At the University of Chicago, in an atmosphere of interdisciplinary scholarship and discovery, the Pritzker School of Medicine is dedicated to inspiring diverse students of exceptional promise to become leaders and innovators in science and medicine for the betterment of humanity.
69th Annual Senior Scientific Session

Wednesday, May 20, 2015

Oral Presentations
1 PM - 4 PM | Biological Sciences Learning Center - Room 115

Poster Presentations
4:15 PM - 6:30 PM | Gordon Center for Integrative Science - 3rd Floor Atrium

2015 Session Chair

Jessica Kandel, MD
Mary Campau Ryerson Professor of Surgery;
Chief, Section of Pediatric Surgery; Surgeon-in-Chief, Comer Children’s Hospital

2015 Presentation Judges

Arshiya Baig, MD, MPH
Department of Medicine

Jacqueline Bernard, MD
Department of Neurology

Anthony Chang, MD
Department of Pathology

Marshall Chin, MD, MPH
Department of Medicine

Harriet de Wit, PhD
Department of Psychiatry and Behavioral Neuroscience

Dana Edelson, MD, MS
Department of Medicine

Scott Eggener, MD
Department of Surgery

Lucy Godley, MD, PhD
Department of Medicine

Elbert Huang, MD, MPH
Department of Medicine

R. Stephanie Huang, PhD
Department of Medicine

Megan Huisingh-Scheetz, MD, MPH
Department of Medicine

Catherine Humikowski, MD
Department of Pediatrics

Scott Hunter, PhD
Department of Psychiatry and Behavioral Neuroscience

Kristen Knutson, PhD
Department of Medicine

John Kwon, MD, PhD
Department of Medicine

Andrea Lo, MD
Department of Surgery

Doriane Miller, MD
Department of Medicine

Mark Musch, PhD
Department of Medicine

Sola Olopade, MD, MPH
Department of Medicine

Tipu Puri, MD, PhD
Department of Medicine

Stephen Small, MD
Department of Anesthesia & Critical Care

Audrey Tanksley, MD
Department of Medicine

Larry Thaete, PhD
Department of Obstetrics and Gynecology
NorthShore University HealthSystem

Monica Vela, MD
Department of Medicine

Olga Zaborina, PhD
Department of Surgery
Welcome & Opening Remarks
Biological Sciences Learning Center - Room 115

1 PM  Holly J. Humphrey, MD
Ralph W. Gerard Professor in Medicine
Dean for Medical Education

Jessica Kandel, MD
Mary Campau Ryerson Professor of Surgery
Chief, Section of Pediatric Surgery; Surgeon-in-Chief, Comer Children’s Hospital

Oral Presentations
Abstracts on Pages 13-23

1:15 PM  Claire Shappell; Mentor: Valerie Press, MD, MPH
Preventing Hospitalization in COPD: An Intervention and Qualitative Study of Patient Perspectives

1:30 PM  Camil Correia; Mentor: Jayant Pinto, MD
Multisensory Impairment is Prevalent and Correlates with Physical Performance and Function in Older Adults in the United States

1:45 PM  Claire Beveridge; Mentor: Vineet Arora, MD, MAPP
Characterizing Sleep and Activity Recovery After Hospitalization: Dream On?

2:00 PM  David Binder, PhD; Mentor: Hans Schreiber, MD, PhD
Antigen-Specific Bacterial Vaccine Combined with Anti-PD-L1 Rescues Dysfunctional Endogenous T-Cells to Reject Long-Established Cancer

2:15 PM  Stephanie Kim, PhD; Mentor: Tong-Chuan He, MD, PhD
Skeletal Expression of BMP-9 Causes a Scoliosis-Like Phenotype

2:30 PM  BREAK

2:45 PM  André Davies; Mentor: Christopher Gomez, MD, PhD
Drug Discovery Targeting a Novel Genetic Mechanism for SCA6

3:00 PM  John Lim; Mentor: Joel Pekow, MD
Elevated Serum Vitamin D Levels are Associated with Improved Epithelial Barrier Function and Decreased Mucosal Inflammation in Patients with Ulcerative Colitis

3:15 PM  Oluwafikunmi Sobowale; Mentor: Victoria Ngo, PhD (Rand Corporation)
Barriers to Mental Health Care Among Low-Income Women in Vietnam and Their Role on Effectiveness of Primary Care-Based Depression Intervention

3:30 PM  Cassandra Fritz; Mentor: Karen Kim, MD, MS
Knowledge of Polyp History and Recommended Follow-Up Among African Americans and the Impact of Patient Navigation

3:45 PM  Jack Peace; Mentor: Dana Edelson, MD, MS
The Use of End-Tidal Carbon Dioxide Cutoffs for Predicting Death During In-Hospital Resuscitations
Poster Presentations
4:15 PM - 6:30 PM | Gordon Center for Integrative Science - 3rd Floor Atrium
Abstracts on Pages 24-68

4:15 PM
Katlynn Adkins
Rachel Allon
Philip Carullo
Anne Castro
Rachel Chen
Alexander Cole
Michael Cui
Meghan Daly
Kyle Ericson
Alexandra Garnett
David Goese
Dominic Harris
Michael Hayes
Justin Hellman
Arielle Hirschfeld
Kevin Hodges
Jennifer Kraninger
Yimo Lin
Elise Madrid
Jennifer McCoy
Claire Naus
Melissa Naylor, PhD
Patricia Osmolak
Rishi Pandya
Paras Patel
Joanna Perdomo
Lorenzo Rinaldo, PhD
Christopher Rishel, PhD
Richard Schroeder
Brittany Seidensticker
Nan Sethakorn, PhD
Jonathan Stein
Kevin Stephens, Jr.
Emily Stockert, MBA
Christina Suh
Nathan Swallow
Brian Thurber
Kiara Tulla
Vaibhav Upadhyay, PhD
Yan Wang
Michael Yee

5:45 PM Presentation Judging for the Following Awards

ORAL PRESENTATIONS

*Catherine Dobson Prize*
For the best oral presentation given by a student in the area of Scientific Investigation in Clinical Research or Social Sciences

*Leon O. Jacobson Basic Science Prize (MD/PhD students)*
Granted to the MD/PhD student whose Basic Science Research is judged to be the most meritorious from among session participants

*Leon O. Jacobson Prize (non-PhD students)*
For the best oral presentation given by a non-PhD student in the area of the Basic Biological Sciences

*Medical and Biological Sciences Alumni Association Prize*
For the best presentation made by a student in the area of Applied Scholarship (Global Health, Community Health, Medical Education, or Quality & Safety)

POSTER PRESENTATIONS

Award for Best Poster Describing Applied Scholarship
Award for Best Poster Describing Scientific Investigation in Basic Sciences
Award for Best Poster Describing Scientific Investigation in Clinical Research or Social Sciences

6:15 PM Closing Remarks & Awards Presentation

Jessica Kandel, MD
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CLINICAL RESEARCH/SOCIAL SCIENCES (CONT)
The annual Senior Scientific Session was founded by Dr. Leon Jacobson in 1946 to highlight the caliber of Pritzker student scholarship and the quality of their medical education. Dr. Jacobson, a native of Sims, North Dakota, received a Bachelor of Science degree from North Dakota State University in 1935 and his Medical Doctorate from the University of Chicago in 1939. His professional career—invested entirely at the University of Chicago—included serving as Director of the Argonne Cancer Research Hospital, as well as Dean of the Division of Biological Sciences.

In 1942, during his residency at the University of Chicago Hospital, Dr. Jacobson was recognized for his scholarly promise. He was tasked with the responsibility of protecting the health of the staff of the Manhattan Project. Dr. Jacobson was chosen for this important position because of his research on the biological effects of radiation, as well as his reputation as one of the first doctors to treat blood disorders with radioactive phosphorus. By the conclusion of the Manhattan Project in 1945, Dr. Jacobson and his staff had pioneered several medical advances, including testing the first forms of chemotherapy used to fight cancer. He was later credited with creating the foundation for bone marrow transplantation and initiating the search for the erythropoietin, a hormone that regulates red blood cell production. Erythropoietin is now the basis for a drug that treats chemotherapy-induced anemia in many cancer patients, a revolutionary treatment in the field of oncology.

The Senior Scientific Session is upheld as an annual tradition. By providing graduating Pritzker students with the opportunity to disseminate their research and scholarship through oral and poster presentations, the legacy of Dr. Jacobson’s commitment to innovation through research continues.
2014-2015 Calvin Fentress Fellowship Recipients

Kyle Ericson  
Mentor: Scott Eggener, MD

Dominic Harris  
Mentor: Sandi Lam, MD, MBA, Baylor College of Medicine

Justin Hellman  
Mentor: Susan Ksiazek, MD

John Lim  
Mentor: Joel Pekow, MD

Yimo Lin  
Mentor: Sandi Lam, MD, MBA, Baylor College of Medicine

Patricia Osmolak  
Mentor: David Glick, MD, MBA

Rishi Pandya  
Mentor: Sola Olopade, MD, MPH

Richard Schroeder  
Mentor: William Myers, MD

Claire Shappell  
Mentor: Valerie Press, MD, MPH

Oluwafikunmi Sobowale  
Mentor: Victoria Ngo, PhD, RAND Corporation

2014-2015 John D. Arnold, MD Scientific Research Prize Recipients

Claire Beveridge  
Mentor: Vineet Arora, MD, MAPP

Cassandra Fritz  
Mentor: Karen Kim, MD

Jennifer McCoy  
Mentor: William Meadow, MD, PhD
2014-2015 JOHN D. ARNOLD, MD
MENTOR AWARD RECIPIENTS

In 2012, a grateful alumnus, Dr. Charles Pak, established the John D. Arnold, MD, Scientific Research Prize. This prize was established in recognition of the impact that his mentor had on his education and future career in research. The Arnold Scientific Research Prize recognizes students whose research accomplishments as medical students are based on ongoing, sustained work with a single faculty mentor. The goal of the Arnold Scientific Research Prize is to provide support for the continuation of the mentoring relationship and collaborative research experience during the student’s fourth year of medical school. As part of the application, students are asked to comment on the contributions that their mentors have made towards their professional growth and development. Mentors of the selected students are honored with the 2014-2015 John D. Arnold, MD, Mentor Award for sustained excellence in mentoring medical students.

This year’s John D. Arnold, MD Mentor Awards are bestowed upon:

Vineet Arora, MD, MAPP

Dr. Vineet Arora is an academic hospitalist, Assistant Dean for Scholarship & Discovery, and Director of GME Clinical Learning Environment and Innovation at the University of Chicago. Through her leadership roles, Dr. Arora enables incoming medical students to participate in longitudinal mentored scholarly projects. In the latter role, she bridges educational and hospital leadership to integrate residents and fellows into hospital quality, safety, and value initiatives. An accomplished researcher, she has developed and evaluated novel interventions that combine systems change with adult learning theory to improve care and learning in teaching hospitals. Through AHRQ funding, Dr. Arora has developed tools to evaluate handoff quality among hospitalists and residents. As PI of an NHLBI R25 grant, she is investigating the effect of sleep loss on hospitalized patients and working to create novel interventions to optimize patient experience in hospitals through workplace learning and systems change. Through R-01 funding, Dr. Arora currently is studying the impact of a novel teen-led social media intervention to boost interest of youth in research careers. She has authored over 100 peer-reviewed publications, many of them with medical students in the Summer Research Program or Scholarship & Discovery Program. She was recently awarded the Fred Brancati Leadership & Mentorship Award from the Society of General Internal Medicine.

Dr. Arora received the John D. Arnold MD Mentor Award for her work with fourth year student Claire Beveridge. Dr. Arora and Claire focused diligently on better understanding sleep and physical activity in older hospitalized patients. Commenting on Dr. Arora’s outstanding style of mentorship, Claire noted: “[Dr. Arora is] very hands-on and active in students’ education, which is something I was looking for. Working with this mentor has shown me how it is possible to balance clinical and research duties, which was important to me considering my goal of entering medicine as a specialty.”
Karen Kim, MD, MS

Dr. Karen Kim is a Professor of Medicine, Dean for Faculty Affairs for the Division of Biological Sciences, and Director of the University of Chicago Medicine Comprehensive Cancer Center Office of Community Engagement and Cancer Disparities. She has been actively involved in community-based participatory research focusing on understanding the attitudes, knowledge and beliefs regarding cancer screening among minority populations, specifically to understand the impact of culturally competent, linguistically specific educational messaging on improving cancer awareness and prevention among African American and Asian American communities. Dr. Kim is a principal investigator of an NCI P20 grant (Chicago South Side Cancer Disparities Initiative) to develop an interprofessional cancer disparities program for Chicago State University’s Master’s of Public Health program (a minority serving institution) and the University of Chicago Pritzker School of Medicine. Dr. Kim is a nationally recognized leader in research and public policy focused on Asian Americans and serves as the principal investigator of the Partnership for Healthier Asians, an AHRQ supported program to develop a market oriented dissemination model to improve cancer screening among Asian American immigrants. Dr. Kim has over 15 years of experience in research, advocacy and civic engagement. Finally, as a community member, faculty and advocate, Dr. Kim is committed to leading advocacy efforts to improve health equity for Asian Americans.

Dr. Kim received the John D. Arnold, MD Mentor Award for her work with fourth year student Cassandra “Cassie” Fritz. Dr. Kim and Cassie worked attentively together on a patient navigation project, working to increase the rates of Colorectal Cancer screening among minority groups and medically underserved patients. Writing about Dr. Kim’s consummate mentorship, Cassie commented:

“One of her best qualities as a mentor is that she provides the appropriate guidance as to what I should be working towards, but she allows me to make and learn from my own mistakes. She provides the perfect balance between support and autonomy, and I truly believe this is one of the main reasons I have enjoyed working with her for so long.”

William Meadow, MD, PhD

Dr. William Meadow is an expert in neonatology who specializes in the treatment of complications related to premature birth. Dr. Meadow’s research focuses on medical ethics in the field of neonatal epidemiology; specifically, he has examined resource allocation, as well as issues of informed consent, in neonatal intensive care units. With strong commitment to medical education, Dr. Meadow has mentored several fellows and medical students in both their clinical training as well as in research design and implementation. Dr. Meadow has authored more than 75 articles in scientific and medical journals, 40 book chapters and a book on neonatal bioethics, and is frequently invited to speak at conferences on medical ethics and neonatal care.

Dr. Meadow received the John D. Arnold, MD Mentor Award for his work with fourth year student Jennifer “Jenny” McCoy. In their work together, Dr. Meadow and Jenny undertook a qualitative investigation of parental perceptions of NICU intervention among extremely premature infants. Jenny spoke highly of the impact that Dr. Meadow had on her professional development, writing:

“Dr. Meadow is a clinician scientist who has established himself as a leading ethicist in the field of neonatology...Working with him has been a valuable experience that has contributed to my development as a clinician and a researcher...He provides excellent guidance and feedback, but also allows me to have valuable autonomy so I can develop my own ideas around a project.”
Oral Presentations
Preventing Hospitalization in COPD: An Intervention and Qualitative Study of Patient Perspectives

Claire Shappell

**Mentor:** Valerie Press, MD, MPH, Department of Medicine, Section of Hospital Medicine

**Co-Authors:** Aaron Tannenbaum, MD; Michael Miller, BA; Stephen White, MD; Tina Shah, MD, MPH

**Background:** Chronic obstructive pulmonary disease (COPD) is the third leading cause of death and the third leading cause of hospital readmissions in the US. The direct costs of COPD care total nearly $50 billion, with $13.2 billion spent on in-hospital care alone. Since October 2014, COPD is included in the Medicare Hospital Readmissions Reduction Program (HRRP), legislation enacting financial penalties for hospitals with above-expected rates of 30-day readmissions. Therefore, there is a growing focus on improving quality of COPD care and reducing readmissions. However, few data exist to support the effectiveness of readmissions-reduction interventions. University of Chicago Medicine has developed and implemented a novel COPD Readmission Reduction Program (CRRP) with the objective of reducing all-cause 30 day readmissions. In addition to investigating the efficacy and costs of the intervention, understanding patient perspectives on COPD (re)admissions and barriers to care is critical.

**Methods:** The CRRP, a Quality Improvement (QI) program to reduce COPD readmissions, was started in February 2014; it has been revised in August and October of 2014 using the Plan-Do-Study-Act QI method. The primary aims of the QI project were to determine if readmissions could be reduced and in a cost-savings manner. Our secondary aims are to: (1) elucidate patients' beliefs about why they have been admitted or readmitted for COPD; (2) identify potential targets for future interventions to improve COPD care and reduce hospitalizations; and (3) evaluate patients' understanding of and attitudes toward the institution's new CRRP. To achieve these aims, we will conduct in-depth semi-structured interviews with 30 patients admitted for COPD exacerbations or until thematic saturation is reached. Potential subjects will be identified using the CRRP screening algorithm and approached in-person for participation. Written consent will be obtained. Interviews will be conducted using an interview guide in participants’ hospital rooms by trained interviewers with audio recording. Transcribed recordings will be analyzed using a modified grounded theory approach. Data will be sorted into coding categories that are developed a priori and into categories that emerge during analysis; coding by a second independent coder will be compared for agreement. Themes will be extracted by investigators in a group process and theoretical saturation will be determined. Atlas.TI software will be utilized for analysis.

**Results:** Between February 2014 and January 2015, 327 patients were admitted for COPD. Median age was 64.3 (SD 11.6), 58.5% were female, 90.0% were of Black race. 61 patients (18.7%) were readmitted within 30 days. The average readmissions rate over four months at program initiation (February-May 2014) was 25%. The average readmissions rate over most recent four months with available data (October-December 2014) was 12.7% for a reduction in admissions of 50%. The survey tools have been developed and refined through pilot interviews with data collection expected to start in April 2015.

**Conclusion:** The CRRP appears to be effective at reducing 30 day admissions for COPD patients. Better understanding of our patients’ views of hospitalizations and program benefits and shortcomings will enable us to improve the CRRP and potentially illuminate subgroups for whom the program may need to be refined.

