

**Cover image courtesy of
Thomas Johnson, MS2**

The cover image is an epifluorescent micrograph depicting a neuron that was generated in culture by differentiation of a neural stem cell. The soma and neurites were visualized using immunofluorescence with a monoclonal antibody raised against neuron-specific class III beta-tubulin cytoskeletal protein. The neural stem cell line that gave rise to this neuron was isolated from the subventricular zone of the lateral ventricle of an adult mouse brain, a region which harbors a stem cell population that continuously repopulates neurons in the olfactory bulb via the rostral migratory stream. Part of our ongoing research aims to characterize the effects of developmentally-regulated CNS signaling molecules on the cell fate choices of neural stem cells as well as on the ability of differentiated neurons to generate and extend long-range cellular processes.

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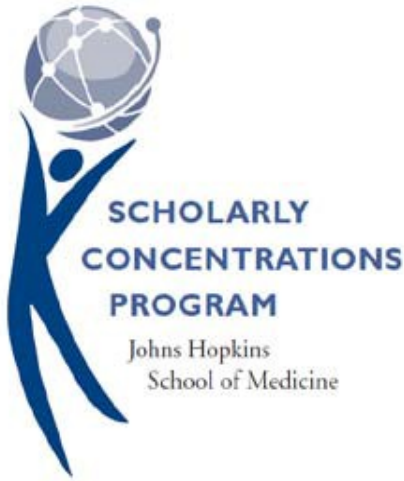
Medical Student Research Day 2012

We are pleased to have you join us for the 4th annual Medical Student Research Day of the Johns Hopkins University School of Medicine. As clinicians in training, we are fortunate to work among faculty who conduct a broad range of investigation that yields discoveries that advance the knowledge of human health. For the past three years, we have been fortunate to have an event that presents the extensive endeavors that students take to advance this mission at the school.

The mission of the The Johns Hopkins University School of Medicine is to educate medical students, graduate students, and postdoctoral fellows in accordance with the highest professional standards; to prepare clinicians to practice patient-centered medicine of the highest standard; and to identify and answer fundamental questions in the mechanisms, prevention and treatment of disease, in health care delivery and in the basic sciences.

The aim of the pre-doctoral curriculum of the School of Medicine is to produce leaders in Medicine who will take the foundation of a broad education in Medicine to improve health through patient care, research, and education.

Medical Student Research Day is a forum for medical students at Johns Hopkins to present their own research to the greater Hopkins community. It is an opportunity for students to participate in the exchange of intellectual ideas in a professional format and meet faculty who relish the pursuit of better science and more effective medicine. Our mission is for Medical Student Research Day to foster the development of young researchers who will aid in the advancement of scientific medicine for years to come.



The Scholarly Concentration (SC) program is a faculty-mentored scholarly experience for medical students. This program provides the infrastructure and mentoring necessary for students to produce a scholarly project in an area of individual interest, and encourages the acquisition of attitudes and skills for lifelong learning and scholarship. The SC program offers the following five areas of study:

Basic Science	Jon Lorsch, PhD
Clinical Research	Kelly Gebo, MD, MPH Jennifer Haythornthwaite, PhD Steve Sozio, MD, MHS John J. Strouse, MD, PhD
History of Medicine	Randall Packard, PhD Graham Mooney, PhD
Medical Humanities Bioethics and The Healing Arts	Joe Carrese, MD, MPH Gail Geller, ScD, MHS
Public Health and Community Service	Eric Bass, MD, MPH David Friedman, MD, PhD

The overall goals of the SC program are to promote intellectual curiosity, appreciation of scholarly inquiry, flexibility, passion for discovery, openness to new ideas, and the ability to work both independently and collaboratively.

PROGRAM SCHEDULE

12:00 – 1:00 PM

Poster session

*AMEB Main Lobby & 2nd Floor
Refreshments will be served*

1:00-3:00 PM

Podium presentations

AMEB Lecture Hall

3:00-4:30 PM

Poster Session

AMEB Main Lobby & 2nd Floor

4:30 PM

Keynote speaker, *Dr. Jeremy Sugarman*

AMEB Lecture Hall

5:00 PM

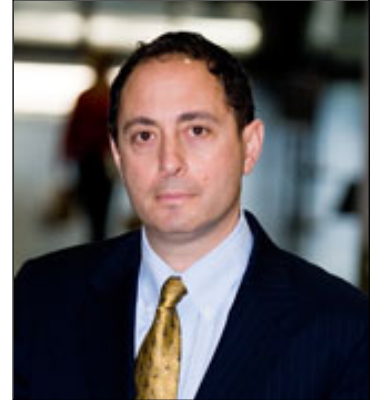
MSRD Award Ceremony

AMEB Lecture Hall

KEYNOTE SPEAKER

Jeremy Sugarman, MD, MPH

*Harvey M. Meyerhoff Professor of Bioethics and Medicine
Deputy Director for Medicine, Johns Hopkins Berman
Institute of Bioethics
Professor of Health Policy and Management*



Jeremy Sugarman is an internationally recognized leader in the field of biomedical ethics with expertise in the application of empirical methods and evidence-based standards for the evaluation and analysis of bioethical issues. His contributions to both medical ethics and policy include his work on the ethics of informed consent, umbilical cord blood banking, stem cell research, international HIV prevention research, and research oversight.

Dr. Sugarman is the author of over 200 articles, reviews and book chapters. He has edited or co-edited four books (*Beyond Consent: Seeking Justice in Research*; *Ethics of Research with Human Subjects: Selected Policies and Resources*; *Ethics in Primary Care*; and *Methods in Medical Ethics*). He is an associate editor of *Clinical Trials*, a contributing editor for *IRB*, and is on editorial boards of several academic journals.

Dr. Sugarman consults and speaks internationally on a range of issues related to bioethics. He is a senior adviser to the Presidential Commission for the Study of Bioethical Issues. He previously served as a senior policy and research analyst for the White House Advisory Committee on Human Radiation Experiments and a consultant to the National Bioethics Advisory Commission.

He was the founding director of the Trent Center for Bioethics, Humanities and History of Medicine at Duke University where he was also a professor of medicine and philosophy. He is a faculty affiliate of the Kennedy Institute of Ethics at Georgetown University.

Dr. Sugarman currently serves on the Maryland Stem Cell Research Commission, the Scientific and Research Advisory Board for the Canadian Blood Service, the Ethics and Public Policy Committee of the International Society for Stem Cell Research, and the Board of Directors of PRIM&R (Public Responsibility in Medicine and Research). He is co-chair of the Johns Hopkins Institutional Stem Cell Research Oversight Committee. In addition, he is chair of the Ethics Working Group of the HIV Prevention Trials Network and is the ethics officer for the Resuscitation Outcomes Consortium.

Faculty Judges

Meredith Atkinson, MD, MHS
Assistant Professor of
Pediatrics

Eric Bass, MD, MPH
Professor of Medicine

**Mary-Catherine Beach, MD,
MPH**
Associate Professor of
Medicine

Dana Boatman, PhD
Associate Professor of
Neurology and Otolaryngology

Henry Brem, MD
Professor and Chairman of
Neurosurgery

Ali Bydon, MD
Assistant Professor of
Neurosurgery

Andrew Cameron, MD, PhD
Assistant Professor of Surgery

James Campbell, MD
Professor of Neurosurgery

Joseph Carrese, MD, MPH
Associate Professor of
Medicine

Michael Choi, MD
Associate Professor of
Medicine

Sarah Clever, MD, MS
Assistant Professor of
Medicine

David Cooke, MD
Associate Professor of
Pediatrics

Charles Flexner, MD
Professor of Medicine

**David Friedman, MD, MPH,
PhD**
Professor of Ophthalmology

Kelly Gebo, MD, MPH
Associate Professor of
Medicine

Gail Geller, ScD
Associate Professor of
Pediatrics

Khalil Ghanem, MD, PhD
Associate Professor of
Medicine

Mitchell Goldstein, MD
Assistant Professor of
Pediatrics

J. Marie Hardwick, PhD
Professor of Microbiology &
Immunology

Adam Hartman, MD
Assistant Professor of
Neurology & Pediatrics

**Jennifer Haythornthwaite,
PhD**
Professor of Psychiatry &
Behavioral Sciences

Craig Hendrix, MD
Professor of Medicine

Alexander Hoon, MD, MPH
Associate Professor of
Pediatrics

Mark Hughes, MD, MA
Assistant Professor of
Medicine

Thomas Koenig, MD
Associate Dean for Student
Affairs

Eric Kossoff, MD
Associate Professor of
Neurology & Pediatrics

Michael Lim, MD
Assistant Professor of
Neurosurgery

Nisa Maruthur, MD, MHS
Assistant Professor of
Medicine

Christina Miller, MD
Assistant Professor of
Anesthesiology & Critical Care
Medicine

Edgar Miller, MD, PhD
Associate Professor of
Medicine & Epidemiology

Lawrence Nogee, MD
Professor of Pediatrics

Ben Ho Park, MD, PhD
Associate Professor of
Oncology

Peter Pronovost, MD, PhD
Professor of Anesthesiology &
Critical Care Medicine

Lorraine Racusen, MD
Professor of Pathology

Adam Schiavi, MD, PhD
Assistant Professor of
Anesthesiology & Critical Care
Medicine

Robert Silicano, MD, PhD
Professor of Medicine

Stephen Sozio, MD, MHS
Assistant Professor of
Medicine

Stacy Suskauer, MD
Instructor, Physical Medicine &
Rehabilitation

Patricia Thomas, MD
Associate Professor of
Medicine

Thomas Trail, MD
Professor of Medicine

Roy Zeigelstein, MD
Professor of Medicine

Schedule of Podium Presentations

1:00 pm	Hansen Bow MS2	<i>Microchip-based intracranial temozolomide delivery in a 9L rat glioma model</i>
1:12 pm	Alessa Colaianni MS2	<i>MS-1: Lessons from the First Year</i>
1:24 pm	Saami Khalifian MS2	<i>Vascularized Autogenous Bone Provides Superior Outcomes in the Management of the Complex Cranioplasty</i>
1:36 pm	Rachel Meserole MS2	<i>Assessment of Health Related Quality of Life Six Years after Early Cochlear Implantation</i>
1:48 pm	Amir Mohareb	<i>Disaster preparedness in the age of molecular diagnostics: a national survey of hospital laboratories</i>
2:00 pm	Vanessa Pascoe MS2	<i>Anxiety is Associated with Increased Sexual Risk Behaviors in Baltimore Women Presenting to an STI Clinic</i>
2:12 pm	Jacob Ruzevick	<i>The Haptoglobin 2-2 gene is associated with increased aneurysm formation in a novel model of aneurysm formation</i>
2:24 pm	Sarah B. Sunshine	<i>Nitric Oxide's role in Dry and Wet Age-related Macular Degeneration (AMD)</i>
2:36 pm	Anne van Beuningen, MS2	<i>The role of GDE2 in motor neuron maintenance and survival</i>
2:48 pm	Erin Zingarelli MS2	<i>The Best Things in Life Are Free: development of open-access, interactive 3D modules for gross anatomy education using publicly available data and low-cost software tools</i>

POSTER PRESENTERS

Listed Alphabetically by Research Category and Location

BASIC SCIENCE: AMEB 2nd Floor

#	Name	Title
1	Joani Christensen	Inflammatory Cell Homing Using Near Infrared Fluorescence Labeling with Indocyanine Green
2	John Fan	Intrinsic Photosensitivity and Non-Visual Pigments in the Chicken Iris
3	Yarden Fraiman*	Identification of a Flt-3 Ligand surge in pediatric leukemia patients receiving myelosuppressive therapy.
4	Caleb Gardner*	Stress-Induced Epigenetic Changes in the Brain
5	Paul Gilbert*	Endophyte Derived Novel Therapeutics for MRSA
6	Valerie Gordon*	Conditional knockout of Kir4.1 in NG2 cells of the adult brain
7	Annie Hsu	The effect of advanced glycation end products on choroidal neovascularization
8	Thomas V Johnson	Small molecule protein kinase inhibitors for neuroprotection in glaucoma
9	Andrea Jones	Evaluation of the Conformer Selection Protocol in Rosetta 3.0
10	Krishna R. Juluri	The Role of Inositol Hexakisphosphate Kinase in Dynamin Mediated Endocytosis
11	Allison Kaeding*	MLL Rearrangement and Age at Diagnosis Are Strongly Associated with High Level Surface FLT3 Expression and Ex Vivo Sensitivity to FLT3 Inhibition: A Prospective Analysis of 54 Consecutive Infants with ALL
12	Molong Li	Characterizing ENCODE DNaseI Hypersensitivity Data and Evaluating Its Use In Identifying Functional Variants
13	Jose Soria Lopez*	Duplication of the ZEB2 Gene in a Young Child Diagnosed with Autism and Self Injurious Behavior

14	Kyle Mahoney	Using artificial antigen-presenting cells to provide CD27 co-stimulation to antigen-specific CD8+ T cells.
15	Marcus Messmer	Development of a Breast Cancer Stem Cell Vaccine in Mice
16	Devin T. Miller	Defining the O-GlcNAcome of Cells and Tissues Subjected to Ischemic Injury
17	Stuart Mitchell*	Loeys-Dietz Syndrome Affects Bone Microarchitecture
18	Camilo A. Molina*	Optimizing magnetic nanoparticle mediated thermoablative therapy on a human adenocarcinoma metastatic spine rat tumor model.
19	Kathryn Morton*	Analysis of Transcription Factor Activity in Head and Neck Squamous Cell Carcinoma (HNSCC)
20	Daniel Noguee*	Development of Chip-Based Antibiotic Susceptibility Detector
21	Thomas E Rappold*	Novel Method to Quantify Expression of Site Specific Mutants in Transgenic Mice: Application to Troponin I Transgenic Mice
22	Paul Sampognaro	Assessing the degree of SMN insufficiency in human SMA patients
23	Emily Silverman*	"LBH is Differentially Expressed in the Retina and May Be Important for Photoreceptor Development."
24	Ashley Smith	Do Acute Myelogenous Leukemia Antigens Induce T Regulatory Cells that Ultimately Suppress the Immune System?
25	Robert Wicks*	Local Delivery of Glioma Metabolic Inhibitors in Combination with Temozolomide and Radiation Therapy
26	Elizabeth Yiru Wu*	Enhanced aggressiveness in human glioblastoma after withdrawal of glycolysis inhibition: Implications for treatment of recurrent tumors
27	Harold Wu*	Plant Endophyte Extracts as Potential Therapeutic Agents against KCNQ2 Potassium Channels
28	Patricia Zadnik	Generation of a novel bone-seeking human breast adenocarcinoma cell line in a rat model of metastatic spinal metastases

*MSRD Competitor

CLINICAL RESEARCH: AMEB 1st Floor

#	Name	Title
29	Solomon Abay	Patient Outcomes in the Surgical Treatment of Atypical Trigeminal Neuralgia.
30	Demetri Arnaoutakis*	Salivary Rinses Collected with and without an Exfoliating Brush from Patients with Head and Neck Cancer Share Similar Promoter Hypermethylation Pattern
31	Paul Bixenstine	Catastrophic Medical Malpractice Payouts in the U.S.
32	Christine Boone	Arteriovenous Malformation Database
33	Michael Brener	Epicardial Fat is Associated with Subclinical Coronary Atherosclerosis in the Multicenter AIDS Cohort Study (MACS)
34	Vivek Charu*	Identifying co-morbidities associated with Pneumocystis jirovecii pneumonia in the HIV-negative population of the United States (1986-2005)
35	Sean Chen	Decision Making Amongst Primary Care Physicians on Prostate Cancer Screening
36	Jonathan Dattilo	Liposclerosing Myxofibrous Tumor: Is it a real entity?
37	Carla De la Cruz	Systematic review of age-related comorbidities in HIV-infected individuals
38	Kristina Eipl	Seroprevalence of unexpected red cell antibodies among pregnant women in Uganda
39	Farzana Faisal	Induction chemotherapy followed by radiation therapy is associated with better survival for patients with locally advanced pancreatic cancer.
40	Mark Fisher	Critical Concepts in Composite Facial Reconstruction: The Role of Aesthetic Units, Skeletal Buttresses, Soft Tissue Volume Contour, and Local Cutaneous Replacement.
41	Sara Fuhrhop	Natural History of Hip Dysplasia in Multiple Epiphyseal Dysplasia
42	Natasha Gupta	Identifying barriers to living kidney donation
43	Kurt Herzer, MSc*	Vitamin A supplements for preventing mortality, illness, and blindness in children aged under 5: systematic review and meta-analysis
44	Kevin Hur*	Patient-Reported Assessment of Functional Gait Outcomes Following Superior gluteal artery perforator (SGAP) Reconstruction

