (CP) is the most common motor disability in childhood, with an estimated worldwide prevalence rate of 1.5-4 of 1,000 live births. Up to 72% of spastic quadriplegic CP patients develop scoliosis. Most of these patients need surgical spine fusion to enhance their quality of life by improving sitting ability. However, there is a complication rate of nearly 30% associated with spinal fusions in patients with CP. Patients with CP are at a higher risk for perioperative complications due to their diagnoses of co-morbidities. Many CP patients are also treated with intrathecal baclofen (ITB) pumps for their muscle spasticity. The safety and efficacy of ITB pumps have been evaluated, but there are significant complications associated with their placement before, during or after spinal fusion in patients with CP. Whether ITB pumps increase the progression of scoliosis in CP patients has not been proven.

OBJECTIVE: We hypothesize that complications and surgery time increase in CP patients with ITB pumps compared to patients without ITB pumps. Aim 1: Determine if ITB pumps placed in CP patients for spastic quadriplegia cause more complications and longer surgery time for scoliosis surgery compared to CP patients without ITB pumps who also undergo scoliosis surgery. Aim 2: Measure the rate of progression of scoliosis in CP patients with ITB pumps compared to those without to further explore the possible complications associated with ITB pumps. METHODS: An IRB proposal was prepared and approved for the study. The retrospective study involved gathering data from the electronic medical records of 141 patients identified by ICTR based on billing codes for posterior spine fusion and ITB pump insertion with CP and scoliosis diagnosis codes. So far, 78 patient charts have been analyzed with 39 patients qualifying for the study. Data collection regarding complication rates associated with surgery and the spinal curve measurements is still ongoing and will be analyzed by a statistician. RESULTS: Data collection is still ongoing. IRB approval was successfully established. I learned the process of analyzing electronic medical records and measuring Cobb angles of spinal curves. CONCLUSIONS: Research is a time-consuming process, especially when collecting data from CP patients with many co-morbidities and with records of varied formatting. I look forward to continuing the research study and the implications that may be found regarding best practices.
Apicidin Inhibits Major Vascular Smooth Muscle Cell Pathogenic Phenotypes

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Mentor(s): K. Craig Kent, MD; Lian-Wang Guo, PhD

Support: Shapiro Summer Research Program; Department of Surgery A.R. Curreri Chair Account

BACKGROUND: Intimal hyperplasia leads to failure of 20-50% of vascular reconstructions. The underlying cause is smooth muscle cell (SMC) pathophysiology characterized by proliferation, migration, and dedifferentiation. Apicidin, a class I histone deacetylase (HDAC3) inhibitor, has been shown to have a potent anti-proliferative effect in a number of cancers. The mechanism of its effect appears to be through activation of tumor suppressor proteins. OBJECTIVE: To evaluate the effectiveness of Apicidin in preventing recurrent stenosis after vascular reconstruction. METHODS: In vitro assays included proliferation (CellTiter-Glo), migration (scratch assay), and western blotting. In vivo analysis was conducted using a rat model of carotid balloon angioplasty. RESULTS: Rat SMCs were pretreated (2 hours) with Apicidin and then stimulated with 10% Fetal Bovine Serum (FBS) for 72 hours followed by measurement of proliferation. Based upon an initial dose response curve, we found the optimal concentration of Apicidin to be 500nM, which reduced proliferation by 72.9% ± 5.3% (p < 0.05). Pretreatment of SMCs with Apicidin also reduced SMC migration by 77.1% ± 2.0% (p < 0.01) at 24 hours in response to 10% FBS. We have previously shown that the combination of TGF-β/Smad3 is a potent stimulant of SMC dedifferentiation. To evaluate whether Apicidin can reverse this effect and promote differentiation, SMCs transfected with Smad3 were pretreated for 2 hours with Apicidin and then stimulated with TGF-β (10ng/mL) for 48 hours. Reductions of several proteins indicative of SMC differentiation by TGF-β/Smad3 were rescued by Apicidin by the following percentages: Calponin (22.3%), Myosin Heavy Chain (108.9%), and Smooth Muscle Actin (30.0%). Blots were re-probed for acetylated histone, which was increased 14.3 ± 2.1 fold (p < 0.05). Finally, adult rats underwent carotid balloon angioplasty with periadventitial application of Apicidin (500µg) in 23% pluronic gel. Carotid samples were harvested at 21 days, yielding preliminary results indicating that Apicidin reduces neointimal area by 55% while preserving luminal integrity. CONCLUSION: The HDAC3 inhibitor, Apicidin, can reduce SMC pathophysiology, and subsequently lead to a significant reduction in intimal hyperplasia. Inhibition of HDAC3 could be an effective therapy for the prevention of recurrent stenosis leading to improved outcomes in patients treated for vascular disease. (Continued experimentation is in progress.)
Integration of Conventional Medicine and Traditional Medicine in Hmong Communities of Vietnam and China

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Mentor(s): Elizabeth Jacobs, MD, MPP; Jacob Hickman, PhD

Support: Shapiro Summer Research Program; UW Carbone Cancer Center Pilot Award

BACKGROUND: It has been 40 years since the first wave of Hmong refugees have resettled in the United States. Hmong immigrants and their children often use both traditional Hmong healing practices and modern biomedicine, which can be frustrating and challenging for both patients and physicians. Not much is known about how this use of both modern biomedicine and traditional Hmong ethnomedicine affect health disparities and quality of care for this population.

OBJECTIVE: To gain a better understanding of how Hmong residents of Vietnam and China view and use modern medicine and traditional Hmong healing systems. METHODS: We interviewed adult Hmong residents of Sapa, Vietnam or Wenshan, China. The semi-structured interview guide was designed to elicit attitudes and perceptions that Hmong individuals and their healthcare providers have about conventional biomedicine and traditional Hmong healing practices, how they integrate these two approaches to health, if at all, and how they make decisions about using these two different approaches. A final codebook was developed after a systematic review of field notes and recordings in the analysis of the data to identify common themes.

RESULTS: A total of 43 adult individuals were interviewed (19 males, 24 females): 31 with Hmong adults who were not trained physicians or healers (14 males, 17 females) and 12 healthcare contributors (8 Hmong shamans, 4 clinical care providers). Twenty-seven participants (10 males, 17 females) were from Sapa, Vietnam and 16 participants were from Wenshan, China (9 males, 7 females). All the Hmong participants interviewed in Sapa, including the Hmong shamans, from Sapa used some form of both Hmong practices and clinical biomedicine. In contrast, only 25% of Hmong individual from Wenshan, including the Hmong shamans, used both types of care. All the healthcare contributors acknowledged the limits to their medical model, be it traditional or modern. Each participant provided some positive and negative insights to Hmong ethnomedicine and clinical biomedicine. CONCLUSIONS: Preliminary analysis suggest that familiarity with the metaphysical-psychosocial components of Hmong traditional medicine and physical element in clinical biomedicine were important in their integration for health seeking Hmong individuals. Additionally, Hmong traditional medicine was utilized by more participants in Sapa compared to those in Wenshan, suggesting the important role that different socio-political pressures play in influencing the preferred medical model of choice amongst Hmong patients.
Building Relationships With African American Patients: A Qualitative Evaluation of Clinician Behaviors

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Mentor(s): Jonas Lee, MD

Support: Prevention Innovation in Medical Education (PRIME) Madison Program

BACKGROUND: African Americans living in Madison and Dane County, Wisconsin experience disparities greater than that of the remainder of the state and nation on virtually every indicator of health and social well-being. When controlling for other factors, race remains a significant, independent risk factor for disparities. Positive patient-physician interactions can foster trust and decrease feelings of perceived discrimination. Patient perception of discrimination by their physician results in lower satisfaction with care received and can result in less continuity of care and worse health outcomes. Therefore, we conducted a qualitative evaluation with African Americans to define the factors that lead to positive and productive health care interactions. OBJECTIVE: The primary objective of this project is to determine specific physician behaviors which foster a sense of trust and partnership between African Americans and health care providers. METHODS: Nine semi-structured, qualitative interviews were conducted with a total of 10 African Americans living in Dane County. Interviewees were identified through a review of clinic schedules and through snowball referral, and interviews were conducted during May-August 2015 in Madison, WI. Eight of the interviewees were female, while two were male. Nine interviewees were Wingra Clinic patients, while one was a community member. An appreciative inquiry method of interview was employed to focus on positive interactions and solutions from the point of view of patients and community members. Interviews were digitally recorded, professionally transcribed, coded, and analyzed by the research team to identify major themes that lead to positive patient-physician interactions. RESULTS: Six key themes emerged that can lead to positive patient-physician interactions. Of these six themes, five of them related directly to physician behaviors: Health Literacy and Education, Relationship-Building, Adequate Time, Patient-Centered, and Equality. The final theme that emerged, Patient Self-Efficacy, is a behavior that patients can do to improve interactions. CONCLUSIONS: Interviews confirmed the importance of physicians developing a supportive, therapeutic relationship with shared decision-making. Patient behaviors, including self-advocacy and willingness to develop a relationship with a provider are also important. These results are consistent with current literature but provide a unique perspective by employing an open-ended, patient-centered, and solution-focused approach. After identifying key domains in which to improve the patient-physician interaction, we recommend that Wingra Clinic physicians are educated regarding these findings and that a toolkit is developed to support clinicians across these domains. Future studies should be conducted to assess for generalizability of the obtained results.
Liver Surface Nodularity Measurement at Computed Tomography (CT) for Predicting Degree of Hepatic Fibrosis

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Mentor(s): Perry Pickhardt, MD; Meghan Lubner, MD

Support: Shapiro Summer Research Program; Department of Radiology

BACKGROUND: Liver fibrosis from chronic liver disease is a major public health problem throughout the world. Staging of hepatic fibrosis is critical to the proper care and management of patients presenting with hepatic disease. The current gold standard used by clinicians for staging the degree of liver fibrosis is a liver biopsy; an invasive procedure with a risk of bleeding complications and mortality. Currently, cirrhosis may be detected in some patients who have undergone an abdominal Computed Tomography (CT) scan. Key changes in the liver morphology can be detected, namely the presence of large regenerative nodules. Additional signs of hepatic decompensation may also be present, such as esophageal varices or splenomegaly. The liver surface nodularity tool is a non-invasive way to measure the surface nodularity of the liver on CT. Further, it can possibly detect the degree of fibrosis present. This method could prove useful in the staging of hepatic fibrosis and in confirming the presence of cirrhosis in patients with hepatic disease. OBJECTIVE: A simple retrospective CT tool for objectively sampling liver surface nodularity was applied to patients with varying degrees of hepatic fibrosis (Metavir pathologic fibrosis stages F0-F4) to assess its predictive value. METHODS: We evaluated 367 total patients (mean age, 51.1 years; 191M/176F), including a healthy (F0) control group (n=119) and fibrosis stages F1 (n=47), F2 (n=38), F3 (n=67), and F4/cirrhosis (n=97). Contrast-enhanced abdominal MDCT scans (120 kVp, variable mA, PV phase, 5x3 mm sections) were assessed utilizing a validated surface nodularity tool. A series of ≥10 consecutive measurements along the anterior liver, totaling ≥80 cm in length, were made using the left lateral lobe as default. Fibrosis stages F1-F4 were based on liver biopsy within one year of CT, except for 49 cases of cirrhosis (F4) where chronic end-stage liver disease based on hepatic decompensation (eg, esophageal varices, portal hypertension, thrombocytopenia, splenomegaly, and hepatic encephalopathy) and cirrhotic morphology supplanted biopsy for safety reasons. RESULTS: CT-based liver nodularity scores increased with stage of fibrosis: 2.00±0.28 for F0, 2.34±0.39 for F1, 2.38±0.40 for F2, 2.88±0.68 for F3, and 4.10±0.95 for F4. Mean time to perform series of measures per-patient was 126±74 seconds. For discriminating F0-F3 vs. F4, the ROC area-under-the-curve (AUC) was 0.959 (95% CI, 0.942-0.977) and sensitivity and specificity using a threshold >2.81 was 98.0% and 84.8%, respectively. For discriminating F0-F2 vs. F3-F4, the ROC AUC was 0.932 (95% CI, 0.906-0.958) and sensitivity and specificity using a threshold >2.53 was 89.0% and 84.2%, respectively. CONCLUSIONS: Objective measurement of liver surface nodularity at CT allows for discrimination between stages of hepatic fibrosis, especially at more advanced levels. Unlike liver biopsy and MR elastography (interpretation of hepatic stiffness from an applied pulsation), this simple assessment can be performed retrospectively without the need for any additional equipment or patient time, and could conceivably be combined with other imaging parameters (e.g, volumetric changes in the regions of the liver associated with cirrhosis).
Obese Patients Have Increased Risk of Surgical Site Infections But Not Major Complications Following Renal Surgery

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Mentor(s): E. Jason Abel, MD

Support: Department of Surgery NIH T35 Training Grant

BACKGROUND: Extreme or class 3 obesity (BMI ≥ 40) may be associated with increased morbidity following surgery. Obese patients have been shown to have an increased perioperative morbidity after general abdominal surgeries.

OBJECTIVE: The objective of this study was to evaluate if patients with extreme obesity had worse perioperative outcomes following renal surgery.

METHODS: Comprehensive medical records were reviewed for all patients treated with partial nephrectomy, radical nephrectomy or nephroureterectomy at our institution from 2000-2014. Complications occurring within 90 days were recorded and classified according to the Clavien-Dindo system. Univariable and multivariable models were used to evaluate the association of obesity with major complications (≥Clavien 3a), surgical site infections (SSI), blood transfusion (BT) rates and readmission rates.

RESULTS: A total of 1109 patients were evaluated including 114 (10.3%) patients with BMI ≥40. Perioperative complications were identified in 279 (25.5%) patients including major complications in 80 (7.3%). Patients with BMI ≥40 were not at increased risk for major complications (p=0.2). Independent predictors of major complications included Charlson Comorbidity Index and surgical approach (open vs. laparoscopic). A total of 217 (19.6%) patients received BT during the initial hospitalization following surgery. BMI ≥40 was not associated with increased risk of BT (p=0.9) SSI were observed in 60 (5.5%) patients. Patients with BMI ≥40 had an increased risk of SSI, OR 2.3 (95% CI 1.2-4.5). A total of 59 patients (5.4%) were readmitted to the hospital with 30 days following surgery. BMI ≥40 was not associated with increased risk of readmission (p=0.4).

CONCLUSIONS: Extreme obesity is associated with increased risk of wound complications but not a higher risk of major complications, BT, or hospital readmission following renal surgery. When feasible, laparoscopic surgery may be associated with lower major complication rates.
Impact of Brain Tumor Location and Language Lateralization on Perisurgical Morbidity: A Retrospective fMRI Study

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Mentor(s): Vivek Prabhakaran, MD, PhD

Support: Shapiro Summer Research Program; Department of Radiology

BACKGROUND: Functional MRI is being used with increasing frequency as a tool for preoperative neurosurgical planning because it allows for the triangulation of patient-specific areas of eloquent cortex. While previous studies have delineated the general relationships between lesion location, fMRI activation centers, and patient deficits, these relationships need to be further explored in order to gain greater clinical relevance. OBJECTIVE: Our study honed the relationships between ‘lesion to activation distance’ (LAD, defined as the distance from the tumor border to the functional activation center), language lateralization, and perioperative morbidity. METHODS: This study included patients diagnosed with primary or metastatic brain tumor who underwent preoperative fMRI-based motor mapping (n = 217) and/or language mapping (n = 193). Morbidity and operative data were collected from patient electronic medical records. The effects of language lateralization and LAD to Broca’s, Wernicke’s, arm, and leg activation centers was analyzed with respect to functional deficits in terms of morbidity (paresis and aphasia). RESULTS: Significant relationships between arm and leg LAD and postoperative paresis (P = 0.003 and P = 0.02, respectively) and between Broca LAD and postoperative aphasia (P = 0.04) are demonstrated. Analysis revealed a significant relationship between Broca LAD and extent of tumor resection (P = 0.036). Finally, a relationship was discovered between language lateralization and perioperative aphasia varying by tumor lateralization (P < 0.02 and P = 0.008, respectively). CONCLUSIONS: The data indicate that LAD is a reliable predictor for postoperative motor and language deficits. This study also illuminates that patients with smaller LADs are more likely to have less tumor ultimately resected. Patients with right-lateralized language were found to be at greater risk for preoperative aphasia regardless of tumor hemisphere, while only those with right-lateralized language in combination with right hemispheric tumor were at increased risk for postoperative aphasia. These findings support the use of fMRI as a tool for presurgical planning and are directly applicable to surgical decision-making and patient counseling.
Evaluating the Quality of Care Transitions Following Outpatient Surgery

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Mentor(s): Herbert Chen, MD; Courtney J. Balentine, MD, MPH

Support: Department of Surgery NIH T35 Training Grant

BACKGROUND: Improving the quality of care as patients transition from the hospital to home has been highlighted by the Institute of Medicine and the Centers for Medicare and Medicaid Services as a priority area for enhancing patient-centered care. The quality of care transitions has been assessed for complex inpatient medical and surgical patients but has never been evaluated for outpatient surgery. OBJECTIVE: The purpose of this study was to use a validated transitions instrument to determine how well patients were being prepared for outpatient surgery at an academic hospital. We hypothesized that our extensive preoperative education and patient support services would result in excellent preparation for surgery and would be reflected by higher scores on the instrument. METHODS: We administered the Care Transitions Measure (CTM), a validated assessment of care transition quality, to patients undergoing outpatient endocrine surgery. The survey measures patient comprehension of medications, treatment and discharge plans. Participants were surveyed at three time points: the pre-operative clinic visit, after surgery on the day of discharge, and at the post-operative clinic visit. The primary endpoint was CTM score at each time point. Secondary outcomes included postoperative complications. RESULTS: We approached 110 patients and 92 (84%) agreed to participate. Mean CTM scores for complex medical and surgical inpatients typically range from 65-70 on a 100 point scale, but our patients had considerably higher scores at all time points. After the initial clinic visit, mean CTM was 89 ±2. After surgery, CTM scores remained high with a mean of 92 ±1.7 on the day of surgery and 90 ±2 at the postoperative visit, though none of the differences was statistically significant. These scores indicated that our patients had excellent comprehension of treatment plans, understood their medications, and felt that follow-up plans were adequately explained throughout their surgical experience. There was no significant difference in CTM scores between patients with postoperative complications and those without complications. CONCLUSIONS: Overall CTM scores in our population were extremely high following outpatient endocrine surgery. There are many mechanisms used at our institution to enhance patient understanding and care coordination including dedicated nursing staff, carefully constructed written educational material, easy access to surgeons by phone/e-mail and reinforcement of education in the clinic. Further work will explore which of these mechanisms is most responsible for our high quality care transitions.
Resource Navigator Pilot Program- Evaluation Development

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Department: Center for Patient Partnerships, University of Wisconsin Law School; Department of Pediatrics, University of Wisconsin School of Medicine and Public Health

Mentor(s): Rachel Grob, MA, PhD; Amanda Eggen, PhD

Support: Shapiro Summer Research Program; UW Center for Patient Partnerships

BACKGROUND: In response to the national call for collaborative, multi-stakeholder approaches to address the socioeconomic influence on health and development, the Center for Patient Partnerships, in collaboration with the HungerCare Coalition, aims to pilot a clinic-based Resource Navigator Program. This clinic-based initiative seeks to screen families for socioeconomic health challenges, including food insecurity and stable housing, and connect these families with existing community resources to alleviate these challenges. It is the expectation that this program will craft more strategic linkages and better coordination of families to community resources and provide a more holistic approach to clinical encounters.