**Acknowledgements/Disclosures:** My M4 S&D work is one arm of a larger study which received the 2014 University of Chicago Medicine Innovations Grant. The University of Chicago Calvin Fentress Fellowship Recipient.
Multisensory Impairment Is Prevalent and Correlates with Physical Performance and Function in Older Adults in the United States

Camil Correia

**Mentor:** Jayant Pinto, MD, Department of Surgery, Section of Otolaryngology-Head & Neck Surgery

**Co-Authors:** Kevin Lopez, BS; Kristen Wroblewski, MS; Megan Huisingh-Scheetz, MD; MPH, David Kern, MA; Rachel Chen, MS4; L. Philip Schumm, MA; William Dale, MD, PhD; Martha McClintock, PhD

**Background:** Age-related decline of the senses (sight, smell, hearing, touch, and taste) poses significant burdens on older adults. The prevalence and co-occurrence of sensory deficits and their combined effects on physical performance and function are not well characterized.

**Methods:** The National Social Life, Health, and Aging Project, a representative, population-based study of community dwelling older US adults (57-85 years of age), collected biomarkers, social and health history, and other physiological measures, including sensory and physical function. We determined the prevalence and patterns of sensory impairments, defined associated risk factors, and assessed an integrated index of global sensory dysfunction. We hypothesized that sensory deficits would be common and increase with age, and that multisensory impairment would be closely associated with concurrent physical performance (Timed Up and Go [TUG]) and disability (Activities of Daily Living [ADL]).

**Results:** 73% of older adults had an impaired sense of taste; 69% had decreased sense of touch; 21% had decreased olfaction; 19% of older adults had decreased vision; and 17% had diminished hearing. Over 94% suffered from at least one sensory deficit and 67% experienced two or more. Older adults, men, African Americans, and those with lower socioeconomic status had greater multisensory impairment (p<0.05, all), even after adjusting for factors that might account for these disparities. Increased sensory dysfunction was associated with longer TUG times (OR 1.13, 95% CI 1.05 – 1.23) and increased number of ADL deficits (OR 1.16, 95% CI 1.07-1.25) in multivariate models.

**Conclusion:** Sensory impairments are common and are affected by age, gender, race, and socioeconomic status. Global sensory impairment is associated with decreased physical performance and disability and warrants further study.

**Acknowledgements/Disclosures:** National Institutes of Health R01AG021487, R37AG030481, and R01AG033903 including National Institute of Aging, Office of Research on Women’s Health, Office of AIDS Research and National Heart, Lung, and Blood Institute grant: 1R25HLO96383.
Characterizing Sleep and Activity Recovery After Hospitalization: Dream On?

Claire Beveridge

Mentor: Vineet Arora, MD, MAPP, Department of Medicine, Section of General Internal Medicine

Co-Authors: Kristen Knutson, PhD; Lisa Spampinato, BS; Andrea Flores, MA; David Meltzer, MD, PhD; Eve Van Cauter, PhD

Background: Hospitalization is a period of marked sleep disruption and low physical activity, which are two contributors to what has been described as a “post-hospital syndrome” that contributes to functional decline. To date, no study has described sleep and activity recovery among medical patients after hospital discharge. Understanding these patterns could help establish interventions to address post-hospital syndrome. This study aims to use objective methods to characterize daytime activity, sleep duration, and sleep efficiency among patients both in the hospital and after discharge.

Methods: Patients aged 50 and over, community-dwelling, ambulatory, discharged from hospital to home without an ICU stay, and wore the actiwatch in the hospital for at least 2 nights and after the hospital for at least 3 nights were eligible. Objective physical activity (average activity counts/minute), sleep duration (minutes), and sleep efficiency (% of time asleep over time in bed) were measured. Daytime sleepiness was determined on admission by the Epworth Sleepiness Scale (ESS) and baseline sleep duration was determined using self-reported values on the Pittsburgh Sleep Quality Index (PSQI). Length of stay and demographics were collected from charts. Descriptive statistics were used to summarize data. Random effect linear regression models, clustered by subject, were used to examine the association between sleep duration, sleep efficiency, and daytime activity before and after hospitalization, as well as with increasing day after discharge.

Results: From October 2012 to December 2014, 185 nights of sleep and 177 periods of activity were sampled from 25 patients. Most patients were African American (84.0%), female (68.0%), with a median length of stay in the hospital of 3 days (IQR=24). On admission, 36.0% were categorized as excessively sleepy. Prior to hospitalization, mean self-reported sleep duration was 368 minutes ± 1.75. In-hospital mean sleep duration via actiwatch was 349 minutes ± 120. Mean in-hospital sleep efficiency was 74.9% ± 16.2. In-hospital mean activity level over the waking period was 141 ± 72.9, corresponding to sitting while eating. Post-discharge mean sleep duration via actiwatch was 353 ± 132 minutes and sleep efficiency was 71.4% ± 19.2, with no significant difference from hospitalization. Post-discharge sleep did not increase for each day enrolled in study. Post-discharge mean activity level was 205 ± 112, corresponding to sitting while being active with hands. In regression models controlling for subject, post-discharge period was associated with higher activity counts than in-hospital activity counts (+53 counts/minute 95%CI [32, 74], p<0.01). Daytime physical activity also increased by 10 counts/minute for each day enrolled in the study (95%CI[6, 14], p<0.01).

Conclusion: While it is thought sleep loss is acute during hospitalization, patients in this study do not experience sleep recovery after discharge. On the other hand, patients’ activity levels improve for each day after discharge, possibly indicating improved health and physical function. Longer follow-up may be needed to understand if patient sleep is eventually restored to baseline after discharge or if hospitalization is associated with a more chronic sleep disorder.

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Antigen-Specific Bacterial Vaccine Combined with Anti-PD-L1 Rescues Dysfunctional Endogenous T Cells to Reject Long-Established Cancer

David Binder, PhD

Mentor: Hans Schreiber, MD, PhD, Department of Pathology

Co-Authors: Boris Engles, PhD; Ainhoa Arina, PhD; Ping Yu, MD, PhD

Background: Cancer cells express tumor-specific antigens that can elicit a CD8+ T cell response. However, tumor-specific CD8+ T cells eventually become dysfunctional and are unable to control tumor progression. Rescuing T cell responses with PD-1 and CTLA-4 blocking antibodies only provides clinical responses in 40% of melanoma patients. Here we engineered a new therapeutic vaccination approach that uses the attenuated Salmonella Typhimurium A1-R strain to deliver exogenous tumor specific antigen into tumors for coordinating antigen delivery and TLR signaling to antigen-presenting cells. We tested the capacity of this approach to rescue T cell responses in tumors refractory to PD-1 and CTLA-4 blockade.

Methods: B16 melanoma cancer cells expressing the tumor specific model antigen OVA were injected into C57BL/6 mice. We tested the capacity of different approaches to rescue CD8+ T cell function by T cell peptide-stimulation assays and tumor treatment experiments.

Results: Long-established B16-OVA tumors, established for at least 2 weeks and larger than 100mm3, were heavily infiltrated by endogenous dysfunctional PD-1+ OVA-specific CD8+ T cells. B16-OVA tumors were resistant to treatment with the αPD-L1 and αCTLA-4 blocking antibodies. Treatment of B16-OVA-bearing mice with antigen-producing A1-R rescued the endogenous tumor-specific CD8+ T cell response: proliferation was restored in the lymphoid organs and effector function was gained in the tumor. While antigen-producing A1-R treatment resulted in tumor eradication in about one third of mice, consistent eradication was achieved by combining antigen-producing A1-R with αPD-L1.

Conclusion: Therapeutic vaccination using tumor-targeting A1-R in combination with αPD-L1 can achieve relapse-free destruction of long established tumors by rescuing dysfunctional endogenous CD8+ T cells. This approach deserves further investigation for treating clinical tumors refractory to PD-1 and CTLA-4 blockade.

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Skeletal Expression of BMP-9 Causes a Scoliosis-Like Phenotype

Stephanie Kim, PhD

Mentor: Tong-Chuan He, MD, PhD, Department of Orthopaedic Surgery & Rehabilitation Medicine

Co-Author: Ning Hu, MD, PhD; Ruidong Li, MD, PhD; Jianli Gao, PhD

Background: By understanding molecular pathways important for bone development, we can gain insight into the pathogenesis of musculoskeletal disease and develop targeted strategies for regenerative medicine in bone. Our lab was the first to identify Bone Morphogenetic Protein-9 (BMP-9) as one of the most osteogenic BMPs in an in vitro and in vivo screening of all 14 human BMPs. Despite a powerful capacity to form bone, BMP-9’s physiologic role in the in vivo musculoskeletal system is unknown. Bone Morphogenetic Proteins (BMPs) are a historically important family in bone development. Osteogenic BMPs rhBMP-2 and rhBMP-7 are approved for certain orthopaedic uses including open fractures and spinal fusion. By evaluating BMP-9’s role in vivo we can gain insight into its therapeutic or pathologic potential in the musculoskeletal system. Here we demonstrate that over-expression of BMP-9 in the mouse skeletal system can lead to a syndrome reminiscent of Adolescent Idiopathic Scoliosis.

Methods: Immunohistochemistry of BMP-9 was performed on mouse intervertebral discs. A Cre-Lox mediated conditional BMP-9 over-expression mouse (CoBMP-9) was generated. To over-express BMP-9 in the skeleton, CoBMP-9 mice were mated to 2.3CollI-Cre mice. The gross skeletal structure of CoBMP-9+, 2.3CollI-Cre+ mice was characterized using micro-CT. Intervertebral disc histology was visualized using H&E. Newborn spines were visualized using Alizarin red/ Alcian blue stain. Immortalized mouse intervertebral disc (iMID) cell lines were created and characterized as annulus fibrosus (AF) or nucleus pulposus cells (NP) using RT-PCR. We characterized BMP-9’s effect on iMID proliferation and differentiation using flow cytometry, Alkaline phosphatase (ALP) assay, ALP stain, osteopontin and osteocalcin stain, Alizarin Red stain and ectopic injection.

Results: IHC showed that BMP-9 expression in the cells of the prenatal and postnatal intervertebral disc. CoBMP-9+, 2.3CollI-Cre+ mice have smaller size and kinky tails. Micro-CT shows progressive thoracolumbar spinal curvature, but an otherwise grossly normal skeleton. Whole mount Alizarin Red/ Alcian blue stain of newborn CoBMP-9+, 2.3CollI-Cre mice shows that the spinal curvature is not present at the time of birth. Histology shows irregular disc morphology with increased AF thickness. IHC shows that BMP-9 is over-expressed in the intervertebral disc. AdBMP-9 expression in AF iMID cells induces Notch mediated osteogenic differentiation as shown by ALP assay and stain, osteopontin and osteocalcin IHC, and Alizarin red. AdBMP-9 transduced AF iMID cells produce a trabeculated ectopic bony mass in the nude mouse, while NP cells produce a smaller cartilaginous mass.

Conclusion: BMP-9 skeletal over-expression results in a scoliosis-like syndrome. To our knowledge, this is the first model of postnatal and progressive scoliosis confined to the axial skeleton resembling AIS. Histology and in vitro and in vivo iMID studies suggest that the deformity may be caused by increased proliferation and osteogenic fate change of AF cells. This study highlights a role for BMP-9 in axial pathogenesis and/or development in conjunction with the Notch pathway. We believe our mouse model and iMID cells will be of great clinical value in studying the cellular and molecular mechanisms behind scoliosis and other degenerative disc diseases.

Acknowledgements/Disclosures: none.
Drug Discovery Targeting a Novel Genetic Mechanism for SCA6

André Davies

Mentor: Christopher Gomez, MD, PhD, Department of Neurology
Co-Author: Xiaofei Du, PhD

Background: Spinocerebellar Ataxia 6 (SCA6) is a rare, autosomal dominant disorder that presents late in adulthood and progressively worsens. SCA6 is characterized by dysarthria, oculomotor disorders, incontinence, peripheral neuropathy, and ataxia of gait, stance, and the limbs due to cerebellar dysfunction. Currently, there is no treatment for SCA6. SCA6 is a result of an expansion of polyglutamine (polyQ) encoding CAG repeats encoded by a newly identified 47th exon within the CACNA1A gene. CACNA1A is a bicistronic gene, and that the single mRNA product transcribed codes for two proteins, $\alpha_1$A and $\alpha_1$ACT. It does so using a cryptic internal ribosomal entry site (IRES). $\alpha_1$ACT, which contains the polyQ tract, is enriched in cerebellar nuclei and is stable. Normally, $\alpha_1$ACT is a transcription factor involved in cerebellar cortical development. $\alpha_1$ACT with the expanded polyQs does lead to toxicity that increases with age. It would therefore be advantageous to decrease $\alpha_1$ACT with the expanded polyQs before the onset of SCA6 symptoms. The aim is to demonstrate that $\alpha_1$ACT expression can be selectively decreased without effecting $\alpha_1$A expression, using selected drugs.

Methods: HEK293 cells were transfected following TransIT protocol. 2 vectors were used, named PRF, and PR100TF. After transfection cells were subjected to 1,200 drugs from the Prestwick library. All plates were subjected to drug conditions for 72 hours. The cells were then collected, and lysed. Using a luminometer and Dual Luciferase assay to measure the expression of Renilla and firefly; the data was recorded in Excel. HEK293 stably transfected with flag tagged $\alpha_1$A were subjected to 7 drugs that were shown to decrease $\alpha_1$ACT expression without affecting $\alpha_1$A expression in the luciferase assay of 1,200 drugs. Cells were collected after 72 hours. Cells were lysed and prepared for protein collection. Protein samples were subjected to Western Blot analysis using 8% gel. The gels were transferred to a nitrocellulose membrane and subjected to antiflag antibody (1:20,000). The membranes were then developed and imaged via fluorescence.

Results: The following drugs were found in the luciferase assay to effect IRES activity: bromphenimarine, chlorambucil, deferoxamine, diethylstilbestrol, lycorine, nocardazole, sulfasalazine, lynestrenol, and eburnamone. The concentrations used of each drug and length of time cells were subjected to the drugs were chosen based on previous studies. 7 of these drugs were given to cells and then worked up in western blot. In comparison to the control, cells that were transfected with a vector containing the entire IRES and were subjected to nocardazole, diethylstilbestrol, and licorice HCl demonstrated reduced $\alpha_1$ACT expression in comparison to $\alpha_1$A expression in western blot, as well as showed decreased expression with increasing concentration. In contrast, no change was seen with chlorambucil, bromphenarimine, deferoxamine, and sulfasalizone.

Conclusion: A subset of the drugs selected were proven via luciferase assay as well as the gold standard western blot to selectively decrease $\alpha_1$ACT expression without dramatically effecting $\alpha_1$A expression. Therefore these drugs may be applicable for future treatment options for patients with SCA6.

Acknowledgements/Disclosures: none.
Elevated Serum Vitamin D Levels Are Associated with Improved Epithelial Barrier Function and Decreased Mucosal Inflammation in Patients with Ulcerative Colitis

John Lim

Mentor: Joel Pekow, MD, Department of Medicine, Section of Gastroenterology
Co-Authors: Katherine Meckel; Marc Bissonnette, MD

Background: Several epidemiological studies looking at rates of inflammatory bowel disease development based on geography support a role for vitamin D in the pathogenesis of IBD. Furthermore, data from our laboratory indicates that vitamin D is protective of colitis by reducing inflammation and improving barrier function. In preliminary studies, we have demonstrated for the first time that serum vitamin D levels have an inverse correlation with mucosal inflammation with ulcerative colitis. To test the hypothesis that serum vitamin D is protective of epithelial barrier function and associated with decreased inflammation, we examined expression of tissue VDR, junctional proteins, and pro-inflammatory cytokines in this cohort.

Methods: Mucosal biopsies were obtained from the sigmoid colon at the time of colonoscopy and serum collection for 25-OH vitamin D in subjects with ulcerative colitis. Immunohistochemistry was performed on 74 patients distributed by Mayo endoscopy scores. Slides were stained for e-cadherin, VDR, claudin-2, zo-1, and occludin. Semi-quantitative scoring was performed by 3 blinded investigators and comparisons made between subjects with low (<20ng/mL) and high (>30ng/ml) serum vitamin D levels. Quantitative real time PCR (qPCR) was performed for TNFα, VDR, e-cadherin, zo-1, occludin, and claudin-2 on 57 patients evenly distributed by Mayo endoscopy scores and compared between subjects with low vs. high serum vitamin D levels.

Results: By immunohistochemistry, expression of VDR (p = 0.02) and e-cadherin (p = 0.04) demonstrated increased expression with increased vitamin D levels at the luminal surface regardless of degree of mucosal inflammation. Expression of occludin was non-significantly increased in subjects with elevated serum vitamin D. No association was observed between zo-1 or claudin-2 protein expression and serum vitamin D levels although differences in expression between patients were difficult to quantitate because of the focal nature of the staining. By qPCR, tissue expression of VDR (2.5-fold, p = 0.06) and Ecadherin (2.6-fold, p = 0.02) were increased, while TNF-α (2-fold, p = 0.03) was decreased in patients with high vitamin D levels compared to those with low levels. There was no association between serum vitamin D levels and zo-1 transcript expression. Studies examining transcript expression of occludin and claudin-2 are in progress.

Conclusion: Vitamin D deficiency is common in patients with ulcerative colitis. Moreover, we demonstrated an inverse correlation between serum vitamin D level and mucosal inflammation. The finding that serum vitamin D levels correlated with VDR, ecadherin, and occludin and inversely with TNFα supports the hypothesis that vitamin D deficiency may contribute to disease activity in ulcerative colitis through disruption of epithelial barrier function.