45	Melissa Hutchinson	The efficacy of five weeks of escalating and fixed contingency management reinforcement on illicit drug use in opioid-dependent pregnant patients
46	Khalda Ibrahim	Survival following lung metastasectomy for soft-tissue sarcomas
47	Sebastian Jara	The diagnostic and financial implications of BRAF mutation testing of fine-needle aspiration biopsy samples 'suspicious for papillary thyroid cancer'
48	Christine Johnson	The Relationship of Preoperative ASA Score to Complications Following Total Shoulder Arthroplasty
49	Andrea Jonas	Effect of impaired fasting glucose on lung function in cystic fibrosis related diabetes
50	Brian J. Lee*	External validation of postoperative nomogram for early prostate cancer recurrence following radical prostatectomy.
51	Xuan Le-Nguyen	An interesting case of non-progressive Amyotrophic Lateral Sclerosis with possible reversal of course: A case report.
52	Anne Leonpacher	Depressive Episodes of Unipolar Relatives in Bipolar and Unipolar Pedigrees
53	Carol Li	BRAF V600E Mutation and its Association with Clinico-pathologic Features in Patients with Papillary Thyroid Cancer: A Meta-analysis
54	Michael Lin	Tailored Rapid Interactive Mobile Messaging (TRIMM) to Promote Weight Loss
55	Susan Lin*	Vesicoureteral reflux, urinary tract infections, labial adhesion and meatal stenosis are the most common causes of surgical intervention in children with urinary incontinence
56	Timothy Markman	Examination of functional cortical interactions during attention to and distraction from painful cutaneous laser stimuli
57	Joseph Molenda	Dural Arteriovenous Fistulae at the Craniocervical Junction: A Systematic Review and Analysis of Clinical Features and Treatment Outcomes
58	Shalini Moningi	The Role of Adjuvant Therapy in the management of low-grade pediatric spinal cord tumors
59	Amanda Morris*	A comparison of patient outcomes after repeat and first-time thoracotomies
60	Ashley Nieves	Surgical outcomes in infantile hemangiomas treated with corticosteroids, propranolol, or expectant management: a retrospective cohort analysis
61	Jason Norman	Prehospital Care, Scene Times, and Signs of Life: A Retrospective Study of Trauma Deaths

62	Dare Olatoye	Stepwise examination of prostate cancer clinical trial participation.
63	Ravi Pandit	Electronic Health Record (EHR) Deployment in Outpatient Ophthalmology
64	Ju Park*	Benign Anastomotic Strictures after Esophagectomy: Long-term Effectiveness of Balloon Dilatation and Factors Affecting Recurrence in 155 Patients
65	Janaki Paskaradevan*	Analgesic efficacy of intravenous magnesium infusion: a systematic review and meta-analysis
66	Aymen Rashid	Reliability and Reproducibility of Optical Coherence Tomography Images in Patients with Age-related Macular Degeneration
67	Mona Rezapour	Prospective Evaluation of Risk Factors for Symptomatic Hemorrhoids
68	Danielle Rochlin	Improvement Following Surgical Intervention for Neurogenic Thoracic Outlet Syndrome is Sustained Over Time
69	Robert Same*	Young Men's Interest and Experience with Sexual & Reproductive Health Services
70	Claire Sampankanpanich	Lymphedema may be treatable at early and later stages with acupuncture therapy: a pilot study.
71	Patrick Sayre	Effect of rifampin and rifabutin on the pharmacokinetics of the next generation HIV integrase inhibitor, dolutegravir
72	James Schroeder, PhD	MELD Score Predicts Mortality Following Orthotopic Heart Transplant
73	Brett Shannon	Relationship between long-term bisphosphonate therapy and cortical thickness of the proximal femur
74	Sonal Sodha	Clinical Significance of the Gagey Sign for Examination of the Shoulder
75	Amar Srivastava*	Comparisons of features of double-positive disease with anti-GBM disease and ANCA-associated vasculitides
76	Erika Tanaka	Analysis of Diagnostic Evaluations and Outcomes in Birdshot Chorioretinitis (BSCR)
77	George Tang	Does Neoadjuvant Treatment Site Matter? Pathologic Response and Overall Survival Rates Following Esophageal Cancer Resection are Independent of the Treatment Center
78	Linnan Tang	ICU Alcohol Withdrawal Syndrome Treatment is Highly Variable at JHH

79	Ye Tao	Risk factors for permanent pacemaker implantation after AVR
80	Kanika Trehan	Increased/Decreased Smoking Recidivism after Minimally Invasive Surgery for Lung Cancer
81	Suzanne van Landingham	Driving Cessation, Driving Restriction, and Driver Preference in Older Adults with Glaucoma
82	Kipp Voth	Rates of Abdominal Imaging and Complications Following Transperitoneal and Extraperitoneal Prostatectomy
83	Katie Washington	Demographic and Clinical Outcomes are Different in Transgendered Persons Living with HIV
84	Aaron Wild*	Effect of chemoradiation-related lymphopenia on survival in patients with unresectable, locally advanced pancreatic adenocarcinoma
85	Wendy Ying*	Low incidence of severe mucositis after myeloablative, HLA-matched bone marrow transplantation and high dose, post-transplantation cyclophosphamide
86	Xun Zhou	The Fate of Driveline Infections: Outcomes in Patients on Ventricular Assist Device Support

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HISTORY OF MEDICINE: AMEB 2nd Floor

#	Name	Title
87	Michael Baxter	Dengue's Rise in the Philippines 1900-1950
88	Laura Beth Kaplan	Dissecting Birth: A Case Study in Anatomy, Obstetrics, and Newborn Care in the Early United States
89	Rebecca McLaren	A Public Health Perspective of Traffic Injuries in the Developing World
90	Gino J. Scalabrini*	Tactical Emergency Medicine (TEMS): A Historical Overview

*MSRD Competitor

MEDICAL HUMANITIES, BIOETHICS, and the HEALING ARTS: AMEB 1st Floor

#	Name	Title
91	Catherine Bennet	The Student Preceptor Program (SPP): Teaching 4th year medical students to be effective clinician educators in preparation for residency

92	Yishan Cheng	Developing a Protocol: How to rigorously study Traditional Chinese Medicine without deconstructing a holistic system.
93	Alexander Cole	Ethical Reasoning and Error Disclosure
94	Nick Cuneo	Exculpation and Equivocation: The Scientific Depoliticization of the Zimbabwean Cholera Outbreak
95	Matthew Molloy*	Factors Associated with Patient-Provider Concordance in Prenatal Genetic Screening
96	Neil M. Neumann	Assessing Patient Attitudes Towards Induced Pluripotent Stem Cell Research
97	Max Romano	Overcoming barriers to quality hypertension care: A qualitative study of health system leaders
98	Vivian Wang*	Highlighting Health Disparities: a Photo-Essay to Illustrate Highlandtown Clinic Patients Beyond the 15-Minute Interview
99	Shira G. Ziegler	From Bench to Bedside Through Visual Art: Enhancing Empathy for Patients with Undiagnosed Diseases

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PUBLIC HEALTH and COMMUNITY SERVICE: AMEB 2nd Floor

#	Name	Title
100	Andrew Bissonette	Simple Solutions for Big Problems
101	Rachel Blair	Limited Availability of Industry-Sponsored Inflammatory Bowel Disease Trial Results on ClinicalTrials.Gov
102	Martha Brucato*	Community Adolescent Sexuality Education (CASE) Program Needs Assessment and Curriculum Update
103	Jina Chung	Studying the effects of nicotine on HIV+/- adult brains using Diffusion tensor imaging
104	Mariyam Faiz	Mortality Burden of Behavioral Risk Factors in Bangladesh
105	Rebecca Greene	Learning how to assess the “world of drugs” related to malaria in Ghana
106	Jennifer Im*	Retreatment Decision-Making in Treating Age-Related Macular Degeneration: A Comparison of Optical Coherence Tomography and Fluorescein Angiography
107	Alexander Jenson*	Gender and performance of Community Treatment Assistants in Tanzania

108	June-Ho Kim	Avoidable Cancer Deaths in the Developing World
109	Mimmie Kwong	Exploring Trauma Care Services in India: A Systematic Review of Pre-Hospital, Hospital, Clinical, and Operational Components for the Care of the Injured Patient.
110	HeeWon Lee*	The Effect of Public Reporting on Central Line Associated Blood Stream Infections
111	Kimberley Lee*	Stress and stressors in a low-income inner-city out-patient population.
112	Lorena Leite*	Dial, Text, or Browse: Improving Access to HIV Education & Testing in Baltimore Latinos
113	Melissa Liu	Assessment of time-domain and spectral-domain ocular coherence tomography in the management of diabetic macular edema with anti-VEGF therapy
114	Susan Matesanz	Adherence to Recommended Follow-up Care after Abnormal Cytology in Paracentral El Salvador
115	Rebeccah McKibben	Reducing Surgical Site Infections Associated with Cesarean Sections: A Review of Reviews
116	Matthew Mesias	The Role of For-profit Hospital Status in Traumatic Brain Injury
117	Luis A Murillo	Influenza sub-typing analysis of a patient population at Johns Hopkins Hospital during the 2010-2011 influenza season
118	Atul Nakashi	Online Social Networks: A Description of Networks that Connect Users to Physical Activity Partners
119	David Narotsky	Are Marathons Dangerous? A Review of Mortality Data over 10 years
120	Angeline Nguyen*	Impact of home- and community-based service use on nursing home placement in persons with probable Alzheimer's disease
121	Ralph J Passarella*	Capturing Patient Input on Patient Safety via Novel Machine Learning Tool
122	Michelle Peng	Visual Disturbances Following Laser Peripheral Iridotomy
123	Christine Sailer	Multiplex Allele-Specific PCR for Detection of MDR-TB in Panama

124	Ellie Souganidis	Determinants of Anemia Clustering Among Mothers and Children in Indonesia
125	Yong Suh*	Comparative Effectiveness of Insulin Delivery and Glucose Monitoring Methods for Improving Weight Management in Diabetes Patients
126	Ruth Tamrat	Hospitalist Unit Sleep Hygiene (HUSH) Project
127	Julia Thorn*	Effects of manipulating attention on the neural response to threat stimuli in children with and without anxiety disorders
128	Beth Vrabel	Projected Effects of Medicaid Reimbursement Rates on Primary Care Physician Participation and Perceptions
129	Sharon Weeks*	Is the Kampala Trauma Score An Effective Predictor of Mortality In Low-Resource Settings? A Comparison of Multiple Trauma Severity Scores
130	Carla Williams*	Evaluation of Stakeholder Engagement in Comparative Effectiveness Research

*MSRD Competitor

2011 MSRD Student Awardees

RICHA GUPTA

Henry Strong Denison Research Scholar

A Feasibility Study of Combination Therapy with Trastuzumab (T), Cyclophosphamide (CY), and an Allogeneic GM-CSF-secreting Breast Tumor Vaccine for the Treatment of HER-2+ Metastatic Breast Cancer

IAN HSU

Harold Lampert Research Scholar

Providing Support to Patients in Emotional Encounters: Recognizing Opportunities for Empathy and Problem-Solving

ALEXANDER HARDING

W. Barry Wood Research Scholar

Using limes and synthetic psoralens to enhance solar disinfection of water (SODIS): A laboratory evaluation with mouse norovirus, E. coli, and MS2

BRIAN GOLDNER

Excellence in Medical Student Research

Methicillin-resistant Staphylococcus aureus (MRSA) colonization increases risk of subsequent infection in children hospitalized in the pediatric intensive care unit (PICU)

WORAWAN LIMPITIKUL

Excellence in Medical Student Research

High Levels of Serum Biomarkers for Inflammation (C-reactive Protein, Interleukin-6) and Myocardial Injury (cardiac Troponin T, myoglobin) Are Strong Predictors for Sudden Cardiac Death

DAVID LIU

Excellence in Medical Student Research

Active Surveillance for Low-Risk Prostate Cancer; A Clinical Decision Analysis

MINGHAO LIU

Excellence in Medical Student Research

Frailty is Associated with Short Term Outcomes after Kidney Transplantation

DIANNA LIU

Excellence in Medical Student Research

AS-OCT Detects primary Angle closure Earlier Than Gonioscopy

HEATHER LYU

Excellence in Medical Student Research

Genomic Changes in Hepatitis B Virus Closely Associated with the Development of Hepatocellular Carcinoma: a Cohort Study in Patients with Chronic Hepatitis B of Genotype C2

ERIC MILLS

Excellence in Medical Student Research

Role of the micorRNA cluster miR-143/145 in vivo

KURUN OBEROI

Excellence in Medical Student Research

Characterization and Treatment of Abnormal Skull Development in a Novel Mouse Model of Beare-Stevenson Syndrome

JOHN PANG

Excellence in Medical Student Research

The use of sRAGE to attenuate arterial restenosis in the rat - dose and effect

RALPH PASSARELLA

Excellence in Medical Student Research

Functional characterization of novel class large noncoding RNAs regulated by the tumor suppressor p53 and their role in cancer

HAOMING QIU

Excellence in Medical Student Research

Hearing Loss and Tumor Control Following Fractionated Stereotactic Radiation Therapy (FSRT) for Vestibular Schwannoma (VS): The Johns Hopkins Hospital (JHH) Experience

NATHAN SKELLEY

Excellence in Medical Student Research

Biomechanical Evaluation of Open Suture Anchor Fixation versus Interference Screw for Biceps Tenodesis

TRANG VU

Excellence in Medical Student Research

Baseline Liver Stiffness Measured by Transient Elastography is Independently Associated with Risk of End-Stage Liver Disease and Death among HIV/HCV Co-infected Adults

ACKNOWLEDGEMENTS

The MSRD Organizing Committee would like to thank the following people for their support putting this event together. Without their help, this day would not have been possible.

Faculty Judges

The Office of Student Affairs

Victor Raspa

Doug Hughes

John Steele

Michelle R. Moody

The Scholarly Concentrations Faculty

2012 MSRD Organizing Committee

Student Members:

Melanie McNally, Co-Chair

Anubhav Amin, Co-Chair

Sherveen Salek, Co-Chair

Alex Harding

Brian Goldner

Faculty Members:

Dr. Thomas Koenig

Dr. Mary Catherine Beach

Michele Massa

PODIUM PRESENTATION ABSTRACTS

Listed Alphabetically

Hansen Bow, MS2

Mentor: Henry Brem, M.D.

MSRD Podium Competitor

Microchip-based intracranial temozolomide delivery in a 9L rat glioma model

Background: Implanted drug delivery systems offer many advantages compared to oral or injection methods, including ease of concentration maintenance in a narrow therapeutic window, consistent local drug delivery to difficult locations, and decreased systemic toxicity. While drug eluting materials are the most common system today (e.g. Gliadel), they are limited in their inability to release a complex combination of multiple drugs, on demand, and after a delay.

In this project, we engineered intracranially-implantable microchips that overcame these limitations. These microchips had 3 membranes that could be opened independently by applying electric current: opening more membranes resulted in faster drug delivery. In addition to examining the kinetics and timing of drug release, we also compared the efficacy of microchip to polymer-based drug delivery.

Methods: Sixty-four rats were divided into 8 groups: no-treatment, unactivated-device, 2 5-mg temozolomide wafers implanted on day 5, 3m/0d (a microchip with 3 membranes opened on day 0), 3m/3d, 3m/5d, 2m/0d, and 1m/0d. All rats were implanted with intracranial 9L gliosarcoma and/or a microchip containing 10-mg temozolomide on day 0.

Results: Control animals and animals with unactivated microchips had median survivals of 14 and 17 days, respectively. Rats with 3 membranes activated on day 0, 3, and 5 had median survivals of 41, 25, and 24 days. Rats with 3, 2, and 1 membranes activated on day 0 had median survivals of 41, 29, and 22 days. The rats with 2 temozolomide wafers implanted on day 5 had median survival of 35 days.

Conclusion: Our results show that releasing drugs earlier and faster resulted in improved median survival. The polymer wafers resulted in better survival, most likely because they were able to release drug omni-directionally. In conclusion, we have demonstrated the first successful microchip-based intracranial drug-delivery system.