OBJECTIVE: Development of an evaluation tool to assess the impact of the Resource Navigator Program, with focus on patient experience outcomes, provider input and resource navigator proficiency outcomes, and identify viable health outcome metrics to be integrated into the evaluation tool.

METHODS: A comprehensive literature review synthesizing results of similar designed clinical programs was conducted to lend greater support to the importance and necessity of implementing similar programs across the Madison area and to identify strategies and metrics utilized to monitor long-term health outcomes. Through small group meetings and focus groups with program stakeholders, short-term and long-term evaluations were designed to track patient, provider and resource navigator experience.

RESULTS: Salient literature of similarly designed programs centered primarily upon the medical-legal partnership model, a collaborative approach that bridges legal services into the health care setting to address health inequities among vulnerable populations. Three key domains were identified: impact on patient health and wellbeing, impact on health provider knowledge and financial impact. Integrating metrics spanning these domains with stakeholder evaluation goals, pre and post patient assessments were crafted, tracking changes in self-reported wellbeing, perceived stress and patient activation. Evaluation tools were also developed to measure provider and resource navigator knowledge of and ability to assist patients screening for unmet social disparities.

CONCLUSIONS: Evaluation development alongside program implementation has identified three key domains to concretely measure the effectiveness of the Resource Navigator pilot program- patient health outcomes, primarily self-reported, provider and resource navigator impact and financial impact, with focus currently on developing tools to assess patient health impact and provider/resource navigator skill development. Consolidation of metrics and survey templates is still underway.
Background: There is increasing evidence that socioeconomic factors affect patient outcomes after traumatic brain injury (TBI). However, these factors are often considered in isolation. Objective: The goal of the present study was to assess the effect of race/ethnicity and method of payment on hospital length of stay, mortality, and discharge disposition after TBI. Methods: A retrospective cohort study using the National Trauma Data Bank years 2002-2012 was performed. Patients aged 14-89 with ICD-9 codes for TBI were analyzed. Univariate logistic and linear regression was used to assess the effect of demographic and injury characteristics on each outcome variable. All significant predictors were included in the multivariate models for hospital length of stay, mortality, and discharge disposition. Results: The sample consisted of 201,553 TBI patients, including 2.5% Asian, 12.0% Black, 10.1% Hispanic, 0.7% Native American, and 74.7% White patients. Of these, 9.0% had Medicaid, 25.2% had Medicare, 12.3% had other insurance, 37.9% were privately insured, and 15.6% were uninsured. Compared to White patients, Black and Hispanic patients were less likely to die in the hospital (Blacks OR=.792, p<.001; Hispanics OR=.840, p=.002), had longer hospital lengths of stay (Blacks coeff=.451, p<.001; Hispanics coeff=.249, p<.001), and were less likely to be discharged to inpatient rehabilitation (Black OR=.885, p<.001; Hispanic OR=.703, p<.001). Compared to the Privately Insured, the Uninsured were more likely to die in the hospital (OR=1.487, p<.001), less likely to receive any continuing care after discharge (OR=.564, p<.001) including inpatient rehabilitation (OR=.516, p<.001), and had shorter lengths of stay (coeff=-.095, p=.042). Patients with Medicaid were more likely to die in the hospital (OR=1.166, p=.019), had longer lengths of stay (coeff=1.493, p<.001), and were more likely to receive continuing care after discharge (OR=1.396, p<.001) including inpatient rehabilitation (OR=1.141, p<.001) than the Privately Insured. Conclusions: Race/ethnicity and insurance status both significantly affect patient’s outcomes after TBI. The strongest disparities can be seen for uninsured patients who are more likely to die in the hospital, less likely to receive any continuing care after discharge, particularly any inpatient rehabilitation, and have shorter lengths of stay than any other group. These socioeconomic outcome differences warrant further investigation into their root cause.
Sustaining and Expanding Directly Observed Therapy For LTBI at Community Clinics in Milwaukee

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Mentor(s): Paul Hunter, MD; Sarah Bleything, PA; Jonathan L. Temte, MD, PhD

Support: Department of Family Medicine and Community Health Student Summer Research and Clinical Assistantship Program

BACKGROUND: A previous study compared completion of treatment of latent tuberculosis infection (LTBI) with 12 weekly doses of isoniazid (INH) plus rifapentine (RPT) administered as directly observed therapy (DOT) to 9 months of daily self-administered INH. Study participants were patients seen in 2012 and 2013 at a community health center serving low-income Hispanics. Overall completion rates were 77.8% (35/45) for INH-RPT combination therapy and 52.1% (49/94) for INH monotherapy. OBJECTIVE: To determine the logistic characteristics of LTBI program that may contribute to the high completion rates, with the long-term goal of implementing similar programs at other community clinics in Milwaukee.

METHOD: With the same statistical methods used for patients seen in 2012 and 2013, we compared completion rates for INH-RPT vs INH monotherapy for patients seen in 2014. One author (LM) interviewed key program personnel to learn history of LTBI program development and implementation at the community health center and visited other community clinics to determine need for targeted TB testing. RESULTS: Among patients who agreed to treatment, INH-RPT combination therapy was still associated with higher completion rates (79.7%) when compared to INH only (0%). Operational practices unique to the study clinic are associated with high completion rates. Interviewees suggested that improved BadgerCare+ TB enrollment may support completion, whereas off-site radiology may undermine completion. CONCLUSION: The DOT strategy and shorter regiment contributes to high treatment completion rates. Shortening the interval between patient agreeing to treatment and receiving the first dose of medication may increase and maintain high completion rates by reducing patient loss to follow-up.
Reduced WM Integrity in Acute Stroke Patients With Language Deficits: A Tract-Based Spatial Statistics Study

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Mentor(s): Vivek Prabhakaran, MD, PhD; JoAnne Robbins, PhD

Support: Shapiro Summer Research Program; NIH K23 Award for Brain Plasticity and/or startup funds from Radiology

BACKGROUND: Reduced white matter integrity in brain regions is associated with cognitive impairment and functional deficits. OBJECTIVE: Microstructural abnormality in specific white matter tracts would show significant reduction in stroke patients with language deficits. METHODS: Stroke patients with language deficits (N = 10, mean age = 56.3 years, within 7 days from stroke onset, normed verbal fluency score of less than -1.5), and age- and gender-matched healthy controls without language deficits (N = 10, mean age = 55.6 years, normal verbal fluency score) were scanned on GE750 3T MRI scanners. 3D T1-w whole brain BRAVO and DTI data (56 directions, b value = 1000 s/mm2) were collected. Verbal fluency test was administered to all subjects. Fractional anisotropy (FA) maps were generated from a tensor-model fit of eddy current corrected DTI data using FSL software. The skeletonized and fully non-linearly registered FA data were obtained using Tract-Based Spatial Statistics (TBSS) implemented in FSL, and then they were used for voxel-wise statistical analysis across subjects. Corona radiata (CR) (anterior, superior, posterior), cingulum, superior longitudinal fasciculus (SLF), and uncinate fasciculus of both right and left hemisphere from Johns Hopkins University (JHU)-ICBM-DTI-81 white matter labels atlas were used to identify significantly affected white matter tracts revealed by TBSS. Student t-tests were used to compare group means for normally distributed data and Mann–Whitney U tests to compare group means for non-normal data. Statistical analysis was performed using StatPlus package. Significance was set at p < .05. RESULTS: There was a significant reduction of FA in the left SLF, left superior CR, and both right and left posterior CR of stroke patients with language deficits compared to healthy controls. A slight trend toward significant reduction of FA was also seen in right superior CR (p = 0.089) of stroke patients with language deficits. No significant group differences in FA value were seen in uncinate fasciculus and cingulum. CONCLUSIONS: Stroke patients with language deficits showed significant reduction in FA values in functionally relevant white matter tracts such as the left SLF, left superior CR, and both right and left posterior CR.
Household Food Insecurity and Dietary Intake Among Rural and Urban American Indian Families

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Mentor(s): Alexandra Adams, MD, PhD; Emily Tomayko, PhD, RD

Support: Shapiro Summer Research Program; NIH Grant # 1 R01 HL114912-01

BACKGROUND: Food insecurity has been shown to be high in American Indian (AI) communities. Few studies, however, have examined the factors that contribute to these high rates, or how household food insecurity may impact the dietary intake patterns of AI families. OBJECTIVE: To describe the nature and extent of food insecurity in rural and urban AI communities, and to determine if household food insecurity is associated with altered dietary intake. METHODS: Survey data were collected from 450 adult-child (age 2-5 years) pairs living in five diverse rural and urban AI communities and enrolled in the Healthy Children, Strong Families (HCSF) intervention trial. Food security was determined using two previously validated questions. Descriptive analyses and logistic regression were used to characterize food security and to define predictors. Child and adult food frequency data were used to calculate mean daily intake of various food items by household food security status, which were compared using t-tests. RESULTS: Household food security was assessed in 438 households (53 % rural). Overall, 61 percent of households were food insecure. Household food insecurity was more prevalent in urban communities (79.5%) than in rural communities (45%). In the rural communities, single adult households had significantly greater odds (P=0.005) of being food insecure; and households whose primary caregiver had attained a college degree or higher were at significantly lower odds of being food insecure (P=0.031). In urban communities, the odds of food insecurity decreased with increasing distance traveled to purchase food (P=0.023), and the odds of food insecurity increased with increasing number of children in the household (P=0.038). Food insecure adults had lower mean intake of vegetables (P=0.031) and higher mean intake of fruit juice (P=0.001), other sugar-sweetened beverages (P=0.015) and fried potatoes (P<0.001) than food secure adults. Mean daily intakes of fried potatoes (P=0.033), soda (P=0.010) and sports drinks (P=0.049) were significantly higher in food insecure children compared to food secure children. CONCLUSIONS: This study demonstrates extremely high rates of food insecurity in the communities participating in the HCSF intervention trial, and that food insecurity may be an important influence on the diets of AI families. These findings also highlight that the nature and extent of food insecurity is different in urban and rural AI communities, and future interventions should account for these different contexts.
Inpatient Outcomes and Adequate ED Analgesia in Pediatric Trauma Patients

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Mentor(s): Michael Kim, MD, MPH

Support: Shapiro Summer Research Program; BerbeeWalsh Department of Emergency Medicine

BACKGROUND: Pain management during the evaluation of children with multi-system trauma has been shown to be variable and often inadequate. In the surgical arena, adequate analgesia has been strongly linked to improved outcomes across a wide range of metrics. Despite this, outcomes associated with adequate analgesia in children with multisystem trauma has not been fully described. OBJECTIVE: To determine the impact of adequate opioid administration during the multisystem trauma evaluation on inpatient outcomes such as length of inpatient stay and the amount of inpatient pain medication administered.

METHODS: A chart review was conducted at an academic pediatric level one trauma emergency department. Charts were analyzed for all children who presented as level 1 and 2 traumas between 5/1/2010 and 5/15/2012. Patients were excluded if discharged from ED, had surgery, or became deceased during their stay. Data abstracted include pre-ED and ED opioid administration, IP opioid administration, ISS, and IP length of stay. Patients were categorized to 1) group A: those who received an adequate weight-based dose of fentanyl (1.5 mcg/kg IN, 1 mcg/kg IV/IO), morphine (0.05 mg/kg IV/IO/IM), hydromorphone (0.005 mg/kg), or oxycodone (0.1 mg/kg PO) within 2 hours of the ED visit and 2) group B: those that did not. Length of inpatient stay was analyzed using linear regression, and the cumulative medication administration during the first 3 days of IP stay was analyzed for a 95% confidence interval for the two study groups. All analyses were performed controlling for age, gender, sex, and ISS.

RESULTS: A total of 334 patients were analyzed. Of these, 176 (52%) received at least 1 dose of opioid in the ED or pre-ED. Of these, 162 received it within the two hours. Of these, 97 (29% of total) met the criteria for group A—adequate dose of opioid within the first 2 hours. Group B consisted of the remaining 237 patients. Patients in group A were associated with longer inpatient stays (+65%, p<0.0001) and were more likely to receive inpatient pain medications (morphine OR: 5.2, 95% CI [2.8, 9.7], oxycodone (OR: 4.8, 95% CI [2.2, 10.2])) Assessment of pain score’s impact on opioid administration is pending.

CONCLUSION: Only 1/3 of admitted trauma patients received adequate opioid analgesia in the ED and they were associated with longer IP stay and more IP opioid administration during first 72 hours. The nature of this association is yet to be determined.
Using Plasma Prostaglandin E2 Levels to Customize Type 2 Diabetes Therapy

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Mentor(s): Michelle E. Kimple, PhD; Dawn Davis, MD, PhD

Support: Shapiro Summer Research Program; Wisconsin Academy for Rural Medicine (WARM) Program; Department of Medicine; PhRMA Foundation

BACKGROUND: Prostaglandin E2 (PGE2) expression has been shown to be upregulated in the pancreatic islets of diabetic mice and humans. It is believed that increased levels of PGE2, as well as associated inflammatory response mediators, may have an inhibitory effect on certain cell-surface receptors that are targeted by type II diabetes (T2D) therapies in order to stimulate release of insulin. This may explain why up to 30% of T2D patients are nonresponsive to treatment using glucagon-like peptide 1 (GLP-1).

OBJECTIVE: The primary objective of this research was to determine what correlations, if any, existed in the relative expression of genes related to the expression of prostaglandin E2. Among these are GNAZ and EP3, a g-protein and receptor combination heavily affected by obesity and diabetes, Ptgs1, Ptgs2, Ptges1, Ptges2, and Ptges3, which are all involved in steps leading up to the biosynthesis of PGE2, and IL-6, IL-11, IL-1β, and TNF-α, which are all associated with general inflammatory pathways.

METHODS: The relative expression of these genes was determined via quantitative real-time PCR (qPCR) analysis. Primers were designed for the selected genes and used to run qPCR reactions on DNA isolated from human pancreatic islet cells. Analysis of qPCR data was performed by standardizing expression of the selected genes against a β-actin gene standard, allowing for direct comparison of relative values.

RESULTS: Pancreatic islet cells were obtained from 48 individuals of varying demographics. Efforts to obtain samples specifically from T2D patients were relatively unsuccessful as only 3 were acquired. Nonetheless, correlations were found between expression levels of several genes. Some were unsurprising, such as that between IL-1β and TNF-α; IL-1β is known to augment TNF-α inflammatory responses. Others were potentially more intriguing—such as statistically significant correlations being found between GNAZ and EP3 (p = 0.0128, r^2 = 0.1246), Ptges2 (p < 0.0001, r^2 = 0.3978) and Ptges3 (p < 0.0001, r^2 = 0.2866).

CONCLUSIONS: There were a number of correlations found between the tested inflammatory genes tested. The implications are not immediately clear, but may help in explaining results of future research studies. Further research should focus on acquiring a larger pool of islet samples from T2D patients for study as well as including genes for which primers were not able to be successfully created in this study, namely interferon gamma (IFN-γ).
Regulation of Chondrogenic Differentiation of Mesenchymal Stem Cells (MSC) and Cartilage Homeostasis by LCN2

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Mentor(s): Wan-Ju Li, MS, PhD

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: In osteoarthritis (OA), the articular cartilage undergoes erosion due to deterioration of metabolic efforts of chondrocytes, accompanied by their progressive loss stemming from a decrease in differentiation of human mesenchymal stem cells (hMSC). An adipokine Lipocalin-2 (LCN2) is expressed abundantly in articular cartilage from OA patients; however it is not clear whether its presence has an effect on decrease in cartilage synthesis or on the decrease of hMSC differentiation to chondrocytes.

OBJECTIVE: Given the extensive presence of LCN2 in patients with OA and its abundance in diseased cartilage, it was tested whether LCN2 regulates the differentiation of hMSCs to chondrocytes.