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Barriers to Mental Health Care Among Low-Income Women in Vietnam and Their Role on Effectiveness of Primary Care-Based Depression Intervention

Oluwafikunmi Sobowale

Mentor: Victoria Ngo, PhD, RAND Corporation

Co-Authors: Bahr Weiss, PhD; Lam Tu Trung, MD

Background: Despite an increased risk of developing depression, low-income women are less likely to receive mental health care. In order to better understand the barriers to care these women face, we assessed structural, attitudinal, social and psychological barriers. Further, we examined the effect of these barriers on help-seeking behavior and completion of a primary care-based depression intervention.

Methods: We interviewed 188 low-income women presenting at four primary care clinics in Vietnam at baseline and after completion of a combined poverty alleviation and depression group therapy intervention. We assessed barriers to care and predictors of these barriers (socio-demographics, etc.) based on a literature review. Next, we analyzed the effect of barriers to care on help-seeking behavior at baseline and post-intervention. Finally, we used mixed-methods analysis to evaluate whether barriers predicted session attendance for the intervention. We used nested multivariable linear and logistic regressions as well as t-tests for analyses. We performed all analyses using STATA 12.0 and set significance at P <.05. For qualitative interviews (n = 27), three raters used structural analysis to code questions of barriers to care.

Results: At baseline, 90% of women endorsed at least one structural barrier to care. There was a moderate amount of depression stigma and less than half of women had adequate mental health literacy. Higher goal self-efficacy was consistently associated with lower endorsement of time-related structural barriers. Women with more children (standardized regression coefficient (β) = 0.25, p = <0.001) or with negative attitudes (β= 0.15, p = 0.02) toward treatment endorsed more structural barriers. Participants with higher social support (OR = 1.02, p = 0.03) and social capital (OR = 2.18, p = 0.009) had higher mental health literacy. Women who knew someone with depression had lower stigma (β = -0.16, p = 0.02) and negative attitudes (β = -0.19, p = 0.003) towards treatment. Only 34% of women sought care for mental health in the last year, while 85% sought care for physical illness. Participants with high social capital were twice as likely to seek help for mental illness, while those with negative attitudes were three times less likely to seek help. Higher social capital predicted group therapy attendance (β= 0.24, p = 0.04), though many women endorsed structural barriers such as work conflicts and child care in qualitative interviews. All barriers decreased for the intervention group, but not the control group.

Conclusion: Low-income women in Vietnam face numerous barriers to mental health care beyond traditional attitudinal and structural barriers. A psychosocial intervention based in primary care appears to effectively decrease barriers to care. However, accommodating women's work and family obligations is necessary to improve the intervention. Mental health care in low- and middle-income settings should be integrated in primary care and responsive to the type of barriers individuals face to better deliver care to underserved populations.

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Knowledge of Polyp History and Recommended Follow-Up Among African Americans and the Impact of Patient Navigation

Cassandra Fritz

Mentor: Karen Kim, MD, MS, Department of Medicine, Section of Gastroenterology

Co-Author: Keith Naylor, MD

Background: Minorities are less likely than whites to receive colorectal screening (CRS). CRS rates in minority and uninsured patient populations have been improved by patient navigation (PN) interventions. Although initial access to CRS is important, patient knowledge of colonoscopy results and follow-up recommendations have been implicated for nonadherence in colonoscopy follow-up. However, patient knowledge of colonoscopy results and follow-up recommendations has not been described in a predominately African American (AA) or navigated patient population. Therefore, our objectives were to determine patient knowledge of colonoscopy results and follow-up recommendations within an AA patient population and to compare post-colonoscopy knowledge among patients who received either PN or usual care.

Methods: This is a prospective observational study of patients (age >45) who underwent screening colonoscopy between January and June 2014 at the University of Chicago (UC). The PN intervention utilized community-based navigators, who were recruited and trained by the American Cancer Society. Navigators worked with patients to reduce barriers to screening, including vouchers for transportation, bowel preparation instructions and appointment reminders. Usual-care patients accessed the UC gastrointestinal procedure unit through the open access endoscopy (OAE) system. UC affiliated referring physicians may request a colonoscopy without prior gastroenterology consultation and are responsible for providing any additional education. A brief semi-structured telephone survey assessed patient knowledge of colonoscopy results, knowledge of follow-up recommendations, beliefs regarding colorectal cancer prevention, and intent to obtain next colonoscopy. Patient responses were compared with medical records. Statistical analysis included Wilcoxon rank sum test, Pearson’s Chi-square or Fisher’s exact test, and multivariate logistic regression.

Results: Of the 96 patients surveyed, 83% accurately reported if polyps were detected and 66% accurately reported their recommended follow-up. The identification of adenomatous polyps on colonoscopy was a predictor of accurate recall of colonoscopy results and follow-up recommendations. An educational attainment of high school or less was a predictor of poor follow-up recall. Eighteen patients received PN and 78 patients received usual care. The two cohorts were similar in sex, age, race, ethnicity, and educational attainment. Both cohorts were predominately AA, 89% navigated vs. 64% usual care (p = 0.36). The two cohorts differed in identification of a primary care physician (56% navigated vs. 94% usual care; p=<0.01), age (navigated 58.2 ±6 vs. 64.3 ± 9 usual care; p<0.01), insurance status (p <0.01), and estimated household income <$25,000 (78% navigated vs. 40% usual care; p=0.02). The navigated cohort more accurately identified if polyps were found on their exam (100% vs. 79.5%; p = 0.035). The rates of accurate follow-up recall were similar (44% vs. 71%; p = 0.053) between the two cohorts.

Conclusion: In a predominantly AA population, post-colonoscopy polyp recall rates were similar to those described in white populations. Uninsured patients who completed PN were more likely than insured usual care patients to accurately report the presence of polyps on colonoscopy. Future studies should continue to focus on long-term outcomes of PN programs among underserved populations in order to ensure equitable benefit from CRS and to reduce disparities from this often-preventable cancer.

Acknowledgements/Disclosures: The University of Chicago John D. Arnold, MD Scientific Research Prize Recipient.
The Use of End-Tidal Carbon Dioxide Cutoffs for Predicting Death During In-Hospital Resuscitations

Jack Peace

**Mentor:** Dana Edelson, MD, MS; Department of Medicine, Section of Hospital Medicine

**Co-Authors:** Nicole Twu, MS; Richa Adhikari, MPH; Matthew Churpek, MD, MPH

**Background:** Longer resuscitation duration has been associated with increased survival in hospitalized patients. However, longer resuscitations are also associated with high costs and still have very low survival rates. An end-tidal carbon dioxide (ETCO2) value of less than or equal to 10 mmHg at 20 minutes has been proposed as an accurate predictor of mortality but has not been tested in the setting of optimized CPR quality. The aim of this study was to validate an ETCO2 cutoff of 10 mmHg at 20 minutes as a predictor of death and to determine if different cutoff values could be used as predictors of mortality.

**Methods:** We conducted a prospective, observational study of consecutive in-hospital cardiac arrests at two academic medical centers between May 2006 and May 2013. A CPR-sensing monitor/defibrillator which provided real-time audio visual feedback regarding CPR deficiencies was used. The device collected CPR quality data (compression depth and rate) and ETCO2 values via a monitor connected in line with the endotracheal tube. Patient outcome data were abstracted via chart review, with death during hospitalization as the primary outcome. Two-sided t-test and Receiver Operator Characteristics (ROC) were used to compare outcomes and assess ETCO2 timepoints and cutoffs. Test characteristics for ETCO2 cutoffs were generated using descriptive statistics.

**Results:** Outcomes and ETCO2 data were available for 877 patients. Return of spontaneous circulation (ROSC) was achieved in 57.6% of cases, and 12.7% of patients survived to hospital discharge. Mean compression depth was 49 ± 14 mm and mean rate was 107 ± 9 compressions per minute, and did not differ significantly among outcomes. Using the previously proposed 20-minute ETCO2 cutoff of 10 mmHg for predicting mortality yielded a sensitivity of 10.7%, a specificity of 100%, and a positive predictive value (PPV) of 100%. When other timepoints were tested, the ETCO2 cutoffs associated with a 100% PPV of death were 7, 13, 16, and 16 mmHg at 15, 30, 45, and 60-minute intervals, respectively.

**Conclusion:** We demonstrated that in the setting of high CPR quality, ETCO2 cutoffs at certain time intervals are highly specific for death during hospitalization, and have high positive predictive value. This study validated the prognostic value of the ETCO2 value at 20 minutes, even suggesting that the cutoff may be higher than 10 mmHg. The results of this study indicate that delayed ETCO2 cutoffs at timepoints other than 20 minutes may also be used as accurate predictors of mortality. These cutoffs could be used by resuscitation teams, along with other relevant clinical data, to help determine when resuscitative efforts are futile. These data could be combined with other variables during a resuscitation to generate a more accurate prognostic model. Future studies could use ETCO2 cutoffs to determine wasted resuscitation time and the cost of utilizing resources on futile resuscitations.

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Applied Scholarship
Documentation of Reproductive Health Counseling at Primary Care Visits

Katlynn Adkins

Mentor: Debra Stulberg, MD, Department of Family Medicine

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Background: Primary care providers have a unique opportunity to help women achieve well-timed, healthy pregnancies by providing reproductive health services. However, previous studies of documentation of reproductive care in the primary care setting suggest that there is a large unmet need for preconception and contraception services among women of reproductive age. Many barriers exist to the achievement of the CDC recommendation that women receive reproductive care at every primary care visit. This study aimed to determine the rates of documentation of preconception and contraceptive counseling in a patient population at high risk for unintended pregnancy.

Methods: We conducted a chart review of a random sample of women between the ages of 18-45 at a community health center serving a low-income, underserved population on the west side of Chicago. The primary outcome was physician documentation of reproductive health services in the electronic medical record (EMR). Secondary outcomes were association of documentation of services with type of visit and association with health conditions that may complicate pregnancy including diabetes and obesity. We determined documentation from free text, reproductive health forms in the EMR, and ICD-9 codes.

Results: 119 charts were extracted for analysis. Mean age of patients was 30 years old and 98.3% of patients were African American. Reproductive care was documented at 56% of visits, with preconception care at 22% of visits and contraceptive care at 45% of visits. A multivariable model showed that patients over the age of 35 and patients who were seen by an attending physician were less likely to have any reproductive health services documented. Patients with diabetes were significantly more likely to have preconception care documented. There was no significant association between type of visit or other comorbidities and documentation of reproductive care.

Conclusion: This study found high rates of documentation of reproductive health care compared to national estimates. Providers were successful at documenting care even in acute settings where reproductive care was not the reason for visit. Further studies are needed to determine the degree of unmet need for reproductive health services in this population since this study did not include consideration of pregnancy intention. Work is underway to identify whether patient and provider centered interventions impact documentation of reproductive health services. While our study found a relatively high rate of documentation of reproductive care compared to national averages, it is likely that there is unmet need for services given high rates of health conditions and risk factors and low rates of preconception compared to contraceptive care.

Acknowledgements/Disclosures: Primary Care Clinical Scholars Fellowship: Community Preceptor Training Grant.
Predicting Food Insecurity in Caregivers of Hospitalized Pediatric Patients

Meghan Daly

**Mentor:** Stacy Tessier Lindau, MD, MAPP, Department of Obstetrics & Gynecology

**Co-Authors:** Jennifer Makelarski, PhD, MPH; Veronica Escamilla, PhD

**Background:** A third of caregivers at one urban children’s hospital were not getting enough to eat while caring for their hospitalized child; 66% were also living in food insecure homes. Hospital food insecurity, defined as not getting enough to eat during a child’s hospitalization, may interfere with a caregiver’s ability to engage with, advocate for, and make decisions on behalf of their ill child. This study aimed to develop a brief screening tool to identify caregivers at risk of food insecurity in order to effectively intervene during a child’s hospitalization.

**Methods:** Caregivers of hospitalized pediatric patients at a 155-bed acute care urban academic children’s hospital were surveyed between 6/11-12/11 about food access. Bivariate analysis was used to identify variables, including demographic factors and items from established household food insecurity scales, associated (p<.10) with caregiver food insecurity during a child’s hospitalization. These variables were entered into a backward stepwise logistic regression model to identify independent correlates (p<.05) with caregiver hospital food insecurity. Using previously established methodology, odds ratios for the 4 significant correlates identified in this model were rounded to the nearest integer to create risk points for a screening tool to identify caregivers at risk of hospital food insecurity. A second survey was administered in 2014 to 198 caregivers in the same setting to validate the screening tool. A receiver operator curve was generated to determine performance of the tool and to identify a cutpoint to optimize sensitivity.

**Results:** The first survey enrolled 192 caregivers. Fourteen characteristics were associated with hospital food insecurity in bivariate analysis. Multivariable analysis identified 4 items independently associated with hospital food insecurity that were used to create the screening tool: 1) “You have transportation to get food while your child is at the hospital” (5 points); 2) “In the past month, was there any day when you or anyone else in your family went hungry because you did not have enough money for food?” (4 points); “In the past twelve months, you worried whether your food would run out before you got money to buy more” (3 points), and; “What race do you consider yourself to be?” (3 points). At a cut-off score of ≥3, the screening tool predicted hospital food insecurity with a maximum sensitivity of 79%, a specificity of 36%, a positive predictive value of 52% and a negative predictive value of 66%. A cut-off score of ≥5 optimized both sensitivity (66%) and specificity (61%). Using a cut-off score of ≥3, this tool also predicted household food insecurity with a maximum sensitivity of 99%, a specificity of 49%, a positive predictive value of 58%, and a negative predictive value of 98%. A score cut-off of ≥6 optimized both sensitivity (89%) and specificity (84%) for household food insecurity prediction.

**Conclusion:** Identification of caregiver food insecurity at the beginning of a child’s hospitalization can be accomplished with a 4-item screening tool to facilitate early intervention and effective utilization of hospital food assistance programs. The same screening tool identifies household food insecurity, and can be used for discharge planning.

**Acknowledgements/Disclosures:** There are no conflicts. Support for the research was provided by the UChicago Medicine Urban Health Initiative, generous individual donors to the Comer Food Pantry, and the Comer Development Board.
The Community Yoga Project: Health Benefits of Yoga in Underserved Clinical Settings

David Goese

Mentor: Kohar Jones, MD, Department of Family Medicine

Co-Authors: Gregory Van Hyfte, MA; Dagmara Moscoso, BS; Angela Cano-Garcia, BS; Sonia Oyola, MD; Loretta Cain, PhD; Mari Egan, MD, MHPE

Background: Health benefits of yoga include reduction in stress and anxiety levels, decreased musculoskeletal disease symptoms, and benefits related to many chronic diseases. Despite its popularity as one of the most commonly used integrative medicine therapies, yoga is not commonly taught in clinical settings. Underinsured, uninsured, or publicly insured patients who receive care at Federally Qualified Health Centers (FQHC) are disproportionately affected by stress, anxiety, and several chronic diseases. The geographic distribution and cost of yoga classes further renders underserved populations less likely to uptake yoga. To our knowledge, no studies have been published investigating the health effects of FQHC-based yoga programs. The Community Yoga Project is a study of four yoga classes offered at no cost by four volunteer yoga instructors inside two FQHC’s on the South Side of Chicago. The yoga classes featured gentle (Hatha), therapeutic (Iyengar), and restorative yoga and were designed to be personalizable and accessible to all community members.

Methods: Goals of the project include 1) to evaluate the effects of FQHC-based yoga classes on stress and pain levels, 2) to understand motivations and barriers for attending the yoga program, and 3) to develop best practice models for integrating yoga programming into underserved community health centers. A 23 question mixed-methods survey was created in both English and Spanish with the primary outcome of self-reported stress and pain levels. The qualitative portion of the survey assessed barriers and motivations related to yoga use. The survey was administered at baseline, after the first class, and again after study participants had attended yoga classes over three months. Data was collected between March 2013 and January 2014. Quantitative analyses of ANOVA and Wilcoxon signed rank sum test were performed using SAS. Qualitative results were independently analyzed by four study authors using an open coding whole text analysis method based on grounded theory. Themes that emerged were subsequently narrowed and tallied by all data analysts collectively using selective coding.

Results: 70 participants filled out an initial (pre-test) survey. 44 participants completed the pre-test, post-test, and 3 month post-test survey. Study demographics indicate a predominantly female (92%) African American (55%) and Latina (42%) population with a mean age of 52 (SD = 15.3). The average class size was 7.67. Pre-test versus 3 month post-test pain scores significantly decreased (2.56 ± 2.9 versus 1.85 ± 2.4, p=0.0463). Pre- to 3-month post-test stress scores also significantly decreased (3.33 ± 3.14 versus 2.07 ± 3.0, p=0.0047). Common themes emerged from the quantitative data analysis. The most beneficial parts of the program were relaxation, breath work, and flexibility. Participants appreciated personal attention, knowledgeability of yoga instructors, and social connections made with classmates. The two most commonly cited reasons for difficulty with the classes were physical challenges and scheduling issues.

Conclusion: Participants in an FQHC-based yoga program experienced a significant lowering of pain and stress over 3 months. Limitations include a small sample size, lack of a control group, poor generalizability, expectancy bias, and loss to follow-up.

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Creating a Healthy Cooking Resource for Community Members in the South Side of Chicago

Joanna Perdomo

Mentor: Mari Egan, MD, MHPE, Department of Family Medicine

Background: From May–June 2013, a pilot survey was conducted with patients at two federally qualified health centers (FQHCs) in the South Side of Chicago to learn about the cooking, eating, and grocery shopping behaviors of community members in the area. This 43 item survey queried 65 patients about demographics, health, ingredient usage, cooking methods, food preferences, and interests for a healthy cooking resource. The results showed the majority of patients know how to cook (93.8%) and enjoy cooking (76.9%). Patients largely eat fruits (73.8%) and vegetables (76.9%) every day. Community members with self-reported weight problems cooked a significantly greater number of meals at home and had a significantly lower number of meals with fruit per day. A 160 item list of foods participants like to cook and a 113 item list of foods participants like to eat was generated. These findings proved there is an audience of community members with and without weight problems who enjoy cooking and are interested in healthy cooking resources. The data gathered informed the creation of a culturally tailored, area resource-specific healthy cooking tool for community members in the South Side of Chicago.