Alessa Colaianni, MS2

Mentor: Wayne Biddle

MSRD Podium Competitor

MS-1: Lessons from the First Year

Background: Physician-writers have long drawn on their clinical experiences as fodder for creative or reflective writing. Practicing medicine is laden with meaningful and emotionally charged events; much can be gained from reading about other physicians' experiences, coping strategies, mistakes, and triumphs. Though many physicians have written books or articles about their experiences, few accounts exist that are written from the perspective of medical students. The aim of this project is to use creative nonfiction essays to explore several watershed moments or themes that arose during the first year of medical school, to give outside readers a sense of the first year's strangeness and ethical complexity.

Methods: Each essay tells a story from my first year that struck me as formative, ethically questionable, interesting, or otherwise meaningful. After drafting each essay, I went through several rounds of edits with my mentor and several additional trusted editors. I asked one medical student, one physician, and several non-physicians for comments.

Results: I outlined, wrote, edited, and finalized five creative nonfiction pieces over the summer, entitled "The Role Model," and "The First Patient," about specific clinical experiences, "Como Agua de Pozo," about a global health trip to Bolivia, "Detachment, Clinical and Otherwise," about Anatomy laboratory, and "Moral Luck and Medical Murder," about physician participation in the Holocaust. Each essay is between fifteen and twenty pages long. Two pieces are underway, one entitled "Shadowing" about a night spent shadowing a trauma surgeon, and the other, as yet untitled, taking stock of the changes I've undergone since coming to medical school.

Conclusion: I found the exercise of putting pen to paper immensely helpful in processing issues that arose during my first year of medical school. I plan to continue to write nonfiction essays throughout my four years, and will consider publishing them as a collection in the future.

Saami Khalifian, MS2

Mentor: Amir Dorafshar, M.D.

MSRD Podium Competitor

Vascularized Autogenous Bone Provides Superior Outcomes in the Management of the Complex Cranioplasty

Background: Many patients who undergo reconstruction of calvarial defects are at high risk for post-operative complications, including infection, hardware exposure, and degenerative changes that can lead to unacceptable cosmetic results and repeat reconstruction. In this study we seek to determine which type of cranioplasty is superior in decreasing unwanted outcomes and minimizing post-operative complications.

Methods: We assembled a retrospective cohort of all patients at Johns Hopkins Hospital who received a cranioplasty between 1991 to 2010. Data were collected on demographics, causes, materials used, outcomes, and risk factors. The data was analyzed using Fisher's exact T-test.

Results: 198 patients were identified who underwent primary cranioplasty over the prior 19 years. The most common causes of calvarial defects were due to neoplasia (42%). Patients who had received radiation treatment prior to cranioplasty were more likely to have flap loss or resorption ($p=0.0034$). Factors associated with fluid collections, hardware malfunction, and exposure included: trauma ($p=0.02$), congenital defects ($p<0.001$), the use of alloplastic cranioplasty ($p=0.03$), and frontal location ($p=0.05$). Patients with frontal sinus involvement or previous radiation exposure had increased risk for sinus formation or CSF leak ($p<0.001$ and $p=0.06$, respectively) and those with greater than 2 prior cranioplasties were at increased risk for failure ($p=0.02$). Vascularized autogenous cranioplasty had fewer unwanted outcomes, post-operative complications, and re-operations ($p<0.05$).

Conclusion: Patients who underwent radiation therapy suffered more unwanted outcomes and repeat operations. These patients fail all types of cranioplasty, including autogenous, alloplastic, and free flap combinations, although vascularized autogenous performs the best of the three. Furthermore, the number of cranioplasty (3 or more) and a frontal location predispose patients to failure, and this is compounded further if the frontal sinus is also involved in the procedure. If this scenario cannot be avoided, vascularized autogenous cranioplasty performs the best and was shown to have the fewest post-operative complications.

Rachel Meserole, MS2

Mentor: John K Niparko, MD

MSRD Podium Competitor

Assessment of Health Related Quality of Life Six Years after Early Cochlear Implantation

Background: Patient-reported outcomes are essential for assessing treatment impact and cost-effectiveness. To date, the impact of cochlear implants (CIs) on children's health-related quality of life (HRQL) has been assessed by parent-proxy. Here, we provide the first simultaneous child- and parent-report of HRQL of CI children.

Methods: This prospective, longitudinal 6-center study of children implanted before age 5 years (n=188) investigated HRQL assessed using the Child Health and Illness Profile (CHIP). HRQL 6 years post-CI was compared with a normal hearing (NH) control group (n=97) and a comparison NH group (n=185) from the CHIP standardization sample matched to the CI group for wider socioeconomic comparability. Differences in HRQL were investigated through multivariable analysis, controlling for age, gender, maternal education, and income. The role of family stress was investigated.

Results: Six-year follow-up questionnaires were completed for 134 CI recipients (71%) and 60 NH controls (62%). CI children reported HRQL as high as NH peers, and rated their satisfaction higher than the comparison sample ($p < 0.05$). CI parents reported lower scores in several domains (p 's < 0.001) and the global CHIP score ($p < 0.05$) than parents of the NH controls. In contrast, CI parents reported better scores than comparison NH parents in three domains and the global score (p 's < 0.05). Family stress scores correlated negatively both with child-report HRQL in comfort, risk avoidance, and global score (p 's ≤ 0.001), and with every parent-reported outcome (p 's < 0.001). The CI group showed higher parent-child agreement in global score ($r = 0.48$) than the control group ($r = 0.42$) or the comparison group ($r = 0.35$).

Conclusion: Early CI recipients report HRQL comparable to NH peers, indicating that CI substantially mitigated the impact of deafness on children's HRQL. Parents' scores for CI children fell in-between those of two NH groups, highlighting the socio-demographic advantage of the original NH control group. Family stress associated with lowered perceived HRQL, underscoring a potential therapeutic target. Parent-child agreement in HRQL was higher for CI children than NH peers, indicating strong concordance within the parent/CI child dyad.

Amir Mohareb, MS3

Mentor: Richard Rothman, MD, PhD

MSRD Podium Competitor

Disaster preparedness in the age of molecular diagnostics: a national survey of hospital laboratories

Background: The 2009 H1N1 influenza pandemic was a recent infectious outbreak that tested national clinical and laboratory testing capacity. The CDC protocol for responding to such outbreaks requires that isolates suspicious of emerging infections be sent to public reference laboratories for definitive pathogen identification. Large outbreaks have the potential to overwhelm this protocol and create a delay in treatment. However, many hospitals have in-house laboratories equipped with advanced molecular testing techniques, such as PCR, which can provide timely and accurate results to clinicians. It is unknown how many hospitals have such technical capacities. The purpose of this study was to estimate the number of laboratories with advanced diagnostic capabilities and to assess their level of preparedness for responding to an emerging infectious event.

Methods: Cross-sectional, geographically weighted survey of US hospitals. Laboratory directors were queried in detail regarding disaster preparedness, personnel/ equipment, and experiences with the H1N1 pandemic (as a surrogate for future outbreaks).

Results: Of 150 hospitals surveyed, 122 (81%) microbiology laboratories agreed to participate in the survey. Of these, 22.8% routinely conducted molecular diagnostic testing for infectious diseases. These laboratories were distributed between private, public, and academic hospitals across the US. They reported an aggregate testing capacity of 420 H1N1 samples per day during the 2009 pandemic. Notably, they provided results within 24 hours at the peak of the pandemic, while the median turnaround time from their local reference laboratory was >7 days. 95% have written protocols to follow during a surge, but only 31% include plans to increase staffing if overwhelmed.

Conclusion: Molecular diagnostic laboratories provide shorter turnaround times for results compared to reference laboratories during an outbreak. However, there is a high variability in their level of preparedness and surge capacity. The current national response system does not fully utilize their potential to assist in pathogen identification.

Vanessa Pascoe, MS2

Mentor: Geetanjali Chander, MD, MPH

MSRD Podium Competitor

Anxiety is Associated with Increased Sexual Risk Behaviors in Baltimore Women Presenting to an STI Clinic

Background: Compared to the general population, anxiety is more prevalent in women and among those presenting to sexually transmitted infection (STI) clinics. While depression is associated with both substance use and sexual risk behaviors, studies examining anxiety have shown mixed results; anxiety may be protective or it may be harmful. We examined the relationship between generalized anxiety and sexual risk behaviors among women presenting to an STI clinic. We hypothesized that higher levels of anxiety would be associated with decreased risk behaviors.

Methods: We conducted a cross-sectional survey of 190 women presenting to a Baltimore STI clinic with STI complaints during August 2008. Subjects reported demographic characteristics, illicit substance and alcohol use, unprotected vaginal or anal sex while high, and completed the GAD-7 Anxiety Scale and a 2-question depression scale. We used chi-squared and logistic regression analyses to examine the association between anxiety and sexual risk behaviors. Analyses were adjusted for age, substance use, and depressive symptoms.

Results: The sample's median age was 27 years. 87% were African-American. 25% reported unprotected sex while high (USWH). Overall, 27% reported experiencing anxiety, and 21% reported drug use. Women with anxiety were ~3 times more likely to engage in USWH ($p=0.045$, 95% Confidence Interval(CI)=1.02-6.68, Odds Ratio(OR)=2.61). No interaction was seen between anxiety and depression. Increased likelihood of engaging in USWH was found in: drug users (heroin and cocaine) ($p=0.048$, CI=1.01-5.75, OR=2.41) and alcohol users ($p=0.001$, CI=1.79-10.46, OR=4.33). Drug users and alcohol users were also 7x and 5x more likely to suffer from anxiety, respectively. Conversely, women with an education beyond high school were less likely to engage in USWH ($p=.007$, CI=0.09-.678, OR=0.25).

Conclusion: Anxiety, drug, and alcohol use are significantly and independently associated with engaging in sexual risk behaviors in Baltimore women presenting to an STI clinic. These results underscore the importance of addressing underlying mental illness and substance use in high-risk individuals.

Jacob Ruzevick, MS3

Mentor: Rafael Tamargo, MD

MSRD Podium Competitor

The Haptoglobin 2-2 gene is associated with increased aneurysm formation in a novel model of aneurysm formation.

Background: The purpose of this study is to determine if the haptoglobin (Hp) 2-2 genotype is associated with increased aneurysm formation. Hp is a serum protein that functions to decrease the toxic side effects of extracorporeal hemoglobin. Humans have two alleles for Hp and studies have shown the Hp2-2 genotype is overrepresented in inflammatory diseases. Small clinical studies have implicated with Hp2-2 and 2-1 genotype with increased rate of aneurysm formation, but no controlled experiments have proven the Hp locus' role in aneurysm formation.

Methods: Wild-type (Hp1-1) and C57Bl6 transgenic Hp2-2 mice received sham surgery (n=5), angiotensin II only (n=5), elastase only (n=10), or elastase + angiotensin II (n=10). After 14 days, the carotid artery was dissected and sectioned. The outer circumference of each aneurysm was measured and analyzed using a two-way ANOVA with bonferroni post-test. Sections were immunostained for T cells, B cells, macrophages, and neutrophils, to assess the degree of inflammation between genotypes. The degree of inflammation in each treatment group was determined using counts per high-powered field and compared using a 2-way ANOVA with bonferroni post-test.

Results: No significant difference in aneurysm size existed between Hp1-1 and Hp2-2 mice treated with sham surgery (Hp1-1: $1356.8 \pm 65.1 \mu\text{m}$, Hp2-2: $1464.5 \pm 37.8 \mu\text{m}$, $p=0.15$) or angiotensin II (Hp1-1: $1446.9 \pm 17.0 \mu\text{m}$, Hp2-2: $1397.0 \pm 44.1 \mu\text{m}$, $p=0.24$). In mice receiving elastase (Hp1-1: $1890.0 \pm 74.2 \mu\text{m}$, Hp2-2: $2094.0 \pm 59.5 \mu\text{m}$, $p=0.03$) or elastase + angiotensin II (Hp1-1: $2449.1 \pm 53.1 \mu\text{m}$, Hp2-2: $2658.3 \pm 63.8 \mu\text{m}$, $p=0.01$), Hp2-2 mice had statistically significant larger aneurysms as compared to Hp1-1 mice ($p=0.01$). There was no difference in blood pressure between Hp1-1 and Hp2-2 genotypes in all treatment groups ($p=0.13$).

Conclusion: Conclusion: The Hp2-2 genotype is associated with increased aneurysm size in a novel model of aneurysm formation, which is mediated in part via inflammatory cells. Results of this study suggest patients with the Hp2-2 genotype may benefit from increased surveillance for the presence of aneurysms.

Sarah B. Sunshine, MS3

Mentor: James T. Handa, MD

MSRD Podium Competitor

Nitric Oxide's role in Dry and Wet Age-related Macular Degeneration (AMD)

Background: AMD, the most common cause of blindness among the elderly in the US, has two forms; the “dry” form, characterized by retinal pigment epithelial (RPE) cell apoptosis and the “wet” form, characterized by pathologic angiogenesis. Nitric Oxide (NO) is a chief component of cigarette smoke (CS), the strongest risk factor for AMD. NO activates the cytoprotective transcription factor Nrf2. CS and NO induce RPE apoptosis, vascular permeability, and angiogenesis unless neutralized. NO from CS or neuronal nitric oxide synthase (nNOS), the predominant isoform in the RPE, could injure the RPE by impairing the Nrf2 response. We hypothesize that acute NO exposure induces the Nrf2 response whereas chronic NO causes Nrf2 failure, leading to dry AMD, and through NO's proangiogenic properties, activate wet AMD.

Methods: NO was measured (DAF2DA) in ARPE19 cells treated with CS, SNAP (NO donor), or transfected with nNOS. The Nrf2 response was tested by measuring Nrf2-responsive gene (GCLM, NQO1, HO1) expression by RT-qPCR. Control and nNOS deficient mice were treated with NOS's substrate, Arginine(70mg/ml), to increase NO, or water for 1-6 months. Laser induced rupture of Bruch's membrane was used to generate choroidal neovascularization (CNV).

Results: CS and nNOS transfected ARPE19 cells showed increased NO (10 and 2-fold) and increased expression of Nrf2(30.6%,p=0.05), GCLM(160%,p=0.02), NQO1(99.3%,p=0.005). Mice treated with arginine had increased expression of GCLM(210%,p=0.02), NQO1(185%,p=0.04), HO1(225%,p=0.03) at 6-months in the RPE, and no Nrf2 response in nNOS deficient mice. The CNV area was paradoxically decreased by 41%(p=0.004) in arginine treated mice.

Conclusion: Nrf2 protects the RPE from acute NO stress. NO from nNOS production likely mediated the Nrf2 response in the RPE of mice chronically exposed to arginine. A dramatic decrease in CNV size was observed in mice treated with arginine possibly through activated arginase. Further investigation of arginase is warranted as a potential new therapy for wet AMD.

Anne van Beuningen, MS2

Mentor: Shanthini Sockanathan, Ph.D

MSRD Podium Competitor

The role of GDE2 in motor neuron maintenance and survival.

Background: Our aim is to evaluate the role of GDE2 in spinal motor neuron (MN) maintenance and survival. GDE2 is a six transmembrane protein that is expressed in all MNs. In vivo gain and loss of function analyses reveal that GDE2 is necessary and sufficient for the differentiation of subsets of limb-innervating MNs during embryonic development. However, whether GDE2 has additional functions in MN function or survival remains unknown.

Methods: Spinal cords were harvested from paraformaldehyde perfused six-week and nineteen-month old Gde2 +/+ and Gde2 -/- animals and embedded in paraffin. Embedded spinal cords were sectioned and analyzed by H&E stains, TUNEL, and by immunocytochemistry using antibodies against neurofilament (NF), ubiquitin, TDP-43, and GFAP. Electron microscopy (EM) of spinal cord and sciatic nerves of nineteen-month old Gde2 -/- mice was performed. Motor function of Gde2 -/- animals was evaluated by standard behavioral tests.

Results: MNs of six-week Gde2 -/- animals displayed NF accumulation and mislocalized cytoplasmic TDP-43. Analysis of 19-month Gde2 -/- mice revealed a more severe phenotype with spinal cords containing apoptotic cells and vacuolated MNs with dystrophic axons. MNs in these animals exhibited NF accumulation and ubiquitinated TDP-43 aggregates, a pathological hallmark of sporadic ALS in humans, while EM analysis identified myelination abnormalities in both spinal cord axons and the sciatic nerve. White matter astrocytes showed increased GFAP expression in Gde2-/- animals at both time points, indicating a reactive astrogliosis in response to the degenerative changes detected. Behavioral testing showed impaired grip strength in older Gde2 -/- mice, consistent with the progressive degeneration phenotype observed.