METHODS: hMSCs were isolated from femoral head and neck bone marrow of patients undergoing hip replacement surgery. LCN2 effects on hMSC prior to chondrogenic differentiation were tested by culturing cells under its exposure. An optimal concentration at which maximal effects on gene expression were seen was chosen and used to check for LCN2 effects on hMSC proliferation. This same concentration was used to test the effects of LCN2 on hMSC chondrogenic differentiation. RT-PCR analysis was used to evaluate gene expression. Additionally, sGAG quantification and HE and Alcian Blue staining were used to evaluate chondrogenesis. DNA quantification was used to evaluate hMSC proliferation.

RESULTS: Exposure of undifferentiated hMSCs to 0, 20, 100, and 500 ng/mL of LCN2 showed a 1.25 (±0.15)-fold increase in PPARγ expression at 100 ng/mL (p < 0.05); while not showing any differences in expression of SOX9, CBFA1, NANOG, and Oct3/4 at any other concentrations. At 100 ng/mL LCN2, no differences were observed in hMSC proliferation. However, when exposed to 100 ng/mL pre-differentiation followed by chondrogenic differentiation at the same LCN2 concentration, sGAG/DNA ratio decreased to 0.85 (±0.06) (p < 0.05), when compared to untreated cells. ACAN showed a reduction to 0.36 (±0.02) (p < 0.05), COL2 showed a reduction to 0.25 (±0.15) (p < 0.05), and SOX9 showed no difference in gene expression, when compared to untreated cells. Alcian blue staining demonstrated a decrease in cartilage deposition under LCN2 exposure.

CONCLUSIONS: Presence of LCN2 inhibited the differentiation of hMSCs to chondrocytes, suggesting its possible involvement in OA. Our current studies are evaluating correlations between LCN2 concentrations in femoral bone marrow and age, BMI, and diabetes status.
Generation of an NRL -/- hESC Line for Enrichment of Cone Photoreceptors

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Mentor(s): David Gamm, MD, PhD; Divya Sinha, PhD; Elizabeth Capowski, PhD

Support: Shapiro Summer Research Program; The Dan and Ellie Albert Student Vision Research Award

BACKGROUND: Photoreceptors make up the first neuronal gateway for light signal to be transmitted to the brain. While rod photoreceptors function in low light settings, cone photoreceptors play a crucial role in fine acuity and color vision. Cones are concentrated in the macula, and are progressively and irreversibly lost in patients with macular degenerative diseases such as age-related macular degeneration, Stargardt’s disease and cone dystrophies. Efforts have been made to differentiate cone photoreceptors from human pluripotent stem cells for transplantation therapy, but their yield has not been optimal for this purpose in terms of efficiency, cellular heterogeneity, and length of time required for differentiation. OBJECTIVE: The objective of this research was to develop an efficient method to generate cone photoreceptors without significant cellular heterogeneity. METHODS: The first step towards achieving this goal was to generate a human pluripotent stem cell line where neural retina-specific leucine zipper protein (NRL), an essential rod genesis transcription factor, was deleted using CRISPR/Cas9 gene editing tool. For this purpose, guide RNA sequences were designed and then validated in iCRISPR hiPSC line. Next, plasmids carrying guide RNA encoding sequences were created and transfected, along with Cas9-GFP plasmids, into a reporter human embryonic stem cell (hESC) line to knock out the NRL gene expression. Cells transfected with Cas9-GFP plasmids were sorted using fluorescence-activated cell sorting and cultured in hPSC media. T7 endonuclease I assay and DNA sequencing were then performed on individual cell colonies to select for clones that had been edited at the NRL loci. RESULTS: Several guide RNAs were successfully identified and cloned in relevant vectors. Using the CRISPR/Cas9 gene editing tool, two NRL -/- hESC lines were identified that showed evidence of deletion at NRL exon 1. CONCLUSION: CRISPR/Cas9 is an extremely useful tool for gene editing in hPSC lines. The generation of NRL -/- hESC lines lays out important groundwork for future molecular, cellular and electrophysiological analyses to test whether the absence of NRL will result in enrichment of cone photoreceptors.
Resident Readiness: Evaluation of Errors During Complex Bladder Catheterizations

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Mentor(s): Carla M. Pugh, MD, PhD, FACS

Support: Department of Surgery NIH Grant T35DK062709; DoD Grant W81XWH-13-1-0080

BACKGROUND: Although nurses perform a majority of urinary bladder catheterizations in the hospital, physicians are called on for more difficult catheter placements. Errors committed during urethral catheterizations are shown to contribute to the incidence of catheter-associated urinary tract infections, which are currently the number one hospital-acquired infection in the United States (2). OBJECTIVE: The purpose of this study is to examine the relationship between the number of errors committed by residents during a urinary bladder catheterization procedure and their self-assessment scores. We hypothesize that residents will be overly confident in their abilities and underestimate the potential for case complexity.

METHODS: PGY 2-4 surgery residents (n=45) had 45 minutes to complete three of four bladder catheterization simulations as part of a larger study. The simulations represented well-known clinical scenarios: a female trauma patient, a female post-op patient, a male with a partial urethral blockage, and a male with a full urethral blockage. Participants were given the option to place a urology consult at any point in the simulation. One investigator reviewed videos of each procedure and evaluated procedure performance using the ACS/APDS Technical Skills Curriculum (1). Pre- and post-simulation participants rated the perceived procedure difficulty and their personal confidence level using a 5-point Likert scale. Multiple linear regression analysis was used to look for predictors of procedure performance. RESULTS: Participants made a total of 348 errors with an average of 7.73 errors (SD=3.16) per participant. The lower the resident's pre-simulation confidence in problem-solving, the more errors they committed during the simulation (beta=-1.91, t=-3.89, p=.001). Participants that predicted less difficulty in problem solving for the catheter insertion also made more errors during the experiment (beta=-.452, t=-3.109, p=.004). Average pre-simulation confidence was 4.42 out of 5, while average post-simulation confidence was 3.56 out of 5. There was no correlation between post-simulation confidence level and total errors (p>.05). Participants with higher pre-simulation confidence in problem solving abilities took less time before deciding to place a urology consult (beta=-1.53, t=-4.32, p=.001). Those who placed a urology consult during the simulation were less confident about problem solving (F(1,42)=6.16, p=.017). CONCLUSIONS: The residents did not perform as well as they anticipated when presented with more complicated bladder catheterization scenarios. Simulation can be used to identify and expose potential errors that may occur during complex presentations of basic procedures. This type of training and assessment may facilitate mastery.
Impact of Drain Placement on Infection, Seroma, and Return to OR in Expander-Based Breast Reconstruction

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Mentor(s): Ahmed Afifi, MD

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: The relative risks and benefits of drain placement following breast tissue expander placement continues to be a point of discussion among reconstructive plastic surgeons; the anatomic plane of drain placement, number of drains used, and duration of drain placement are all variables that differ among practicing surgeons without any clear evidence recommending for or against a particular technique. METHODS: In this retrospective cohort study, we compared two groups of patients with drains placed after breast tissue expander placement; in the first group a single subcutaneous drain was placed, and in the second group both a subcutaneous and a submuscular drain were placed. These groups were evaluated on their relative duration of drain placement, incidence of seroma formation, incidence of infection, and rates of complication necessitating return to operating room. RESULTS: The single-drain group was determined to have a significantly shorter duration of drain placement (14.58 versus 22.84 days, \( p = < 0.01 \)) as well as return to OR (8.3% versus 17.6%, \( p = 0.040 \)), with no difference in rate of seroma formation (6.9% versus 14.7%, \( p = 0.114 \)). Differences in rate of infection between the two groups were determined to be insignificant (1.4% in the single-drain group versus 8.8% in the two-drain group, \( p = 0.054 \)). CONCLUSIONS: Therefore, we conclude that a single subcutaneous drain was a superior modality as compared to the two-drain approach given its shorter duration of drain placement and lower rate of complication requiring return to OR while not resulting in higher rates of seroma or infection.
Healthcare Provider Knowledge, Attitudes and Practices Surrounding Long-Acting Reversible Contraception in WI

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Mentor(s): Deborah Ehrenthal, MD, MPH, FACP; Nicholas Schmuhl, PhD

Support: Shapiro Summer Research Program; Wisconsin Partnership Program Lifecourse Initiative for Healthy Families

BACKGROUND: Long-acting reversible contraceptives (LARC), specifically implants and intrauterine devices (IUDs), are highly effective, low maintenance forms of birth control. Not all healthcare providers who provide contraception counseling receive formal education on LARC, especially in regards to insertion technique. The limited number of surveys assessing LARC provision as related to training shows that LARC-specific educational experiences vary by specialty and year of residency training. Many of these studies imply having more recent specialized LARC training increases a provider’s likelihood to provide LARC because training provides accurate knowledge about patient eligibility and improves insertion skills. However, regardless of misinformation and amount of training, providers face systemic limitations such as cost and on-site device availability. In an effort to understand both educational and systemic barriers to providing LARC, this particular study evaluates knowledge, attitudes and current practices among Wisconsin healthcare providers. METHODS: The 8-page self-administered survey was tested for reliability and validity using semi-structured cognitive interviews with 10 clinicians who currently provide contraceptive care. Five Obstetrician-Gynecology residents participated in a focus group assessing the survey instrument quality. Clinicians suggested revisions and points of confusion, and survey questions were revised accordingly. Survey administration to 3,000 Wisconsin healthcare providers will occur in fall 2015. RESULTS: Survey domains include provider demographics, current practice with regard to providing contraception (both in general and specific to LARC), training and confidence in LARC insertion, knowledge about patient eligibility, immediate post-partum LARC provision and factors that potentially limit LARC provision. The sampling scheme of Wisconsin clinicians includes: all licensed Obstetrician-Gynecologists (n=1,022); all licensed nurse-midwives (n=467); approximately 20% of licensed family practice providers (n=1,000), and approximately 35% of licensed pediatrics providers (n=511). CONCLUSIONS: Survey results will inform the development of educational and marketing initiatives directed at improving LARC provision and use across Wisconsin.
**4D Flow MRI during Hypercapnia Identifies Cerebrovascular Dysfunction in Young Adults With Metabolic Syndrome**

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**Mentor(s):** William G. Schrage, PhD; J. Mikhail Kellawan, PhD

**Support:** Shapiro Summer Research Program; UW Cardiovascular Research Center

**BACKGROUND:** Metabolic Syndrome (MetSyn) increases the risk of developing cerebrovascular diseases (e.g. stroke). This may be related to impaired cerebral perfusion autoregulation pathways that lose the ability to respond normally to challenges such as hypercapnia (elevated pCO2). Vasodilation in response to hypercapnic challenge has been shown to diminish in older adults, and newer research has investigated possible impairment in the cerebrovasculature of younger adults with metabolic syndrome.

**OBJECTIVE:** We tested the hypothesis that MetSyn impairs cerebral dilation to hypercapnia, and the attenuation may be non-uniform, given the regional disease prevalence.

**METHODS:** Macroscopic cerebral blood flow (CBF) was measured with a novel 4D Flow MRI approach at 3T using radial undersampling to quantify regional vasodilation to hypercapnia in 10 healthy controls and 8 MetSyn patients as defined by 3 or more risk factors (obesity, prehypertension, low HDL, high triglycerides, blood glucose >100). Blood pressure, O2 Saturation (SaO2), end-tidal CO2 was measured, and Cerebral Blood Flow was calculated for five intracranial arteries: Middle [MCA] x2, Anterior [ACA] x2, and Basilar [BA] (ml/min/100mmHg) and four extracranial arteries: Internal Carotid [ICA] x2, and Vertebral [VA] x2. Due to differences in BP (control vs Metsyn values here), CBF was normalized to BP, where an increase in CBF indicates cerebral vasodilation.

**RESULTS:** Resting CBF was lower in MetSyn (ml/min) compared to controls (ml/min). Preliminary data show that healthy adults increase total CBF in response to hypercapnia, whereas patients/subjects with MetSyn exhibit an increase. The group differences in CBF/CVC were greatest in the ACA, and not apparent in a MCA and extracranial arteries.

**CONCLUSIONS:** MetSyn patients exhibit markedly reduced resting CBF, and impaired overall hypercapnic vasodilator responses. The largest vasodilator deficits appear directed more to regions of the brain supplied by the ACA. This non-uniform cerebrovascular dysfunction occurs early in adulthood, which may contribute to poor cerebral vascular outcomes in MetSyn.
Effects of Pre-operative Opioid Use on Post-operative Patient Health Outcomes After Spinal Surgeries

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Mentor(s): Alaa Abd-Elsayed, MD

Support: Shapiro Summer Research Program; Department of Anesthesiology

BACKGROUND: Opioid use in the United States has dramatically increased since the 1990’s and is now considered the mainstay for both chronic and acute pain management therapy. Hydrocodone combined with acetaminophen continues to be one of the nation’s most prescribed drugs. Although opioids are effective analgesics, the risk of addiction and physical dependence, a plethora of side effects, and increased use of opioids as a chronic therapy, have all lead opioids to be the subject of controversy and continuous research within the medical community. Opioids are commonly prescribed for pre-operative pain management in patients prior to spinal fusion surgeries. Understanding the implications of chronic pre-operative pain management on post-operative health outcomes could improve current pre-operative pain management protocols. One self-reported study concluded 24-hour pre-operative opioid use in spinal surgery predicted worse health outcomes for patients. Our study includes a great multivariable analysis with more reliable data sets, a greater chronological assessment of health outcomes and scores, and documentation of opioid use for an extended period of time. These additional factors may produce a more statistically significant study that will maximize its impact on influencing pre-operative spinal surgery protocol. OBJECTIVE: We hypothesize that patients treated pre-operatively with opioids prior to lumbar, thoracolumbar, or cervical spinal surgeries will have worse post-operative health outcomes when compared to patients that have no pre-operative opioid use. METHODS: This is a retrospective chart study of information collected from 244 patients who underwent lumbar, thoracolumbar, or cervical spinal surgery at UW Hospital from May 5, 2014, to September 17, 2014. Information obtained from the electronic medical record (EMR) includes pre-operative, peri-operative, and post-operative opioid usage duration and amount, pre-operative and post-operative pain, Oswestry Disability Index, and Neck Disability Index scores. Opioid usage is standardized using an equianalgesic chart. RESULTS: We are still in the process of data collection. Our preliminary analysis shows that patient who used opioids before surgery had significantly higher pain scores in the first 24 hours after surgery. Our final analysis will include more outcomes variables that will be very comprehensive. CONCLUSION: Our preliminary results show worse pain scores in patient who used opioids before surgery as compared to patients who did not use opioids. More conclusions will be drawn from this study after finishing the data collection and final analysis.
Assessment of a Newborn Care Training Program for Community Health Workers in Two Rural Districts in Uganda

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Mentor(s): Cynthia Haq, MD

Support: Farrell Public Health Scholars Program

BACKGROUND: Neonatal mortality accounts for a high proportion of under-five deaths in Uganda. The World Health Organization has found home-based newborn care (NBC) provided by community health workers to be an effective intervention to reduce neonatal mortality. In response, Uganda’s Ministry of Health has recently implemented programs for training its community health workers, known as Village Health Teams (VHT), in newborn care practices. A training program was initiated in Kamwenge and Kabarole districts in 2012. There is a need to evaluate the effectiveness of trainings as well as current VHT knowledge to optimize success.

OBJECTIVE: The goals of this study were to assess knowledge of NBC practices amongst VHTs, assess effectiveness of current training of VHT supervisors responsible for training and supporting VHTs, and integrate these findings to provide quality improvement recommendations for future trainings.

METHODS: Twenty-one VHT supervisors at one NBC training and 26 VHTs in two rural districts were administered a common survey tool. The survey consisted primarily of open-ended questions that required participants to demonstrate knowledge by listing essential NBC practices and newborn danger signs, which are health markers indicating need for referral. The tool was administered a single time for VHTs and pre- and post-training for VHT supervisors. Data was analyzed separately for VHTs and supervisors. Pre- and post-training data was compared for supervisors. Common indicators of NBC knowledge were compared between VHTs and supervisors to identify overlapping trends.

RESULTS: Supervisor training significantly improved knowledge of NBC practices (p = 0.046). Areas of lower knowledge in both VHTs and their supervisors included thermal care practices and umbilical cord care. VHTs were able to list 3.7 (SD 1.7) essential care practices, and knowledge of danger signs was adequate for number of signs reported (n = 4.1, SD 2.1) but showed poor consolidation and prioritization. Consolidation and messaging of danger sign knowledge showed qualitative improvement with training.

CONCLUSIONS: Training of VHT supervisors is effective in improving NBC knowledge, and trainer knowledge corresponds with that of VHTs. There is a need for improvement in VHT knowledge of NBC practices and danger signs. Recommendations for training include a greater emphasis on thermal care, standardized messaging about umbilical cord care, and consolidating newborn danger signs into the most important and relevant signs for VHTs.
Opioid Use in Chronic Non-Cancer Pain Management

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Mentor(s): Fabiana Kotovicz, MD; Dennis J Baumgardner MD

Support: Aurora Health Care

BACKGROUND: Chronic non-cancer pain (CNCP) is highly prevalent and can have significant impact on quality of life. Despite controversial efficacy of opioids for CNCP, use has dramatically risen over the past decade. Given that inappropriate opioid use is associated with harmful health and social-related consequences, adherence to guidelines is essential for safer, more appropriate CNCP management.