Methods: Recipe creation was conducted based on survey results. Dishes were selected for creation by choosing the most popular items respondents reported liking to cook and/or eat. Ingredients were purchased from stores at which people reported shopping. Cost analysis was conducted, with a goal of creating recipes under $1/serving for nonmeat dishes and under $2/serving for meat-containing dishes. Cooking methods were selected for their health benefits, use of accessible kitchen instruments, and quick preparation time. Efforts were made to create diabetic-friendly, low-sodium, and kid-friendly recipes. Nutrition facts were calculated for each recipe using the website NutritionData.com.

Results: 29 original recipes were published on the University of Chicago Family Medicine website (http://familymedicine.bsd.uchicago.edu/MedicalStudents/Nutrition/Recipes) along with South Side healthy food resources. The site continues to be updated as new recipes are created. In collaboration with another student, basic nutrition information will be added to the website. The recipes have been used for the advanced cooking class series at the Komed Holman Health Center, an FQHC in the South Side. Feedback obtained from the recipes indicates enthusiasm for them given their easy preparations and accessible ingredients. Recipes have also been demonstrated and shared with patrons of the 61st Street Farmers Market in Woodlawn and the KLEO Center food pantry in Washington Park.

Conclusion: The recipe collection continues to be a work in progress. A call for recipes from the Pritzker community has been made and new recipes will be added in April 2015 following submissions. The recipes will continue to be used by the Komed Holman Health Center in their cooking class series, the Mission: Nutrition group for cooking lessons and by students, community members, and health care providers. It is hoped that the recipe site will serve as a dynamic tool which students can update over time and community members and health care providers can use to promote healthy, accessible cooking practices in the South Side of Chicago.

Acknowledgements/Disclosures: University of Chicago Department of Family Medicine.
Screening to be “Double Sure”: Breast Cancer Risk Perceptions and Illness Etiologies Among Nigerian Women

Claire Naus

Mentor: Funmi Olopade, MD, Department of Medicine, Section of Hematology/Oncology
Co-Author: Linda Patrick-Miller, PhD

Background: Breast cancer has been the subject of numerous studies in the United States and Western Europe; however, less attention has been paid to public awareness of breast cancer risk factors and prevention outside of the Western context. The Nigerian Breast Cancer Study, which seeks to identify genetic and non-genetic factors that contribute to breast cancer risk and disparities in breast cancer outcomes, has identified families with BRCA1/2 mutations. The purpose of this study was to explore breast cancer knowledge and attitudes about genetic testing to reduce risk in the Nigerian context.

Methods: This study, which was conducted in the community and at University College Hospital (UCH) in Ibadan, Nigeria, used qualitative methods, namely semi-structured interviews and participant observation, to assess knowledge about causes of illness, in general, and breast cancer, in particular, as well as perceptions of genetic risk information among Nigerian women. Questions related to notions of risk explored the repercussions of knowing one is at an increased risk for breast cancer given a positive genetic test.

Results: Of the 51 women interviewed, the majority were married and belonged to the Yoruba ethnic group. Their ages and education levels varied; however, their religious affiliations were split evenly between Christianity and Islam. Two thirds of respondents said they “did not know” the causes of breast cancer, and knowledge about breast cancer was exceedingly limited. With regard to risk perceptions, women from the community and various UCH clinics, including a group of breast cancer patients, shared misgivings about undergoing a prophylactic mastectomy and stated a preference for screening if faced with an increased risk for breast cancer in the form of a positive genetic test. They cited a need to confirm a cancer diagnosis via screening before proceeding with a surgical intervention. In addition, apprehensions about surgery and failure to recognize themselves as seriously ill led some breast cancer patients to disappear from the healthcare system for months or years following their diagnosis only to reappear with more advanced disease.

Conclusion: This study explores causal explanations of illness, knowledge of breast cancer, and perceptions of risk among women in southwestern Nigeria in order to anticipate the sociocultural and psychosocial ramifications of introducing genetic testing into this community and to inform the development of a culturally appropriate genetic counseling program.

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Implications of a Cookstove Intervention on Household Air Pollution and Maternal Health

Rishi Pandya

Mentor: Sola Olopade, MD, MPH, Department of Medicine, Section of Pulmonary/Critical Care
Co-Author: Donee Alexander, PhD

Background: More than 40% of the world's population use solid fuels (including firewood) for cooking and energy needs, producing high levels of household air pollution (HAP) with elevated levels of particulate matter (PM) and other pollutants. Kerosene, a popular alternative to solid fuels, also produces PM levels that exceed WHO standards. HAP can lead to elevated blood pressure (BP), which is an important risk factor for cardiovascular disease (CVD), the leading cause of mortality worldwide. Previous studies have examined improved cookstoves as a means to reduce HAP and improve BP. Ours is the first to evaluate the effects of HAP on BP through a randomized controlled intervention study comparing a clean-burning ethanol cookstove with traditional solid fuel and kerosene stoves.

Methods: As part of a larger study evaluating the associations between pregnancy outcomes and HAP, we recruited 300 pregnant women from 2 clinics in Ibadan, Nigeria. The participants were < 18 weeks gestational age and use firewood or kerosene as their primary fuel and had no history of smoking or hypertension. Those eligible were randomized to the control arm (continuing use of firewood or kerosene) or the intervention arm for which they received an ethanol cookstove. Both groups participated in an education program on the dangers of smoke exposure and means to reduce it. All subjects had six BP measurements during antenatal visits and 1 measurement 6 weeks post-delivery.

Results: We have randomized 294 women thus far, with similar mean baseline systolic blood pressure (SBP) and diastolic blood pressure (DBP) between the intervention group (ethanol users) and the control group (kerosene and firewood users). Among women who have already delivered (n = 154), mean SBP in the intervention group at last measurement before delivery was 110.7 mm Hg, significantly lower than the control group's mean SBP of 115.1 mm Hg (p = .02). Mean DBP was also significantly lower in the intervention group at this time (69.5 vs. 74.5 mm Hg, p = .001). The number of participants with a post-pregnancy BP measurement is small (n = 90), and the difference in mean SBP and DBP between the 2 groups is not significant. Comparing the last BP measurement before delivery between the intervention group (n = 83) and kerosene users alone (n = 54), mean SBP in the ethanol group was significantly lower (110.7 vs 116.2 mm Hg, p = .007). Difference in mean DBP among these groups was again significant (69.5 vs. 75.7 mm Hg, p = .0002). Comparing the last BP measurement before delivery in the intervention group versus firewood users alone (n = 17), differences in mean SBP and mean DBP were not significant but the latter sample size is small.

Conclusion: Our study has found a significant reduction in systolic and diastolic blood pressure with a clean-burning ethanol cookstove intervention over the course of pregnancy but not post-pregnancy. However the final results and full implications of our study will not be clear until all participants have been randomized and their pregnancies carried to term.

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Empathy in Third Year Medical Students: Tracking Changes and Understanding Causes in Clinical Clerkships

Alexander Cole

Mentor: Tamara Vokes, MD, Department of Medicine, Section of Endocrinology, Diabetes, and Metabolism

Background: The medical education literature documents consistent and reproducible declines in empathy that begin with clinical training in medical school and continue throughout medical practice. Stronger empathic traits in physicians have been associated with a variety of clinical outcomes including improved hemoglobin A1c and LDL levels and improved ease and accuracy of diagnosis by the physician. Previous studies have demonstrated some success with educational interventions aimed at empathy preservation, suggesting this trait may be malleable rather than fixed. However, little work has been done to understand the causes of empathy decline during clinical work, and no studies have been done to document empathy declines over timescales shorter than one year in medical students.

Methods: Students completing the internal medicine, surgery, and psychiatry clerkships during the winter 2015 quarter were asked to voluntarily participate in this study. Participation entailed completion of pre-clerkship and post-clerkship surveys; the former was completed at the start of the clerkship and the latter was completed after the completion of the clerkship. Both surveys included the Jefferson Scale of Empathy (JSE), a validated survey tool used to quantify empathic traits, as well as questions probing students' life and clerkship experiences believed to have an impact on empathy. JSE scores before and after the clerkship were compared and personal and clerkship experiences correlated to changes in JSE scores.

Results: A total of 27 students completed the pre-clerkship survey and 18 students completed the post-clerkship survey. Nine participants (33%) did not complete the post-clerkship survey, and 3 participants provided invalid participant codes that did not match previously collected codes and were excluded from analysis. The mean change in JSE score for the entire dataset was -2.9 (SD 9.33), which was not statistically significant (p=0.1981). JSE score changes by clerkship were 1.8 (SD 13.44) for internal medicine, -2.9 (SD 5.17) for surgery, and -7.8 (SD 9.20) for psychiatry. These differences were not statistically significant by ANOVA. Clerkship factors most strongly associated with preserved empathy included the ability to form bonds with patients and their families (r=0.5836, p=0.0110), the feeling of being an integral member of the care team (r=0.5511, p=0.0178), and the feeling of performing meaningful clinical work (r=0.4664, p=0.0510).

Conclusion: No statistically significant differences between any sub-groups of our study with respect to change in JSE scores were identified, though the largest absolute changes in JSE scores were identified in our clerkship sub-group, general specialty interest sub-group, and personal exposure to illness sub-group. Aspects of the clerkship experience most strongly associated with preservation of empathy suggests that student involvement in meaningful clinical work, interaction with patients and their families, and positive faculty/resident role models may preserve empathy during clinical training. Narrative comments collected with the post-clerkship survey suggest witnessed poor treatment of other medical providers and staff by attending physicians, limited interaction with patients by medical teams, and witnessed behavior interpreted not to be patient-centered may have a qualitatively negative impact on students’ development of empathy.

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How Do Medical Students Define Lifestyle?

Alexandra Garnett

**Mentor:** Shalini Reddy, MD, Department of Medicine, Section of Hospital Medicine

**Co-Authors:** Kimberly Clinite, MS4; Stephanie Kazantsev, MS4; Jennifer Kogan, MD; Kent DeZee, MD

**Background:** Specialty lifestyle is known to be an important consideration in medical student career choice, but how medical students conceptualize lifestyle remains unknown. Previous investigations of lifestyle and specialty selection have relied on inconsistent definitions provided by the investigators, or have left this concept undefined. The purpose of this study was to determine how medical students themselves define the concept of lifestyle.

**Methods:** First-year medical students at 11 allopathic schools were surveyed at matriculation in 2012. Fourth-year medical students at the same 11 schools were surveyed after the NRMP main residency match in 2013. Students were asked to provide free text responses to the open-ended question, “When someone says ‘That specialty has a good lifestyle,’ what does that mean to you?” Data was analyzed using a directed content approach. Descriptive statistics of the themes were calculated and analyzed by student variables, including first-year versus fourth-year status.

**Results:** 57.4% (979/1704) of first-year students and 54.0% (919/1701) of fourth-year students completed the survey and provided an answer to the open-ended question about lifestyle. Student responses encompassed three major themes: physician schedule (95% of students), income (35%), and professional life (22%).

**Conclusion:** Medical students’ definition of lifestyle most frequently involves the theme of physician schedule. A number of students include income and aspects of professional life in their conceptualizations of lifestyle. The themes identified in first-year and fourth-year students’ definitions of lifestyle aligned in content, though not in frequency. Future research into lifestyle influences on specialty selection should utilize these three themes.

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Nutritional Attitudes and Knowledge of Medical Students and the Impact of a Culinary Medicine Activity

Elise Madrid

**Mentor:** Sonia Oyola, MD, Department of Family Medicine

**Co-Authors:** Geeta Maker-Clark, MD; Debra Stulberg, MD

**Background:** Several studies have shown medical students and residents rate their nutrition education as inadequate. We aimed to evaluate a novel culinary medicine extracurricular activity and whether it changes the self-perceived proficiency, attitudes, and knowledge of Pritzker medical students.

**Methods:** Questions for the survey were taken from several different validated surveys. Several questions were slightly altered to better reflect the objectives of the culinary medicine extracurricular activity. The multidisciplinary culinary medicine activity has been adapted from the Goldring Center for Culinary Medicine’s curriculum. The survey was distributed to all Pritzker School of Medicine students. Unique anonymous identifiers were included to link pre and post results.

**Results:** Preliminary results before the activity show Pritzker students are not satisfied with their nutrition education. When asked if they were satisfied with the quantity and quality of their nutrition education 76% and 65% respectively responded Strongly Disagree and Disagree. However, the MS3s & MS4s did tend to rate their self-perceived proficiency towards nutrition counseling in most categories more highly than the MS1s and MS2s. Yet only 11% of MS3s and MS4s rated that they were able to provide patient-centered multicultural nutritional counseling.

**Conclusion:** In conclusion the preliminary results show of the students that responded they are not satisfied with their nutrition education showing that there is room for improvement. The Culinary Medicine activity could address this gap. It also has the potential to give students additional confidence in providing nutritional counseling.

**Acknowledgements/Disclosures:** The Goldring Center for Culinary Medicine for providing coursework for the Culinary Medicine activity. The University of Chicago’s Women’s Board.
Home Work: Quality and Timing of Attending Attestations in the Electronic Health Record

Kiara Tulla

Mentor: Jeanne Farnan, MD, MHPE, Department of Medicine, Section of Hospital Medicine

Co-Authors: Shannon Martin, MD, MS; David Meltzer, MD, PhD; Vineet Arora, MD, MAPP

Background: Current health information technology has made the electronic health record (EHR) accessible to review clinical information remotely. Attending remote use of the EHR is unexplored, specifically with regard to off-hours use and quality of documentation. We aimed to characterize how attendings remotely utilize the EHR, and how these patterns may influence supervision of trainees.

Methods: Attending physicians on the Medicine teaching service at a single academic center from January-April 2012 were consented for participation and surveyed regarding their use of EHR during their service. Five patient charts from the attending’s time on service were randomly selected. Attending attestations of housestaff documentation were audited to evaluate timing and quality of the history and physical (H&P) and one progress note (PN). Timing was defined as time of attending signature; quality of attestation was determined by the presence of any additional comments added to the attestation. Descriptive statistics were performed, and proportions were compared using Pearson’s chi-square test.

Results: 88% of attendings participated (22/25). 96% report use of the EHR from home. Nearly 70% of attendings spent 60-90 minutes daily using EHR outside of rounds, and at least 30-60 minutes using it remotely. H&Ps were most frequently signed after 3pm on the postcall day; PNs were most often signed after 8pm. The timing of the attestation was not associated with additional comments in documentation. Only 34% of resident H&Ps were signed within 8 hours of completion, 25% within 8-12 hours, 29% within 12-24 hours and 11% greater than 24 hours. For quality of attestations, 58% and 55% of H&Ps and PNs respectively contained comments in attestations. Attendings reporting frequent EHR use outside of rounds included comments 65% and 63% of the time in H&Ps and PNs respectively compared to those reporting infrequent use (H&Ps 33%, PNs 40%, p<0.05). Attendings with 0-7 years of experience were more likely to include information in their attestation than more senior colleagues (H&P: 75% vs. 46%, p<0.05; PN: 87% vs. 34%, p<0.05). Notes written by self-identifying general internists included comments more often than those written by hospitalists and subspecialists (H&P: internists 67% vs. hospitalists 40% vs. subspecialists 45%, p<0.05; PN: internists 67% vs. hospitalists 28% vs. subspecialists 40%, p<0.05). Attendings who reported thoroughly reading H&Ps were more likely than those who did not to include information in attestations (67% vs. 40%, p=0.036). Attendings reporting changes in patient management occurring due to their own discovery of clinical findings when viewing the EHR were more likely to include comments than those who did not report discovering information when using the EHR independently (H&P: 62% vs. 33%, p<0.05; PN: 58% vs. 40% p=0.037).

Conclusion: There is significant variability in timing of attending attestation documentation, which is an example of clinical care activities occurring outside the hospital setting. Increased content in attending notes is associated with electronic supervision activities such as attending-driven changes in patient management due to independent discoveries in the EHR. It will be important to understand implications of these findings for attending satisfaction, workload and risk for burnout, as well as resident education.

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Assessing the Medical Neurobiology Laboratory Curriculum Using Post-laboratory Formative Evaluations

Michael Yee

**Mentor:** Peggy Mason, PhD, Department of Neurobiology

**Co-Authors:** Valeriy Poroyko, PhD; So Watanabe, MD, PhD; Duo Jiang, BS; James Lane, BS; Marcella deTineo, BSN; Fuad Baroody, MD; Robert Naclerio, MD

**Background:** The Medical Neurobiology course is evaluated through a standard summative evaluation administered at the end of the course. However, these evaluations are not designed to provide pinpoint feedback on each laboratory experience in the course. Formative evaluations that are given immediately following an experience can be a useful hypothesis-generating method. When combined with inductive qualitative analysis, they can be an essential tool in identifying areas of improvement that are not otherwise captured in summative evaluations.

**Methods:** Students were asked to complete a three question formative evaluation online immediately following each laboratory experience. Surveys asked what was most helpful, least helpful and what should be changed about each lab experience. There were 9 total surveys in 2013 and 8 total surveys in 2014. Responses were analyzed using inductive qualitative analysis. A second rater was used for a comparative analysis resulting in multiple major themes and subthemes for each question.

**Results:** Total response rate varied from 20-50% per lab with an average response rate of 33%. Inter-rater reliability was 91%. 5-10 themes emerged for each question during analysis. However, the three most common themes for each question contained 77%, 80% and 70% of all codes for that question respectively. The top three themes remain the same when separated by year, suggesting consensus between years. Students said that the teacher assistants and teachers were the most helpful component of lab followed by specific lab experiences and the handout (32%, 28% and 17% of all codes respectively). The most common complaint was problems with the lab handout, followed by problems with lab activities and no problems (31%, 27% and 22% of all codes respectively). Further analysis showed that students praised or struggled with the handout or lab activities depending on the lab experience. Changes to the lab handout were the most common suggestion followed by requests for additional resources and no change (34%, 22% and 15% of all codes respectively). Within this theme, 36% of students said that the handout needed more diagrams, charts or images. These critiques had not been specifically identified in previous summative evaluations of the course.