Conclusion: In the absence of GDE2, spinal MNs undergo slow, progressive degeneration leading to impaired motor function. The pathologies observed bear striking similarities to ALS suggesting that Gde2-/- animals might be a useful tool to model human motor neuron degenerative disease.

Erin Zingarelli, MS2

Mentor: Donna Magid, MD, MEd

MSRD Podium Competitor

The Best Things in Life Are Free: development of open-access, interactive 3D modules for gross anatomy education using publicly available data and low-cost software tools

Background: Traditional approaches to teaching gross anatomy focus on classroom-based lectures and cadaveric dissection. Recently, anatomy education has been transformed by a surge in three-dimensional (3D) imaging resource development. Despite the variety of 3D materials available, the cost of commercially developed tutorials creates a barrier to access. Moreover, these materials may neglect students' individual learning styles.

Methods: Digital Imaging and Communications in Medicine (DICOM) datasets were acquired using the National Cancer Institute's National Biomedical Imaging Archive (NBIA), a publicly accessible, searchable repository of patient imaging records. Three-dimensional volume renderings of CT and MRI scans were produced using OsiriX, a free, open-source DICOM processing software. Files were exported in QuickTime Virtual Reality (QTVR) format. Educational content was embedded using VR Worx 2.6, a low-cost virtual reality authoring and editing program. Interactive QTVRs and self-assessment modules were displayed on TeamRads.com, an educational website used in conjunction with the JHU SOM's anatomy course. Tutorial utility was assessed via an anonymous survey under JHU SOM IRB approval.

Results: One hundred and five of 120 students completed the survey. Seventy-four percent of students indicated that the QTVRs were "somewhat helpful" to "very helpful," as did the majority of students stratified by self-reported learning style (69% of visual learners, 75% of somewhat visual learners, and 85% of non-visual learners). Additionally, 56% reported the low-cost nature of the files as one of the top three reasons for accessing them.

Conclusion: Incorporating QTVRs into anatomy education benefits medical students of all learning styles by "giving life" to clinical imaging data free of charge. Furthermore, this study demonstrates a novel use of the NBIA, which was created to improve image-based malignancy detection. This unique partnering of OsiriX and the NBIA provides students with an opportunity to create customized learning materials and engage in self-directed learning.

BASIC SCIENCE
POSTER ABSTRACTS

Listed Alphabetically

#1: Joani Christensen, MS3

Mentor: Justin Sacks

Inflammatory Cell Homing Using Near Infrared Fluorescence Labeling with Indocyanine Green

Background: Cellular homing is particularly relevant to the differentiation of inflammatory processes. Currently, biopsy and radioactive cell tagging are available for tracking inflammatory cell movements to sites of infection and inflammation. Therefore, a less invasive, non-radioactive mechanism for accurately tracking inflammatory cells would be of great clinical utility. We aim to tag monocytes using the only FDA-approved near infrared dye, indocyanine green (ICG), and assess their homing after systemic administration using clinically-applicable laser angiography in the rat hind paw.

Methods: Monocytes are isolated from rat peripheral blood using density gradient centrifugation and co-incubated with ICG. The isolated cells are then washed and examined for fluorescence. Small boluses of monocytes loaded with ICG will first be injected locally to establish visibility *in vivo*, then systemically through an indwelling intravenous catheter. Injections will be made into animals with induced focal inflammation of the hind paw. Whole animal, non-invasive, near infrared imaging will be completed using a modified pulsed diode laser, and videos obtained will be processed for image analysis using custom-built perfusion algorithms.

Results: The monocyte fraction can be quickly isolated and readily takes up ICG. When examined *in vitro*, more than 60% of living cells within a high powered field have high fluorescent intensities of >3000 normalized units. In previous studies, such bright cells could be visualized in within animal vasculature. Animal models of acute localized inflammation are currently being developed. We hope to see localized fluorescence with systemic injection of loaded cells as compared to control animals.

Conclusion: Development of a technique to rapidly, non-invasively image inflammation without using radiation can have applications in the diagnosis of many pathological conditions.

#2: John Fan, MS2

Mentor: King-Wai Yau, Ph.D

Intrinsic Photosensitivity and Non-Visual Pigments in the Chicken Iris

Background: The presence of non-visual photoreceptors in vertebrates has been well established for many years, and the known functions of such tissues include circadian rhythm entrainment and pupillary constriction. It has recently been theorized that chick embryo irises, which show intrinsic photosensitivity, constrict as a result of cryptochrome based light transduction. The purpose of our project was to confirm cryptochrome's role in phototransduction in chicken iris and to elucidate potential mechanisms of its transduction cascade.

Methods: Chicken embryos (E15-E18) were sacrificed and enucleated. The iris sphincter muscle was dissected and removed and mounted to a custom force transducer while being maintained in physiological conditions. Spectra analysis was performed using filtered light between 370-550nm. The maximum and sustained forces generated were recorded. During pharmacological studies, the irises were bathed in the drugs for one hour prior to exposure to light stimulation and maximum force of contraction was recorded.

Results: Spectra analysis revealed peak sensitivity at 430nm wavelength of light. Maximum force of contraction occurred an average of 1.8 seconds after stimulation, and was followed by a slight decrease and a plateau at 8.7 seconds. A minimum 8.3 second refractory period was required to reproduce maximal force. Contraction was sustainable for up to 2.5 hours continuously. Thapsigargin reduced the force of contraction by 64%, while U-73122 had no measurable effect on contraction force.

Conclusion: The maximum force of contraction was measured at a wavelength consistent with the maximum absorbance of cryptochrome, and unlike with other opsin based pigments, desensitization was not observed. Additionally, the kinetics of the chicken iris muscle contraction differed from those of other animals whose photosensitivity is known to be opsin based. Pharmacological studies showed inhibiting calcium release decreased force of contraction, however no decrease was observed when inhibiting phospholipase C.

The results of our studies support the hypothesis that intrinsic photosensitivity in chicken embryo iris is governed by cryptochrome and that its phototransduction cascade is almost certainly different from that of other photosensitive pigments.

#3: Yarden Fraiman, MS2
MSRD Poster Competitor

Mentor: Patrick Brown, M.D.

Identification of a Flt-3 Ligand surge in pediatric leukemia patients receiving myelosuppressive therapy.

Background: Flt-3 hematopoietic progenitor cell tyrosine kinase is important in cell survival, proliferation, and differentiation of lymphocytes. Flt-3 is normally activated by Flt-3 Ligand (FL) but certain leukemias have been found to upregulate or constitutively activate Flt-3. Consequently, Flt-3 inhibitors are being investigated in the treatment of leukemias with Flt-3 activating mutations.

It has previously been reported that adults with Acute Myeloid Leukemia (AML) have a surge of endogenous Flt-3 Ligand (FL) levels in response to myelosuppressive therapy. Additionally, increased levels of exogenous FL decreases the efficacy of Flt-3 inhibitors in leukemia-model cell lines. (Levis et al, 2011)

Patrick Brown is currently engaged in Children's Oncology Group clinical trial using CEP-701 (Lestaurtinib), a Flt-3 inhibitor, in the treatment of pediatric patients with Flt-3 activated Acute Lymphoblastic Leukemias. Due to prior studies, we were interested in identifying if there was a FL surge in pediatric patients receiving myelosuppressive therapy because of the potential of identifying resistance mechanisms to treatment.

Methods: FL levels were quantified in Peripheral Blood plasma collected from three COG clinical trials at designated timepoints using Quantikine Human Flt-3/Fik-2 Ligand ELISA according to the manufacturer's protocol.

Results: Data from three pediatric clinical trials with varying chemotherapy regimens +/- CEP-701 showed a significant surge in FL in response to myelosuppressive therapy. Furthermore, in patients who had a majority of timepoints, data suggests that surges occur on day 9 of each cycle of therapy with each subsequent cycle associated with progressively higher surges of FL.

Conclusion: This is the first time a Flt-3 Ligand (FL) surge has been documented in the pediatric leukemia population. The FL surge, shown in three different pediatric trials, illustrates the predictable host response to myelosuppressive therapy, and suggests possible mechanisms of resistance to therapy and further areas of investigation to maximize efficacy of pediatric leukemia treatment.

#4: Caleb Gardner, MS2
MSRD Poster Competitor

Mentor: James Potash, MD

Stress-Induced Epigenetic Changes in the Brain

Background: The field of epigenetics explores the molecular mechanisms behind differential gene expression and the way in which related molecular marks are passed on during cell division. The most studied marks involve DNA methylation and histone modifications, and examination of these has shed light on the effects of chronic stress in the brain. Study of brain epigenetics may provide a concrete illustration of the essential interrelatedness of “nature “ and “nurture,” and eventually advance the treatment of patients suffering from mental disorders such as major depression.

Methods: Literature review was performed in the areas of epigenetics, stress, and their impact on the brain and psychiatric illness.

Results: Key findings have been those of stress-induced epigenetic modifications of genes involved in the hypothalamic-pituitary-adrenal axis stress response. Differential DNA methylation of the glucocorticoid receptor gene was observed in mice subjected to early-life stress, and childhood abuse in humans has been associated with similar persistent DNA methylation changes. Another central gene, FKBP5, whose product is a regulator of glucocorticoid receptor activity, has been shown to be up-regulated by glucocorticoid exposure in mice through a decrease in DNA methylation. Recent work aims to dissect further these relationships by distinguishing between different cell types, as, for example, neurons and glial cells may vary in their baseline methylation patterns, and in their epigenetic responses to stress. Genome-wide approaches are now being employed in these investigations.

Conclusion: These findings have clear implications for the study of stress-related psychiatric disease, and studies have already found associations between FKBP5 variants and mental disorders such as major depression and post-traumatic stress disorder. Continued research is needed to illuminate further the nature of these connections and, eventually, to begin exploring how knowledge of epigenetic regulation of the stress response might translate into new therapies.

#5: Paul Gilbert, MS2
MSRD Poster Competitor

Mentor: Jon Lorsch, Ph.D.

Endophyte Derived Novel Therapeutics for MRSA

Background: MRSA (Methicillin resistant *Staphylococcus aureus*) is a dangerous and challenging pathogen with resistance to beta-lactams and emerging strands resistant to vancomycin; thus, the need for novel therapeutics is great. A potential solution may be searching for novel natural products produced by endophytes (symbiotic microorganism in plants) that have activity against MRSA. In particular, “medicinal” plants may have endophytes that are responsible for their “acclaimed” curative properties. Furthermore, growing endophytes in specific conditions may induce the expression of antimicrobial products.

Methods: We screened a library containing 114 different fungal extracts for anti-microbial activity against MRSA using a Resazurin cell viability assay. Overnight cultures of MRSA grown in brain-heart infusion broth were diluted to an OD of .01 and incubated for 3 hours with serial dilutions of the extracts; this was followed by a 1 hour incubation with the Resazurin dye. The 96-well plates were read for color change and fluorescence to determine inhibition of MRSA. Microscopy was performed at 1000X oil immersion with Trypan Blue stain and images were captured with a HV-C20 camera. Fungal growth assays were performed in 24-well plates under various conditions: salt concentration, carbon source, pH, added nutrients. Extracts from the various growth conditions were tested for anti-microbial activity. Lastly, TLC fractionation was used to separate the active fraction followed by spectroscopy.

Results: A dozen mildly potent extracts were identified, but one extract was particularly potent with MRSA inhibitory effects to a dilution of 1:320. Varying fungal growth conditions yielded less potent extracts; extracts derived from growth on standard potato dextrose consistently yielded the most potent anti-MRSA effects. An active TLC fraction was identified and found to be UV active, visibly brown, and yellow with N-Anisaldehyde dye.

Conclusion: The fungus tested in this project shows promising results in producing a yet to be determined anti-microbial product effective against MRSA.

#6: Valerie Gordon, MS2
MSRD Poster Competitor

Mentor: Dwight Bergles, Ph.D

Conditional knockout of Kir4.1 in NG2 cells of the adult brain

Background: Kir4.1 channels are inward-rectifying potassium channels widely expressed in CNS glia, including NG2 cells (oligodendrocyte progenitors). Knockout of Kir4.1 leads to a severe phenotype that includes ataxia, paralysis, seizures, and demyelination. To elucidate the specific contribution of NG2 cells to this phenotype, we have generated a conditional NG2 cell-specific Kir4.1 knockout.

Methods: We used a line of transgenic mice, PDGF α R-CreER⁺Z/EG⁺Kir4.1f/f, to conditionally knock out Kir4.1 from NG2 cells in the adult brain. 4-hydroxy-tamoxifen was administered at 4-6 weeks. 10-14 days after induction, single-cell patch clamp recordings from hippocampal NG2 cells were used to test for the presence of Ba²⁺-sensitive Kir4.1 channels. In a separate cohort, BrdU was administered for 7 days beginning 1 week after induction to mark proliferating cells. Immunofluorescence staining was performed and the number of NG2⁺ cells, NG2⁺/BrdU⁺ cells, and NG2⁻/Olig2⁺/BrdU⁺ cells was quantified.

Results: Hippocampal NG2 cells from a control animal displayed Ba²⁺-sensitive inward current, which was absent in 72% (8/11) of EGFP⁺ cells across 3 Kir4.1f/f animals. Cells without Ba²⁺-sensitive current had less increase in membrane resistance than controls upon Ba²⁺ administration (22.6% vs. 341.0%, p=0.008). The two groups had equivalent resting membrane potentials. NG2 cell density in the corpus callosum was reduced in Kir4.1 knockouts (426 vs. 570 cells/mm², p=0.003), but not altered in gray matter. Knockouts also showed a marked decrease in the density of BrdU⁺ cells (287 vs. 480 cells/mm², p=0.015), no change in density of NG2⁺/BrdU⁺ cells, and decreased density of NG2⁻/Olig2⁺/BrdU⁺ cells (45 vs. 113 cells/mm², p=0.03) compared to controls.

Conclusion: We find that this genetic strategy can be used to conditionally remove Kir4.1 from NG2 cells. Kir4.1 knockout resulted in decreased NG2 cell density and decreased differentiation to oligodendrocytes in white matter. These studies suggest that Kir4.1 is important for regulating the proliferation and differentiation of NG2 cells in white matter.

#7: Annie Hsu, MS2

Mentor: James Handa, MD

The effect of advanced glycation end products on choroidal neovascularization

Background: Wet age-related macular degeneration (AMD) is characterized by abnormal vessel growth from the choroid into the subretinal space that can distort the macula and lead to vision loss. Advanced glycation end products (AGEs) have been implicated in this process, but their specific role is unknown. AGE's have been shown to accumulate in AMD and aging eyes and to induce the release of vascular endothelial growth factor (VEGF), a potent angiogenic cytokine, from retinal pigment epithelium (RPE) cultures. Because of this, we hypothesize that increased AGE accumulation in AMD eyes magnifies the proangiogenic milieu, worsening the severity of choroidal neovascularization. We thus treated mice with D-galactose (D-gal), which induces AGE accumulation, as well as N-phenacylthiazolium bromide (PTB), which cleaves AGE crosslinks, in order to determine whether AGE's increase the size of laser-induced CNV's and whether this effect can be reversed.

Methods: 2 month-old C57BL/6 mice were treated daily for 8 weeks: (1) 12 received subcutaneous PBS, (2) 12 received subcutaneous D-gal (50 mg/kg), (3) 12 received subcutaneous D-gal (50 mg/kg) and intraperitoneal PTB (10 mg/kg). Afterwards, all mice received 4 laser spots in each eye, followed 10 days later by perfusion with FITC-dextran dye. Eyes were enucleated and flat-mounted for quantification of CNV area (using AxioVision).

Results: There was no difference in the total size of CNV's across groups. However, there was a statistically significant difference in CNV composition, between control and D-gal groups (Turkey Kramer, $p = 0.017$), where the D-gal group had a smaller area of central hyperfluorescence with a larger hypofluorescent rim.

Conclusion: D-gal treatment appears to induce a more fibrotic (hypofluorescent) rather than vascular (hyperfluorescent) CNV phenotype. This could reflect an increase in the rate of CNV involution. It could also reflect an inducing effect of AGE's on pro-fibrotic platelet-derived growth factor (PDGF), which is in keeping with previous studies.