OBJECTIVE: To provide a baseline assessment of current CNCP management in two academic primary care clinics. METHODS: A retrospective baseline assessment of 50 adult CNCP patients on opioids for at least 90 days seen at Aurora Sinai or St. Luke’s primary care clinic was conducted from 8/2014-3/2015. Demographic and health information were collected. An opioid appropriateness score was calculated based on documentation of nine items. A focus group explored major challenges providers face diagnosing and treating CNCP. Basic statistical analysis was performed using SPSS and MiniTab; multivariate models were analyzed with ordinal logistic regression. RESULTS: Of CNCP patients using opioids (mean age 55yrs and morphine equivalent dose 35mg/day), 22% used more than one chronically. Psychiatric conditions, severe COPD, and OSA were reported in 74%, 8%, and 32% of patients, respectively. The median opioid appropriateness score was 5/9. Only 6% and 18% of patients had opioid agreements and urine drug screens documented, respectively. Providers reported lack of multidisciplinary collaboration and training as significant challenges. Univariate analysis demonstrated that age and location were predictive of opioid appropriateness (p=0.005 and p=0.048, respectively); only age remained significant in multivariate analysis. CONCLUSIONS: Overall, opioid use in CNCP lacks consistency and adherence to recommended guidelines. It is unknown if specific clinic populations confound the correlation between age and appropriateness. Provider education may help ensure safety, homogeneity, and more appropriate management of CNCP patients.
Vancomycin Use in the Emergency Department: A Questionable Target for Improved Antibiotic Stewardship

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Mentor(s): Michael Pulia, MD

Support: Shapiro Summer Research Program; BerbeeWalsh Department of Emergency Medicine

BACKGROUND: Antibiotic resistant bacteria are a growing public health concern and inappropriate antibiotic use is the primary, modifiable driver of this trend. Vancomycin has been the gold standard for treating serious infections due to methicillin-resistant Staphylococcus aureus (MRSA) for decades. Optimizing the use of vancomycin is critically important as over 30 vancomycin-resistant S. aureus strains have already been identified. Studies examining vancomycin use in the ED have reported inappropriate use rates as high as 90%. However, these studies utilized appropriate use criteria that do not accurately reflect current antibiotic use practices in the ED, especially regarding patients with suspected sepsis.

OBJECTIVE: To determine the appropriateness of prescribing and dosing of vancomycin using criteria that accurately reflect current standards of care in the ED. METHODS: This retrospective cohort study was conducted on 150 consecutive patients who were prescribed vancomycin in the ED of a tertiary care university hospital from 2014-2015. Data collected included demographic information, vitals and SIRS criteria, laboratory values, risk factors or prior history of MRSA, vancomycin dosing, and past medical history. The primary outcome variable, appropriateness of vancomycin use, was defined prior to the data collection based on national guidelines and established MRSA risk factors. Dosing was evaluated based on recommendations by the Infectious Disease Society of America. We analyzed our outcomes with X2.

RESULTS: 2% of vancomycin use was considered inappropriate. MRSA was cultured in 8 of the 147 patients who appropriately received vancomycin, and in none of those who did not meet any of the criteria for receiving the drug. Emergency physicians (EPs) ordered a correct dose (15-20 mg/kg) of vancomycin for 78 patients (52.3%). After Pharmacist review, only 81 patients (54.4%) ultimately received a correct dose. When weight-based dosing was utilized by the EP, 67.3% of patients were administered the correct dose (p = 0.026).

CONCLUSION: These data suggest that vancomycin use in our ED is appropriate in the vast majority of cases and much higher than previous reported rates. Dosing outside of the recommended range for empiric treatment of MRSA was very common at this institution, despite the presence of ED based pharmacists who review all medication orders. The use of weight-based dosing by the EP significantly increased the rate of appropriate dosing.
Transcriptionally-Mediated Effects of Ionizing Radiation on Immune Susceptibility in Murine Melanoma

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Support: Shapiro Summer Research Program; St. Baldrick's Summer Fellowship

BACKGROUND: Ionizing radiation (RT) is a common treatment modality used in clinical oncology. While RT is thought to chiefly elicit an anti-tumor response through induction of DNA damage, we and others have demonstrated a cooperative interaction between RT and the anti-tumor effects of various immunotherapies. In prior studies using B78 murine melanoma cells we observed that this interaction may critically depend upon phenotypic changes in the expression of certain immune susceptibility markers following RT, including up-regulation of the death receptor Fas. Here, we examine the time course of such changes using real-time polymerase chain reaction (RT-PCR). OBJECTIVE: The goal of this study is to determine the effect of RT on the transcription of specific immune susceptibility markers in B78 murine melanoma, focusing on death receptor and T cell co-stimulatory/co-inhibitory molecules.

METHODS: B78 murine melanoma cells were grown in RPMI media with 10% FBS. Cells were irradiated (12 Gy) 2, 7, or 14 days prior to RNA isolation. RNA was isolated from cells, concentration was determined, and cDNA was generated. Primers for RT-PCR were designed using Primer3. RT-PCR was run on each sample for the target genes to determine relative gene expression compared to non-radiated control cells. Experiments were performed using biological and technical triplicates. Analysis was completed using Prism. RESULTS: To begin, we verified prior flow cytometry experiments and determined that transcription of the death receptors, Fas and DR5, both increase in B78 cells following RT with a time-course mirroring that observed by flow cytometry. RT modulates expression of additional immune susceptibility markers with the most typical pattern showing an increase in gene expression between days 2 and 7. This finding correlates with a delayed increase in tumor sensitivity to immunotherapy that we observed following RT with this model in vivo. CONCLUSIONS: Our results suggest that transcriptionally mediated changes in gene expression following RT correlate with a time period of enhanced susceptibility to anti-tumor immune response. We are investigating whether this time-dependent increased susceptibility may directly result from known DNA damage repair pathways. Our findings suggest an opportunity for further translational research exploring the capacity of gene expression profiles to serve a predictive role in enhancing the anti-tumor efficacy of regimens combining RT and immunotherapies.
Sport Specialized Training Prevalence and the Risk of Injury in Young Athletes

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Mentor(s): Alison Brooks, MD, MPH; David Bell, PHD

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: Early focus in a single sport at the exclusion of other sports (sport specialization) is theorized to increase the risk of overuse injuries. New tools have been developed to better classify athletes into specialization categories. However, injury risk patterns and prevalence of sport specialization have yet to be investigated using this new methodology. OBJECTIVE: Our primary aim was to identify the prevalence of sport specialization in youth athletes involved in summer sport events. A secondary aim was to determine whether degree of sport specialization and training volume are associated with increased odds of overuse injury. METHODS: Athletes ages 12-18 were recruited from sport events throughout Wisconsin. Participants completed a survey regarding their sport participation patterns, injury history, and training volume. Degree of specialization was classified using a scale based on answers to the following questions: 1) Do you train in 1 sport more than 8 months a year, 2) Have you quit another sport to focus on a single sport, 3) Do you consider your primary sport more important than other sports. This scale classifies athletes as either low, moderate, or highly specialized. RESULTS: A total of 1430 athletes completed the surveys. Overall, 73.9% of athletes were classified as moderate to highly specialized (moderate (n=534, 37.3%), high (n=523, 36.6%)). Females were more likely to be highly specialized compared to males (p=0.01). Highly specialized athletes were more likely to report any previous overuse injury (OR=1.55, p<0.01), upper body overuse injury (OR=1.9, p<0.01), or lower body overuse injury (OR=1.49, p<0.01). Athletes presenting with a previous overuse injury participated in their primary sport more months of the year (p<0.01) and more hours per week (p<0.01) than athletes with no previous overuse injury. Of the 3 questions comprising the specialization scale, training more than 8 months per year was the best determinant of reporting a previous overuse injury (OR=1.83, p<0.01). CONCLUSION: Sport specialization was very common in youth athletes, with almost three quarters classified as moderate or highly specialized. Highly specialized athletes and those with higher training volume were more likely to report a history of overuse injuries to the upper and lower extremity. Physicians, parents, coaches, and athletes should be aware that higher degree of sport specialization and increased training volume may influence injury risk.
Identification of Risk Factors for Cataracts in a Rural Community in Imo State, South-Eastern Nigeria

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Mentor(s): Olachi J. Mezu-Ndubuisi, MD, OD

Support: Shapiro Summer Research Program; Department of Pediatrics

BACKGROUND: Volunteer mission trips alleviate the global burden of disease in resource-limited areas. Mezu International Foundation (MIF) integrates medical and vision care with health education during medical missions in a rural community in Imo State, Nigeria. In 2014, MIF found a high prevalence (64%) of early cataracts in the adult working population, which may create a significant economic burden and health disparity in the community due to low vision. OBJECTIVE: This study aimed to investigate the risk factors for cataracts in this community to effectively guide the development of a sustainable community vision educational program. METHODS: During the 2015 MIF medical mission, 61 patients were selected from over 2000 attendees for a case-control study using a questionnaire to determine health habits, socioeconomic status, and diet choices. RESULTS: 54 patients with complete records were analyzed (52% with and 48% without cataracts). Eye complaints were the most frequent reason for seeking care (56%), followed by malaria (19%) and arthritis/joint pain (19%). There was no difference in comorbidities, such as refractive error (p=0.101), ocular allergy (p=0.999), hypertension (p=0.4), and arthritis/joint pain (p=0.787) between patients with or without cataracts. People without cataracts had more formal education than people with cataracts (p=0.013); 11% of people with cataracts reported that their highest level of education attained was primary school compared to 0% without; while 50% of people without cataracts studied beyond secondary school compared to 22% with cataracts. People with higher SES scores were less likely to have cataracts (p=0.011), but both groups had low frequency of routine medical visits (p=0.234) and were equally likely to obtain medications from pharmacies without a prescription (p=0.999). There was no difference in risk factors for cataracts such as length of direct sunlight exposure (p=0.305), multivitamin intake (p=0.802), use of sunglasses (p=0.318), or brimmed hats (p=0.831). CONCLUSION: Although people with more formal education and higher SES scores were less likely to develop cataracts, lack of finances and poor health knowledge likely negatively affected health care behaviors in both groups. Development of a sustainable community intervention to prevent cataracts should include socio-economic strategies such as education on risk factors and better health practices, as well as ways to subsidize treatment cost.
Learning to Practice: Identifying Deficits in Pediatric Resuscitation Education in the Community

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Support: Shapiro Summer Research Program; Department of Pediatrics

BACKGROUND: Each year in the United States, 16,000 children suffer from a cardiopulmonary arrest with significant morbidity and mortality. Better adherence to resuscitation guidelines has been shown to improve mortality rates in children with a cardiac arrest, suggesting that some of the morbidity and mortality is preventable. Resuscitation education is a critical and necessary element of performance and adherence to resuscitation guidelines. OBJECTIVE: We sought to elucidate current education patterns, needs and desires for further education, barriers to obtaining further education, subjective competence with pediatric resuscitation, and other barriers to resuscitating children according to resuscitation guidelines. METHODS: Semi-structured key informant interviews were conducted with ten individuals who were purposefully sampled based on their practice setting, scope of practice, and role as an educator. All had various levels of certification in basic or advanced pediatric life support. Interviews were audio-recorded, transcribed, and coded independently by two authors for the identification of key themes and findings. This was considered program development and therefore IRB review was not required. RESULTS: The following findings were identified: 1) simulation and active learning methods were strongly desired; 2) providers with greater resuscitation experience desired more education, while those with less experience felt their current certification course was sufficient; 3) providers hoped for more context and content specificity of simulation cases relevant to their work setting; 4) providers preferred educators with pediatric-specific resuscitation experience; 5) situational and emotional stress was a significant barrier to performance and competence; 6) time, cost, and availability of courses are additional barriers to education. CONCLUSIONS: Context- and case-specific curricula beyond standard certification courses should be offered. Additionally, simulation curricula should incorporate situational stress and address the emotional impact of a pediatric resuscitation on providers. Future efforts should develop curricula incorporating these findings to improve pediatric resuscitation education, and ultimately reduce some of the preventable morbidity and mortality.
Awake Versus Asleep MRI Guided STN DBS for Parkinson Disease: A Comparison of Outcomes Using Levodopa Equivalents

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Mentor(s): Wendell Lake, MD

Support: Shapiro Summer Research Program; Department of Neurological Surgery

BACKGROUND: Deep brain stimulation (DBS) for Parkinson disease (PD) has traditionally been performed in awake patients. This required anti-parkinsonian medications to be held for a significant period prior to surgery to allow for microelectrode recording (MER) for verification of appropriate electrode placement. Some patients are unable to tolerate awake surgery or extensive time off their medications, which has previously limited surgical options for these patients. Recently, asleep image-guided lead placement using intraoperative MRI or CT for verification has been proposed as an alternative for patients unable or unwilling to undergo awake DBS surgery. OBJECTIVE: Assessing the viability of asleep MRI-guided DBS as an alternative to the traditional awake method. METHODS: We conducted a retrospective chart review comparing PD patients at our institution who either underwent asleep MRI-guided subthalamic nucleus (STN) DBS lead placement or awake neurophysiologically-guided STN DBS lead placement. Both groups’ levodopa equivalent daily doses (LEDDs) and complications at approximately 6-month follow-up were compared, along with operative times. RESULTS: Both groups show statistically similar reductions in LEDD at 6 months of therapy, with similar complications. Operative times were initially longer for MRI-guided DBS, but have improved with surgical experience. CONCLUSION: Asleep MRI guided DBS is a viable option for PD patients unable or unwilling to undergo awake placement with likely equivalent results in terms of LEDD reduction and complications.
Implementation of Electronic ED Sepsis Screen and Alert: Effect on Compliance With Proposed Sepsis Quality Measures

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Mentor(s): Brian Sharp, MD

Support: Shapiro Summer Research Program; Wisconsin Academy for Rural Medicine (WARM) Program; BerbeeWalsh Department of Emergency Medicine

BACKGROUND: The Center for Medicare and Medicaid Services recently announced sepsis quality measures including IV fluid and antibiotic administration and lactate measurement within the first three hours of care. Many organizations have implemented sepsis screening via electronic medical record (EMR) with little known of their effect. OBJECTIVE: Examine the effect an ED EMR sepsis alert has on compliance with time sensitive sepsis measures. METHODS: Our ED electronic sepsis alert combines nurse screening questions and abnormal vital signs. When criteria are met, an alert triggers, prompting ordering of basic labs and IV fluids. We performed retrospective chart review on adult ED patients with SIRS criteria pre-implementation (9/13 to 12/13) and post-implementation (9/14 to 12/14). Patients were reviewed that by vital signs alone triggered an alert or would have triggered from respective time frames (nurse screening questions were not present in the pre-implementation period). Two blinded reviewers determined whether patients met criteria for sepsis, severe sepsis or septic shock with tiebreaker review if needed. Variables abstracted: time to lactate measurement, antibiotic administration and IV fluid administration. Fisher's exact test with 2 tailed p-values was used for comparisons. RESULTS: 656 patient encounters were reviewed: 337 before and 400 after implementation. In the pre-alert period, 225 patients were determined to have sepsis and 60 with severe sepsis/septic shock. In the post-alert period, 306 patients with sepsis alerts were determined to have sepsis and 79 with severe sepsis/septic shock. When comparing pre- and post-implementation periods, for patients with sepsis, the following metrics were met within three hours: IV fluids administered 72.4% (163/225) min compared to 79.7% (244/306) (p=.06); lactate drawn 50.2% (113/225) compared to 77.8% (238/306) (p<.001); and antibiotics 58.2% (131/225) and 53.9% (165/306) (p=.33). For patients with severe sepsis/septic shock the following metrics were met within three hours: IV fluids 78.3% (47/60) compared to 88.6% (70/79) (p=.11); lactate obtained 86.7% (52/60) and 93.7% (74/79) (p=.24); and antibiotics 80% (48/60) and 72.2% (57/79) (p=.32). CONCLUSIONS: Implementation of an EMR sepsis alert demonstrated improved compliance with obtaining lactate in patients with sepsis but no significant change in other proposed CMS sepsis quality measures for matched sepsis and severe sepsis/septic shock groups.
Primary Hyperparathyroidism: A Case Study

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Support: Department of Family Medicine and Community Health Student Summer Research and Clinical Assistantship Program

BACKGROUND: Primary hyperparathyroidism (PHPT) is an uncommon endocrine disorder that is characterized by overproduction of parathyroid hormone (PTH) by a parathyroid gland that has lost its normal negative feedback which causes hypercalcemia. OBJECTIVE: Here we report four cases of PHPT and review the epidemiology, diagnosis, and treatment of PHPT as well as discuss a potential association between PHPT and autoimmune disease. METHODS: After IRB approval and patient consent was obtained, a chart review of the four patients was performed. An anonymized search of the electronic health record was performed to find the annual incidence rate of PHPT in 20 academic family medicine clinics in Wisconsin. A literature search of PubMed was performed using the MeSH headings for PHPT and autoimmune disease. RESULTS: The average combined yearly incidence from the 20 clinics was 34.4 PHPT cases/100,000 patients. This rate falls in the range reported in the literature of 26.1-59.1 PHPT cases/100,000 patients. The incidence reported in the literature is 2-3 times higher in women than men. Racial disparities in incidence also exist. PHPT is often first detected with an asymptomatic elevation in serum calcium. A history and physical exam should be done, focusing on signs and symptoms of hypercalcemia. PTH levels should be checked. If PTH is low, other causes of hypercalcemia should be considered, such as malignancy. If PTH is high, PHPT is likely and a referral to an endocrine surgeon is appropriate or to an endocrinologist if the diagnosis of PHPT is less clear. A link between PHPT and autoimmune disease has been reported in the literature with prevalence of PHPT 3-4 times higher in patients with autoimmune diseases. CONCLUSION: Here we report 4 cases of PHPT that presented to their primary care provider. While we did not see a temporal trend in our incidence data, the incidence reported by others continues to change. The manner in which PHPT presents is also changing, from a disease that presents with the classic syndrome of “bones, stones, moans, and groans” to an asymptomatic disease presenting with hypercalcemia without other symptoms. When PHPT is diagnosed, medical treatments can limit the symptoms and effects of the disease, but parathyroidectomy is the only curative treatment. Three out of the four cases above had autoimmune diseases comorbid with PHPT. More research is needed to determine if there is a link between autoimmune pathology and PHPT.
Clinical and MDCT Findings for Predicting the Need for Surgical intervention in Small Bowel Obstruction