**Conclusion:** Formative evaluations were useful for identifying unique areas of improvement within the Medical Neurobiology laboratory curriculum. A majority of student responses converged into one of three common themes for each question, indicating consensus on strengths and weaknesses of the current labs. Analysis demonstrated that teacher assistants are the most useful adjunct to the labs when they are well prepared and gave reviews. Many students found the lab handout and specific laboratory experiences such as optical illusions hampered with their learning experience. In order to improve the labs, the handout for several labs needs to be edited and more diagrams should be included to increase the clarity of the information. However, given that 23% of responses stated nothing obstructed their learning and 17% said no change was needed, we anticipate the need to make only several minor and specific changes to accommodate a majority of students.

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An Under Appreciated Ethical Problem: Delays in Death Certification by Physicians

Philip Carullo

**Mentor:** Daniel Sulmasy, MD, PhD, Department of Medicine

**Background:** The death certificate is a legal document used for mortality statistics and to finalize end of life tasks by families of the decedent. Previous studies have shown that residents and physicians are poorly trained at accurately completing the death certificate. This is the first study to examine the phenomenon of delays in death certification due to physician deferral or refusal and the effects this has on families awaiting them.

**Methods:** Hour long qualitative interviews first obtained with hospital staff from academic medical centers across the US. Upon hospital staff enrollment, funeral home and medical examiner staff were contacted and interviewed for each geographic area. A phenomenological analysis was performed along with dual coding of data to identify key themes.

**Results:** Twelve academic medical centers, 10 funeral homes, and 8 medical examiner’s offices throughout the United States participated. Several themes were identified including process and policy matters that prevent timely completion as well as emotional and practical consequences for families awaiting certificates.

**Conclusion:** Delays by physicians are common across the country and increase workloads for others in the death certification process. They most immediately affect the families of the decedent resulting in serious emotional and practical burdens. We believe our results suggest a long neglected ethical problem, that as a final act of care to patients, many physicians are remiss in their death certificate responsibilities.

**Acknowledgements/Disclosures:** none.
The Relationship Between Adherence to 2014 Surgical Care Improvement Project Measures and Post-Operative Complications

Anne Castro

Mentor: David Glick, MD, MBA, Department of Anesthesia & Critical Care

Background: The Surgical Care Improvement Project (SCIP) was created in 2006 through a partnership of national quality organizations with the goal of decreasing preventable surgical complications by 25% by 2010. Measures were chosen based on early clinical trials; however, to date, studies have not demonstrated a consistent relationship between SCIP criteria adherence and reduction in post-operative complications. The purpose of this study was to investigate the relationship between 2014 hospital compliance with core SCIP measures and general post-operative complications, including whether complication rates in hospitals with very high overall SCIP compliance (>99%) differed from hospitals with lower compliance levels. It was hypothesized that increasing SCIP performance would be associated with lower complication rates.

Methods: Publicly available data were accessed from the Healthcare Compare website for U.S. hospitals who reported performance on 2014 SCIP core measures (qualitynet.org). Only hospitals performing 10 or more cardiac valve (n=573) and/or cardiac bypass procedures (n=607) were included in the analysis. Average compliance with 2014 core SCIP measures was calculated for each hospital, which included CARD2 (patients on beta-blocker therapy prior to arrival received perioperative beta-blocker), VTE2 (appropriate venous thromboembolism prophylaxis within day before/after surgery), INF1 (prophylactic antibiotics received within one hour of surgical incision), INF2 (appropriate prophylactic antibiotic selection), INF3 (prophylactic antibiotics discontinued within one day after surgery), INF4 (cardiac surgery patients with controlled post-operative blood glucose), and INF9 (urinary catheter removed on POD1 or 2). Each hospital's average SCIP compliance was compared with volume of valve/bypass surgeries and PSI90, a composite score of eight common post-operative complications (pressure ulcers, iatrogenic pneumothorax, central venous catheter-related infections, hip fracture, PE/DVT, sepsis, wound dehiscence, and accidental puncture/laceration). Statistical analysis including normality tests, paired t-tests with Welch corrections, and Spearman's correlations were performed using STATA 13.

Results: For hospitals performing cardiac bypasses, Spearman's correlation demonstrated a very weak but significant relationship between SCIP compliance and PSI90 (rs = 0.096, p=0.02). Hospitals with >99% overall compliance with SCIP measures demonstrated a statistically significant, lower PSI90 score than hospitals with <99% compliance (p<0.01, 95% CI [0.008, 0.5]). However, for hospitals performing cardiac valve procedures, there was no significant relationship between SCIP compliance and PSI90 (rs = 0.02, p=0.60), and hospitals with >99% overall average SCIP compliance did not have a significantly lower PSI90 score (p=0.07, 95% CI [0.5, 0.52]).

Conclusion: For hospitals performing cardiac bypasses, these results demonstrated a very weak but significant relationship between increased SCIP compliance and decreased post-operative complication rates, as well as a significant relationship between decreased post-operative complication rates and highest (>99%) compliance. This effect was not shown in hospitals performing cardiac valve procedures. These results suggest that although there may be some value in current SCIP measures, the weak/absent nature of correlation warrants further research to identify process measures that are more reliably linked to outcomes.

Acknowledgements/Disclosures: none.
Baseline Assessment of Home Health in the Primary Care Group

Jennifer Kraninger

**Mentor:** Lisa Vinci, MD, MS, Department of Medicine, Section of General Internal Medicine

**Background:** With the aging population of the United States, the utilization of medical services, including those in the patients’ homes continues to grow. By the year 2050, 27 million people are predicted to require long term care, with a large proportion of that taking place in the community. Furthermore, although home health is a service that is frequently utilized in the healthcare setting, many healthcare professionals have a poor understanding of the requirements and services offered. Through this study, we aimed to understand the complexity of coordinating home health.

**Methods:** Stakeholder interviews of nursing and secretarial staff as well as home health employees were conducted in order to better analyze the process. Using input from these interviews, a simplified process map was generated. Through review of faxed paperwork received between 9/1/14 and 11/30/14 in the Primary Care Group, a convenience sample of 122 patients was identified. Information from the paperwork was gathered including the name of the Home Health Agency (HHA); dates of fax receipt, paperwork signature, and fax return; period of home health certification, and services ordered. Patients to whom this paperwork corresponded were identified. Through chart review, data including age, gender, race, documentation of functional status, specific use of the term “homebound”, documentation of HHA contact information, and date of last primary care visit was collected. Review was conducted by examining three consecutive primary care visits with the first date overlapping with the certification period of home health. The term “homebound” was searched for through the entire chart. The terms “home health” and the name of the HHA were searched for when identifying recorded contact information.

**Results:** Paperwork was reviewed with 281 separate fax samples (939 pages) related to home health collected. These samples related to 122 individual patients in the care of 34 signing attending and resident physicians. The HHAs chosen for the patients were diverse with 68 distinct agencies utilized. Average time from fax receipt to fax return was 7.7 days. The majority of this time was attributed to the delay between fax receipt and physician signature, which was an average of 7.11 days. A homebound equivalent was reported about 60% of the time with the most common documentation being use of assistance devices for mobility. The term “homebound” was used in only one patient chart. Progress notes mentioned that the patient was receiving home health services in about 50% of the cases. Overall, contact information was documented for 61% of the patients receiving home health care. Of the patients where it was recorded, the information was found in a telephone encounter 82% of the time.

**Conclusion:** Through this study, the process of establishing home health and navigating paperwork related to the service was further examined. More than paperwork, the documentation of home health examined with exceedingly low rates of both functional status and record of home health within progress notes (60% and 50%, respectively). Potential future interventions include a generic electronic face-to-face form, a dot phrase for homebound status, and an educational intervention.

**Acknowledgements/Disclosures:** Nursing staff of the University of Chicago Primary Care Group and the Quality and Safety Track Leaders, Dr. Lisa Vinci and Dr. Julie Oyler.
Evaluation of Surgical Flap Outcomes in Patients Who Received Angiotensin-Converting Enzyme Inhibitors or Angiotensin-II Receptor Blockers Preoperatively

Brittany Seidensticker

**Mentor:** Avery Tung, MD, Department of Anesthesia & Critical Care

**Co-Authors:** Shivani Amit Patel, PharmD; Amanda Dugal, PharmD

**Background:** Angiotensin-converting enzyme inhibitors (ACEi) and angiotensin-II receptor blockers (ARBs) are associated with hypotension in patients undergoing general anesthesia, with some studies finding an increased vasopressor requirement to maintain hemodynamic stability. The clinical relevance of this hypotension and/or pressor requirement, however, is unclear, especially in flap procedures that rely on intact perfusion and hemodynamic stability for success. The aim of this study is to examine the association of preoperative ACEi/ARB use and intraoperative vasopressor use and whether this combination is associated with worse flap outcomes.

**Methods:** We performed a retrospective observational chart review of 151 patients over the age of 18 who underwent a flap procedure at the University of Chicago Medicine between September 1, 2010 and September 30, 2013. Patient demographics, antihypertensive medication use, intraoperative blood pressures, fluid administration, vasopressor requirements, and flap outcomes were recorded. Data were analyzed using Fisher’s exact test on SPSS to compare outcomes of patients who received ACEi or ARB preoperatively and vasopressors intraoperatively with patients who did not receive these two medications, to compare whether ACEi/ARB use was associated with increased use of vasopressors compared to patients who did not receive ACEi/ARBs, and lastly to compare the amount of fluids given intraoperatively between patients who received ACEi/ARBs and those that did not. “Poor” flap outcomes were defined as necrosis, thrombosis, flap failure, abscess formation, wound dehiscence, and/or hematoma, with a “good” outcome being none of these present.

**Results:** Of the 151 patients that met the inclusion criteria, 109 had electronic medical records or scanned paper charts available. 70% of patients who received an ACEi or ARB preoperatively also required intraoperative vasopressors (19/27). This was significantly higher than the 45% in patients who did not receive an ACEi or ARB preoperatively (37/82; P= 0.027). Despite greater vasopressor use, the incidence of good flap outcomes did not differ between patients who received an ACEi/ARB in combination with a vasopressor compared to patients who received only an ACEi/ARB, no ACEi/ARB, or only a vasopressor (P=0.601). Additionally, the amount of fluids administered was not different between patients who received an ACEi/ARB preoperatively to those who did not (P= 0.524).

**Conclusion:** While patients who are on ACEi/ARBs were more likely to require vasopressors intraoperatively during flap procedures compared to patients who are not on ACEi/ARBs preoperatively, our data suggest that this increased vasopressor use does not have an effect on flap outcomes.

**Acknowledgements/Disclosures:** none.
Population Segmentation and Risk Prediction of MA and MMAI Patients

Kevin Stephens, Jr.

**Mentor:** Lisa Vinci, MD, MS, Department of Medicine, Section of General Internal Medicine

**Co-Author:** George Weyer, MD

**Background:** The University of Chicago Medical Center (UCMC) is entering the risk-sharing health insurance marketplace with two small plans, a Medicare-Medicaid Alignment Initiative (MMAI) plan and a Medicare Advantage (MA) plan. In order to best serve these populations, UCMC must develop population health management capabilities. The first step to creating a population health management system is to risk stratify the patient population in order to understand the risk profile of the entire population and the specific needs for smaller subsets. The objective of this project is to evaluate the performance of several nonproprietary risk-adjustment/stratification instruments in predicting healthcare utilization in this specific population.

**Methods:** All patients seen by the UMC Primary Care Group with ICD9 claims data and internal charge data between the years 2012 and 2014 (n = 438) that were enrolled in the Cigna-HealthSpring Medicare Advantage contract or the MMAI managed care contract were studied. 5 models were evaluated: Hierarchical Condition Categories (HCC), Elder Risk Assessment (ERA), Chronic Comorbidity Count, Charlson Comorbidity Index, and Minnesota Health Care Home Tiering. Logistic regression models using demographic characteristics and diagnoses from 2012-2014 were used to segment the population by healthcare utilization and internal charge data over that time period with binary outcomes (hospitalizations and high charge users in the top 20%) using the C-statistic and goodness of fit. Then, on a smaller subset of patients (n = 336) logistic regression models using demographic characteristics and diagnoses from 2013 were used to predict healthcare utilization and charges for 2014 with the same binary outcomes using the C statistic and goodness of fit among the top 20%.

**Results:** Between 2012 and 2014, the HCC and ERA model outperformed the others in predicting hospitalizations C-statistics of 0.85 (95% CI: 0.81-0.88) and 0.85 (95% CI: 0.81-0.88), and high charge users with C-statistics of 0.83 (95% CI: 0.79-0.88) and 0.81 (95% CI: 0.76-0.86), respectively. In 2013, 48% and 53% of the top 20% of HCC and ERA were hospitalized, respectively, compared with 15% of the entire population. 60% and 55% of the top 20% of HCC and ERA were high charge users, respectively. 73% of patients who were members of both top 20% (n = 37) were hospitalized while 78% were high charge users. In 2014, of the patients identified as the top 20% in 2013, 39% of HCC and 51% ERA were high charge users while 36% of HCC and 61% ERA were hospitalized. For those that were in the top 20% of both metrics, 57% were hospitalized and 51% were high charge users. Overall, in 2014, 17% were hospitalized.

**Conclusion:** For the UCMC patient population, the HCC and ERA models were the best predictors of hospitalization and high charge utilization. The analysis also revealed that UCMC’s ICD9 coding most likely underrepresents certain medical conditions (e.g., stroke and mental health disorders) that are important to risk stratification. However, the results show that these models can be used to predict utilization in combination with clinical evaluation.

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Dynamic Operational Mapping: Tracking Key Decision Points in Microvascular Breast Reconstruction and Their Impact on Surgical Teamwork

Emily Stockert, MBA

Mentor: Alexander Langerman, MD, Department of Surgery, Section of Otolaryngology-Head & Neck Surgery

Co-Authors: Julie Park, MD; David Song, MD

Background: Our objective is to create a novel multimedia tool, the Dynamic Operational Map (DOM), through translation of a complex series of steps, interactions, and variability of microvascular breast reconstruction. The DOM highlights processes, responsibilities, decision points, and potential outcomes from the perspective of the surgical team, anesthesia, the scrub, and the circulator. The DOM facilitates transparent communication and more efficient coordination in the operating room.

Methods: A single-site, observational study of microvascular breast reconstruction procedures was performed at an academic medical center. Case progression and decision points for participants were recorded through in-person observation. Interviews with OR team members augmented our understanding of intraoperative decision-making and identified reasons for non-ideal case progression.

Results: A complete DOM for microvascular breast reconstruction was created, including visual representation of major events (black lines). OR team members are color-coded (sterile indicated by solids). Tasks (rectangles), decision points (circles), branching outcomes from decisions, and team ‘time out’ and ‘debriefs’ are identified. Decision nodes for the surgical team include patient positioning, DIEP vs. SIEA flap, number of perforators harvested, recipient vasculature quality, number and type of venous anastomoses, volume of flap, initial flap perfusion and appearance, and wound closure. Anesthesia nodes include the location and number of venous access, need for arterial line, response to blood pressure changes, and plans for intubation/extubation. The circulator and scrub nodes include room readiness, instruments readiness, microscope calibrated and draped.

Conclusion: The Dynamic Operational Map has applications for directing flow in the operating room, assessing supply chain needs, educating staff and trainees, and informing patient discussion. The visibility and integrated nature of the DOM hold the promise of enhancing OR efficiency, improving team coordination and communication, decreasing procedure variability, and reducing unnecessary costs.

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Proposed Process for Efficient Collection of Risk Assessment Information for Patients Enrolled in Cigna-HealthSpring Medicare Advantage Program

Nathan Swallow

Mentor: Lisa Vinci, MD, MS, Department of Medicine, Section of General Internal Medicine

Background: The Population Health Management Team at the University of Chicago has started an initiative with a pilot population enrolled in Cigna-HealthSpring Medicare Advantage program. A component of this initiative is collecting a comprehensive health risk assessment, recorded by Medicare as a basis for reimbursement. The importance of this risk assessment is two-fold as it is also integrated with grading the quality of care the health plan provides the patients. Medicare uses many of the quality metrics recorded in the health risk assessment for bonus payments or penalties. The form Cigna-HealthSpring uses to collect this risk assessment data is called the 360 comprehensive assessment.

Methods: The objective of this project is to develop a process to obtain all necessary patient information for the 360 comprehensive assessment and have it signed by a physician without significantly disrupting the flow of normal clinic. In developing this process, we created an initial process map, with a timeline to efficiently gather pre-visit information. Collecting pre-visit information is critical to the process so the physician can use information gathered to perform a more focused assessment and avoid an increase in visit time due to the increased number of questions required from the comprehensive risk assessment form compared to a normal exam. In addition to pre-visit information, our process specifies when and how to notify physicians who will be examining the enrolled patients, and briefly educate them on how to evaluate patients and what is required. Our process also includes a proposed time frame and procedure for completing forms after a physician encounter. Enrolled patients can be seen at the Primary Care Group or geriatrics clinic of University of Chicago Hospitals.

Results: Evaluation of the process will be done on a weekly basis and discussions held at weekly Population Health Management Team meetings. Small adjustments will be implemented often. Our team members involved with the 360 comprehensive assessments will undergo training on how to fill out the form properly. Cigna-HealthSpring also provides feedback on how well we fill out the form, in terms of completeness and appropriateness as we collect them, which aids our evaluation.

Conclusion: Although continuous adjustments to the process can be made, after 46 weeks of collecting data, receiving feedback, and adjusting the process to determine best practices, we anticipate our process to be relatively optimized and further efforts to actively shape our process can be reduced. If the process is still failing to accurately and efficiently assist us in completing the risk assessment, we will propose a more drastic change in process structure.