#8: Thomas V Johnson, MS2

Mentor: Donald J Zack, MD, PhD

Small molecule protein kinase inhibitors for neuroprotection in glaucoma

Background: Glaucoma is characterized by progressive retinal ganglion cell (RGC) injury and death, optic nerve degeneration, and vision loss. Lowering intraocular pressure is the mainstay of current treatment but is not always achievable. Even when achieved, vision loss sometimes progresses. Therefore, developing adjunctive neuroprotective strategies to inhibit RGC death could improve glaucoma treatment options. Recently, the Zack Laboratory, through a high-content small molecule library screen, identified several protein kinase inhibitors (PKIs) capable of promoting survival in primary dissociated murine RGC cultures. The current study evaluated the neuroprotective properties of these compounds in an organotypic retinal explant tissue culture model.

Methods: Neural retinae of 8-week-old rats were cultured in organotypic fashion for seven days in defined serum-free culture medium, supplemented with vehicle (0.1% DMSO) or the following PKIs at dosages corresponding to peak effects in dissociated RGC culture: sunitinib (200nM, 500nM, or 1 μ M); PKI-2 (1 μ M or 3 μ M); PKI-3 (1 μ M or 3 μ M); and PKI-4 (300nM or 1 μ M). Fixed tissue was cryosectioned and processed for immunohistochemistry to analyze tissue morphology and quantify survival of NeuN+ and Islet-1+ RGCs.

Results: Sunitinib treatment was associated with dose-dependent increases in RGC survival: a maximally effective dose of 1 μ M increased the linear density of NeuN+ cells in the RGC layer by 25.2 \pm 4.0% (p <0.001); increased the Islet-1+ cell linear density by 148.9 \pm 16.4% (p <0.001); and increased the thickness of the inner plexiform layer, which harbors RGC dendrites, by 24.6 \pm 2.5% (p =0.001). Comparable levels of RGC neuroprotection were observed following treatment with PKIs 2-4. Unexpectedly, some of the PKIs also prevented deterioration of photoreceptor layer thickness (p <0.05).

Conclusion: The RGC-neuroprotective effects of several PKIs were verified in organotypic retinal explant culture. Moreover, a previously unrecognized neuroprotective effect on photoreceptors was identified. Continuing investigations aim to identify the neuroprotective mechanism(s) of these compounds and evaluate their potential therapeutic use for glaucoma and photoreceptor degeneration.

#9: Andrea Jones, MS2

Mentor: Jeff Gray, Ph.D

Evaluation of the Conformer Selection Protocol in Rosetta 3.0

Background: Protein interactions form the basis of biochemical processes and faulty interactions underlie the pathophysiology of disease. In protein binding there are often significant changes in backbone conformation that are important to the understanding of the interactions. Modeling this backbone flexibility is the most difficult challenge in accurate computational predictions of docking. The conformer selection model was shown to be an effective and computationally efficient way to implicitly model backbone flexibility. It was validated in Rosetta 2.0 and has not been tested in Rosetta 3.0.

Methods: The protocol was tested on a subset of the docking targets that had been used to evaluate the Rosetta 2.0. Backbone flexibility was limited to the ligand and docking was restricted to local docking. For each of the five docking targets tested, 1000 decoys were produced and the top decoy was evaluated and used to compare the protocol in Rosetta 3.0 with that from Rosetta 2.0.

Results: For each of the five docking targets tested, the top decoy was of lower quality than that produced by the same algorithm in Rosetta 2.0. For the two targets for which Rosetta 2.0 produced decoys with low Fnat scores (0.00 and 0.08), the top decoys produced by the two Rosetta versions had similar L_rmsd and I_rmsd scores. For the three targets for which Rosetta 2.0 produced decoys with higher Fnat scores (0.45, 0.59, and 0.74), the top decoys produced by Rosetta 3.0 were of significantly lower quality and had much higher L_rmsd and I_rmsd scores.

Conclusion: The ensemble docking protocol in Rosetta 3.0 does not currently perform as well as that in Rosetta 2.0. Some bugs may have emerged in the code when the new version was created. The inaccuracy of the predictions is due to a sampling error, or a lack of predicted structures that recapitulate the known bound conformation.

#10: Krishna R. Juluri, MS2

Mentor: Solomon H. Snyder, MD

The Role of Inositol Hexakisphosphate Kinase in Dynamin Mediated Endocytosis

Background: The higher inositol phosphate diphosphoinositol pentakisphosphate, or IP7, which is synthesized by inositol polyphosphate hexakisphosphate kinase (IP6K) enzymes, have been implicated in regulating a number of cellular processes including apoptosis, chemotaxis, telomere maintenance, DNA recombination, vesicular trafficking, and insulin signaling. We have identified the large GTPase dynamin, an integral part of the clathrin mediated endocytosis machinery, as a binding partner of IP6Ks. IP6K binds to dynamin within its GTPase effector domain (GED) and pleckstrin homology (PH) domain and may regulate its function through this interaction.

Methods: We performed binding experiments in HEK293 cells using overexpressed IP6K and dynamin-1 fused to a GST or myc tag. Cell lysates were incubated with glutathione sepharose beads and the bound proteins were separated on SDS-PAGE and analyzed by Western blot. By generating truncated versions of IP6K or dynamin, we were able to determine the region on dynamin 1 that is necessary for binding.

Results: In pulldown assays using GST-tagged IP6Ks and myc-tagged dynamin, dynamin bound to all three mammalian isoforms of IP6K. When using GST-tagged fragments of IP6K, dynamin bound to multiple regions of IP6K1. In experiments using C-terminal deletion fragments of dynamin fused to GST and myc-tagged IP6K1, IP6K1 bound to fragments including the PH and GEF domains, suggesting that these regions mediate the interaction.

Conclusion: We found that dynamin interacts with all three members of the IP6K family and that this interaction is at mediated at least in part by the PH and GEF domains of dynamin. The interaction between IP6K and dynamin, which is a critical mediator of clathrin mediated endocytosis along with previous findings from our laboratory and others implicates IP7 as a regulator of endocytotic processes. This finding can ultimately help to explain the basic processes underlying endocytosis which is vital in regulating the neuronal processes of learning and memory and conditioning.

#11: Allison Kaeding, MS4
MSRD Poster Competitor

Mentor: Patrick Brown, MD

MLL Rearrangement and Age at Diagnosis Are Strongly Associated with High Level Surface FLT3 Expression and Ex Vivo Sensitivity to FLT3 Inhibition: A Prospective Analysis of 54 Consecutive Infants with ALL

Background: Approximately 80% of infant acute lymphoblastic leukemia (ALL) harbors MLL gene rearrangement (MLLr), which confers poorer prognosis compared to wild-type MLL (MLLwt), especially in cases diagnosed at <90 days of age. Retrospective studies suggest that MLLr infant ALL expresses high levels of FLT3 receptor tyrosine kinase and may be selectively sensitive FLT3 inhibitor-induced cytotoxicity compared to MLLwt ALL, leading to an ongoing clinical trial of the FLT3 inhibitor lestaurtinib (AALL0631).

Methods: We prospectively characterized 54 infant ALL diagnostic specimens enrolled on AALL0631: 1) Quantitative surface FLT3 (s-FLT3) expression using FACS; 2) lestaurtinib ex vivo sensitivity using 48-hour WST-1 cytotoxicity assays; 3) Identification of a putative leukemia stem cell (LSC) population via flow cytometric immunophenotyping (CD34+, CD38-). We subsequently learned patient age at diagnosis, MLL rearrangement status and fusion partner.

Results: Of 54 cases, 22% were MLLwt and 78% were MLLr. All cases diagnosed at <90d were MLLr. Surface FLT3 was higher in MLLr than MLLwt cases (34.2 vs. 11.6, $p=0.03$) and strikingly higher in MLLr cases diagnosed at <90d than >90d (62.6 vs. 22.0, $p<0.0001$). MLL rearrangement was associated with sensitivity to lestaurtinib (Chi square 4.125, $p=0.042$). Drug-sensitive samples trended towards higher s-FLT3 than resistant samples (31.3 vs. 16.7, $p=0.17$). A clearly identifiable LSC-like population (>0.5% of total leukemia) was present in 65% of samples and had significantly higher s-FLT3 than the remaining "bulk" leukemia cells (40.4 vs. 31.2, $p=0.05$).

Conclusion: Prospective comparison of infant ALL cases confirmed that MLLr disease expresses more FLT3 and is more sensitive to FLT3 inhibitor-induced cytotoxicity. Notably, MLLr disease in the youngest infants expresses strikingly high FLT3. Furthermore, phenotypically-defined LSC-like subpopulations are present in most cases and express more FLT3 than the remaining leukemia cells. If these findings correlate with clinical response to lestaurtinib, they may spotlight predictive biomarkers for selecting patients eligible for FLT3-targeted therapy

#12: Molong Li, MS2

Mentor: Aravinda Chakravarti, PhD

Characterizing ENCODE DNaseI Hypersensitivity Data and Evaluating Its Use In Identifying Functional Variants

Background: Genome-wide association studies have been used to identify associations between genetic loci and phenotypes, but as yet have been unable to identify the causal functional variant(s). In this study, we look at the feasibility of using DNaseI hypersensitivity (DNaseHS), a marker for open chromatin, to identify functional variants, especially in noncoding DNA. Since DNaseHS regions are more accessible to regulatory proteins, we hypothesize that DNaseHS can be used as a marker for a wide range of regulatory element classes. Furthermore, we hypothesize that variants found within regions of DNaseHS are likely to be functional.

Methods: We have analyzed DNaseHS data from multiple cell lines produced by groups at the University of Washington (UW) and Duke University and made available through the encyclopedia of DNA elements (ENCODE) project. This analysis was done using originally written scripts, BEDTools and the UCSC genome browser.

Results: We found that among cell lines used by both the UW and Duke groups, there is only 26% concordance for genomic regions annotated as DNaseHS. In the UW data, genomic coverage for DNaseHS does not seem to saturate despite having analyzed 78 cell lines. In both datasets, as compared to the genome average, there is a 2-3 fold enrichment of DNaseHS in exons and a 2 fold enrichment within 5kb of transcription start sites. DNaseHS regions defined by UW are enriched for SNPs (28%) as well as phenotype-associated SNPs (81%).

Conclusion: The currently available DNaseHS data produced by the two groups seem to differ due to a number of experimental differences. While there is enrichment within DNaseHS sites for variants in general, and for phenotype-associated SNPs, this enrichment is small. The lack of data saturation suggests existence of additional cell type specific DNaseHS sites. Thus, currently available DNaseHS annotation has limitations in accurately predicting functional variants in non-coding DNA.

#13: Jose Soria Lopez, MS2
MSRD Poster Competitor

Mentor: Jonathan Pevsner, Ph.D

Duplication of the ZEB2 Gene in a Young Child Diagnosed with Autism and Self Injurious Behavior

Background: Self-injurious behavior (SIB) is a serious behavioral disorder exhibited by many individuals with autism and has a significant adverse impact on health, family functioning and quality of life. Previous research has established that single gene mutations cause syndromes strongly associated with SIB. Children with intellectual disabilities and SIB diagnoses are treated in the Neurobehavioral Unit at Kennedy Krieger Institute where they receive targeted therapies.

Methods: We use Affymetrix single nucleotide polymorphism (SNP) microarrays and Penn CNV copy number detection software to analyze chromosomal abnormalities in a patient for whom detailed clinical and behavioral data were also available. The proband was diagnosed with autism and SIB during early childhood with no family history of mental disability.

Results: We identified a rare de novo duplication of the ZEB2 gene located on chromosome 2 which may be causal for this patient's phenotype. Deletions and mutations in ZEB2 gene have previously been associated with the Mowat Wilson Syndrome and Hirschsprung Disease, although amplifications have not been previously described. ZEB2 is a transcriptional repressor that plays a role in the migration of neurocrest cells during development in mice and could potentially be responsible for the autism and SIB observed in this patient.

Conclusion: Future studies measuring ZEB2 protein expression levels in cells from this proband, and the creation of a mice model with this mutation are needed to characterize the relation between ZEB2 duplication and the phenotype observed in this patient. This study contributes to a growing body of knowledge about the neurodevelopmental disorders that can potentially allow the creation of therapies and more personalized care for similar patients.

#14: Kyle Mahoney, MS2

Mentor: Dr. Jonathan Schneck M.D., Ph.D.

Using artificial antigen-presenting cells to provide CD27 co-stimulation to antigen-specific CD8+ T cells.

Background: Cytotoxic T lymphocytes (CTL), capable of directly killing tumor cells, are important in the anti-tumor response but ineffective at completely eliminating the tumor. Numerous techniques enhance the anti-tumor response by manipulating the activation of tumor-specific T-lymphocytes. Normally, T-lymphocytes are activated by antigen-presenting cells that provide at least 2 necessary signals: signal 1 is a foreign antigen presented by a major histocompatibility complex (MHC) molecule and signal 2 is a co-stimulatory signal. Our lab has developed a bead-based artificial antigen-presenting cell (aAPC) designed to activate T-lymphocytes by providing signals 1 and 2. The current study will assess the co-stimulatory molecule CD27 in its ability to expand influenza-specific CTLs using aAPCs. Importantly, CD27 has previously been shown to provide co-stimulation in a variety of experimental models, both in vivo and ex vivo.

Methods: We isolated CD8+ T-lymphocytes from peripheral blood mononuclear cells of two different donors. The cells were cultured with aAPCs containing MHC-Ig molecules loaded with M-1 influenza peptide and one of the following antibodies to act as co-stimulatory signals: anti-CD27, anti-CD28, or both. Cells were counted and analyzed each week for 4 weeks using flow cytometry to assess specificity, phenotype, and functionality.

Results: Among the different aAPCs used, there was no apparent difference in the number or percentage of M-1 peptide-specific CD8+ T-lymphocytes generated at any time point. Phenotypically, all cells expressed similar levels of CD27 and CD28. Functionally, the cells produced similar amounts of the cytokine IFN- γ in response to activating target cells.

Conclusion: Based on the initial results, co-stimulation with CD27 seems to produce activation of influenza-specific CTLs comparable to that of CD28 with no added benefit of having both molecules on the aAPCs; however, this was only observed in 2 samples. Further studies might increase the sample size or explore other co-stimulatory molecules, such as 4-1BB.

#15: Marcus Messmer, MS2

Mentor: Jonathan Powell M.D., Ph.D.

Development of a Breast Cancer Stem Cell Vaccine in Mice

Background: Many researchers have demonstrated the existence of a subset of cancer cells that is able to self-renew and differentiate into different lineages, sometimes referred to as cancer stem cells. These cells are resistant to traditional chemotherapy, and may account for the ability of cancer cells to persist after therapy has eliminated all evidence of the tumor. This study seeks to create a vaccine against breast cancer in mice using a population of breast cancer cells that is enriched for stem cells through growth in non-adherent culture conditions. Cells grown in these conditions have been shown to exhibit a stem cell-like phenotype, including the ability of a small number of cells to initiate tumors in SCID mice.

Methods: A1.8 breast cancer cells were grown for 1 week on non-adherent culture plates, in specially formulated media. The cells were combined with a GMCSF secreting cell line, irradiated, and injected subcutaneously into the inguinal region of 5 BALB/c mice. Negative controls included 5 mice injected with GMCSF secreting cells alone and 5 mice injected with GMCSF secreting cells and A1.8 cells grown under normal conditions. After 1 week, 5×10^4 4T1 breast cancer cells were injected into the contralateral flank of each mouse. The growth of the tumors was monitored using calipers.

Results: Using flow cytometry, we demonstrated that these cells are CD44 high and CD24 low, a phenotype often used to identify breast cancer stem cells. The primary endpoint of the in vivo experiment, tumor size, showed no statistical difference between the groups.

Conclusion: We have shown that sphere-forming culture conditions may be an efficient method of enriching cancer lines for stem cells. Our next step is to further characterize the stemness of the sphere forming cells. We hope to apply this method to a mouse model that may better represent de novo tumorigenesis.

#16: Devin T. Miller, MS2

Mentor: Natasha Zachara Ph.D.

Defining the O-GlcNAcome of Cells and Tissues Subjected to Ischemic Injury

Background: Elevated levels of O-linked β -N-acetylglucosamine (O-GlcNAc) modification on nuclear, cytoplasmic, and mitochondrial proteins prior to or directly following the induction of cellular stress is protective in models of ischemia reperfusion injury as well as other forms of injury such as heat stress, oxidative stress, hypoxia, and trauma hemorrhage. These data show promise in elucidating a novel method of retarding cellular death following tissue ischemia, in both the myocardium and other tissues, such as those involved with organ transplantation. However, the molecular mechanisms by which O-GlcNAc regulates protein function, thus, leading to enhanced cell survival and cardioprotection have not been identified.