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Mentor(s): Perry J. Pickhardt, MD; Meghan G. Lubner, MD

Support: Shapiro Summer Research Program; Department of Radiology

BACKGROUND: Small bowel obstruction (SBO) is a common and important condition that requires prompt evaluation to effect appropriate management. Multidetector computed tomography (MDCT) plays a central role in the evaluation of suspected SBO. OBJECTIVE: The purpose of this study is to assess the potential value of a large panel of clinical and CT variables and attempt to formulate a clinicoradiologic model for predicting the need for urgent surgical intervention (<72 hours), presence of bowel ischemia, and need for bowel resection in patients with suspected SBO. METHOD: MDCT studies performed at the time of admission for suspected SBO in 179 consecutive adults (mean age, 55.8 years; 86M/93F) were each systematically reviewed by three board-certified radiologists. In addition to assessing individual CT features, each radiologist scored the overall likelihood of each main-outcome-measure using a 5-point scale. All relevant clinical and laboratory data was abstracted from electronic medical record (EMR) review. Univariate and multivariate analysis was performed. RESULTS: Among all 179 patients with suspected SBO, 56 (31.3%) underwent urgent surgical intervention, 10 (5.7%) had ischemia at surgery, and 9 (5.1%) required small bowel resection. At univariate analysis, multiple CT findings were highly significant (p<0.01) for predicting the main surgical outcomes, including degree of obstruction, radiology likelihood scores, and the presence of transition point, closed loop, and mesenteric congestion. None of the objective clinical/laboratory variables (including serum lactate) reached this level of significance. At multivariate analysis, forward step-wise logistic regression with 0.05 significance level cut-off included both degree of obstruction (p<0.001) and closed loop (p<0.01), whereas the 0.2 significance cut-off also included transition point (p=0.081). CONCLUSION: A number of findings at abdominal MDCT are associated with the need for surgery and other important surgical outcomes in patients with suspected SBO, whereas objective clinical and laboratory values appear to be of limited value. Clinical Relevance Statement: We have shown that MDCT findings alone can be used to predict need for surgical intervention in suspected SBO, allowing radiologists to help guide surgeons to appropriate diagnosis and treatment.
Standardizing the Delivery of 20 μL during Patch Testing

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Mentor(s): Margo Reeder, MD

Support: Shapiro Summer Research Program; Department of Dermatology

BACKGROUND: Patch testing, a tool used to diagnose allergic contact dermatitis, begins with a nurse or technician hand dispensing allergens from a pre-loaded syringe onto aluminum chambers. Due to human error, this technique produces inaccurate and inconsistent results, leading to confusion for both the patient and the physician. Recent studies have demonstrated that 20 μL is the optimal amount to be loaded onto Finn Chambers. **OBJECTIVE:** To create a device that accurately and efficiently dispenses 20 μL and to compare the design to the current hand dispensing technique and a commercial device, the TruVol, in order to find the most accurate and efficient method. **METHODS:** A device was created using Solid Works program. The device consists of a threaded plunger that inserts into a 1cc syringe with threads that were designed with a specific pitch that correlates to one revolution dispensing exactly 20 μL. Ten devices were then printed using 3D printing in order to compare to other available methods. Five nurses in our Contact Dermatitis Clinic were asked to load 10 Finn chambers using the current technique. Assembly time, volume of hapten, and accuracy of placement were measured. The process was repeated with the commercial loading device (TruVol, SmartPractice) and our new device, called the Revolution. Each device was tested three separate times. After the three trials, the nurses completed a survey, which consisted of 10 questions that were specific to the usefulness and accuracy of each device. **RESULTS:** The results from testing the current technique showed a large variation in the amount of hapten used when the hapten is dispensed by hand. The amount dispensed ranged from 17 μL to 80 μL. The TruVol design is accurate and consistent; however it received the lowest survey score out of all three methods and resulted in a significant amount of hapten wasted. The Revolution design is accurate and consistent and received the highest score out of all three methods, with no allergen wasted. **CONCLUSION:** The current hand dispensing technique is not accurate and does not allow the nurses to consistently dispense 20 μL. The nurses are at our clinic dispensed an average of 30-40 μL with a large variation between nurses and also between the 3 separate trials. Our results have shown the Revolution has the potential to be an accurate and consistent method that can help standardize the patch testing method.
Predictors of Significant Weight Loss Following Bariatric Surgery: A Propensity Score Analysis

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Mentor(s): Luke Funk, MD, MPH

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: Laparoscopic vertical sleeve gastrectomy (LSG) has replaced laparoscopic Roux-en-Y gastric bypass (LRYGB) as the most commonly performed bariatric operation in the U.S. Identifying variables associated with optimal bariatric surgery outcomes remains challenging. OBJECTIVE: We sought to compare 90-day and one-year outcomes following LSG or LRYGB and identify predictors of >50% excess body weight loss (EBWL) at one year using propensity score analysis. METHODS: Billing data from the University of Wisconsin Hospital were obtained to identify morbidly obese patients who underwent LRYGB or LSG from January 2010 to March 2014. Electronic health records were reviewed to extract preoperative and postoperative variables, including one-year weight loss and comorbidity resolution. Patient age, sex, comorbidities (coronary artery disease, type 2 diabetes and gastroesophageal reflux disease) and surgeon age were hypothesized a priori to be independently associated with type of surgery and were included in a multivariable model to generate a propensity score for each patient. Propensity score-adjusted multivariable odds ratios for variables hypothesized a priori to be independently associated with EBWL >50% were calculated. RESULTS: 74 LSG and 270 LRYGB patients were included. Mean preoperative body mass index (BMI) was similar between the cohorts (47.8 kg/m2 for LSG vs. 47.0 for LRYGB; p=0.43). The LSG group had more males (36.5% vs. 18.5%; p=0.002), coronary artery disease (16.2% vs. 5.9%; p=0.01) and was older (mean age of 50.6 vs. 47.3; p=0.04). 90-day complication rates were similar between both groups (8.1% vs. 10.7%; p=0.67). LSG was associated with less one-year EBWL (44.3% vs. 61.1%; p<0.001). Female sex (OR 2.52 [95% CI 1.31-4.84]), surgeon age >40 (OR 2.09 [95% CI 1.11-3.94]) and surgery performed before 2013 (OR 6.83 [95% CI 3.69-12.65]) were independent predictors of undergoing LRYGB. On propensity score-adjusted multivariable analysis, BMI <45 (OR 3.00 [95% CI 1.66-5.40]), absence of type 2 diabetes (OR 2.55 [95% CI 1.43-4.54]) and undergoing LRYGB (OR 5.29 [95% CI 2.52-11.09]) were associated with EBWL >50%. CONCLUSIONS: Lower BMI, the presence of type 2 diabetes and gastric bypass surgery (compared to sleeve gastrectomy) were independently associated with greater weight loss after bariatric surgery. These findings contribute to a growing understanding of optimal candidates for bariatric surgery.
Rib Fracture Number Thresholds Independently Predict Worse Outcomes in Older Adults

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Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: Rib fractures in older adults have been associated with significant morbidity and mortality. Contemporary studies have reported that when adjusted for age, comorbidities and trauma burden, the number of rib fractures is not an independent predictor of worse outcomes. OBJECTIVE: Our study investigated this risk-adjusted relationship in older adults. We hypothesized that the number of rib fractures was a significant predictor of worse outcomes independent of patient comorbidities and trauma burden. METHODS: A retrospective review of the American College of Surgeons’ National Trauma Data Bank registry was performed. A query was made for all patients 65 years of age and older who had suffered a known number of rib fractures between 2009 and 2012. Patients with accompanying sternal fractures and those with penetrating or burn mechanisms were excluded for a total cohort of 67,695 patients. Data for the number of rib fractures was quantified using International Classification of Diseases coding. Data collected for risk-adjustment included age, gender, injury severity score, mechanism of injury and comorbidities. Outcome data was collected for eleven different measures including hospital mortality, ICU length of stay (LOS), ventilator duration and complications. Bivariate analysis was performed for all predictor and outcome pairs to identify significant factors (p<0.1) for inclusion in multivariate models. Multivariate logistic regression analysis was performed for all dichotomous outcomes and log-transformed multiple linear regression analysis was performed for all continuous outcomes. RESULTS: Sustaining eight or more rib fractures was associated with increased hospital mortality, ICU LOS, need for mechanical ventilation, ventilator duration, and the occurrence of pulmonary complications, unplanned intubation, and acute respiratory distress syndrome. Sustaining six or more rib fractures was associated with increased LOS, need for ICU care, the occurrence of any complication, and that of pneumonia (all p<0.001). In a subset excluding patients with serious injuries in extrathoracic regions, sustaining six or more rib fractures was associated with all aforementioned outcomes except for ventilator duration. In this subset, every additional rib fracture increased LOS and the need for ICU care (all p<0.03). CONCLUSION: In older adults, the number of rib fractures is a significant predictor of trauma outcomes independent of comorbidities and trauma burden.
Evaluating the Effect of the Reach Out and Read Program on Clinic Values, Attitudes, and Knowledge

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Mentor(s): Dipesh Navsaria, MD, MPH, MSLIS

Support: Shapiro Summer Research Program; Department of Pediatrics

BACKGROUND: Reach Out and Read (ROR) is a clinical early childhood literacy promotion program in which physicians give out free books and prescriptions for reading at pediatric well-child checks in an effort to facilitate literacy discussion and encourage family reading at home. Although many studies have been performed regarding the efficacy of this program, no previous studies have examined the effect of ROR implementation on the clinic itself. With an increasing number of clinics implementing ROR in the near future, it is important to understand what changes may occur in clinics as a result of starting this program. OBJECTIVE: This research sought to understand how clinic values, attitudes, and knowledge relating to early childhood literacy are affected by the ROR program and how employees feel that ROR has changed their clinics. METHODS: To answer these questions, semi-structured key informant interviews were performed with 10 clinics with ROR and 7 clinics that are applying for ROR but have not yet implemented the program. Interviews were transcribed, coded, and analyzed for core themes according to standard qualitative research protocol. Transcripts from clinics with ROR and clinics in application for ROR were compared to look at differences in clinic morale and attitudes towards early childhood literacy. A secondary analysis looked at the transcripts from clinics with ROR to directly examine how employees felt the ROR program had changed their clinics. RESULTS: The coded interview transcripts showed that ROR boosted clinic morale, increased provider satisfaction, improved patient-clinician relationships, and promoted a literacy-rich environment in the majority of clinics where it was implemented. Clinics with ROR felt that clinicians have a larger role in promoting early childhood literacy and had more consistent literacy discussion in visits than clinics applying for ROR. The only disadvantage of the program consistently mentioned by clinics with ROR was funding. DISCUSSION: Understanding the potential changes that can occur in clinics because of the ROR program is crucial to help clinics adequately prepare for the implementation process. The knowledge that ROR has many advantages and few disadvantages in clinics may encourage more hesitant clinics to apply for the program. Further research should be performed comparing clinics with ROR to those that with no interest in the ROR program to see if the results from this study are generalizable.
Not Just Little Adults: A Literature Review on Limited English Proficient Pediatric Encounters

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Support: Shapiro Summer Research Program; Wisconsin Academy for Rural Medicine (WARM) Program; Department of Medicine; University of Wisconsin Carbone Cancer Center; NIH/NCI P30 CA014520- UW Carbone Cancer Center; Health Innovation Program

BACKGROUND: It is well-established that adult patients who are “limited English proficient” (LEP) experience disparities in health care. Children whose parents do not speak English well are even more vulnerable. It is not clear how much research has been done to investigate disparities experienced by LEP children or the effectiveness of interventions to reduce them. OBJECTIVE: To conduct a systematic review of the literature on language barriers in health care in encounters with pediatric patients.

METHODS: We conducted a search in PubMed using the following search terms: (interpreters[All Fields] OR interpreter[All Fields]) AND "communication barriers"[MeSH Terms] AND ("infant"[MeSH Terms] OR "child"[MeSH Terms] OR "adolescent"[MeSH Terms]). We reviewed all abstracts to include only those with data on interpretation in pediatric encounters or children acting as interpreters. RESULTS: We identified 77 manuscripts of which 31 were eliminated because they did not meet inclusion criteria for reasons such as pertaining to adult medicine or not involving interpretation. 46 manuscripts were included in the final review. Topics covered in these manuscripts included quantifying interpreter use (n=15), assessing clinical outcomes of LEP children (n=12), and children as interpreters (n=9). The research documented that professional interpreters are more accurate than ad hoc, yet they were consistently underutilized. LEP children experienced a number of disparities, exacerbated when their families did not have access to interpreter services. Parent satisfaction was commonly measured, but children’s view of the quality of the interaction only measured in 1 manuscript. There was little consensus on the issue of utilization of children as interpreters; some dramatic cases exemplified the inappropriateness of using children as interpreters while others claimed that under appropriate circumstances, they were beneficial. LEP parents often overestimated their own English literacy, and this too lead to clinical consequences for the child. Cultural competence of providers had positive influence on LEP pediatric encounters.

CONCLUSIONS: The consensus was the same as that found in LEP adult patient literature: professional interpretation is best. Still, further research should include exploration of the child’s perspective, the role of healthcare professionals’ supplementary utilization of basic language skills, and expansion of studies beyond specialty to general pediatrics.
Perioperative Management of Patients With SMA Presenting for Nissen Fundoplication: A Retrospective Chart Review

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Support: Shapiro Summer Research Program; Wisconsin Academy for Rural Medicine (WARM) Program; Department of Anesthesiology

BACKGROUND: Spinal muscular atrophy (SMA) is an autosomal recessive disease associated with progressive neuromuscular degeneration due to mutations of the survivor motor neuron gene (1). Nissen fundoplication surgery is recommended for SMA patients because bulbar dysfunction, respiratory muscle fatigue, and malnutrition lead to aspiration events and respiratory tract infections increasing risks of life threatening pneumonia (2). No current procedural or anesthetic standard exists for the perioperative care. We aim to expand the knowledge of best practices for SMA patients undergoing Nissen Fundoplication.

METHODS: We completed a retrospective chart review on all patients with the diagnosis of SMA who underwent Nissen fundoplication surgery at our tertiary care children’s hospital between 2000-2015. Demographic, clinical, and outcome data was extracted using electronic or paper medical records and subsequently analyzed via descriptive statistics. RESULTS: Thirty-nine children with SMA (30 type I, 9 type II) underwent a Nissen fundoplication. The average age of the SMA I patients (11 months) was considerably younger than that of the SMA II (87 months) cohort. Of the patients presenting for surgery 51% were previously dependent on technology support and 54% were administered TPN prior to surgery for nutrition supplementation. The most frequent anesthetic techniques include inhalational induction (77%), and maintenance with potent volatile anesthetics (97%). Airway management included direct laryngoscopy (95%), and postoperative extubation often occurred in the operating room (86%). Difficult intubation (8%) was rare. No intraoperative anesthetic complications were noted. 30% of patients had postoperative complications, the most common being atelectasis. Pain was successfully managed with epidural analgesia (63%), opioids (33%), and acetaminophen/NSAIDs (95%). The average postoperative length of stay was 4 days with 1.2 days in the ICU. CONCLUSIONS: Children with SMA have repeated need for general anesthesia, surgical intervention, and technology support. SMA patients can be safely managed with inhaled anesthetics, non-depolarizing neuromuscular blockers, epidural analgesia, acetaminophen/NSAIDs, and judicious administration of opioids. Atelectasis is the most common postoperative complication and airway clearance should be maximized for prevention. This study builds on data published in by Graham by demonstrating safe and effective care of patients with SMA (3), with emphasis on SMA I patients presenting for Nissen fundoplication.

References:

Unwanted Variations in Specialty Clinic Rooming: A Time Study Tool and Analysis

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Support: Shapiro Summer Research Program; Systems-Based CVD Prevention Protocols for Rheumatology Teams: A low-cost multidisciplinary approach (Independent Grants for Learning and Change-Pfizer; PI-Bartels); Stepping Up in Specialty Clinics to Reduce Blood Pressure (NCATS 9U54TR000021, part of the National Institutes of Health (NIH) through a UW CTSA Clinical & Community Outcomes Research Pilot; PI-Bartels); National Institute of Arthritis and Musculoskeletal and Skin Diseases, part of NIH, under Award Number K23AR062381

BACKGROUND/PURPOSE: Facing fixed time for specialty visits, the time staff spends on rooming patients is a premium, but remains poorly understood. We conducted a time study, a basic systems engineering approach, to examine the frequency and duration of all visit related tasks performed by clinic staff (medical assistants (MA) or nurses) between the waiting room and the entry of the rheumatologist.