Acknowledgements/Disclosures: Public Health Management Group at the University of Chicago.
Scientific Investigation in Basic Sciences
Regulation of Cardiac Hypertrophy by MicroRNA-130a

Kevin Hodges

Mentor: Gene Kim, MD, Department of Medicine, Section of Cardiology

Co-Authors: Cynthia Harmon, MS; Jordan Green, MS2; Saoirse McSherry, BS; Tyler Calway, BS

Background: MicroRNAs (miRNAs) are a class of 18-22bp noncoding RNA molecules, which regulate gene expression by suppressing translation of target mRNAs or reducing their stability. Numerous miRNAs have been shown to regulate cardiac development, function, and disease. MiR-130a has been implicated in arrhythmogenesis through downregulation of the gap junction protein, Cx43. Computational models predict that miR-130a targets multiple transcripts with known cardiac function, including PPARγ and Smad4, which have been implicated in cardiac hypertrophy. We hypothesize that miR-130a also regulates cardiac hypertrophy through a distinct mechanism, including the downregulation of Smad4 and PPARγ.

Methods: Fluorescent in situ hybridization (FISH) for was used to confirm endogenous miR-130a expression in mouse cardiomyocytes. To investigate the role of miR-130a overexpression on cardiac hypertrophy, we employed a cardiomyocyte-specific, inducible transgenic model. Structural effects of miR-130a overexpression were characterized by left ventricular wall thickness, cardiomyocyte size, cardiomyocyte fractional shortening, and degree of cardiac fibrosis. To identify potential targets of miR-130a, protein was isolated from doubletransgenic and nontransgenic mice after 8 weeks of miR130a overexpression. Microwestern blot was carried out for 96 potential targets of miR-130a through the University of Chicago genomics core. SDSPAGE and conventional western blot analysis were performed investigate the effects of miR-130a overexpression on PPARγ expression.

Results: FISH performed in non-transgenic mice confirmed endogenous expression of miR-130a in cardiomyocytes. MiR-130a overexpression resulted in a significant increase in LV wall thickness (0.91mm vs 0.72mm, p<0.05), cardiomyocyte size (1528.5 pixels² vs 3233.9 pixels², p<0.05), and degree of cardiac fibrosis. Meanwhile, there was a significant decrease in LV fractional shortening (28.4% vs 33.2%, p<0.05) in the setting of miR-130a overexpression. Micro-western blot analysis revealed that several genes with known cardiac function are down regulated in the setting of miR-130a overexpression, including MTOR, PDK1, Src, NF-κB p65, EGFR, DHPRα1, Cx43, Neuregulin, and Smad4. Conventional western blot demonstrated that PPAR-γ gamma expression is reduced by 50% in double transgenic mice after 8 weeks of miR-130a overexpression (p=0.12).

Conclusion: Cardiomyocytespecific overexpression of miR-130a leads to cardiac hypertrophy, fibrosis, and decreased contractility characteristic of the pathological changes seen in heart failure. Further, miR-130a overexpression is associated with down regulation of target genes which have been established roles in cardiac hypertrophy, including PPARγ and Smad4. Further studies are needed to investigate this hypothesis. In vitro luciferase reporter assays can be used to confirm regulation of PPARγ and Smad4 expression by miR-130a, and immunohistochemistry can be used to visualize changes in PPARγ and Smad4 expression. A thiazolidinedione can be used to enhance PPARγ signaling. If PPARγ downregulation is responsible for miR-130a mediated hypertrophy, then these agents should mitigate the effect by augmenting PPARγ signaling. Finally, emerging technology allows for targeted in vivo inhibition of microRNA activity with synthetic oligonucleotides. Inhibition of miR-130a would be a powerful tool to assess its importance in regulating hypertrophy in response to physiologic stress induced by transaortic constriction banding or angiotensin II infusion.

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Muscarinic Receptor Activation Affects Plasticity at Parallel Fiber-Purkinje Synapses

Lorenzo Rinaldo, PhD

Mentor: Christian Hansel, PhD, Department of Neurobiology

Background: Endocannabinoid (CB) release can block the induction of presynaptically expressed long-term potentiation (LTP) at parallel fiber-Purkinje cell synapses. The activation of muscarinic acetylcholine receptors (mACHRs) has been shown to trigger CB release and alter plasticity in a variety of brain systems. There are five known isoforms of mACHRs (M1-5), all of which have been found in the cerebellar cortex and are located predominantly in the vestibulocerebellum. Furthermore, cholinergic inputs to the cerebellum arise mainly from the vestibular nucleus of the brainstem. Using the non-specific muscarinic agonist oxotremorine-m (oxo-m), we aimed to investigate the effect of mAChr activation on plasticity at the parallel fiber-Purkinje cell synapse.

Methods: Patch-clamp recordings of Purkinje cells were performed in cerebellar slices from rats aged P22-32 and mice aged P22-34. Cells were voltage-clamped at -70 mV during baseline and post-tetanization periods. Slices were perfused with ACSF + picrotoxin (100 uM) throughout the recording and other pharmacologic agents were administered at various times throughout the recordings as indicated in the results. Parallel fiber synapses were stimulated by placing an electrode in the molecular layer.

Results: Under control conditions, LTP was induced by delivering 120 PF stimuli at 8 Hz. In contrast, no LTP was observed when oxo-m was present during tetanization. LTP was restored when the cannabinoid receptor 1 (CB1) antagonist N-1-(2,4-dichlorophenyl)-5-(4-iodophenyl)-4-methyl-N-1-piperidinyl-1H-pyrazole-3-carboxamide (AM251) was coapplied with oxo-m. Furthermore, the suppressive effect of oxo-m on PF-LTP was abrogated by the GDP analog GDP-β-S (applied intracellularly), the phospholipase C inhibitor U-73122, and the diacylglycerol lipase inhibitor tetrahydrolipstatin (THL), suggesting that cannabinoid synthesis results from the activation of Gq-coupled mAChRs present on Purkinje cells. The oxo-m-mediated suppression of LTP was also absent in M1/M3 receptor double-KO mice, identifying either M1 or M3 receptors as the primary oxo-m targets.

Conclusion: We demonstrate that the muscarinic agonist oxotremorine-m (oxo-m) blocks the induction of presynaptic long-term potentiation (LTP) at parallel fiber-Purkinje cell synapses in a CB1R-dependent manner. Our findings allow for the possibility that cholinergic signaling in the cerebellum—which may result from long-term depression (LTD)-related disinhibition of cholinergic neurons in the vestibular nuclei—suppresses presynaptic LTP to prevent an up-regulation of transmitter release that opposes the reduction of postsynaptic responsiveness.

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Independent Category and Spatial Encoding in Parietal Cortex

Christopher Rishel, PhD

**Mentor:** David Freedman, PhD, Department of Neurobiology

**Co-Author:** Guang Huang

**Background:** The posterior parietal cortex plays a central role in spatial functions, such as spatial attention and saccadic eye movements. However, recent work has increasingly focused on the role of parietal cortex in encoding nonspatial cognitive factors such as visual categories, learned stimulus associations, and task rules. The relationship between spatial encoding and nonspatial cognitive signals in parietal cortex, and whether cognitive signals are robustly encoded in the presence of strong spatial neuronal responses, is unknown.

**Methods:** We directly compared nonspatial cognitive and spatial encoding in the lateral intraparietal (LIP) area by training monkeys to perform a visual categorization task during which they made saccades toward or away from LIP response fields (RFs).

**Results:** We show that strong saccade-related responses minimally influence robustly encoded category signals in LIP.

**Conclusion:** This suggests that cognitive and spatial signals are encoded independently in LIP and underscores the role of parietal cortex in nonspatial cognitive functions.

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Determining an Ideal Concentration of Povidone-Iodine for Conjunctival Antisepsis Before Cataract Surgery: An In Vitro Study

Richard Schroeder

Mentor: William Myers, MD, NorthShore University HealthSystem, Department of Ophthalmology

Background: The incidence of post-operative endophthalmitis following cataract surgery is about 0.048%. The causative organism most often responsible for post-operative endophthalmitis is staphylococcus epidermidis followed by staphylococcus aureus and streptococcus species. Povidone-iodine is an antiseptic proven to reduce the rate of bacterial endophthalmitis. It is toxic to the conjunctiva at high concentrations, however. Lidocaine gel is increasingly used pre-operatively for topical anesthesia, and previous studies have shown that when applied at 1% to the conjunctiva before surgery the bactericidal effect of povidone-iodine is decreased. HOCl is a bactericidal agent used in wound cleaning which is less toxic to human tissue than povidone-iodine and may have a role in pre-operative antisepsis. The purpose of this project is to determine the ideal concentration of povidone-iodine necessary to kill staphylococcus on a blood agar plate as a surrogate for the corneal conjunctiva before cataract surgery. Furthermore, to confirm in vitro that the use of lidocaine gel at concentrations of both 1% and 2% if applied to an agar plate before povidone-iodine will allow growth of staphylococcus epidermidis. Finally, to evaluate the use of HOCl as a bactericidal agent before cataract surgery by determining its effect on staph aureus in vitro.

Methods: A standard 0.5 MacFarlane solution of staphylococcus epidermidis was applied generously on blood agar plates. Some plates were treated with povidone-iodine at concentrations of 5%, 2.5%, 1%, 0.25%, 0.01%, and 0.025% for 30 seconds. Other plates were treated with HOCl at concentrations of 0.01% and 0.03%. A final set of plates were first coated in 1% and 2% lidocaine gel, then treated with 5% povidone-iodine. All plates were then allowed to incubate for 24 hours. Microbial growth was evaluated by one grader as a percentage of plate covered by bacterial growth.

Results: Povidone-iodine is effective at killing staph epi at high concentrations (0.25% and above) but not at low concentrations (0.1% and below). Lidocaine gel at 1% and 2% effectively limit the bactericidal effect of povidone-iodine. HOCl showed limited ability to act as a bactericidal agent in this model.

Conclusion: Povidone-iodine is the standard of care for preoperative antisepsis, but its use before surgery is not standardized to a specific concentration. Its toxicity to the conjunctiva prompts the need to use a minimum concentration which is an effective bactericidal agent while causing the least amount of damage possible. Our study shows that concentrations as low as 0.25% povidone-iodine can be used as a bactericidal agent. Other studies in vivo have also suggested this concentration can be used perioperatively to limit the rate of endophthalmitis. Further studies can be conducted to confirm in vitro that 0.25% povidone-iodine when applied at regular intervals will allow for full bactericide. In addition we believe a new model may be necessary to further simulate the conjunctival surface and confirm the efficacy of povidone-iodine at low concentrations.

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Regulator of G Protein Signaling (RGS3) Is a Novel Regulator of Epithelial to Mesenchymal Transition Signaling Pathways in Breast Cancer Cells

Nan Sethakorn, PhD

Mentor: Nickolai Dulin, PhD, Department of Medicine, Section of Pulmonary/Critical Care

Co-Authors: Jacob Kach, PhD; Douglas Yau, PhD

Background: Epithelial-to-mesenchymal transition (EMT) represents a potential mechanism by which epithelial-derived solid tumors acquire invasive and metastatic properties. Although TGF-beta has been established as one of the major pathways inducing EMT, factors that regulate TGF-beta signaling-mediated EMT are not as well understood. G protein-coupled receptor (GPCR) agonists have also been demonstrated to induce some characteristics of EMT, however the signaling pathways mediating these effects have not yet been elucidated. GPCRs signal through heterotrimeric G proteins, which are in turn regulated by a family of GTPase-activating proteins (GAPs) called Regulator of G protein Signaling, or RGS proteins. One member of the family, RGS3, can also inhibit TGF-beta signaling in addition to its canonical GAP activity. A few studies have linked RGS3 and various cancer types, including mammary carcinoma. Although RGS3 has been shown to inhibit signaling pathways that promote proliferation and migration, the contribution of RGS3 to cellular function is poorly understood. Additionally, the mechanism by which RGS3 controls the behavior of cancer cells was not thoroughly investigated.

Methods: RGS3 knockdown: Lentivirus encoding shRNA targeting RGS3, or non-targeting control, co-expressing a GFP selection marker were generated. GFP-positive cells were selected by fluorescence activated cell sorting, expanded in culture, and used for the following experiments. Western blotting: Cells were treated as described, lysates prepared for Western blotting, and developed by enhanced chemiluminescent reaction. Real-time semi-quantitative PCR: Cells were treated as described, RNA isolated, and used to generate cDNA. Genes of interest were amplified, each sample normalized to 18S, and delta-delta CT was calculated. Proliferation: Proliferation was measured with the CyQuant fluorescent dye protocol. Migration: Migration was measured with the Transwell assay. Dataset analysis: RGS3 expression data were extracted from the NKI breast cancer dataset, and fit to a survival curve. Statistical Analysis: All the data represent the results of at least three independent experiments. Quantitative data were analyzed by the Student’s t test, and values of p<0.05 were considered statistically significant.

Results: We demonstrate that knockdown of RGS3 in the epithelial MCF-7 breast cancer cell line promotes acquisition of mesenchymal morphology, accompanied by expression of markers N-cadherin and vimentin, and decreased expression of the epithelial marker E-cadherin. Additionally, knockdown of RGS3 increased migration and proliferation. Conversely, expression of RGS3 in the mesenchymal-like MDA-MB-231 breast cancer cell line promoted expression of E-cadherin, downregulation of the mesenchymal markers Snail and vimentin, and inhibited migration and proliferation. Using the NCI-60 panel of cancer cell lines, we determined that the PDZ-RGS3 isoform of RGS3 was strongly correlated with epithelial-type cancer cells. In a human breast cancer dataset, RGS3 expression was associated with decreased survival.

Conclusion: Overall, our data indicate that RGS3 regulates EMT in breast cancer cells, and may be a potential novel marker of epithelial cells. However, its role in survival of breast cancer may be multifactorial.

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Diet Drives Changes in Commensal Bacteria Regulated by Lymphotoxin to Enable Obesity

Vaibhav Upadhyay, PhD

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**Co-Authors:** Yuan Zhang; Tae-Jin Kim; Kevin Keegan

**Background:** Both protective and risk variant alleles in the gene encoding lymphotoxin β (LTβ) have been linked to obesity and metabolic illness. Together, this ligand and its receptor (lymphotoxin-β-receptor, LTβR) contribute to gastrointestinal immunity through lymphoid organ development and regulation of the cytokines IL-23 and IL-22. Commensal microorganisms occupying the distal gut live in a symbiotic relationship with the host, principally influenced by such immune responses. Alterations in the distal gut microbiota have been linked to obesity, but how commensal bacteria adapt in response to altered nutrition is poorly defined. We hypothesize that LTβR plays a role in weight gain, and this role is through its ability to regulate composition of the commensal microbiota.

**Methods:** Mice lacking elements of the LT-pathway (Lta-/-, Ltb-/-, Ltbr-/-, and Rorc-/-) were fed a normal or high-fat diet (HFD) along with heterozygous littermate or wild-type controls. We also generated Ltbr-/- germ free mice and challenged them with HFD. We examined hematopoietic cells within the colon using flow cytometry and light microscopy. Cytokine expression was profiled using real-time PCR. We examined variation in the microbiome and colonizing species by shotgun sequencing cecal contents and 16s rRNA sequencing of stool. We also used hydrodynamic injection to restore IL-23/Il-22/IL-17A expression in Ltbr-/- mice. Data were analyzed using Prism 6.0, MOTHUR, and MGRAST.

**Results:** Lta-/-, Ltb-/-, Ltbr-/-, mice resisted diet-induced obesity. Cecal transplantation conferred leanness to wild-type germ free recipients. Ltbr-/- mice differed in microbial community composition compared to their heterozygous littermates, including an overgrowth of Segmented Filamentous Bacteria (SFB). Housing Ltbr-/- mice with their obese siblings rescued the obese phenotype, demonstrating communicability of weight gain. HFD induced LTβ expression, and both LTβR and HFD regulated IL-23 and IL-22 expression within the distal gut. Restoration of IL-22 partially restored weight gain in Ltbr-/- mice. Ltbr+/+ and Ltbr-/- germ free mice were both able to gain weight on HFD, demonstrating dependence of the obese phenotype on the microbiota. The ability to gain weight correlated with splenomegaly. Metagenomic sequencing revealed both HFD and LTβR were required to create a unique microbiome configuration. LTβR repressed metabolism and DNA replication in colonizing species.

**Conclusion:** Our data reveal that host immunity via LTβR responds to HFD intake and regulates bacteria occupying the distal gut to enable weight gain. LTβR is essential for weight gain in our model of diet-induced obesity, but this requirement only occurs in animals colonized with commensal microbiota. Our data also reveals that adaptations in the microbiome in response to a change in diet occur in conjunction with immunity. We propose a three-component model for host physiology where diet, colonic microbiota, and immunity all provide unique contributions to enable weight gain: diet provides a positive energy balance and initiates compositional changes in the commensal microbiota that are regulated by LTβR to enable diet-induced obesity.

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Scientific Investigation in Clinical Research or Social Sciences
High Normal CGG Repeat Number on the Fragile X Mental Retardation (FMR1) Gene is Not Correlated with Diminished Ovarian Reserve

Rachel Allon

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Co-Authors: Ann Schufreider, MD; Dana McQueen, MD; Sang Mee Lee, PhD; Meike Uhler, MD; Jocelyn Davie, MS, CGC

Background: The Fragile X Mental Retardation 1 (FMR1) gene in its fully expanded form is responsible for the condition that is the most common cause of inherited mental retardation and autism. Mutations of the FMR1 gene are categorized by the number of CGG trinucleotide repeats present, with >200 repeats responsible for the Fragile X syndrome. The premutation contains 55-200 repeats and is associated with Primary Ovarian Insufficiency (POI). Several small studies have also reported an association between women with high normal and intermediate CGG repeat numbers (35-54 repeats) and diminished ovarian reserve. However, studies have had conflicting results and this association has not been conclusively demonstrated. Given the varying results demonstrated by prior smaller studies, the objective of this study was to further investigate the possible correlation between high normal CGG repeat numbers and diminished ovarian reserve in a larger population.