Methods: In order to determine how O-GlcNAc mediates cell survival in the setting of ischemia we utilized stable isotope labeling with amino acids in cell culture (SILAC) to identify the proteins that undergo O-GlcNAcylation in response to hydrogen peroxide stress. After obtaining a list of over 150 proteins as putatively modified by O-GlcNAc in response to peroxide stress, we confirmed the O-GlcNAcylation status of key proteins by immunoprecipitation (IP) and western blot (WB).

Results: The SILAC screen identified over 150 proteins including Carm1, OGT, Sec24, and WNK4. Of the subgroup of proteins that were confirmed to be O-GlcNAcyated by IP/WB, Carm1, a protein methyltransferase, was of particular interest in that ~30% of the protein was found to be O-GlcNAcyated and to associate with the O-GlcNAc transferase (OGT) upon stress. Notably, Carm1 was methylated upon stress and this was exacerbated when OGT was deleted, suggesting that the association between OGT and Carm1 regulates methylation of Carm1.

Conclusion: Due to Carm1's role in methylation of proteins such as histones and stress granule components it is possible that this protein may play a pivotal role in the mechanism promoting cell survival initiated by O-GlcNAc modification.

#17: Stuart Mitchell, MS2
MSRD Poster Competitor

Mentor: Ashvin Dewan, MD

Loeys-Dietz Syndrome Affects Bone Microarchitecture

Background: Loeys-Dietz syndrome (LDS) is a recently recognized autosomal dominant connective tissue disorder caused by mutations in transforming growth factor- β receptor (TGF- β R) genes. Most research has examined the vascular manifestations of LDS, but as awareness has grown, many orthopaedic manifestations have been identified. Recent case reports suggest LDS patients may develop early osteoporosis with increased fracture incidence and delayed bone healing. The role of TGF- β R mutations in the pathogenesis of these musculoskeletal manifestations remains unclear. In this study, we investigated the effect of LDS on bone morphology and microarchitecture in a murine model.

Methods: Formalin-fixed femora obtained from 6-month-old LDS and wild-type mice were analyzed using a high-resolution μ CT imaging system. Cortical and trabecular morphometric parameters were examined in diaphyseal and metaphyseal regions, respectively. Student's t-test with $\alpha=0.05$ was employed to compare means.

Results: Cortical parameters including bone volume, bone surface, and cortical thickness were consistent between groups. Trabecular parameters including bone surface density, proportion of bone volume in intramedullary canal, trabecular number, and trabecular thickness, however, were all significantly increased in LDS mice compared to wild-type mice.

Conclusion: LDS mice exhibit heterogeneous bone microarchitecture and thicker, denser trabeculae that could be attributed to disorganized bone remodeling. Bone remodeling, particularly in the cortex, prevents propagation of bone microfractures produced by routine mechanical stressing. TGF- β s play a significant role in orchestrating bone remodeling. An uncoupling of remodeling might account for increased fractures and osteoporosis reported in LDS patients. Further studies examining the effect of LDS on activation status of the TGF- β signaling pathways are needed.

#18: Camilo A. Molina, MS3
MSRD Poster Competitor

Mentor: Daniel M. Sciubba

Optimizing magnetic nanoparticle mediated thermoablative therapy on a human adenocarcinoma metastatic spine rat tumor model.

Background: Among the 1.5 million new cases of cancer diagnosed annually, approximately 3-9% of patients experience symptomatic spinal metastasis. Although advances have been made in the diagnosis of metastatic spine disease, management has not advanced accordingly. The purpose of this study was to use an animal model of metastatic spine disease to investigate nanoparticle based tumor thermoablation as a treatment modality for metastatic spine disease. Ferromagnetic nanoparticles can be delivered by injections to target cancer tissue, and when exposed to an alternating magnetic field (AMF), the magnetic materials generate thermoablative heat.

Methods: Twenty-six female Fischer-rats were randomized into three groups. All groups underwent a transperitoneal approach to the lumbar spine followed by implantation of rat breast-adenocarcinoma tissue into the L6 vertebral body. On post-operative day 13, Group-1(n=4) and Group-3(n=18) received intratumoral nanoparticle injections (5 μ l /cm³ of tumor). Control Group-2(n=4) did not receive particle injection. Only Groups 1 and 2 were subsequently exposed to an AMF ranging from 600-800 Gauss. Heat generation was measured via an intratumoral-temperature probe and compared to core (rectal) temperature. Group-3 animals were sacrificed at 1,3,6,12,24, and 48 hours following particle injection to study intratumoral and systemic particle distribution via gross and histological analysis.

Results: Mean intratumoral-temperature in Group-1 animals was significantly higher than core temperature (42°C versus 35°C, P=0.02). A trend of nonspecific tumor heating was observed in Group-2. All Group-1 and Group-2 animals were ambulatory at 24-hrs status-post AMF treatment. Group-3 systemic distribution analysis at 1,3,6,12,24, and 48 hours did not demonstrate nanoparticles in the spinal cord, lung, liver, or spleen.

Conclusion: Nanoparticles can be safely delivered to tumor tissue without systemic distribution. The selective intratumoral localization of particles can be utilized to specifically deposit thermoablative heat energy within tumor tissue. Further studies will be necessary to determine the effects of AMF alone on tumor tissue.

#19: Kathryn Morton, MS2
MSRD Poster Competitor

Mentor: Joseph Califano, MD

Analysis of Transcription Factor Activity in Head and Neck Squamous Cell Carcinoma (HNSCC)

Background: HNSCC is the 6th most common cancer worldwide with a 5-year survival of only ~50%. Characterization of the molecular expression patterns of these tumors may lead to novel treatments that improve outcomes. In this study we examined transcription factor (TF) activity in a cohort of HNSCC tumors to identify candidate genes that may be exploited for targeted therapy.

Methods: We evaluated TF signatures of 44 HNSCC and 25 healthy oral mucosa samples using an exon array and normalized data to methylation and copy number variations. The array data was ranked by p-value and subjected to unsupervised hierarchical clustering analysis. HPV16 status of each sample was then evaluated using qRT-PCR.

Results: Of the 49 TFs analyzed, STAT1 and STAT3 exhibited the greatest differences in activity in tumors relative to healthy tissue. Unsupervised hierarchical clustering analysis showed that tumors segregated into two populations. Population-A contained 25 tumors and showed significantly increased STAT1 and STAT3 activity ($p < 0.05$), and Population-B contained 19 tumors and showed no significant difference in STAT1 or STAT3 activity ($p > 0.05$). HPV16 analysis revealed that 15 of the 44 tumors were HPV16+, with 12 tumors clustering together in Population-A and 3 in Population-B. Ten of 15 (66.7%) HPV16+ tumors showed >2-fold increase in STAT1 activity compared to 11 of 29 (37.9%) HPV16- tumors. Similarly, 7 of 15 (46.7%) HPV16+ tumors showed >2-fold increase in STAT3 activity compared to 6 of 29 (20.7%) HPV16- tumors.

Conclusion: The elevation of STAT1 and STAT3 activity in tumor samples suggests these TFs may be useful as chemotherapeutic targets. The degree of STAT1 and STAT3 activity varied amongst samples, with HPV16+ tumors showing the greatest increases in STAT activity. Therefore, HPV16 status may be a useful indicator for targeted therapy with STAT inhibitors. To further explore this possibility we will model anti-STAT treatment on HNSCC cell lines and xenografts.

#20: Daniel Noguee, MS2
MSRD Poster Competitor

Mentor: Sam Yang, MD

Development of Chip-Based Antibiotic Susceptibility Detector

Background: Current methods of determining antibiotic resistance properties of microorganisms isolated from clinical samples require significant amounts of time and are vulnerable to inaccuracy from human error. The purpose of this project is to develop and test a microfluidic chip based assay for determining the minimum inhibitory concentration of antibiotics on isolated microorganisms, potentially for use in automated “lab on a chip” set-ups.

Methods: We developed, manufactured, and tested a PDMS chip with micrometer-scale channels created from a silicon mold, and enclosed by a plasma-bonded glass slide. LB media containing *E. coli* cultures was infused into the chip, trapping bacteria in 300 micrometer wide chambers; an ampicillin solution of known concentration was infused through separate channels and serially diluted with LB broth across the chip. Bacterial growth was observed through light microscopy. Optical density measurements were used to quantify ampicillin susceptibility of the *E. coli* strains intended for use in the chip

Results: Preliminary tests with light microscopy showed that the bacteria were able to grow within the culture chambers of the chip. However, the permeability of the PDMS led to evaporation of the media within the chip, making results difficult to interpret: differences in growth at different ampicillin concentrations could not be quantified in the chip.

Conclusion: The preliminary results indicate that the PDMS chip may provide a suitable environment for bacterial growth, a necessary condition for the chip assay to function. Further testing and modification of chip and culture conditions are necessary to optimize bacterial growth. Detection ability may be improved through use of electrochemical-sensitive dyes or direct measurement of electrochemical properties within the culture chambers.

#21: Thomas E Rappold Jr, MS2
MSRD Poster Competitor

Mentor: Dr. Anne Murphy, M.D.

Novel Method to Quantify Expression of Site Specific Mutants in Transgenic Mice:
Application to Troponin I Transgenic Mice

Background: Cardiac troponin I (cTnI) is an essential regulatory protein in the cardiac muscle contractile apparatus. Prior work indicated 3% of African American (AA) population had a cTnI sequence variance, Pro82Ser. Hypertensive AA men with this variant have increased cardiac hypertrophy compared to age-matched AA hypertensive controls. Transgenic mice with the Pro82Ser variant have impaired cardiac muscle relaxation and decreased response to isoproterenol. Studies of transgenic lines with point mutations are limited by the lack of an accurate method to determine the expression of the mutant protein. Our aim was to quantify the amount of cTnI, Pro82Ser in transgenic mouse hearts using a novel method, multiple reaction monitoring (MRM).

Methods: Cardiac myofilaments were isolated from transgenic wildtype and Pro82Ser mouse hearts and separated on 1D SDS-PAGE using 4-12% NuPAGE Bis-Tris gels. Gels were stained using Coomassie blue R-250. The cTnI protein was excised from gels and digested using trypsin. Orbitrap LC/MS/MS was used to identify relevant peptides. The standard peptide NITEIADLTQK* was spiked into mouse heart samples at 1 fmol/ μ l. MRM development, optimization, and validation was by Q-Trap nano-LC/MS/MS analysis. Peak detection and quantification of peak area was determined with Multiquant software version 2.0 (AB SCIEX).

Results: We established a standard calibration curve with the standard peptide to calculate the quantity of wild type protein in each heart sample. Expression of wildtype and mutant (n=8) Pro82Ser cTnI was determined with the MRM assays. Pro82Ser protein was found to be present at 2.2 to 3.5 % of wild type cTnI with mean and standard deviation of 2.94 +/- 0.5 %.

Conclusion: Prior work on other mutants of troponin has noted significant phenotype at low levels of mutant expression. This work has implications for deleterious impact on cardiac function for a variant present in 3% of the AA population.

#22: Paul Sampognaro, MS2

Mentor: Charlotte Sumner, M.D.

Assessing the degree of SMN insufficiency in human SMA patients

Background: Spinal muscular atrophy (SMA), an autosomal recessive motor neuron disease, is the leading inherited cause of infant and early childhood mortality. SMA is caused by mutation of the telomeric survival motor neuron 1 gene (SMN1). SMN1 encodes a protein required for proper assembly of the spliceosome. All patients retain one to four copies of a homologous, centromeric SMN2 gene, but SMN2 produces insufficient levels of SMN protein due to alternative splicing that leads to a truncated isoform. Reduced levels of SMN protein result in motor neuron degeneration by mechanisms that have yet to be defined.

Although the genetic cause of SMA is well-established, to date there is no treatment. However, because all patients retain at least one copy of SMN2 and disease severity correlates inversely with SMN2 copy number, current therapeutic efforts focus on identifying strategies to increase SMN levels in patients. As these promising drug candidates transition to clinical trials in SMA patients, it becomes increasingly important to understand the baseline degree of SMN deficiency in human patients and the magnitude by which SMN must be increased via SMN2 upregulation to ameliorate disease. Here, we characterize SMN expression levels in several tissues isolated from SMA patients and age-matched controls.

Methods: Tissue samples were collected from Type 1 SMA patients (i.e. those with the greatest symptom severity) and unaffected age matched control subjects. Spinal cord and diaphragm tissues were chosen to assess insufficiency in both neural tissue and skeletal muscle alike. RNA and protein isolations were performed, and SMN RNA and protein levels were quantified using qRT-PCR, ELISA, and Western blot methods.

Results: Our preliminary findings show that Type 1 SMA patients have up to a 34.3 % and 31.5% decrease in SMN RNA and protein expression in diaphragm and spinal cord, respectively. Additionally, we also found the housekeeping genes, 18S and TBP, to be the most stable endogenous controls for qRT-PCR when comparing SMN levels across tissues.

Conclusion: These results demonstrate that Type 1 SMA leads to an approximately 66% decrease in SMN levels in both neural and muscle tissue.

#23: Emily Silverman, MS2
MSRD Poster Competitor

Mentor: Maria Canto-Soler, Ph.D

LBH is Differentially Expressed in the Retina and May Be Important for Photoreceptor Development.

Background: LBH, or “Limb-bud and heart homolog”, is a highly conserved nuclear protein and transcription factor that is known to be preferentially expressed in the developing limbs and heart. Preliminary experiments in Dr. Canto-Soler’s lab suggest that LBH is also differentially expressed in the retina, and may play a role in photoreceptor development. The aim of this study is to confirm these findings in situ by detecting mRNA for the LBH protein in different photoreceptor subtypes.

Methods: Eyes of ED20 (embryonic day 20) chicken embryos were sectioned, fixed and processed for in situ hybridization. Single labeling in situ hybridization was used to localize LBH expression in the mature retina, and double labeling in situ hybridization was used to detect the presence of LBH in specific photoreceptor subtypes. Rods, red cones and green cones were identified by rhodopsin, red opsin and green opsin expression, respectively.

Results: Single label in situ hybridization for LBH showed that expression is restricted to the outer segment of the photoreceptor cell layer. The protein seemed to be present in all photoreceptor subtypes. Double labeling in situ hybridization showed that LBH is, indeed, colocalized with all of the opsins studied: red opsin, green opsin and rhodopsin. Interestingly, results suggest that there may be a subpopulation of green cones that do not express LBH.

Conclusion: LBH is a transcription factor expressed in all mature photoreceptor cell types studied: rods, red cones and green cones. Follow up studies will include a more detailed analysis of LBH expression in green cones, as well as a study of the pattern of LBH expression at different landmarks of retinal development.

#24: Ashley Smith, MS3

Mentor: Allan Hess, PhD

Do Acute Myelogenous Leukemia Antigens Induce T Regulatory Cells that Ultimately Suppress the Immune System?

Background: Scholarly Aim: Determine if antigens that are commonly expressed by AML cells somehow evade destruction by dampening the body's immune system.

Background: Early white blood cell counts after chemotherapy for acute myelogenous leukemia (AML) are primarily lymphocytic and peripherally derived. An unusual number of these lymphocytes have been shown to be Foxp3 positive, which is specific to regulatory T cells. T regulatory cells are responsible for suppressing the immune system. Survivin is one of the non-self antigens highly expressed in AML.

Hypothesis: Survivin, which is highly expressed in AML will cause the proliferation of T regulatory cells, which dampens the body's immune system and leads to an overall poor prognosis in AML patients.

Methods: We infused the antigen into blood samples collected from 10 patients. All 10 samples were stimulated by the control and survivin antigen. Three 10 cc green tops of peripheral blood were drawn at 4 different intervals: before treatment at first diagnosis of AML, day 18, day 21, and between days 30 and 40 of recovery. White blood cells counts were measured at those times. Flow cytometry was performed to determine the amount of T regulatory cell proliferation after the control and survivin were introduced to the peripheral blood samples. Bioplex was used to identify the cytokines present after antigen presentation.