METHODS: We developed a time study tool using health system policies and procedure documents, interviews and observations of pre-visit rooming. The tool measured 25 pre-determined tasks at a resolution of 15s=0.25 min. Trained engineering and medical observers measured 190 rooming sequences for a total of 1419 minutes at three rheumatology clinics in an academic multispecialty practice during Fall 2014-Spring 2015. Rooming was performed by nurses or medical assistants (MA) at 2 sites, but otherwise by MAs. Scheduled visits varied from 20-30 minutes. We calculated descriptive statistics on tasks and times, compared frequencies using Fischer’s exact test, and times using analysis of variance. We developed a task taxonomy and described variations in tasks. RESULTS: We observed 18 additional actions beyond 25 expected tasks. We then grouped 15 labeled tasks in 5 categories based on the sequence they occurred and clinical objectives for each task (Table 1). Total rooming time varied widely (2.5-22 min). Mean rooming time was 7.5 ± 3.1 min across clinics (Table 1) and varied between clinics, at 8.8, 6.7, and 7.6 minutes (p<0.001). Vital signs (1.9 ± 0.6 min) and medication reconciliation (1.7 ± 1.3 min) accounted for half of the total rooming time. Maximum time variation was associated with questionnaire administration (±1.8 min), medication reconciliation (±1.3 min), and other conversations (±1.2 min). Only 4 tasks were observed in >90% of the rooming sequences: initiation, pulse, blood pressure measurement, and medication reconciliation. For other tasks, frequencies varied by clinic. For instance, prescription refills occurred in 3 vs. 46% of clinic visits, and pain scores in 17 vs. 98% of visits when stratified by clinic (p=<0.001). Five of nine tasks with high frequency variation were identified to benefit from standardization: height, weight measurement, prescription refill cueing, pain assessment, questionnaire administration (disease activity, new patient) and tobacco history. CONCLUSION: Using time study we developed a practical tool for measuring time spent on each rooming task, and created a taxonomy of rooming tasks. We found that the frequency and timing of rooming tasks varied among encounters and clinics. Implications of this work beyond our institution include methods for (A) identifying and prioritizing opportunities for standardization, (B) offering a platform for decisions regarding changing standards and (C) comparing baseline data for new scheduling or care quality initiatives.
Preoperative Predictors of Discharge to a Higher Level of Care Following Colon Resection

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Mentor(s): Gregory Kennedy, MD, PhD

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: Preoperatively anticipating the discharge destination of patients contributes to quality patient-doctor conversations regarding long term goals and quality of life. Additionally, previous literature has found that early identification of discharge destination may decrease the hospital length of stay and improve patient care planning. OBJECTIVE: The purpose of this study was to identify preoperative predictors of discharge to higher level of care in patients undergoing colectomy. METHODS: Patients undergoing colectomy in 2012-2013 were identified in the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) targeted colectomy database. Exclusion criteria included death before discharge; discharge to a facility that was already home; unknown discharge destination; discharge to a separate acute care facility; outpatient surgery; and ASA Class 5 or unknown. Two cohorts were established based on discharge destination. One group included all patients discharged to home, while the other consisted of those discharged to an increased level of care (ILC), which was defined as a skilled or unskilled nursing facility or rehab that was not originally home. Univariate analysis was performed using Chi-squared tests for categorical variables and Student’s t-tests for continuous variables to identify patient characteristics, comorbidities, and operative factors associated with discharge to ILC. Variables with p-value <0.1 on univariate analysis were included in a multivariate model in order to identify the variables with the largest independent contribution to discharge destination. RESULTS: A total of 36,492 patients were included in this study, with a rate of discharge to ILC of 11.2% (n = 4111). The mean age of the ILC group was 73 years of age, compared to 60 years in those discharged to home (p=<0.001). On univariate analysis, the ILC group had a significantly higher incidence of emergent cases, renal failure, insulin-dependent diabetes, preoperative wound infection, and preoperative systemic sepsis. Multivariate analysis confirms a higher odds ratio for several comorbidities when controlling for cohort differences at baseline. CONCLUSIONS: As expected, discharge to an ILC was associated with a more dependent functional status, preoperative ventilator-dependence, and higher ASA class. These findings may contribute to a more informed discussion of postoperative expectations and planning in patients being considered for colectomy.
Functional Recovery Following Analgesic Femoral vs. Adductor Canal Block for ACL Reconstruction

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Mentor(s): Tamara Scerpella, MD

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: Recent studies indicate a delay in quadriceps strength, functional recovery and return to sport in patients who receive femoral nerve block (FNB) during surgery for anterior cruciate ligament (ACL) reconstruction. An adductor canal block (ACB), which is primarily sensory, but also affects the vastus medialis, has gained popularity as an alternative analgesic approach. **OBJECTIVE:** The aim of this study is to compare the effects of ACB vs. FNB vs. no nerve block (NB) on strength and functional outcomes at 6 months after ACL reconstruction. **METHODS:** Surgical records were reviewed for graft type, concurrent procedures and diagnoses, total tourniquet time and pressure, and block dosage, medication, timing and location. Demographic variables include sex, age, BMI, and side of injury. The main outcome variables (isokinetic flexion and extension strength, functional performance variables (KT-1000, single leg press, Y balance) and functional outcome scores (SF-12, IKDC, SANE)) were compared between block groups. **RESULTS:** There were no statistically significant between-group differences in demographic or functional performance variables at 6 months post-operative. The ACB group had significantly lower isokinetic flexion strength at 240 degrees/second compared to FNB and NB groups. Additionally, the ACB group had significantly lower SANE scores at 6 months post-operative compared to FNB and NB groups. **CONCLUSION:** Adductor canal blockade results in persistent strength and functional outcome score deficits at 6 months post-ACL reconstruction. ACB-associated blockade of the vastus medialis appears to have a more adverse effect on functional outcomes following ACL reconstruction than does FNB.
Can Children's Books Serve as Viral Fomites?

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Mentor(s): Dipesh Navsaria, MPH, MSLIS, MD

Support: Shapiro Summer Research Program; Wisconsin Academy for Rural Medicine (WARM); Department of Pediatrics

BACKGROUND: A major barrier to child literacy promotion is the uncertainty of whether books can serve as credible fomites. This question was first raised at the turn of the 20th century when tuberculosis and smallpox epidemics were claiming thousands of lives. Many recommendations were made but no scientific evidence was published to prove or disprove this question. Although numerous medical advancements have been made since, this question has yet to be answered and remains relevant for clinic policies. OBJECTIVE: The purpose of this study was (1) to investigate the longevity of rhinovirus on hard cover children’s books and (2) to compare the presence of viral particles on hard cover children’s books to other inanimate objects in clinic waiting rooms. METHODS: To assess rhinovirus longevity on books, 50 units of 0.5 mL RG-HRV16 inoculum of 2x10^4 TCID50 units/mL were applied to a hardcover book surface through a simulated sneeze. The surface was sampled 0, 1, 6, 12 and 24 hours post-contamination with a polyester-tipped swab. Serial dilutions were prepared. Cell infectivity assays, using WI38 cells, and quantitative reverse transcription-PCR (RT-PCR), using picornavirus primers, were performed. To compare viral presence on book surfaces to other inanimate objects, non-contaminated books were placed in pediatric waiting rooms and exam rooms of 3 UW Health clinics. Books were sampled after 1 week, at which point inanimate objects in the waiting rooms were also sampled using the technique outlined above. RT-PCR was performed on collected samples. RESULTS: The cell infectivity assay resulted in no cell death at any time point. RT-PCR revealed significant viral presence at time 0, with minimal viral presence after 1-hour. One book placed in an exam room contained significant viral presence, while all other books and surfaces revealed insignificant viral presence. CONCLUSIONS: The rhinovirus concentration of 50 units was not infectious. Future studies could use higher concentrations to determine infectivity. RT-PCR revealed significant viral decline by 1-hour post-contamination. Future studies using infectious concentrations could confirm this pattern. RT-PCR revealed similarly insignificant viral contamination of books in clinic waiting rooms and exam rooms compared to inanimate waiting room objects. One limitation included unknown times between patient contact and sample collection. Future studies could sample at various time points after witnessed contact.
Race and Ethnicity Disparities in Pedestrian Crashes in Wisconsin, 2009-2013

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Mentor(s): Harold Weiss, PhD, MPH, MS; Parvathy Pillai, MD, MPH

Support: Prevention Innovation in Medical Education (PRIME) Madison Program

BACKGROUND: A pedestrian is killed every 2 hours and injured every 8 minutes in the United States. While pedestrians make up 14% of traffic fatalities, walking accounts for just 10.5% of everyday travel. Risk factors that increase the incidence and severity of pedestrian injury include urban areas, male gender, high vehicle speeds, good weather and alcohol consumption. National studies suggest minorities have higher pedestrian mortality rates, but trends in Wisconsin have not been studied. Most previous studies used mortality data while this study uses data from fatal and nonfatal incidents. OBJECTIVE: To explore how pedestrian crash rates in Wisconsin differ by race and ethnicity and how these trends are modulated by age, gender, urbanization, severity and alcohol use. METHODS: Wisconsin Department of Transportation crash data was linked with 16-point probabilistic matching to hospital and emergency department data from the Wisconsin Hospital Association to create the Crash Outcomes Data Evaluation System. Pedestrian crashes in Wisconsin from 2009-2013 were analyzed by race/ethnicity, age, gender, injury severity, alcohol involvement and urbanization. RESULTS: Age-adjusted pedestrian crash incidence rates were calculated for blacks (316.24 per 100,000), American Indians (110.05), whites (56.82) and Asians (56.45). Blacks and American Indians had relative risks (RR) of 5.71 and 1.9 respectively compared to whites. Hispanics had a statistically significant RR of 1.39 compared to non-Hispanics. Black males age 10-14 had the highest incidence with a rate of 548 per 100,000 and a RR of 7.13. American Indians had elevated RRs in both urban and rural settings, 1.4 and 3.83 respectively. Blacks had a RR of 7.04 in urban areas with a rate of 320.47 per 100,000. Blacks had increased risk in all injury severity categories with the greatest relative risk (5.49) for mild injuries. Alcohol was involved (driver and/or pedestrian) most in American Indian pedestrian crashes (25.76%) as compared to white pedestrian (10.94%) or black pedestrian (6.3%) crashes. CONCLUSIONS: In Wisconsin, major disparities exist between white and black pedestrian crash rates across a wide range of co-variables. American Indians had elevated risks, especially in rural areas, and their crashes were more likely to involve alcohol. Future studies are needed to explain why these disparities exist.
Qualitative Aspects of Treatment With Prolotherapy for Knee Osteoarthritis in a Multi-Method Study

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Mentor(s): David Rabago, MD. Chidi N Obasi MD, MS, PhD.

Support: Shapiro Summer Research Program; Department of Family Medicine and Community Health

BACKGROUND: Knee osteoarthritis (KOA) is a common debilitating condition. Prolotherapy, an injection technique for KOA, was associated with improved knee-specific quality-of-life (p<0.05) and improved pain, stiffness and function (p<0.05) compared to baseline status and to control therapies in 52-week randomized and open label studies. These objective outcomes suggest a role for prolotherapy for KOA, however the participants’ qualitative experience is not known. OBJECTIVE: To assess the qualitative response of participants who received prolotherapy for KOA. METHODS: A randomized subsample of participants who received prolotherapy in three randomized and open-label studies participated in semi-structured, in-depth interviews. Transcribed responses were discussed by co-authors to identify major themes; disagreements were resolved by consensus. The setting was primary care, university based, outpatient Family Medicine clinic. Intervention included five monthly prolotherapy treatment sessions included a single intra-articular injection and multiple peri-articular tendon/ligament attachment injections. Outcome measures: Primary: Qualitative interviews; Secondary: Western Ontario McMaster University Osteoarthritis Index (WOMAC; 0-100 points: baseline, 12 and 52 weeks). RESULTS: Participants (n=22) reported improvement in knee-specific quality-of-life; (WOMAC scores; 19.9±12.6 points), consistent with improvement in the three parent studies, in excess of minimal clinical important improvement benchmarks. Four major themes emerged. (1) decreased knee pain and improved ability to perform specific activities of daily living - including both work and leisure (2) no long-term side-effects and minimal, predictable injection-related effects, (3) pre-treatment counseling enhanced adherence, and (4) an overall positive experience with prolotherapy. CONCLUSIONS: Qualitative data supported and supplemented objective findings. For most, prolotherapy improved knee pain and function without side effects. These narratives provide new information about prolotherapy by reporting the patients’ experiences, adding meaning to the intervention in ways that prior quantitative studies cannot; they enable patients to understand what prolotherapy might mean for them and empower clinicians to personalize prolotherapy to each individual patient.
Effect of Perioperative Fluid Class, Volume, and Timing on Incidence of Post-Operative Ileus

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Mentor(s): Gregory D. Kennedy, MD, PhD

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: Postoperative ileus (POI) complicates approximately 20-30% of colon surgeries. It has been proposed that bowel edema at least partially contributes to the etiology of POI. Additionally, previous studies have shown decreased fluid administration can decrease POI incidence. **OBJECTIVE:** We sought to investigate how the class, volume, and timing of fluid administration impact POI incidence.

METHODS: We conducted a retrospective cohort study of 300 patients with rectal cancer who underwent partial colectomy or proctectomy at the University of Wisconsin Hospital and Clinics from 2008 to 2015. Chart review was performed to collect data on intra-operative fluid type and volume as well as fluid volume data for postoperative day one. The primary outcome was POI, defined as presence of a nasogastric tube for nausea or vomiting or NPO status on post-operative day four or later. Volumes of crystalloid (0.9% saline and Ringer’s lactate) were divided into quartiles and volumes of colloid (5% albumin, hydroxyethyl starch, and blood products) were divided based on whether or not colloid was administered intraoperatively. Association with POI was assessed using Chi-square tests and binary logistic regression. Covariates were chosen from comorbidities, demographics, and operation specifics based on relevance to hypothesis and relative significance on univariate analysis. Secondly, we compared the ratio of the rates of fluid administration for the intra-operative period and the period through postoperative day 1. **RESULTS:** A total of 300 patients were included in our study, with an overall POI incidence of 30.0% (90 out of 300). Multivariate analysis confirmed a relationship between intra-operative crystalloid volume and risk of POI [O.R. (95% CI): 1st quartile: reference; 2nd quartile: 2.884 (1.192-6.979) P=0.019; 3rd quartile: 2.973 (1.191-7.418) P=0.020; 4th quartile: 3.417 (1.321-8.842) P=0.011]. Other significant predictors of POI included older age, and operative approach. Additionally, we found no correlation between the incidence of POI and the ratio of fluid administered in the preoperative and postoperative phases of care. **CONCLUSIONS:** In patients undergoing colorectal surgery, lower intraoperative crystalloid administration was associated with lower rates of POI, while colloid did not appear to affect ileus rate. Therefore, limiting the volume of crystalloid administered may be effective at reducing the incidence of POI.
Determining Factors Influencing Hmong China/Vietnam Healthcare Decisions

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Mentor(s): Elizabeth Jacobs, MD, MPP; Jacob Hickman, PhD

Support: Shapiro Summer Research Program; Department of Medicine

BACKGROUND: Since the migration of the Hmong into the United States in the mid-1970s, there has been a significant conflict between the traditional Hmong concepts of health and the biomedical model. The traditional Hmong concept of health recognizes Animism as a key notion. The natural world consists of benevolent, malevolent, and ancestor spirits. The physical and spiritual well-being of the Hmong relies significantly on the relationships and interactions with these spirits. Etiology of illnesses, influence of patriarchal values, modesty, language capability, and mistrust toward the biomedical model are all factors that obstruct quality-standardized healthcare for Hmong patients. Recent research suggests that the Hmong have integrated biomedical concepts while maintaining traditional Hmong concepts of health.

Three main contextual factors determine whether traditional Hmong or biomedical care is sought. They include: (1) the presence and regularity of symptoms, (2) longevity of symptoms, and (3) spiritual visions or manifestations. OBJECTIVE: This study seeks to understand the factors that contribute to how indigenous Hmong populations in Vietnam and China make healthcare decisions, particularly when they engage in traditional Hmong practices versus the biomedical model. This information will be applicable to improving healthcare quality for recent Hmong immigrants and Hmong Americans who lack experience or apprehension of the biomedical model and addressing the health disparities of the Hmong in the United States.

METHODS: The empirical basis for this study was an ethnographic methodology consisting of participant observation and qualitative data collection through in-depth interviews. The participants were indigenous Hmong from Sapa, Vietnam and Wenshan Prefecture of Yunnan Province in China.