Methods: The study included all women who presented for treatment to Fertility Centers of Illinois and underwent both Fragile X testing and ovarian reserve testing from January 2012 to February 2014. Fragile X testing was done with triplet repeat PCR, with confirmation of positives by Southern blot. CGG repeat numbers from both alleles were recorded, and the allele with the higher number of repeats was used for statistical calculations. Women with >54 CGG repeats were excluded from analysis. Ovarian reserve testing was carried out on cycle day 2 or 3 and included measurements of follicle stimulating hormone (FSH), AntiMüllerian hormone (AMH) and antral follicle count (AFC). Characteristics of the subjects were summarized with the use of descriptive statistics. Differences across repeat numbers were assessed by one way ANOVA for continuous variables and chi-square tests for categorical variables. A generalized linear regression model assuming gamma distribution and log link function that controlled for age was used to assess correlation between CGG repeat number and FSH, AMH and AFC.

Results: 1,287 women underwent both FMR1 and ovarian reserve testing. Most women (84%) had <35 repeats (n=1079). 208 women (16%) had high normal repeat numbers, defined as 35-54 repeats. Women in this study had a mean age of 35.9±4.4, mean FSH of 9.1 ±7.3mIU/mL, mean AMH of 2.6±3.1ng/mL, and a mean AFC of 15.2±10.2. Patients were categorized by CGG repeat numbers of <35, 35-39, 40-44, and >44. There were no statistical differences in patient characteristics or ovarian reserve testing amongst groups. As expected, there was a significant correlation between increasing age with increasing FSH and decreasing AFC and AMH for the patients in this study. For every 1 year increase in age, FSH increased by a factor of 1.04, AFC decreased by a factor of 0.93, and AMH decreased by a factor of 0.89. After controlling for age, there was no significant correlation between FMR1 CGG trinucleotide repeat number and FSH (p=0.23), AFC (p=0.14), or AMH (p=0.53).

Conclusion: In contrast to previous smaller studies, this large data set demonstrated that a high normal number of CGG repeats was not significantly correlated with diminished ovarian reserve.

Acknowledgements/Disclosures: Thanks to OB/GYN department for providing support for this project.
Prostate Cancer Detection Rates After Diagnosis of Atypical Small Acinar Proliferation

Kyle Ericson

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Co-Author: Hannah Wenger, MS4

Background: Atypical small acinar proliferation (ASAP) is diagnosed when insufficient features of prostate cancer are present on prostate biopsy. ASAP is found in approximately 5% of prostate biopsies with cancer subsequently diagnosed in 27-59% of patients. Current National Comprehensive Cancer Network guidelines call for rebiopsy within 6 months. Current guidelines are based on several studies from the sextant biopsy era. The purpose of this study is to add to the current understanding of ASAP in the era of 12 core biopsies by reporting the incidence of ASAP and subsequent cancer rates and characteristics at our institution.

Methods: We reviewed patients that underwent prostate biopsy for either an elevated PSA or an abnormal digital rectal exam between 2008 and 2013 at our institution by a single urologist. Men with ASAP without previous cancer were included. Patients were counseled on the current recommendations and were allowed to decide whether to receive a repeat biopsy. Patients that were rebiopsied received 12 core biopsy with additional sampling from the area of the original ASAP lesion. PSA values as well as pathologic biopsy features including the presence of ASAP or cancer, tumor volume, number of involved cores, and Gleason score were analyzed.

Results: Of 1450 men, ASAP was found in 75 (5%) patients. Rebiopsy was performed in 49 (65%) patients at a mean of 6.7 months. 15 (31%) were diagnosed with cancer, 10 (20%) with ASAP, and 24 (49%) were benign. Total incidence of cancer was 35% after cancer was found in 2 patients on subsequent biopsies after ASAP or benign findings at rebiopsy. Prompting PSA and number of ASAP positive cores were not associated with a subsequent cancer diagnosis. Gleason 6 disease was diagnosed in 14 (82%) patients, Gleason 7 in 2 (12%) patients, and Gleason 8 in 1 (6%) patient. The average tumor volume was 2.9 mm. Of the 17 patients diagnosed with prostate cancer, 8 (47%) opted to enroll in active surveillance, 6 (35%) underwent prostatectomy, and 3 (18%) received focal therapy.

Conclusion: The incidence of cancer after ASAP diagnosis in our study was 35%, toward the lower end of the previously reported range. The overwhelming majority of cancers diagnosed after ASAP are low-grade and low-volume. Consistent with prior data, PSA values prompting biopsy and the number of cores ASAP positive did not predict subsequent cancer diagnosis. The majority of cancers diagnosed after finding ASAP would qualify for active surveillance. In an era of increasing comfort with active surveillance and minimizing the overtreatment of prostate cancer, we support a conservative follow-up strategy for patients with ASAP including semi-annual PSA and DRE with repeat biopsy within 1 year.

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Comparative Effectiveness of Surgical Treatments for Pediatric Hydrocephalus Lesions

Dominic Harris

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Co-Author: I-Wen Pan, PhD

Background: Pediatric hydrocephalus represents a high health care burden in the US. Treatments for hydrocephalus most commonly include ventriculoperitoneal shunt (VPS) and endoscopic third ventriculostomy (ETV). The absence of implanted shunt hardware makes ETV an attractive alternative to shunt placement in select cases where ETV may offer a durable treatment. There is increasing interest for examining the comparative effectiveness of these two surgical treatments. This study aims to apply propensity scores matching (PSM) to perform a comparative effectiveness analysis for endoscopic third ventriculostomy (ETV) and cerebrospinal fluid (CSF) shunt placement in pediatric hydrocephalus patients in the US using a large administrative claims database.

Methods: The MarketScan database 2003-2011 was used. Patients aged 19 years or younger at the first occurrence of ETV or shunt during the study period were included. The study outcome, surgery failure, was defined as further surgical treatment for hydrocephalus subsequent to the initial ETV or shunt procedure. Age, etiology of hydrocephalus, and history of shunt were used to create matched samples for the ETV and VPS cohorts. Kaplan-Meier survival curves, stratified log-rank test, and Cox proportional-hazard models were used to analyze the samples.

Results: There were 3231 eligible patients with either ETV or CSF shunt as index treatment for hydrocephalus. 478 (14.8%) patients had ETV and 2753 (85.2%) had CSF shunt placement. The 1-year success rates for the matched sample were 69.9 for ETV and 75.3% for VPS. The 5-year success rates were 61.3% and 61.8%, respectively. Overall, there was no significant difference in failure rates between these two groups. Subgroup analysis, however, showed that patients under 1 year of age had lower ETV success rates than those with shunt (p=0.009).

Conclusion: Overall, there was no significant difference in time to surgery failure between patients undergoing ETV and shunt placement. ETV was associated with higher risk of failure compared to shunt among patients under 1 year of age.

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Comparison of Efficacy, Pharmacokinetics, and Immunogenicity Between Infliximab Mono-Versus Combination Therapy in Ulcerative Colitis

Michael Hayes

Mentor: Atsushi Sakuraba, MD, PhD, Department of Medicine, Section of Gastroenterology

Background: The association of concomitant immunosuppressant use with infliximab (IFX) and therapeutic outcomes in correlation with pharmacokinetic properties in ulcerative colitis (UC) remains unclear.

Methods: A retrospective analysis of UC patients treated with IFX. Duration of efficacious IFX therapy, and serum IFX and antibody-to-IFX (ATI) levels were compared between those receiving IFX as monotherapy and in combination with an immunosuppressant.

Results: Among the 85 UC patients who received IFX, 46 (54.1%) received concomitant immunosuppressants, and 38 (45.9%) received IFX monotherapy. Concomitant immunosuppressant use was associated with increased duration of IFX therapy as 90% of patients receiving immunosuppressants remained on therapy at 1 year versus 61% of patients on monotherapy (Logrank, p = 0.016). Concomitant immunosuppressant use, as compared with monotherapy, was associated with greater IFX levels (20.4 mg/L vs 10.5 mg/L, p = 0.025) and less frequent ATI formation (4.5% vs 33.3%, p = 0.031). Patients receiving greater than 2.0 mg/kg of azathioprine had greater IFX level than those receiving less than 2.0 mg/kg (26.0 vs 10.6 mcg/mL, p = 0.03) and those receiving IFX monotherapy (26.0 vs 11.2 mcg/mL, p = 0.03). The duration of IFX therapy among patients receiving less than 2.0 mg/kg azathioprine was indistinguishable from patients on IFX monotherapy (Logrank, p = 0.95).

Conclusion: Concomitant immunosuppressant therapy with IFX improves outcomes in UC as shown by increased duration of therapy, decreased immunogenicity against IFX, and increased blood levels of IFX. Our data suggest that this benefit may be dependent on the dose of concomitant immunosuppression.

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Simfield: A Computer Simulated Visual Field Test to Screen for Glaucoma

Justin Hellman

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Co-Authors: Marie Perrone, MS3; Hasenin Al-khersan, MS2; Diego Altamirano, MD

Background: The purpose of this project is to evaluate the efficacy of a computer simulated visual field test (Simfield) as a screening tool for glaucoma.

Methods: 36 glaucoma or glaucoma suspect patients (53 eyes) from one ophthalmology clinic used the Simfield program within six months of a reliable performance on a 242 SITA standard Humphrey Visual Field Analyzer Exam. Patients with corrected vision worse than 20/100 were excluded. The exam measured threshold values at the same 54 points as the 242 SITA standard software as well as false positives, false negatives, and fixation losses. Two glaucoma specialists and one general ophthalmologist blindly analyzed the Simfield results and determined whether there was evidence of a glaucomatous defect in any of the 4 quadrants of each field. These results were compared to the corresponding HFA tests to determine sensitivity and specificity.

Results: The sensitivity of Simfield ranged from 51-76% and the specificity was 67-88%. In a sub-analysis that eliminated mild defects, defined as defects in a field with mean deviation < 7.0, sensitivity improved to 75-91% and specificity was 69-91%. The average false positive rate was 5.2%, the average false negative rate was 3.7%, and the average fixation loss rate was 27.7%.

Conclusion: Simfield is an effective test for identifying moderate to severe glaucomatous visual field loss and can be accessed from any home computer. While the cost to detect glaucoma in one patient using current screening methods is estimated at $1000, Simfield can be used for free anywhere that a computer is available.

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The Impact of Insurance and Race on Age at Surgical Intervention Among Children with Craniosynostosis

Yimo Lin

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**Co-Authors:** I-Wen Pan, PhD; Dominic Harris, MS4; Thomas Luerssen, MD

**Background:** Craniosynostosis is a condition involving the premature fusion of one or more cranial sutures. The optimal age of surgical intervention for this disease depends on a number of clinical factors, but recent studies have found that surgical correction at a younger age leads to better intellectual and neurological outcomes. This study aimed to examine the impact of demographic factors, including insurance type, family income, and race/ethnicity, on patient age at the time of surgical intervention for craniosynostosis surgery in the US.

**Methods:** The Kids' Inpatient Database (KID) is the largest publicly-available all-payer pediatric inpatient care database in the United States. Weighted, it contains data from approximately 7 million pediatric discharges each year. The KID was queried for admissions of children younger than 3 years of age undergoing craniosynostosis surgery in 2009. Descriptive data regarding age at surgery for various substrata are reported. Multivariate regression was used to evaluate the effect of patient and hospital characteristics on the age at surgery.

**Results:** Children with private insurance were, on average, 6.8 months of age (95% CI 6.2-7.5) at the time of surgery; children with Medicaid were 9.1 months old (95% CI 8.4-9.8). White children received surgery at mean age of 7.2 months (95% CI 6.5-8.0) and black and Hispanic children at a mean age of 9.1 months (95% CI 8.2-10.1). Multivariate regression analysis found Medicaid insurance (beta coefficient [B] = 1.93, P < .001), black or Hispanic race/ethnicity (B = 1.34, P = .022), and having 2 or more chronic conditions (B = 2.86, P < .001) to be significant independent predictors of older age at surgery.

**Conclusion:** Public insurance and nonwhite race/Hispanic ethnicity were statistically significant predictors for older age at surgery, adjusted for sex, zip code median family income, year, and hospital factors such as size, type, region, and teaching status. Further research into these disparities is warranted.

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Voxelwise Multivariate Analysis of Multimodality Magnetic Resonance Imaging

Melissa Naylor, PhD

Mentor: Wim van Drongelen, PhD, Department of Neurology

Co-Authors: Valerie Cardenas, PhD; Duygu Tosun, PhD; Armin Schwartzman, PhD

Background: Most brain magnetic resonance imaging (MRI) studies concentrate on a single MRI contrast or modality, frequently structural MRI. By performing an integrated analysis of several modalities, such as structural, perfusion-weighted, and diffusion-weighted MRI, new insights may be attained to better understand the underlying processes of brain diseases.

Methods: We compare two voxelwise approaches: (1) fitting multiple univariate models, one for each outcome and then adjusting for multiple comparisons among the outcomes and (2) fitting a multivariate model. In both cases, adjustment for multiple comparisons is performed over all voxels jointly to account for the search over the brain. The multivariate model is able to account for the multiple comparisons over outcomes without assuming independence because the covariance structure between modalities is estimated. To illustrate the power of each approach, we simulate data with multiple outcomes under four different covariance assumptions and analyze a case control study of Alzheimer’s disease, in which data from three MRI modalities are available.

Results: Simulations show that the multivariate approach is more powerful when the outcomes are correlated and, even when the outcomes are independent, the multivariate approach is just as powerful or more powerful when at least two outcomes are dependent on predictors in the model. However, multiple univariate regressions with Bonferroni correction remains a desirable alternative in some circumstances.

Conclusion: When choosing a method to account for multiple comparisons, researchers must consider several factors, including the primary hypothesis, whether the correlations between modalities are of interest, and computational resources.

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The Incidence of Perioperative Deep Venous Thromboses of the Lower Extremities

Patricia Osmolak

Mentor: David Glick, MD, MBA, Department of Anesthesia & Critical Care

Background: Patients undergoing surgery are at risk for developing deep vein thrombosis (DVT). Whereas the general population has an incidence of diagnosed DVT of 5 per 10,000 patient-years (Fowkes et al., 2003), patients undergoing high-risk procedures, such as orthopaedic surgery, can have DVT incidence higher than 50% (Berqvist et al., 1996). The difference is generally attributable to characteristics of the operation itself, including immobilization, tissue trauma, dehydration and transfusion. What is less clear, however, is what effect certain preoperative factors, such as patient gender, ASA status and anticoagulation use, may have on the incidence of perioperative DVT development. We will look at the immediate pre- and post-operative prevalence of DVTs in our patient population and then calculate the post-operative incidence of DVTs at our patients’ three and six-month follow up visits.

Methods: This study is designed as an observational study that does not require placebos or controls. The goal is to enroll 500 patients. Eligible subjects include all patients over the age of 18 having planned surgery at the University of Chicago Hospitals. Exclusions include history of known DVT, PE, or clotting disorder; planned surgery below the knee; and inability to give informed consent. On the day of surgery, consenting patients received a bilateral lower extremity venous duplex exam in the holding area before their procedure. Type of anesthetic administered as well as DVT prophylaxis during surgery, if any, was noted. A repeat exam was performed in the PACU within an hour of extubation in order to compare the prevalence of DVT in patients before and after surgery. If a clot was found during either of these studies, the attending surgeon was notified and the decision regarding how to proceed was made by the surgeon in consultation with the patient. The patient was also made aware of the results of both the pre- and post-operative scans. The patients’ medical records were queried at 3 and 6 months for evidence of the development of DVTs.

Results: At this time, 234 subjects have been enrolled in this study, and their ultrasounds and perioperative data have been tabulated. In our patient population, the immediate pre- and post-operative prevalence of DVTs was determined to be zero. Using Stata statistical analysis software, the three-month incidence of DVTs in our patient population was determined to be 5.8 per 10,000 patient-days (95% CI 3.2, 10.5); the six-month incidence of DVTs was determined to be 3.2 per 10,000 patient-days (95% CI 1.8, 5.6).

Conclusions: The immediate pre- and post-operative DVT prevalence of zero demonstrates that patients without known DVT, PE or clotting disorders are unlikely to present with or to develop DVTs during surgery. The very high incidence of DVTs in our patient population at both three and six months follow up, compared with the general population, supports the assertion that surgery is a strong risk factor for the development of DVT. The next phase of this study will involve looking at specific perioperative factors to see what effect, if any, they may have on DVT development.

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Image Analysis in Chronic Sinusitis: State of the Field

Paras Patel

Mentor: Jayant Pinto, MD, Department of Surgery, Section of Otolaryngology, Head & Neck Surgery
Co-Authors: Samuel Armato III, PhD; Fuad Baroody, MD

Background: Chronic rhinosinusitis (CRS) is a disease characterized by inflammation of the lining of the paranasal sinuses and nasal cavity. CRS has a complex and poorly understood etiology, which complicates the classification and staging of the disease. CT is routinely used in the United States to diagnose CRS and to determine if a patient qualifies for medical or surgical management. Several staging systems exist to aid the clinician in determining the severity of disease on CT, the most popular being the Lund-Mackay (LM) system. LM assigns scores to two-dimensional coronal sections of the sinuses based on zero, partial, or full occlusion of each bilaterally, plus the osteomeatal unit, to generate a score of 0-24. However, the vast majority of these systems, LM included, do not correlate with objective symptom scores as measured by a number of clinical questionnaires. Measurement of the severity of disease is complicated by several factors. Location of disease within the paranasal sinuses, nature of inflammatory infiltrate, and individual anatomy all affect symptoms in ways that are not measured by conventional CT scoring systems. Recently, several authors have put forth modifications to the LM system, in addition to entirely new systems for scoring the severity of CRS. This review article assesses the theory behind these new methods and qualitatively evaluates their potential clinical efficacy and practicality.