Results: Of the 10 samples stimulated by survivin, 6 had a non-significant increase in the proliferation of T regulatory cells compared to stimulation by the control. In those same 6 samples, higher amounts of TGF- β were secreted in response to survivin stimulation than to stimulation by the control. There was no recognizable pattern of secretion of cytokines IL-2, TNF- α , or IFN- γ by the regulatory T cells when stimulated by the control or survivin.

Conclusion: Survivin was not shown to cause significant T regulatory cell proliferation. However, significant TGF- β secretion was induced, which acts primarily to dampen the immune system. This may help to explain why few AML patients go into remission and why those that do tend to relapse.

#25: Robert Wicks, MS4
MSRD Poster Competitor

Mentor: Henry Brem, MD

Local Delivery of Glioma Metabolic Inhibitors in Combination with Temozolomide and Radiation Therapy

Background: 3-bromopyruvate (3-BrPA) and dichloroacetate (DCA) are effective inhibitors of cancer-cell metabolism, but their application in glioma is limited by the inability of 3-BrPA to cross the blood-brain-barrier and the dose-limiting toxicity of DCA. We investigate the safety and efficacy of intracranial delivery of 3-BrPA and DCA. We then assess whether the combination of 3-BrPA or DCA with oral temozolomide (TMZ) and radiation therapy (XRT) provides a synergistic effect.

Methods: Cytotoxicity of 3-BrPA and DCA were analyzed in one human (U87) and two rodent (9L and F98) glioma cell lines. 3-BrPA and DCA were incorporated into biodegradable polymers and the maximally tolerated dose (MTD) was determined in F344 rats. Efficacy of intracranial 3-BrPA polymer and DCA polymer was then assessed in a rodent glioma model.

Results: Both 3-BrPA and DCA were found to be cytotoxic in all three glioma cell lines. The MTD of 3-BrPA polymer was 5%, while the MTD was not achieved for DCA polymer, even when loading was as high as 50%. In the 9L model, 5%3-BrPA had a median survival of 18 days ($p=0.0027$ vs. Control). The median survival of 50%DCA polymer was 17 days significantly increased over oral DCA ($p=0.0050$) and control ($p=0.02$). Oral DCA did not increase survival beyond control. In a separate study, rats given 5% 3-BrPA polymer in combination with TMZ + XRT had significantly increased survival compared with TMZ and XRT alone ($p<0.01$). 50% DCA polymer in combination with TMZ + XRT did not show an increase in survival over either treatment alone.

Conclusion: The intracranial delivery of 3-BrPA and DCA polymer was safe and showed significantly increased survival, a possible novel approach to glioma therapy. Combination intracranial delivery of 3-BrPA with TMZ and XRT has a synergistic effect leading to significantly increased survival compared to either treatment alone.

#26: Elizabeth Yiru Wu, MS2
MSRD Poster Competitor

Mentor: Alfredo Quinones-Hinojosa, M.D.

Enhanced aggressiveness in human glioblastoma after withdrawal of glycolysis inhibition: Implications for treatment of recurrent tumors

Background: Glioblastoma multiforme (GBM) preferentially utilize glucose, making glycolysis an attractive target. Previously, we demonstrated 2-fold increased glucose-6-phosphatase (G6Pase) mRNA in 2-deoxyglucose (2DG, glycolytic inhibitor) treated cells. We hypothesize that 2DG treatment increases apoptosis and decreases proliferation, migration, motility speed, and stemness, and studied response to recovery with or without chlorogenic acid (CHL, G6Pase inhibitor).

Methods: We cultured primary GBM lines in glucose or 2DG-supplemented media and replated in glucose or glucose-CHL. We evaluated stemness, proliferation, migration, speed, and apoptosis using immunocytochemistry, EdU flow cytometry, transwell speed assays, and annexin V flow cytometry. We assessed matrix metalloproteinase 2 (MMP2) and signal transducer and activator of transcription 3 (STAT3) expression using qRT-PCR and western blot, and established significance with one-way ANOVA (GraphPad Prism).

Results: We showed significantly decreased expression of neural stem cell marker nestin with 2DG treatment relative to controls. Nestin expression increased after recovery, but less with CHL addition. We observed decreased proliferation, migration and motility speed with 2DG ($p \leq 0.05$). Moreover, recovery cells were more proliferative and migratory than controls ($p \leq 0.05$). CHL-treated recovery cells remained significantly less migratory than recovery. We demonstrated increased annexin V staining, which marks apoptotic cells, relative to controls, reversed with recovery. Recovery cells with CHL had higher annexin staining relative to recovery and controls. We observed reduced STAT3 activation and MMP2 RNA levels in 2DG-treated cells relative to controls, determined by western blot and qRT-PCR; MMP2 mRNA levels increased significantly with recovery.

Conclusion: 2DG significantly increased apoptosis and decreased stemness, proliferation, migration, and motility speed in GBM, reversed after recovery. We hypothesized that G6Pase was pivotal in survival following 2DG. Decreased active STAT3 and MMP2 (important for oncogenesis and invasiveness) may be related to phenotype. We demonstrate metabolic derangements contributing to GBM adaptation, highlighting chemotherapeutic resistance in recurrent GBM. Elucidating these adaptive mechanisms provide insights into targeted therapies.

#27: Harold Wu, MS2
MSRD Poster Competitor

Mentor: Min Li, Ph.D

Plant Endophyte Extracts as Potential Therapeutic Agents against KCNQ2 Potassium Channels

Background: KCNQ2 channels are potassium voltage gated channels chiefly expressed in central and peripheral neurons. These channels conduct M currents, controlling neuronal sub-threshold excitability to modulate repetitive action potential firing. Such channel activity is particularly important in hyperexcited states such as epilepsy and pain, and specific mutations in KCNQ2 are associated with Benign Familial Neonatal Seizures, a rare autosomal dominant inherited form of epilepsy in newborns. Clearly, KCNQ2 channels are important therapeutic targets. The purpose of this project was to identify potential activators and inhibitors of the KCNQ2 channel.

Methods: Using the thallium flux fluorescence assay, we profiled 138 extracts derived from plant endophytes for potential activity against the KCNQ2 channel. A total of three screens were performed using untransfected and transfected HEK293 cells: 1) extracts in 1% DMSO in both groups of cells, and two additional concentrations in the transfected group (0.1, 0.01% DMSO); 2) three dose response treatments (1, 0.1, 0.01% DMSO); 3) seven dose response treatments (10, 3, 1, 0.3, 0.1, 0.03, 0.01% DMSO). Extracts at concentrations with significant baseline fluorescence were excluded. Statistically significant extract activity ($P < 0.01$) was determined using two-tailed equal variance T-tests and verified via whole-cell patch clamping (protocol: from -80 mV to +60 mV).

Results: Results from the screening identified two extracts with potential activity against KCNQ2 channels: 1) *Camellia sinensis* (green tea) extract with potentiation at 0.01% DMSO ($P=0.003$) and 2) *Echinacea* (purple coneflower) extract with potentiation at 0.01% DMSO ($P=0.003$). The *Camellia sinensis* extract activity was verified with whole cell patch-clamping.

Conclusion: We found extracts derived from *Camellia sinensis* and *Echinacea* that potentiate KCNQ2 channel activity at particular concentrations. Further characterization and isolation of the specific compounds within these extracts may lead to novel therapeutic agents against seizure and pain disorders.

#28: Patricia Zadnik, MS3
MSRD Poster Competitor

Mentor: Daniel M Sciubba, MD

Generation of a novel bone-seeking human breast adenocarcinoma cell line in a rat model of metastatic spinal metastases

Background: Metastatic cancer afflicts thousands of patients each year. More sophisticated animal models are needed to facilitate translation of experimental therapeutics from bench to bedside. In response to this need, we generated a bioluminescent, bone-specific human breast cancer cell line for use in a rodent model of metastatic breast adenocarcinoma. Our hypothesis is that serial culture of metastases from the vertebral bodies will generate a more aggressive, bone-specific breast cancer cell line.

Methods: Six four-week-old female nude rats were injected with 100,000 MDA-MB231 cells in 200 microliters of serum-free media in the left ventricle. These cells express Luciferase and GFP. The animals were monitored via Xenogen imaging for signs of metastases at day 10 and 34. Locations of metastases were recorded. Tumor cells were harvested from the vertebral bodies of two rats and plated for cell culture. Tumor cells exhibiting GFP and Luciferase positivity were injected into the left ventricle of eight four-week-old female nude rats at a concentration of 100,000 cells/200 microliters. These rats were subjected to IVIS imaging at day 11.

Results: At day 35, three rats from the MDA-MB-231 intracardiac injection group exhibited signs of paralysis, indicative of spinal cord compression secondary to tumor growth in the vertebral body. At day 50, a fourth rat was paralyzed. At day 11, no rats in the tumor cell intracardiac injection group were paralyzed, however quantitative comparison of the two groups demonstrated higher rates of bony metastases to the forepaws, hindpaws, tail and femur in the tumor cell group.

Conclusion: This work confirms that GFP and Luciferase positive cells can be recovered following intracardiac injection of GFP/Luciferase positive primary tumor lines. Further, intracardiac injection of tumor cells isolated from the vertebral bodies of rats results in higher rates of bony metastases compared to the primary cell line.

CLINICAL RESEARCH POSTER ABSTRACTS

Listed Alphabetically

#29: Solomon Abay, MS2

Mentor: Michael Lim, MD; Ben Carson, MD

Patient Outcomes in the Surgical Treatment of Atypical Trigeminal Neuralgia.

Background: Patients who present with trigeminal neuralgia of the atypical form (ATN), defined as paroxysmal lancinating pain accompanied by a constant component and numbness, usually have facial pain more refractory to surgical intervention than classic trigeminal neuralgia (CTN) patients. The purpose of our study was to determine which neurosurgical procedures of those offered at the Johns Hopkins Hospital resulted in the most positive outcomes for patients with ATN.

Methods: We conducted a database search of 909 patients of both CTN and ATN who had undergone a neurosurgical procedure at the Johns Hopkins Hospital from 1990 to 2010. We narrowed the field further to just 51 ATN patients who had undergone one or more of five possible procedures. Finally, we used Microsoft Excel Pivot Tables to determine the number of patients who reported a I or II (indicating complete or near-complete relief, respectively) on the Boulder-Stanford pain relief scale for each of the five examined procedures. In addition to this, we also plan on using the same software to determine the average length of pain-free survival for each procedure.

Results: ATN patients who received Gamma Knife radiosurgery were more likely to report a I or II on the BS pain relief scale (7 of 9 total patients, 77%) than any of the other four procedures (Glycerol rhizotomy - 14/26, 53.8%; microvascular decompression [MVD] – 5/7, 71.4 %; nerve block [NB] – 3/4, 75%; and Radiofrequency glycerol rhizolysis – 2/4, 50%). The results for pain-free survival are not yet available.

Conclusion: We found that atypical trigeminal neuralgia patients responded more favorably to gamma knife radiosurgery than to glycerol rhizotomy, MVD, NB, or RF-Gly on the basis of self-reported BS pain relief scores. The duration of pain-free survival will be investigated in the next stage of the study.

#30: Demetri Arnaoutakis, MS2

Mentor: Joseph Califano, M.D.

Salivary Rinses Collected with and without an Exfoliating Brush from Patients with Head and Neck Cancer Share Similar Promoter Hypermethylation Pattern

Background: Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer in the world. The inactivation of tumor suppressor genes (TSGs) caused by epigenetic changes has been well established in the literature. Recently, detection of gene promoter hypermethylation in salivary rinses has been explored as a potential for monitoring HNSCC.

Clinically, salivary rinses can be obtained by a simple rinse and gargle or brushing oral cavity surfaces with an exfoliating brush. The aim of this study is to evaluate the concordance of promoter hypermethylation between salivary rinses collected with and without an exfoliating brush from HNSCC patients.

Methods: 57 paired salivary rinses collected with or without an exfoliating brush from identical HNSCC patients were evaluated for promoter hypermethylation status using quantitative methylation-specific PCR. Target TSG promoter regions were selected based on our previous studies describing a panel for HNSCC screening and surveillance: P16, CCNA1, DCC, TIMP3, MGMT, DAPK and MINT31.

Results: In both salivary rinses collected with and without brush, frequent methylation was detected in P16 (8.8% vs. 5.2%), CCNA1 (26.3% vs. 22.8%), DCC (33.3% vs. 29.8%), TIMP3 (31.6% vs. 36.8%), MGMT (29.8% vs. 38.6%), DAPK (14.0% vs. 19.2%), and MINT31 (10.5% vs. 8.8%).

Spearman's rank correlation coefficient showed a positive correlation between salivary rinses collected with and without brush for P16 ($\rho=0.79$), CCNA1 ($\rho=0.61$), DCC ($\rho=0.58$), MGMT ($\rho=0.70$), DAPK ($\rho=0.51$) and MINT31 ($\rho=0.72$) ($P<0.01$).

Cohen's kappa revealed strong concordance between salivary rinses with and without brush: 96.5% P16 ($\kappa=0.73$), 82.5% CCNA1 ($\kappa=0.53$), 78.9% DCC ($\kappa=0.51$), 84.2% MGMT ($\kappa=0.65$), 84.2% DAPK ($\kappa=0.43$), and 94.7% MINT31 ($\kappa=0.70$).

Conclusion: Our study demonstrated strong correlations of gene promoter hypermethylation between salivary rinses collected with and without an exfoliating brush. Salivary rinse collection without using an exfoliating brush may offer a cost effective, non- invasive, and reliable means for development of epigenetic salivary rinse biomarkers.

#31: Paul Bixenstine, MS2

Mentor: Martin Makary, MD MPH

Catastrophic Medical Malpractice Payouts in the U.S.

Background: Catastrophic medical malpractice payouts (greater than \$1 million) influence physicians' practice, hospital policy, and discussions of healthcare reform. However, little is known about the specific provider, patient, and event characteristics of these payouts.

Methods: We reviewed paid malpractice claims nationwide over a 7-year period (2004 to 2010) using the National Practitioner Data Bank. For each claim, we extracted data on the alleged event, patient characteristics and injury severity, physician year of medical school graduation and previous paid malpractice claims, judgment vs. settlement, and state. We used multivariate regression to identify factors associated with catastrophic and increased payouts.

Results: Claims with catastrophic payouts represented 7.9% (6130/77621) of all paid claims. Factors most associated with catastrophic payouts included patient age less than 1 year (OR, 10.04; 95% CI, 5.58-18.06) and anesthesia-related error (OR, 3.26; 95% CI, 2.06-5.15). Diagnosis-related errors were the most common event for catastrophic (34.2%, 2099/6130) and non-catastrophic payouts (32.1%, 22926/71491). Claims involving quadriplegia, brain damage, or lifelong care were also most associated with catastrophic payouts, with 62.77 times greater odds than insignificant injury (95% CI, 19.99-197.15), which accounted for just 8 catastrophic payouts. Settlement showed smaller odds of catastrophic payout (OR 0.31; 95% CI, 0.23-0.42) and 46% smaller payments (95% CI, 0.46-0.62) than judgment. No difference was found in odds of catastrophic payout based on a physician's years in practice or having previous paid claims, though physicians with previous paid claims paid 14% more (95% CI, 1.08-1.21). New York State had the highest rate of catastrophic payouts per capita (94.1/million). Catastrophic payouts averaged \$1.40 billion per year.

Conclusion: Catastrophic payouts represent a small fraction of all malpractice payouts and of healthcare expenditures. They are most often associated with permanent injury and disability and not with insignificant injury. Identification of associated patient, provider and event characteristics may help guide efforts for prevention.

#32: Christine Boone, MS2

Mentor: Judy Huang, MD

Arteriovenous Malformation Database

Background: Cerebral arteriovenous malformations (AVMs) are rare, congenital vascular lesions in which arteries communicate directly with tortuous, dilated veins. The lack of capillaries between the feeding arteries and draining veins shunts arterial blood into the venous system^{4,6,7}. Individuals may develop symptoms early in life or many decades later, while some may remain asymptomatic. Intracranial hemorrhage (ICH) is one of the major symptoms of an AVM. AVMs cause 4% of all ICHs and as many as 33% of ICHs in young adults. Symptomatic AVMs increase risk of morbidity and mortality^{4,6,7}. For this reason, symptomatic AVMs are usually treated quickly, which hinders determination of the natural history of this disease⁷. The elusive natural history, and the diversity of lesions and treatment options complicate the management of AVM cases. Thus, demonstrating a need for more prospective and retrospective studies that examine a wider array of relevant factors with increased precision. The first step in this direction is to collect and organize the vast amount of data existing in patient records in a way that will facilitate this type of study. The purpose of this AVM database is to develop a comprehensive and precise system of data collection and management of both retrospective data and of prospective data in order to facilitate further investigations of the natural history and treatment of AVMs.