RESULTS: The preliminary findings suggest that the Hmong in China and Vietnam are pragmatic in that they will utilize all available healthcare resources in search of the most optimal outcome. The majority of Hmong interviewees in China pursued biomedicine as the initial treatment referencing the wide accessibility to clinics and hospitals. In contrast, the Hmong interviewees in Vietnam modified their decisions based on contextual factors. Factors such as religion, resources, and severity of symptoms strongly influenced decisions. CONCLUSIONS: Further in-depth analysis of the interviews are currently being conducted. A discourse analysis approach is being utilized to analyze the data.
Impact of an Electronic Sepsis Screening and Alert on Antibiotic Prescribing in the Emergency Department (ED)

Authors: Iris Vuong; Cassandra Schandel; Brian Sharp; Michael Pulia

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Mentor(s): Michael Pulia, MD FAAEM FACEP

Support: Shapiro Summer Research Program; BerbeeWalsh Department of Emergency Medicine

BACKGROUND: Antibiotic timing and selection are critical elements of sepsis management. In order to improve early identification and treatment of sepsis, there is great interest in developing automated, electronic health record (EHR) based screening systems which identify at risk patients. The impact of these screening systems on antibiotic prescribing patterns is unknown. OBJECTIVES: Our objective was to assess the impact of an automated sepsis screening system on antibiotic prescribing in the ED. Our hypotheses were that antibiotic use and time to antibiotics would improve in patients with sepsis while antibiotic overuse would occur in patients identified by the screening tool but who were ultimately not septic. METHODS: An EHR sepsis screen and alert system was implemented in July 2014. This system is triggered by fever plus an abnormal vital (hypoxemia, hypotension, tachypnea, tachycardia) or any two abnormal vitals plus a positive nursing screening question regarding suspected infection or rigors. We performed a pre/post-implementation, retrospective chart review of adult patients who presented to our ED over a four month period in 2013 and 2014 with fever and an additional abnormal vital sign at any point during their ED visit. Two blinded chart reviewers determined if patients met criteria for sepsis with tiebreaker review of any disagreements. Data collected included antibiotic prescribing and time to antibiotics. Outcomes were analyzed with χ2 or t test. RESULTS: 337 patient encounters were identified with fever and an additional abnormal vital sign in the pre-implementation data set, while 323 patient encounters were identified in the post-implementation data set. 225 patient encounters in the pre-implementation group and 211 in the post-implementation group were determined to meet sepsis criteria. 71.6% and 76.7% of septic patients received antibiotics in the pre/post periods respectively (p=0.24). In patients who were not septic, 18.8% in the pre-implementation group received antibiotics compared to 17.0% in the post-implementation group (p=0.73). Time to antibiotic in septic patients was 127 minutes pre compared to 162 minutes post (p=0.004). CONCLUSION: Antibiotic use did not change significantly for either septic or non-septic patients in our ED following the implementation of an EHR sepsis screening system. Time to antibiotics in this cohort of septic patients increased significantly following implementation of the EHR sepsis screening system. This unexpected finding may be reflective of increased utilization of lactate following the EHR prompt. While lactate is critical for stratification of sepsis severity and guiding resuscitation, waiting for this additional lab before initiating antibiotic therapy may result in a significant treatment delay.
An Evaluation of Cookstove Improvements in Rural Guatemala

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Mentor(s): James Svenson, MD, MS

Support: Shapiro Summer Research Program; BerbeeWalsh Department of Emergency Medicine

BACKGROUND: An estimated 3 billion people use wood cookstoves worldwide to cook and heat their homes. Solid biomass (wood, animal dung, charcoal, crop residue) is the typical fuel used and when burned, releases gases and fine pieces of pollution into the surrounding air. A significant amount of research has gone into understanding the complex health effects of cookstoves and ways to improve their efficiency. However, much of the evaluation of improved cookstoves has been done with methods of passively measuring the ambient air. A possible limitation of this method is that it does not evaluate the true effect of improved cookstoves on individuals exposed to the emissions, instead uses ambient air as a proxy for individuals' exposure. OBJECTIVE: To better understand the effects of improved cookstoves on health, non-invasive measurements of blood carbon monoxide levels were taken at community clinics in five rural Guatemalan communities. METHODS: All patients greater than 8 years old evaluated at walk in urgent care clinics at rural villages near San Lucas Toliman, Guatemala were eligible for evaluation. On patient intake, a Masimo pulse CO-oximeter was used to measure heart rate, blood oxygen saturation (spO2), methemoglobin and blood carbon monoxide (CO). Cookstove type (chimney or not), location (outside or inside) and fuel type used by the patient at home were recorded. The patients were asked about common symptoms (back pain, nausea, headache, cough) at the time of evaluation were recorded. RESULTS: For all patients, average CO levels were 5.56%, with a range of 1%-13%. Additionally, total average methemoglobin was 0.77%. Average CO levels by village were: Quixaya (6.0%), Santa Ana (5.9%), Panimaquip (5.9%), San Julian (5.8%), and Vida Nueva (4.6%). Of those reporting use of a chimney, average CO was 4.89% while those reporting no chimney had average CO of 6%. For each symptom, average CO level for the group responding yes was higher than the group responding no; backache (6.1/4.8), nausea (5.75/5.2), headache (5.3/5.1), cough (5.3/5.2), asthma (6.4/5.2), joint aches (6.3/5.0). CONCLUSIONS: Gains have been made in introducing improved cookstoves in to homes of rural Guatemala and these have improved exposure to particulate matter in the home. Our findings suggest that, despite these efforts, there is still significant exposure to carbon monoxide in these communities. There may still be long term health effects from this chronic exposure to blood CO levels.
Prescription Opioid Abuse Behaviors: Exploitation of System Weaknesses

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Support: Department of Family Medicine and Community Health Student Summer Research and Clinical Assistantship Program

BACKGROUND: Despite expansion of the electronic health record, the prescription drug monitoring programs, and the use of abuse-deterrent medication formulations, the majority of abused prescription-based opioids are obtained through a prescription, inferring clinicians can play an important role in reducing the epidemic of prescription opioid abuse and related overdose deaths and heroin abuse. Little is known, however, how patients utilize gaps in the existing system to “procure” prescription opioids that fuel drug abuse. OBJECTIVE: To gain insight into drug procurement methods and behaviors relating to prescription opioid abuse. Design: Multi-perspective, qualitative study. Setting: Community. Participants: Twelve participants (two clinical substance abuse counselors, seven individuals in recovery, a pharmacist, law enforcement officer, and needle exchange program director), representing perspectives of five different “stakeholder groups,” were interviewed. METHODS: Semi-structured in-person interviews were conducted and audio-recorded, transcribed, and openly coded to identify emergent themes. Through inductive reasoning and consensus approach, data was categorized into domains and subthemes. RESULTS: Qualitative analysis identified three major domains, endorsed by at least four out of five groups, related to procuring prescription opioids: “outsmarting” behaviors such as manipulating/lying to clinicians and utilizing user-networks to access information about how to procure prescription opioids; exploiting system weaknesses such as the barriers to sharing of medical information and inconsistencies in clinicians’ prescribing practices; and inadequate patient counseling by clinicians about the harms of and alternatives to prescription opioids. CONCLUSION: Patients who abuse drugs continue to “outsmart” clinicians and utilize healthcare system weaknesses to procure prescription opioids, however risky. Clinicians play a vital role in preventing further growth of the opioid abuse epidemic through detailed patient education about opioid related harm, and increased awareness of characteristics and behaviors of patients affected by opioid use disorders.
Validation of an Instrument to Assess Barriers to Care Seeking for Accidental Bowel Leakage

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Mentor(s): Heidi W. Brown, MD, MAS

Support: Shapiro Summer Research Program; Department of Obstetrics and Gynecology

BACKGROUND: Accidental bowel leakage (ABL), or fecal incontinence, affects 1 in 5 women 45 years and older. ABL is associated with severe negative impact on quality of life as well as increased health care costs and risk of nursing home placement. Despite the existence of effective treatments for ABL, less than 30% of women with this condition seek care. The Barriers to Care-seeking for Accidental Bowel Leakage (BCABL) questionnaire is a patient-centered instrument designed to identify the major obstacles keeping women with ABL from seeking treatment with healthcare providers. OBJECTIVE: To identify factors associated with care seeking for ABL using the Barriers to Care-seeking for Accidental Bowel Leakage (BCABL) questionnaire in a US, English reading, computer-literate population. METHODS: An electronic invitation to participate in this IRB-exempt study was emailed to a mailing list obtained from a company that manufactures a personal hygiene product for ABL. Interested recipients were invited to click on a link providing more information about the study and electronic consent was obtained. Those who consented to participate were screened for relevant inclusion criteria, before being directed to the online questionnaire. In addition to the BCABL instrument, the questionnaire included the Vaizey Incontinence Severity Index, a validated instrument to assess ABL severity, and the Patient Activation Measure (PAM), a validated instrument to assess knowledge, skill, and confidence regarding self-management of medical conditions, as well as questions regarding standard demographics and health insurance status, length of time with ABL, relevant co-morbid medical conditions, perceived general health status, and prior knowledge about ABL. Respondents were invited to complete the BCABL again two weeks later to assess test-retest reliability. Basic descriptive analyses and Chi-square testing were performed using SPSS to characterize respondents and compare those who had and had not previously sought care. RESULTS: Among the 739 participants who clicked on the link to learn more, 693 consented to participate, and 552 had experienced ABL in the past three months. Those who met the inclusion criteria were 83% female and were predominantly white, retired and insured. CONCLUSIONS: The information obtained via the BCABL questionnaire will be used to develop and assess interventions to minimize barriers to care seeking in women suffering from ABL.
Increasing WI HPV Vaccination Uptake With Use of an Environmental Scan

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Mentor(s): Noelle Loconte, MD; Sarah Mroz, MPH

Support: Shapiro Summer Research Program; UW Carbone Cancer Center

BACKGROUND: In the U.S. 91% of cervical and anal cancers, 75% of vaginal, 72% of oropharynx, 69% of vulvar and 63% of penile cancers are attributed to HPV infection. From 2006-2010, an estimated 534 cancer deaths in WI men and women could be attributed to HPV infection. The HPV vaccination offers protection to females and males against HPV infection and HPV associated cancer. However, since the licensure of the first HPV vaccine in 2006, utilization has remained low compared to other adolescent vaccines in WI. OBJECTIVE: Build and leverage efforts to increase HPV vaccine rates in WI by conducting an environmental scan. The long-term goal of this work will be to enhance collaborations to develop research and interventions to increase HPV vaccination uptake in primary care settings in WI.

METHODS: This environmental scan included four-parts: (1) Further examination of vaccination data available through the WI Immunization Registry. (2) A Stakeholder Survey sent to WI HPV Vaccine Summit participants and relevant stakeholder organizations. (3) Comprehensive assessment of current UW research on HPV, HPV-related cancers, and the HPV vaccine. (4) Quality improvement evaluation of the UW provider education series. RESULTS: (1) In 2014, low completion rates were found among both WI females and WI males in the recommended age range (11-12) with the rates being lower among males. The highest initiation rates were found among males and females 13-17 years of age and were seen in Menominee County. In general, teens who had ever been on Medicaid had higher rates of receiving HPV vaccination than those who had never been on Medicaid. (2) Of the 277 stakeholder surveys sent out, 117 (42%) were sufficiently completed and used in the analysis. Ninety-four stakeholders reported being involved in activities focusing on adolescents (girls or boys ages 11-18) and their parents that may increase HPV vaccination. Seventy-six out of the total 117 respondents indicated they were involved with activities focusing on clinical and health professionals that may increase HPV vaccination. Sixty-one stakeholders identified their activities as projects focusing on communities and health systems that may increase HPV vaccination. Eighteen out of the 117 total respondents indicated being involved with activities focused on advocacy and public policy. (3) Five key HPV related activity themes emerged from the interviews: (a) educational presentations of information about the virus, HPV associated cancers, and the HPV vaccine to the community, parents, or providers, (b) analysis of perceptions and opinions of parents, physicians, or stakeholders on HPV vaccine utilization via a survey, (c) research on viral mechanisms and cell changes that occur with HPV exposure, (d) prevalence studies of HPV in cancer cells, especially in head and neck cancers, (e) research on the virus and efficacy of HPV associated cancer treatments. Many of the projects were found to be ongoing, and many of the interviewed researchers were found to have interest or plans in participating in future research projects related to HPV. (4) Comparison of vaccination rates from February 2014 and February 2015, indicate an increase in both initiation rates and completion rates, regardless of gender. CONCLUSION: The assets, needs, and barriers of statewide organizations involved in HPV vaccination uptake identified in this environmental scan will allow UWCCC, key-partners, and stakeholders to more effectively target interventions and/or further research to better increase HPV vaccination uptake in the state. The findings also reveal opportunities for collaborations between organizations. Increases in vaccination rates, post-UW educational series reveal success in this intervention. There is hope in continuing this series around the state.
Comparative Outcomes Among Surgical and Ablative Treatments for Small Localized Renal Cell Carcinoma

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Mentor(s): E. Jason Abel, MD, FACS

Support: Shapiro Summer Research Program; Department of Urology

BACKGROUND: While surgery is the gold standard treatment for small (≤4cm) renal cell carcinoma (RCC), percutaneous cryoablation provides a nephron-sparing alternative that may also result in curative outcomes. In addition, the recent development of high-powered microwave ablation (MWA) may offer potential benefits over cryoablation. OBJECTIVE: The objective of this study was to evaluate disease recurrence after treatment for patients with small RCC treated with ablation or surgery. METHODS: A total of 489 patients were treated with percutaneous ablation or surgery for localized RCC (confirmed with biopsy or surgical pathology) at our institution from 2001-2015. Differences in patient and disease characteristics among patient cohorts were evaluated using t-test or chi squared analysis. RESULTS: Of the 489 patients, 314 (64.2%) were treated surgically, 100 (20.4%) were treated using MWA and 75 (15.3%) had cryoablation. There was no difference in gender, race, body mass index, smoking history, R.E.N.A.L. nephrometry score, laterality, tumor diameter, or histologic RCC subtype among ablative treatments or surgery (p=0.13, 0.08, 0.08, 0.18, 0.16, 0.29, 0.80, 0.3). Patients treated surgically were younger (p<0.0001) with median age 56.9 (IQR 48-66) compared to MWA (median age 67.0 IQR 59-72) or cryoablation (median age 65, IQR 60-74). Patients treated surgically were also more likely to have symptoms at presentation (p=0.01) compared to ablative treatments and more likely to have higher nuclear grade compared to ablative treatments (0.0002). Median Charlson Comorbidity Index was 2 (IQR 1-3) in surgically treated patients, compared to 3 (IQR 2-4) and 3 (IQR 2-4) in MWA and cryoablation respectively (p<0.0001). Median follow-up was 9 months (IQR 6-18) for patients treated with MWA compared to 40 months (IQR 24-60) for cryoablation and 41 months (IQR 15-80) for surgery (p<0.0001). Local recurrence was identified in 11(14.7%) patients following cryoablation compared to 1(1%) patients following MWA or 3(1%) after surgery, (p<0.0001). Development of metastatic RCC was observed in 2 (2.7%), 0 (0%), and 12 (3.8%) of patients following cryoablation, MWA or surgery respectively, (p=0.13).

CONCLUSIONS: Local recurrence is rare after surgery or percutaneous microwave ablation for small localized RCC. Cryoablation is associated with higher rates of local recurrence and retreatment compared to surgery. Future studies with longer follow-up are necessary to determine whether local recurrence rates are superior after treatment with MWA compared to cryoablation.
Multi Model Comparison of Aortic Dissection Hemodynamics

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Support: Shapiro Summer Research Program; Department of Radiology

BACKGROUND: Aortic dissection is a life-threatening condition in which the inner wall of the aorta is disrupted, causing separation of the inner and outer layers of the aortic wall. Blood can flow between the separated layers of the vessel wall, creating a false lumen alongside the original true lumen. This process may occur rapidly and can lead to rupture of the aorta, although in many patients, a dissection can remain stable for years. Altered hemodynamics in stable dissection patients can lead to decreased organ perfusion and organ damage. Surgery is often needed to manage this condition, but the anatomy of each patient and geometry of each dissection result in unique hemodynamics. The conditions resulting in adverse outcomes in patients with chronic aortic dissection are incompletely understood. **OBJECTIVE:** We sought to develop several patient-specific models to compare the hemodynamics of aortic dissection, incorporating data from 4D flow MRI, computational fluid dynamic (CFD), and solid models analyzed by ultrasonic flow probe (UFP).

METHODS: Patient images (MRA and CTA) were segmented using Mimics to create 3D printed models. Medical grade tubing connected to a cardiac bypass pump was used to supply the inflow and outflow of each aortic model. The models were then scanned using high-resolution CTA (CT750, GE Healthcare) and MRA (MR750, GE Healthcare). The CTA was performed using a standard clinical CTA protocol for imaging thoracoabdominal aortic dissections. The MRA consisted of 3D MRA sequences with isotropic spatial resolution (1.25mm^3), 2D flow MRI through the ascending aorta, and 4D flow MRI of the entire aorta. From the CTA and MRA in vitro scans, 3D digital models were generated and segmented using Mimics. CFD analysis was then performed on the 3D models using Fluent. The bypass pump setup was also analyzed using UFP.

RESULTS: Data from each of these modalities was generated. Inflow and outflow velocity measurements made by UFP stood up to a mass balance analysis and agree with 4D flow MRI and CFD data. Color-coded velocity, pressure, and wall shear stress data generated by CFD and 4D flow MRI were studied and show good agreement in both numerical values and in flow patterns. **CONCLUSION:** The models used in this study to characterize the hemodynamics of aortic dissection showed good agreement, and may be further developed to guide surgical procedures used to manage aortic dissection. Future endeavors include introducing a valve system to the bypass pump to achieve pulsatile flow, and using 3D solid models with variable material properties.
Clinics and Pharmacies Use Wisconsin Immunization Registry (WIR) to Increase Vaccination Rates

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Support: Farrell Public Health Scholars Program

The overarching goal for Immunize Milwaukee! (a community wide coalition) is to increase vaccination rates. In 2014 a needs assessment was conducted in which 68% of interviewees stated that work on immunization information systems should be a high priority for Immunize Milwaukee! OBJECTIVE: With this in mind our objective was to determine how clinicians in the greater Milwaukee area are using the Wisconsin Immunization Registry (WIR). METHODS: In 2015 an online, anonymous survey was conducted in order to determine how healthcare professionals utilize the Wisconsin Immunization Registry (WIR). Survey participants included clinicians and clinic staff who were known to be interested in vaccinations, as well as members of the Pharmacy Society of Wisconsin in the metro-Milwaukee area.

RESULTS: Responses from 136 individuals showed that the majority of physicians are made aware that a patient needs a vaccination through their electronic medical record (EMR) while the majority of pharmacists and other healthcare workers directly login to the WIR. Furthermore, physicians also made up the majority of those who were not sure how the WIR is updated. Among all of the respondents 15% of them look up immunization records only through their EMR. Among these EMR-only users the majority of them believe that the WIR is as accurate or more accurate than their EMR and many of them would like to use the WIR. Overall, most individuals have a positive perception of the WIR and feel as though the registry is enhancing vaccination rates in Milwaukee. CONCLUSION: In order to address the clinics’ lack of access to WIR, Immunize Milwaukee! should encourage clinics to send multiple staff members to free WIR training by the state.
Outcomes That Matter to Teens With Type 1 Diabetes

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Mentor(s): Elizabeth D. Cox, MD, PhD

Support: Shapiro Summer Research Program; Department of Pediatrics

BACKGROUND: The teenage years are a critical period in which teens with type 1 diabetes take on more disease management responsibilities in preparation for adulthood. Diabetes control is often sub-optimal for teenagers. Understanding the outcomes that matter to teens could support successful interventions to improve diabetes care. This study examined outcomes that mattered to teens with diabetes who posted on two public forums for type 1 diabetes. OBJECTIVE: To gain an understanding about the outcomes that matter to teens with type 1 diabetes using posts from online communities.