Methods: Literature searches were conducted using the PubMed computerized database and the online search engine Google Scholar. The search was conducted using the following terms: chronic rhinosinusitis, staging, Lund-Mackay, volumetric, and sinusitis. Inclusion criterion was any study that proposed or evaluated a staging system for CRS.

Results: Systems based on the two-dimensional LM method universally failed to correlate with objective symptom scores. Authors unsuccessfully tried to integrate clinical data and radiographic density data with the LM system. In addition, these modified systems required manual analysis of CT scans; they complicated the relatively simple LM system and made the process more laborious and less practical, limiting clinical utility. New systems have been introduced in the last year and use three-dimensional volumetric analysis to stage CRS severity. Pallanch et al. introduced the first volumetric method, which takes 0.4mm spaced coronal CT slices and sums the volume of inflamed tissue contained within each area to approximate the percent occlusion. This is the first method that showed a correlation with objective symptom scores. However, like the LM-based systems, this method requires manual analysis of CT scans and is cumbersome. Likness et al. modified the Pallanch system to take a single three-dimensional section at the level of the osteomeatal complex, resulting in the most practical and clinically correlated system in existence today.

Conclusion: New computing methods to automate the currently manual process of outlining sinus cavities will drastically improve the speed of future staging systems. Automation algorithms for this purpose currently exist but are restricted to closed-source proprietary software platforms. Open-source image interpretation software will allow for far more collaboration among investigators. Pathological data may also be incorporated into future systems to improve correlation with objective symptom scores.

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Validating the Use of Visual Analog Scales to Assess Quality of Life and Sleep Quality in Patients with Inflammatory Bowel Disease

Jonathan Stein

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Co-Authors: Jami Kinnucan, MD; Sarah R. Goeppinger

Background: There is great interest in the health-related quality of life (HRQoL) among inflammatory bowel disease (IBD) patients, and an evolving appreciation for the role sleep and sleep quality play in IBD. In addition, an emerging area of importance by clinicians and regulatory agencies is the use of validated patient-reported outcomes (PROs). In this study of IBD patients, we sought to validate the use of visual analog scales (VAS) in assessing HRQoL measured by the Short Inflammatory Bowel Disease Questionnaire (SIBDQ) and assessing sleep quality using the Pittsburgh Sleep Quality Index (PSQI). Validating VAS as a surrogate for these instruments would allow for a concise and efficient way of collecting PROs.

Methods: We recruited adult patients with a diagnosis of IBD who were seen in the outpatient clinic, procedure unit or hospitalized at the University of Chicago Medicine. Each patient completed a survey consisting of the following tools; SIBDQ, PSQI and two VAS. The SIBDQ is a validated ten-question survey measuring physical, social and emotional status; scores range from 10 (poor HRQoL) to 70 (good HRQoL). The PSQI is a self-rated questionnaire used to assess sleep quality and disturbances, scores range from 0 (good sleep quality) to 21 (poor sleep quality). The VAS were standard 100 mm horizontal lines that represented overall health (SIBDQ) and sleep quality (PSQI), and patients were asked to mark on the line their current state. We measured the distance in mm along the horizontal line to quantify these responses. Statistics included Pearson’s correlation coefficients to compare the SIBDQ, PSQI, and corresponding VAS.

Results: Two hundred ninety-eight patients completed the survey; 158 (53%) female, 187 (62.8%) with Crohn’s disease and 263 (88.3%) Caucasian. The mean age was 40.8 years (SD 15.7), 29.2% smoked cigarettes, 48.3% reported at least weekly alcohol intake and 14.4% had history of depression and/or anxiety. The mean SIBDQ score was 51 (SD 28.7, range 1070). The mean PSQI score was 8.5 (SD 5.3, range 021), 64.1% of patients reported poor sleep quality. There was excellent correlation for the SIBDQ and overall health VAS (r=0.77) and good correlation for the PSQI and sleep quality VAS (r=0.58).

Conclusion: In this cross-sectional study, we have demonstrated excellent correlation between the SIBDQ and a simple VAS, and good correlation between the PSQI with a simple VAS. These results support the ongoing use of VAS instruments in clinical practice and in the evolving area of patient-reported outcomes. Additional studies are underway to assess the relationship between sleep and HRQoL as well as objective measures of sleep.

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Age at the Time of SU Initiation Influences Treatment Outcomes in KCNJ11-Related Neonatal Diabetes

Brian Thurber

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**Co-Authors:** David Carmody, MD; Elizabeth Tadie, BA; Ashley Pastore, BA; Jazzmyne Dickens, BA; Kristen Wroblewski, MS; Rochelle Naylor, MD; Louis Philipson, MD, PhD

**Background:** Subjects with heterozygous activating mutations of the KCNJ11 gene encoding a subunit of the ATP-sensitive potassium channel (KATP) can usually be treated with oral sulfonylurea (SU) pills in lieu of insulin injections. The aim of this study was to test our hypothesis that younger age at the time of initiation of SU therapy is correlated with lower required doses of SU therapy, shorter transition time, and decreased likelihood of requiring additional diabetes medications.

**Methods:** We performed a retrospective cohort study utilizing data on 58 subjects with neonatal diabetes due to KCNJ11 mutations identified through the University of Chicago Monogenic Diabetes Registry (http://monogenicdiabetes.uchicago.edu). We assessed the influence of age at initiation of SU therapy on treatment outcomes.

**Results:** HbA1c fell from an average of 8.5% (69 mmol mol\(^{-1}\)) before transition to 6.2% (44 mmol mol\(^{-1}\)) after SU therapy (p < 0.001). Age of initiation of SU correlated with the dose (mg kg\(^{-1}\) day\(^{-1}\)) of SU required at followup (r = 0.80, p < 0.001). Similar associations were observed across mutation subtypes. 10 subjects required additional glucose lowering medications and all had initiated SU at age 13 years or older. No serious adverse events were reported.

**Conclusion:** Earlier age at initiation of SU treatment is associated with improved response to SU therapy. Declining sensitivity to SU may be due to loss of beta cell mass over time in those treated with insulin. Our data supports the need for early genetic diagnosis and appropriate personalized treatment in all cases of neonatal diabetes.

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The Importance of Lighting in the Home: National Prevalence Of “Real-World” Vision Impairment in Older Adults

Rachel Chen

Mentor: William Dale, MD, PhD, Department of Medicine, Section of Geriatrics and Palliative Medicine

Co-Authors: Martha McClintock, PhD; David Kern, PhD, Jayant Pinto, MD

Background: Field measurement of vision differs from clinical measurement in lighting and contrast. Previous estimates of the national prevalence of vision have not assessed the functional vision of older adults in their home. We estimate the prevalence of vision impairment (VI) in older adults measured at home and determine if low lighting is associated with poor geriatric outcomes.

Methods: We employed data from the National Social Life, Health, and Aging Project (NSHAP), a nationally-representative probability sample of community-dwelling older adults living in the U.S. The study included older adults aged 57 to 85 years at baseline (2005) with follow-up at five years (2010; n=1,417). Data were collected using a structured computer-assisted personal interview (CAPI) by professional, trained survey research staff. Bilateral distance visual acuity was measured using a standardized Early Treatment Diabetic Retinopathy Chart (ETDRS), and home lighting was measured by interviewer rating. We assessed physical performance using the timed up-and-go test, disability by self-reported difficulty with instrumental activities of daily living (IADLs) and activities of daily living (ADLs), self-reported health relative to peers, and mortality. Statistical significance was assessed using multivariate analyses using STATA 12.

Results: The prevalence of VI in U.S. older adults in their homes was 23.3%. Low lighting was significantly associated with worse vision (p<0.05) and independently associated with impaired physical performance, worse perceived relative health, disability, and decreased measures of home orderliness, after adjustment for demographics, geriatric outcomes, and vision itself (p>0.05, all). Older adults with VI were nearly twice as likely to have died after 5 years (OR=1.93, 95% CI 1.25, 2.97).

Conclusion: The prevalence of VI in older adults, as experienced in the home, is severely underestimated in current epidemiological studies. Home lighting should be considered when assessing older adults for health risks and may represent a modifiable target for intervention to reduce risk and improve geriatric outcomes.

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Why Patients Don’t Show

Michael Cui

Mentor: David Meltzer, MD, PhD, Department of Medicine, Section of Hospital Medicine

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Background: Failure to show up to primary care appointments disrupts the main purpose of primary care: providing quality continuous care over time. Missed appointments are a major source of inefficiency in the medical system and lead to poor control of chronic disease, later presentation to care, wasted health care dollars, and ineffective use of provider time. No show rates are a particular problem to clinics that care for the underserved. We sought to characterize the patients who did not show up to appointments.

Methods: Overall patient population for the study was composed of 444 patients at the University of Chicago Primary Care Clinic who were enrolled in the Comprehensive Care Physician (CCP) study. The study currently identifies patients who are at high risk of hospitalization and assigns them 1 of 5 CCP physicians who will act as the patient’s primary care physician and also their physician when/if they are hospitalized. Factors studied were age, gender, race, income, education level, appointment number, having a previous provider, and perceived respect from previous provider.

Results: All results were statistically significant. Our study showed an overall no show rate of 17.1% in all appointments. Younger patients, male, lower income status, and lower education all showed an increase in no show rates. Not having a previous provider, not knowing or having a previous provider never show you respect also resulted in higher no show rates. African American patients had higher no show rates than Caucasian patients but patients who selected “other” had even higher no show rates. However the sample size of these patients is small. As patients have more appointments, those who miss later appointments were more likely to be repeat offenders.

Conclusion: No show rates impede the goal of primary care. Interventions designed to target patients at high risk of no show are needed to help reduce the no show rate and improve patient care.

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Models of Geriatric Care: The Successful Aging and Frailty Evaluation Clinic: A Feasible Interprofessional Approach to Assessing, Managing, and Teaching About Frailty

Arielle Hirschfeld

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Background: The population of the United States continues to age and a well-documented shortage of fellowship-trained geriatricians places the onus of care for the majority of older adults on primary care providers, many of whom do not have the expertise or resources to care for frail elders. Referral clinics for frail elders may help to address the geriatric workforce shortage and augment primary care for older adults by maximizing the impact of limited specialized resources for geriatric care.

Methods: The Successful Aging and Frailty Evaluation (SAFE) clinic at University of Chicago Medicine’s Outpatient Senior Health Center at South Shore provides frailty assessment and comprehensive geriatric evaluation for older adult patients identified as being at increased risk by their primary care providers. Following an evaluation by an interprofessional team, recommendations are made to patients, caregivers, and primary care providers based on frailty status and patient goals. Interprofessional education is provided to trainees in the SAFE clinic during didactic sessions, patient assessments and interprofessional team meetings.

Results: One-year follow up data collected from a subset of SAFE clinic participants (N=80) show stability or improvement in overall frailty status in 76.3% and stability of Montreal Cognitive Assessment, Short Physical Performance Battery and Vulnerable Elders Survey-13 scores.

Conclusion: Requiring minimal equipment and few additional staff, this novel model of care is a feasible strategy to augment primary care for frail older adults.

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Worth A Try? Describing the Experiences of Families During Infant Trial of Therapy in the Neonatal Intensive Care Unit

Jennifer McCoy

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Background: As medical technology has allowed neonatologists to care for increasingly premature and sick neonates, questions arise about the prudence of resuscitating those infants who have a low likelihood of intact survival. Some infants are resuscitated for a ‘trial of therapy’ in the Neonatal Intensive Care Unit (NICU). This trial of therapy can end with the infant dying in the NICU, surviving with disabilities, or surviving intact. Resuscitation of these infants remains controversial and practices vary among providers and institutions. Such cases usually entail negotiated decision-making between the parents and the medical team. Little is known about how parents experience these situations, how they make such complicated decisions, and if they feel that a trial of therapy for such critically ill infants is ultimately worthwhile.

Methods: This is a qualitative, semi-structured interview study. The parents of infants admitted to the NICU were asked to participate in audiotaped interviews. Inclusion criteria to identify those infants undergoing a trial of therapy included: Gestational age 25 weeks or less, ECMO, Grade 34 IVH, Trisomy 13 or 18, and FiO2 >60%+mechanical ventilation after 1 month. Interviews consist of open-ended questions, generally lasting 20-30 minutes. Interviews were conducted privately and audiotaped. The recordings were transcribed and prominent themes identified. Each transcript was coded for prominent themes and frequencies of each theme were tabulated.

Results: 39 infants met the inclusion criteria during study period; 17 were ultimately interviewed. 28 major themes emerged from the data. Of these, 13 identify positive feelings/experiences, 11 identify negative feelings/experiences, 4 are neutral. 9 codes appear in >50% of interviews. The most common themes identified: realism about death or disability (35 times), an appreciation for the efforts of the care team (34 times), fear (32 times), optimism and hope (28 times), importance of faith/religion (22 times), and trust in the care team (21 times). Notably absent from every interview is the theme of futility or suffering for the infant. Concern about the infant experiencing pain or discomfort was mentioned 4 times, and distrust of the care team was mentioned 2 times. Parents also commonly expressed appreciation for the interview and stated that participating in the interview was valuable.

Conclusion: Parents understand the uncertain future for their infants and are realistic about the possibility of death or long-term disability. Parents remain optimistic that their infants may survive, and they appreciate the care they are receiving. No parents reference feeling that NICU trial of therapy is futile, torturous, or causing their infant to suffer. Parents find the NICU experience to be scary and stressful, and they often invoke faith to cope with this experience. Parents trust the teams that are caring for their infants and feel involved in their infants’ care and consider themselves active decision makers for their infants. Our data suggests that for most parents, there is moral value in a trial of therapy, regardless of the ultimate outcome for their infant.

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Is LARC for Everyone? Sociocultural Perceptions and Barriers to Contraception Among Refugees in Ethiopia

Christina Suh

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Background: Ethiopia is home to a large and growing refugee population, including many who come from neighboring Somalia and Eritrea. The International Rescue Committee (IRC), a nonprofit organization, implements health programs in refugee camps throughout Ethiopia, which aim to improve access to and quality of comprehensive reproductive health services. While all modern contraceptive methods are available to women in these camps, few women use long-acting reversible contraceptives (LARC). The purpose of this study was to explore sociocultural perceptions of and barriers to contraceptive use among these refugees, with a particular focus on LARC.

Methods: Qualitative data were collected in four Ethiopian refugee camps (two Somalian, two Eritrean) from January to February 2014, including: 12 focus groups (eight with women, four with men), 10 individual interviews (all women), and 15 key informant interviews with contraceptive providers. Data were translated into English, transcribed verbatim, and coded by two coders. The Social Ecologic Model (SEM) was used to frame contraceptive decision-making within the Individual, Interpersonal, Institutional, Community, and Policy levels of influence. A coding dictionary was developed based on themes from the focus group transcripts and the SEM. Atlas ti, a qualitative software program, was used for data organization and reduction. Salient themes endorsed across interviews are reported.

Results: All participants in the study were originally from Somalia (53%) or Eritrea (47%). 58% were Muslim and the remaining 42% were Christian. 47% of women reported that they currently used a short-acting contraceptive method and 25% reported using the implant. No participants reported using the IUD. When discussing their reproductive plans, both men and women articulated the importance of elements such as desired family size, desired birth spacing, and partner involvement. While they generally desired large families, participants wanted contraception because of the economic stability provided by having a smaller family, especially given their refugee status. Additionally, participants wanted religiously sanctioned reproductive methods, which were used primarily for birth spacing. Some expressed concern over whether LARC methods were religiously permissible. Other barriers to LARC uptake included concerns about the potential side effects and long-acting nature of LARC, particularly for the IUD.

Conclusion: Overall, for this population of Ethiopian refugees, cultural and religious beliefs heavily influence contraceptive selection and uptake. Short-acting methods are preferred over LARC, even when all methods are available free of charge.

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Extensive Workup for Embolic Sources in Lacunar Strokes: Prevalence in an Academic Setting

Yan Wang

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Background: Small subcortical (lacunar) strokes occur in clinical settings and have prognostic implications distinct from infarctions due to large artery occlusions. While the two stroke types share certain risk factors, small subcortical strokes are more commonly caused by intrinsic microvascular disease than by thromboembolism from proximal sources. Thus, the clinical relevance and cost-effectiveness of extensive workup for thromboembolic sources in lacunar strokes has been questioned. A pilot study was designed to describe the practice of extensive etiologic workup in lacunar stroke patients in an urban academic hospital setting.

Methods: All admissions to the University of Chicago Medical Center with a principle diagnosis of stroke over a three year period were classified as lacunar strokes versus other stroke types according to pre-identified criteria. Twenty five lacunar stroke cases and 25 non-lacunar stroke cases were randomly sampled. Clinical feature, echocardiography, and intracranial vascular imaging results were reviewed and recorded. Student’s t-test and Fisher’s exact test were used.

Results: 1,841 patients with a coded diagnosis of stroke were admitted during the study period. There were 637 confirmed ischemic strokes, 293 primary intracranial hemorrhages, 10 combined ischemic and hemorrhagic strokes, 849 non-acute stroke conditions, and 52 uncertain or unclassified cases. Lacunar strokes represented 16% of the 637 ischemic stroke cases. Of the 25 sampled lacunar stroke admissions, 17 had both echocardiography and intracranial vascular imaging; in comparison, 18 of 25 non-lacunar stroke admissions included both types of imaging. Antithrombotic medications were changed in 17 out of 25 lacunar patients and 18 out of 22 non-lacunar patients alive at discharge.

Conclusion: Lacunar strokes represented a substantial fraction of the ischemic strokes admitted in this urban hospital. In the small study sample, these patients typically received extensive work-up for thromboembolic sources at a rate similar to that of large artery strokes. The imaging studies did not directly contribute to antithrombotic medication changes in the lacunar group. Further examination of the clinical utility of the extensive imaging is warranted to guide best clinical practices.

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