DESIGN/METHODS: 72 publicly-available posts from 2011-2013 were randomly selected from the “teen” sections of two major diabetes online forums. Twenty-two posts were eliminated from the initial sample due to 1) although posted in the “teen” section, the poster was not 13-17 years of age (n=13) or 2) lack of relevant content (n=9). From each selected post, the content and descriptive data (e.g., duration of diabetes and age) were collected. Standard open coding techniques were used to analyze content and identify outcomes found in the posts. An outcome was defined as impacts or consequences as a result of type 1 diabetes. Researchers independently examined and recorded their interpretation of each post and then met to discuss the coding. A codebook was jointly developed to facilitate the identification of meaningful outcomes from the posts. RESULTS: 50 posts written by 36 unique teens were examined for outcomes. The average age of teens was 15.7 years old (16 specified their age). From the 18 teens who specified how long they have had type 1 diabetes, the average duration was 6.3 years, with a median of 5 years. The three most common outcomes mentioned in forum posts were 1) control of blood glucose, 2) emotional wellbeing, and 3) positive interactions with peers. Other outcomes mentioned included 4) physical wellbeing, 5) family interactions, 6) education and motivation of others, 7) interactions with others such as school personnel and 8) academics. CONCLUSIONS: Results suggest that teens who post within online diabetes forums convey many outcomes that matter beyond the control of their blood sugar. Healthcare providers and family members may want to consider these outcomes when motivating teens with type 1 diabetes to improve blood glucose control.
The Role of Iliopsoas Tendon Anatomy in Determining Efficacy of Surgical Release for Central Iliopsoas Impingement

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Support: Shapiro Summer Research Program; Department of Radiology

BACKGROUND: The presence of iliopsoas impingement is traditionally diagnosed by the presence of an isolated anterior labral tear at 3 o'clock position in the setting of iliopsoas tendon pathology at that level with the presumed mechanism being that of friction leading to labral tearing. Literature has shown that iliopsoas impingement, traditionally treated with iliopsoas tendon release, demonstrates recurrent or refractory pain in a minority of patients. The typical methods of surgical release most commonly include central release at the level of the acetabular rim, versus peripheral release at the level of the lesser trochanter. The location of iliopsoas tendon release intuitively would provide more variable results when performed centrally, as the tendon components likely have not converged in this more cranial position in all patients. Additionally, the presence of variant anatomy may affect the surgical outcome and improved pre-surgical evaluation of iliopsoas anatomy may improve surgical outcomes. OBJECTIVE: To retrospectively assess the potential role of iliopsoas tendon anatomy variants on postoperative pain and function following central versus peripheral arthroscopic tendon release. METHODS: This IRB approved, retrospective study evaluated 82 patients who underwent iliopsoas tendon (IPT) arthroscopic release for suspected central iliopsoas impingement (IPI), 41 of whom underwent central release and 41 of whom underwent peripheral release, performed by a single surgeon. Retrospective consensus hip MRI review was performed by two musculoskeletal radiologists. The number and cross-sectional area of IPT components were measured at the acetabular rim (RIM), 1.5cm above (ARIM) and below the rim (BRIM), and at the lesser trochanter (LT), and presence of tendon lateral dipping at the rim was documented. A control group of 41 patients (37 females, 4 males, mean age 39yrs) who underwent arthroscopy for femoroacetabular impingement without specific imaging or clinical findings of IPI were analyzed in similar fashion. Other data such as clinical and surgical diagnoses, and Modified Harris Hip Scores (mHHS) were collected via electronic medical record review. Statistical analysis was performed using Fischer's exact test for categorical variables, Student's T-test for continuous variables, and the SAS Mixed Linear Model for pain and function outcomes assessment. RESULTS: Patients with IPI had smaller cross-sectional tendon component areas (mm²) at the acetabular rim (psoas major: mean 129.2(47.1) vs. 152.9(43.8), p=0.0086; medial iliacus: mean 15.0(13.4) vs. 25.5(25.6), p=0.05; accessory iliacus: mean 27.4(16.0) vs. 41.2(37.0), p=0.031) and 1.5cm above the rim (psoas major: mean 109.3(46.9) vs. 144.2(76.36), p=0.0094; medial iliacus: mean 17.6(14.5) vs. 24.4(15.4), p=0.0483; accessory iliacus: mean 18.1(11.5) vs. 26.8(24.3), p=0.0435). There was no significant difference in tendon component number in IPI cases versus controls (ARIM= 2.8:2.8, RIM= 2.6:2.6, BRIM= 1.9:2.0, LT= 1.0:1.2), and no effect of tendon component number or size on post-operative mHHS. There was no significant difference in post-operative pain and function within 1 year for central versus peripheral release patients (43.88(9.08) vs. 42.49(12.84), p=0.5732). Lower post-op mHHS correlated with pre-surgical MRI findings of IPT tendinopathy (-10.02, p=0.0013), iliopsoas bursitis (-7.67, p=0.0392), and cartilage degeneration with articular bodies (-9.44, p=0.0201). CONCLUSIONS: Patients with IPI may show smaller average tendon component diameters at and above the acetabular rim, and a higher prevalence of lateral dipping, but tendon component size and number do not affect operative outcomes post tendon release. Similar post-operative improvement in pain and function occurs following central and peripheral release for IPI, the majority occurring within the first 12 weeks. The presence of a lateral dip, or coexisting iliopsoas tendinopathy, bursitis, or cartilage degeneration are associated with poorer post-operative outcomes.
Assessment of Cerebrovascular Disease Changes in Alzheimer’s Disease Patients

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Mentor(s): Sanjay Asthana, MD; Shahriar Salamat, MD, PhD

Support: Shapiro Summer Research Program; Department of Medicine; NIA grant P50 AG033514

BACKGROUND: Alzheimer’s disease (AD) is the most common cause of dementia in the United States. AD pathology is often comorbid with cerebrovascular disease (CVD) lesions in the brain. CVD can independently contribute to the development of dementia, but the contribution of CVD to dementia in patients with comorbid AD remains unclear. Research on this topic is complicated by a lack of universally accepted standards for grading CVD lesions. OBJECTIVE: We examined the contribution of CVD to dementia in AD by developing a system to grade the extent of CVD and applying it to AD brains. CVD was examined as a predictor of several clinical variables, neuropsychiatric performance and neuroimaging data acquired with MRI. METHODS: Twelve AD brains (mean age 80.8 ± 14.3 years) from the Wisconsin Alzheimer’s Disease Research Center (ADRC) were examined and compared against brains from 4 age-matched and 3 young adults (mean age 38.7 ± 5.3) with no evidence of cognitive decline. All were examined for gross infarcts, hemorrhages and atherosclerosis. A semiquantitative scale for white matter pallor (0-3), arteriolosclerosis (0-3), hemosiderin (0-3), perivascular space changes (0-3), and presence or absence of tortuous vessels (0-1) was applied to microscopic sections of frontal and parietal border zones. The sum of vascular scores was used to estimate CVD. Microinfarcts, cerebral amyloid angiopathy (CAA), thromboemboli and atherosclerosis were also assessed microscopically. All analyses included age and sex as covariates. RESULTS: Linear regression analysis revealed that AD patients had worse atherosclerosis (p=0.002), more infarcts (p=0.037), and more severe CAA (p=0.040) than controls. In addition, AD patients had a higher mean vascular score (p=0.002) and more frontal pallor (p=0.03) than controls. Positive correlations include: frontal pallor with frontal vascular score (p=0.05), clinical dementia rating (CDR) with both mean and parietal vascular scores (p=0.05), and CDR with AD pathology severity rating (p=0.01). CONCLUSIONS: This limited study demonstrates potential for a standard CVD grading system, in addition to suggesting that patients with AD show brain changes consistent with CVD. Future studies should include more patients and controls, and more brain sections should be taken to more closely align with harmonization standards as put forth by the NINDS and other models of CVD as suggested in the field.
Factors Affecting Family Presence and Satisfaction During Fracture Reduction in the Pediatric ED

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Mentor(s): Michael K. Kim, MD

Support: Shapiro Summer Research Program; BerbeeWalsh Department of Emergency Medicine

BACKGROUND: Historically, asking family members to leave during invasive procedures has been common practice across emergency departments. One aspect of patient and family centered care is the option for family presence during treatment. There is currently little literature investigating factors affecting family member presence during fracture reductions, a relatively common procedure. If healthcare is to be truly patient and family centered, family members’ experiences must be understood. OBJECTIVE: This study aims to investigate factors related to family members’ presence and satisfaction during fracture reductions in the pediatric emergency department (ED). METHODS: Role-specific, anonymous surveys were administered in a level 1 trauma center pediatric emergency department. Subjects included a convenience sample of family members and providers of patients who had fracture reductions performed in the ED. Family member survey items included reasons for being inside or outside of the procedure room during the reduction, perception of reduction success, and satisfaction with their decision of where to be during the procedure. All family members were given a choice on where to be during the procedure. Providers were surveyed regarding the difficulty of the procedure. Fisher’s exact test was performed to identify associations between survey responses, and qualitative responses were analyzed for common themes. RESULTS: Twenty-five family members and 41 providers of 18 patients completed surveys. Family member satisfaction with their location during the procedure (median = very satisfied) and perception of reduction success (median = extremely well) were almost uniformly high and not associated with any other variables examined, including anxiety level, previous presence during a medical procedure, or provider-reported procedure difficulty. However, location during the procedure was significantly associated with a desire to be in the same location in the future (p=0.001). Common themes were found among family members’ reasons for their location decisions and satisfaction levels, including a desire to support the patient, high staff competence, and their right as parents to choose their location during the procedure. CONCLUSIONS: Family members’ ability to self-select their location during fracture reduction in the pediatric ED was associated with high levels of satisfaction. Future studies should include a larger sample size, in-depth interviews, and randomization of family member location.
Evaluation of FDG PET as a Predictor of Osteosarcoma Response and Prognosis

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Mentor(s): Steve Y. Cho, MD; Chihwa Song, PhD

Support: Shapiro Summer Research Program; Department of Radiology

BACKGROUND: Osteosarcoma is the most common primary bone cancer in children and teens. Standard treatment consists of neoadjuvant chemotherapy followed by surgical resection of the primary tumor. Upon histologic evaluation, greater than 90% necrosis indicates response to chemotherapy and correlates with better event-free survival (EFS). There has been great interest in assessing the effectiveness of 18F-FDG PET in monitoring treatment response and predicting prognosis in various cancers, as it is non-invasive and can be done prior to resection. Recent studies in osteosarcoma suggest that Maximum Standardized Uptake Value (SUVmax), Metabolic Tumor Volume (MTV), and Total Lesion Glycolysis (TLG) predict histologic response after one cycle of chemotherapy, and MTV and TLG predict metastasis-free survival before chemotherapy. It remains to be seen whether FDG PET parameters can predict histologic response before chemotherapy, and whether parameters other than MTV and TLG can predict EFS.

OBJECTIVE: Assess the ability of various PET parameters (SUVmax, SUVpeak, SUVmean, MTV, TLG, heterogeneity parameters, % change between time points) to predict histologic response and EFS.

METHODS: We performed retrospective analysis of FDG PET/CT scans for 34 osteosarcoma patients from St. Jude Children's Research Hospital between 2008 to 2012. Images were taken at baseline, 5 weeks, and 10 weeks after the start of chemotherapy. Mirada XD3 software was used to quantify FDG PET parameters. Logistic regression, Cox regression, and Kaplan-Meier curves were used to assess the effectiveness of parameters in predicting histologic response and EFS.

RESULTS: Preliminary analysis suggests that SUVmax, SUVpeak, and SUVmean are predictive of histologic response and EFS as early as week 5 (p < 0.05). MTV, and TLG are predictive of EFS at week 10. Due to the unit change selected for regression analysis of MTV and TLG, the significance of these parameters may be underestimated, so analysis will be redone. Data for % change and heterogeneity parameters were recently sent to St. Jude statisticians for analysis.

CONCLUSIONS: The finding that SUVmax, SUVpeak, and SUVmean can predict EFS adds to previous studies. Analysis of % change and heterogeneity parameters may add even more. Various PET parameters seem to be effective in predicting histologic response and EFS after one round of chemotherapy. This is promising to guide future use of FDG-PET in the management and assessment of cancer.
Differential Expression of Adipokines as a Function of Aging and Focal Cerebral Ischemia

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Mentor(s): Uma Wesley, PhD; Robert Dempsey, MD

Support: Shapiro Summer Research Program; Department of Neurological Surgery

BACKGROUND & PURPOSES: Aging is associated with the chronic, low-grade inflammation that amplifies the risk of stroke incidence. Adipokine imbalance is thought to be a key event in promoting the pro-inflammatory state and cerebro-vascular diseases. This correlation emphasizes a need to further characterize the adipokines in aging and post-stroke brains. Previously, Dempsey lab has shown up-regulation of four adipokines: Lipocalin-2 (LCN-2), MCP1, TIMP-1 and Serpin E1 protein levels in both old (11/12 months) rats and stroke induced rats when compared to young (3 months) naive rats. In this study, we examined if up regulation of these adipokines occurred at transcriptional levels. Hence we measured the mRNA levels of these four adipokines among the same comparison groups. METHODS: Spontaneous hypertensive rats (SHR) were used in this study. The rats were divided into four groups: 3 month naive SHR, 3 month SHR in which stroke was induced by middle cerebral artery occlusion (MCAO) surgery with two days reperfusion time, 12 month naive SHR, and stroke induced 12 month SHR with two days reperfusion time. Total RNA was extracted from the rat brain tissues. The cDNAs were synthesized from the extracted RNA using M-MLV reverse transcriptase and Oligo (dT) primer. Quantitative real time PCR was carried out to validate altered adipokine expression at the transcriptional level. Briefly, Q-PCR was performed using a SYBR Green PCR master mix in an ABI 7000 Q-PCR machine. The housekeeping gene β-actin was used as an internal control. Fold-changes in adipokine expression were determined by the delta Ct (ΔΔCt) method. RESULTS: In accordance with the protein levels of LCN-2, MCP-1, TIMP-1 and Serpin E1 observed in post-stroke brains, similar trends in upregulation of these four adipokine mRNAs were observed in both 3 months MCAO rats and 12 months MCAO rats compared to 3 months naive rats. At transcriptional level, no significant change of LCN-2 and MCP-1 mRNA in 12 month naive rats was observed when compared to 3 months naive rats. Slight down-regulation of Serpin E1 and TIMP-1 mRNAs were observed in 12 month naive rats compared to 3 months naive rats. CONCLUSION: These experiments demonstrated altered adipokine expression in the post-stroke brains at the mRNA levels, indicating adipokines over-expression in acute phase may exaggerate pro-inflammatory status and may contribute to increased susceptibility to stroke. The up-regulation of adipokines in aged brain was not observed at transcriptional level but the increased amount of adipokine proteins might still contribute to the exacerbation of stroke.
The Effect of Fish Oil Therapy on Serum Lipid Levels in the Pediatric Population

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Mentor(s): Amy Peterson, MD

Support: Shapiro Summer Research Program, Department of Pediatrics, Division of Cardiology

BACKGROUND: Atherogenic lipid patterns of elevated serum triglyceride and lowered serum high-density lipoprotein cholesterol (HDL) levels are associated with metabolic syndrome and future risk of cardiovascular disease. Omega-3 fatty acids, specifically EPA and DHA found in fish oil, lower adult serum triglyceride levels. Docosahexaenoic acid (DHA) and Eicosapentaenoic acid (EPA) are the active ingredients in fish oil. Pediatric dosage is 2g DHA+ EPA/day. Limited information regarding the effect of fish oil on children’s serum low density lipoprotein cholesterol (LDL), HDL, triglycerides, and non-HDL cholesterol is available. Most available data do not reflect “real-world” use. OBJECTIVE: To assess the impact of fish oil therapy on children’s serum HDL, LDL, non HDL cholesterol, and triglyceride levels in the setting of confounding effects of adherence to lifestyle therapy including change in BMI percentile for age, stage of nutrition change, and exercise therapy. METHODS: A retrospective observational case controlled study was conducted on 63 children treated for dyslipidemia between 2011 and 2015 at the American Family Children's Hospital Pediatric Preventative Cardiology Clinic. All children received nutrition and exercise therapy but the experimental group of 16 added fish oil therapy. Fasting lipid panels drawn prior to treatment and at the first visit following therapy initiation, an interval of 3-6 months, were analyzed to determine the effects of fish oil therapy. Effects of confounding variables identified in the univariate analysis were controlled in the lipid change analysis. This necessitated the use of an estimated population marginal mean (LS-mean) and 95% CI values instead of mean and standard error values. RESULTS: The control group achieved an estimated population marginal mean (LS-mean) rise in HDL of 9%, whereas the experimental group experienced no change in HDL, at p=0.04. There were no statistically significant differences between the two groups regarding serum LDL, non HDL cholesterol or triglyceride levels. Both groups decreased serum triglyceride levels by over 25%. Upon questioning, patients reported that dosage ranged from 0.5 to 4.0 grams, with a mean of 2.28 (STD 1.24)g. CONCLUSION: Nonuse of fish oil was associated with an average 9% rise in serum HDL levels, while fish oil use was not associated with a change in serum HDL levels. Use of fish oil was not associated with any statistically significant change in triglyceride, LDL, or non-HDL cholesterol levels. Lack of a statistically significant correlation between fish oil use and serum triglyceride level reduction may be due to variable patient compliance to fish oil therapy. Poor compliance to dosage, in particular, highlights room for clinical improvement in patient education regarding dosage. Regardless of fish oil use, patients achieved mean serum triglyceride reductions exceeding 25%. This indicates that reduction in triglycerides may be due to lifestyle changes adopted during clinical visits instead of to fish oil therapy.