Methods: The methods used will primarily involve reviewing patient records through the Johns Hopkins Electronic Patient Records system (EPR) and categorizing a broad variety of aspects of each case. The cases included in the database will be those of Dr. Huang and other neurosurgeons in the Johns Hopkins Department of Neurosurgery.

#33: Michael Brener, MS3

Mentor: Wendy Post, MD

Epicardial Fat is Associated with Subclinical Coronary Atherosclerosis in the Multicenter AIDS Cohort Study (MACS)

Background: Cytokines released by epicardial fat are implicated in the pathogenesis of atherosclerosis. We hypothesized that HIV infection is associated with increased epicardial fat, and consequently a greater degree of subclinical coronary atherosclerosis.

Methods: Three hundred seventy seven HIV-infected and 159 HIV-uninfected homosexual men age 45 to 70 were recruited to undergo a non-contrast CT scan to evaluate epicardial fat volume (EFV) (fat within the pericardium) and coronary artery calcium (CAC). Coronary CT angiography performed on select participants determined the total plaque severity score (TPS) (n = 393). We evaluated the associations between EFV, CAC presence, and TPS, adjusting for age and serostatus.

Results: HIV-infected men were younger (54.2 ± 5.8 vs. 57.7 ± 6.7 years) and had lower BMIs than seronegative men (26.1 ± 4.6 vs. 27.8 ± 5.0 kg/m²). Among the entire cohort, the prevalence of CAC was 53.2% and the median TPS was 3.0 (IQR = 1.0-6.0). Although younger and thinner, HIV-infected men had larger EFVs (122.0 ± 58.6 vs. 116.0 ± 58.6 mm³, $p = 0.0001$). Duration of antiretroviral therapy was positively associated with EFV ($p = 0.0004$). EVF was also associated with CAC presence (OR = 1.05, 95% CI = 1.02-1.08, $p = 0.004$). In fact, the median TPS was 0.13 points higher per 10 mm³ of increased EFV. This relationship was statistically significant ($p = 0.002$) even after adding BMI ($p = 0.01$) and visceral adipose tissue volume to the model ($p = 0.03$). EFV was directly associated with increased fasting insulin levels too ($p = 0.0001$). Serostatus exerted no interaction effect on the associations between EFV and either CAC or TPS.

Conclusion: Epicardial fat volumes are larger in HIV-infected men and are directly associated with the duration of antiretroviral therapy. Among both HIV-infected and uninfected men, greater epicardial fat associated with increased subclinical coronary artery atherosclerosis.

#34: Vivek Charu, MS2
MSRD Poster Competitor

Mentor: William Checkley, M.D., Ph.D.

Identifying co-morbidities associated with *Pneumocystis jirovecii* pneumonia in the HIV-negative population of the United States (1986-2005)

Background: Prophylaxis guidelines for *Pneumocystis jirovecii* pneumonia (PCP) in the HIV-negative population are not well established. Previous studies of PCP in this population are limited by small sample size. We utilized a large, nationally-representative hospital discharge database to identify co-morbidities associated with hospitalizations due to PCP.

Methods: We extracted all PCP hospitalizations captured by the National Hospital Discharge Survey Database (NHDS) from 1986 to 2005. We excluded cases based on the presence of an ICD-9 code consistent with HIV or an additional AIDS-defining illness other than PCP. We examined co-morbidities associated with PCP hospitalizations among HIV-negative individuals.

Results: We identified 410 HIV-negative patients with PCP captured by the NHDS from 1986-2005; this corresponds to a rate of ~7 PCP hospitalizations per 100,000 per year. Of the 410 patients, we found that 66% were male, 44% were 30-59 years of age. We estimate a case fatality ratio of 21.5% among patients not mechanically ventilated, and 61.3% among patients receiving mechanical ventilation. We found that 41% of patients had an associated hematologic disease, 22% had a solid organ malignancy, 21% had obstructive lung disease, 12% had a disease of the immune mechanism, 9% had interstitial lung disease, 8% had connective tissue disease, and 7% received an organ transplant. We were unable to identify a statistically significant trend in hospitalizations over the time period studied.

Conclusion: To our knowledge this is largest case-series of patients with PCP in the HIV-negative population. The majority of cases occurred in individuals with hematologic diseases and solid organ malignancies. However, a notable portion of cases occurred among individuals with obstructive and interstitial lung diseases. This data may aid physicians in prophylaxis decisions, or in the more rapid identification and treatment of PCP in HIV-negative immunosuppressed populations.

#35: Sean Chen, MS2

**Mentors: H. Ballentine Carter, M.D.
Craig Pollack, M.D., M.H.S.**

Decision Making Amongst Primary Care Physicians on Prostate Cancer Screening

Background: In 2010, prostate cancer was the second leading cause of cancer death among men. Thus the Prostate-Specific Antigen (PSA) test has become a widely used diagnostic tool. However, the risks and benefits of PSA testing are not evenly distributed across the population. The PSA test is thought to be a source of significant health care expenditures and decrease in the quality of life for those receiving unnecessary treatment. Despite recommendations against routine screening, approximately half of men over 75 years old and a third of those with low life expectancies receive screening. Through a retrospective chart review and survey we sought find what currently informs clinician discussions regarding PSA testing

Methods: Electronic medical record data: The medical records from the Johns Hopkins Community Physicians (JHCP) was reviewed for variations in screening by patient demographics (age, race/ethnicity, socioeconomic and insurance statuses), number of comorbidities, and frequency of PSA tests. Surveys: surveys were distributed to primary care physicians in the JHCP network to assess factors that influence the clinical decision process on prostate cancer screening. Bivariate and multivariable regression analyses were performed to examine how physician characteristics are associated with these perceptions and beliefs.

Results: In 2010, 41,088 men over the age of 40 and without a history of prostate cancer were eligible for PSA testing. Overall, 26% were tested and 424 (1%) were diagnosed with prostate cancer. Over 17% of men aged 75 and over were screened. Among men with diabetes, 28% were screened, and among those with cerebrovascular disease, 20% were screened. For patients with four or more comorbidities, 20% were screened.

Conclusion: There may be under screening of at-risk populations in addition to overscreening of the population of patients where there is unlikely to be a benefit from the PSA test.

#36: Jonathan Dattilo, MS2

Mentor: Edward McCarthy, M.D.

Liposclerosing Myxofibrous Tumor: Is it a real entity?

Background: Liposclerosing myxofibrous tumor (LSMFT) is a well-circumscribed lesion exclusive to the proximal femur that has been correlated with several histopathologic patterns, each characteristic of other well-characterized diseases. LSMFT has been contested as a true clinical entity, and it has been suggested that this lesion is instead the result of chronic degenerative changes of other lesions, most commonly fibrous dysplasia and intraosseous lipomas. Consequently, it is not a universally accepted entity. Elucidation of the pathology is essential in preventing unnecessary biopsies for patients with suspected LSMFT lesions.

Methods: We identified patients presenting in the Johns Hopkins Health System between 1990 and 2011 that met the radiologic diagnostic criteria for LSMFT. Patient characteristics were abstracted from medical records, including presenting symptoms, radiologic and pathologic findings, treatment, and outcomes. Surgical pathology was reexamined to confirm initial diagnoses.

Results: Thirty-three patients meeting our criteria were identified, 18 (55%) of whom underwent biopsy for additional evaluation. Our study population consisted of 20 males and 13 females with a mean age of 46 years and age range 19 to 80 years at time of presentation. Patients who underwent biopsy consisted of 11 males and 7 females with a mean age of 49 years and age range of 19 to 80 years. We found that the most common presenting symptom was pain (30%) and that 6 lesions were discovered incidentally. Surgical pathology revealed that fibrous dysplasia was the most common final diagnosis (66%). Intraosseous lipomas (17%) and pathology consistent with the definition of LSMFT (17%) were also observed. Females also presented at younger ages than males, pathologic fracture presented in older cohorts, and LSMFT presented later in life than non-LSMFT or fibrous dysplasia diagnoses.

Conclusion: We conclude that LSMFT is likely a result of chronic degeneration of fibrous dysplasia or intraosseous lipomas subject to the weight bearing forces placed on the hip over time. We recommend biopsy only in cases where patients must be treated for pathologic fracture or if the patient presents with pain that cannot be otherwise explained, as this may be indicative of a growing neoplasm.

#37: Carla De la Cruz, MS2

Mentor: Keri Althoff, PhD

Systematic review of age-related comorbidities in HIV-infected individuals

Background: Recent epidemiologic studies showed an increased incidence of age-related co-morbidities in HIV-infected individuals. Due to the elusiveness of the demographically-similar HIV-uninfected control groups, the general population is frequently used in studies. This is problematic because HIV-infected adults have an increased prevalence of traditional risk factors for co-morbidities. The purpose of this study is to examine the existing literature and summarize the evidence for a difference in age at co-morbidity diagnosis of myocardial infarction (MI) and end-stage renal disease (ESRD) in HIV-infected adults.

Methods: Systematic reviews of the literature were conducted for MI and ESRD among the electronic databases EMBASE and PubMed. A protocol for this study was developed in collaboration with the Cochran Center for Systematic Reviews. Search strategies were assembled under the guidance of librarians at the Welch Medical Library. Six reviewers participated in a dual review process of the abstracts. Studies were selected if they included an HIV-uninfected comparison group.

Results: A total of 1823 and 2267 studies were identified for MI and ESRD, of which 99 (5%) and 104 (5%) had an HIV-uninfected comparison group, respectively. The concordance rate among reviewers was 97% for MI and 96% for ESRD. The next steps are to 1) classify the HIV-uninfected comparison group; 2) evaluate studies for selection and information bias, and confounding; and 3) conduct a statistical comparison of the pooled results to determine if HIV-infected adults are younger at MI and ESRD diagnosis compared to HIV-uninfected adults.

Conclusion: Although our inclusive search strategies resulted in a large number of studies, few studies ultimately meet our selection criteria. Concordance for inclusion of studies was high for both MI and ESRD. Upcoming steps to evaluate the comparison group, potential biases and confounding, and conducting a meta-analysis will ensure an answer to this pressing question about accelerated aging among HIV-infected adults.

#38: Kristina Eipl, MS2

Mentor: Brooks Jackson, M.D.

Seroprevalence of unexpected red cell antibodies among pregnant women in Uganda

Background: We conducted a population-based, cross-sectional study to determine ABO and Rh blood types among pregnant women in Kampala, Uganda, and to determine the percentage who have unexpected red cell antibodies and their specificities. Currently, the prevalence of the Rh D antigen in the Ugandan population has not been well-studied, nor the prevalence of other unexpected red cell antibodies in pregnant Uganda women. Given the varying prevalence of different red cell antigens throughout the world, further examination of this part of the world is important for clinical care.

Methods: 1001 de-identified blood samples leftover from routine testing at the Mulago Hospital antenatal clinic were collected over a three-week period and typed for ABO blood groups and RH D antigen and screened for the presence of unexpected antibodies.

Results: Of the 1001 maternal samples tested, 48.9%, 26.4%, 21.0%, and 3.8% tested positive for blood groups O, A, B, and AB, respectively, 23 or 2.3% were negative for the Rh D antigen, and 55 or 5.5% were positive for unexpected red cell antibodies. The most frequent antibody specificities were ____ (____%) and ____ (%).

Conclusion: [Final conclusion is still in progress.]

#39: Farzana Faisal, MS2

Mentor: Lei Zheng, M.D., Ph.D

Induction chemotherapy followed by radiation therapy is associated with better survival for patients with locally advanced pancreatic cancer.

Background: Advanced pancreatic cancer has a poor prognosis. At diagnosis, 80% of patients are unresectable, 40% locally advanced. We performed a retrospective analysis of patients treated at JHH to assess the role of chemotherapy and radiation therapy for locally advanced pancreatic cancer.

Methods: Between 6/06-6/10, 1433 pancreatic cancer patients seen at JHH were reviewed. Among them, 67 patients who met the Society of Surgical Oncology criteria for locally advanced pancreatic cancer were treated primarily at JHH. Clinical information from diagnostic CT scans, chemotherapy and radiation therapy was collected. Overall and progression-free survivals were compared among different subgroups by Kaplan-Meier analysis and the Wilcoxon test.

Results: For the 67 patients (37% female, median age 62y), median overall survival was 15.7 months, median progression-free survival 7.9 months. Patients who received combination chemotherapy and radiation had a longer progression-free survival than patients who received radiation alone (12.0 vs. 4.5 mo, $p<0.01$), but there was no difference in overall survival. Patients who received combination chemotherapy and radiation also had a trend for better progression-free survival than patients receiving chemotherapy alone (12.0 vs. 6.8 mo, $p=0.08$), but there was no difference in overall survival. Among patients receiving combination therapy, patients who received chemotherapy first had a significantly longer overall survival and a trend toward better progression-free survival than patients who received radiation first (overall 18.1 vs. 11 mo, $p=0.03$; progression-free 12.6 vs. 8.3 mo, $p=0.15$).

Conclusion: This study suggests that chemotherapy may play an important role in the treatment of locally advanced pancreatic cancer. However, combination chemotherapy and radiation therapy is favored. Historically, radiation has been the preferred treatment for locally advanced pancreatic cancer, but chemotherapy is effective because locally advanced cancer is a systemic disease. We recommend treating patients with induction chemotherapy followed by consolidation with radiation therapy. Optimal combination chemotherapy regimens still need to be developed.

#40: Mark Fisher, MS2

Mentor: Paul Manson, MD

Critical Concepts in Composite Facial Reconstruction: The Role of Aesthetic Units, Skeletal Buttresses, Soft Tissue Volume Contour, and Local Cutaneous Replacement.

Background: Over the last several decades there have been numerous advances in the fields of aesthetic, craniofacial, and microsurgery. Aesthetic units are no longer “skin deep,” but are recognized as being comprised of soft tissue as well as underlying hard tissue. Indeed, hard tissue must be simultaneously reconstructed with soft tissue to recreate the unit. In addition, planning multi-stage reconstructions, which include revisionary procedures, has become necessary to achieve the desired result. Here, we integrate these advancements into seven critical concepts necessary for composite facial reconstruction and provide a patient series to illustrate their success.

Methods: We assembled a multi-center, retrospective cohort review of patients who underwent free tissue transfer of craniofacial defects at the R Adams Cowley Shock Trauma Center and the Johns Hopkins Hospital from 2003 to 2011. Patients were categorized by anatomic aesthetic location and complications recorded.

Results: One hundred eighty four patients with craniofacial defects were identified; 79 females and 105 males, with an average age of 44 years. Etiologies included cancer (51.6%), trauma (39.1%), congenital defects (6.5%), and infection (2.7%). Free tissue transfers included 67 fibula, 42 anterolateral thigh, 41 ulnar, 18 groin, 14 iliac, 3 radius, and 1 vastus lateralis flaps. The success rate was 97.3% and complication rate was 10.8%. Secondary procedures included suction lipectomy, dermabrasion, tissue re-suspension, and cutaneous flap excision followed by full thickness skin grafting or tissue rearrangement.

Conclusion: Aesthetically pleasing results in composite facial reconstruction have been achieved by merging principles of three symbiotic disciplines: aesthetic, craniofacial, and microsurgery. Critical concepts in this approach are aesthetic unit appearance, defect boundaries, lining restoration, provision of vascularized skeletal buttress(s) framework, ample soft tissue volume, early reconstruction, and local revisional cutaneous replacement through multi-stage planning. Integration of these concepts improves patient outcomes, and paves the way to successful facial transplantation.

#41: Sara Fuhrhop, MS2

Mentor: Michael Ain, MD

Natural History of Hip Dysplasia in Multiple Epiphyseal Dysplasia

Background: Multiple epiphyseal dysplasia (MED) is a rare disorder characterized by delayed and irregular ossification of multiple epiphyses. We aim to describe age-related radiographic features of hip dysplasia in MED, and to determine how patient-reported hip pain, hip function, and quality of life change with age.

Methods: We conducted a retrospective cohort study of all JHH MED patients since 1980: fifteen patients (30 hips). We reviewed preoperative lower extremity radiographs and conducted phone questionnaires, including the SF-36 and quantitative hip pain and function scales.

Results: Triradiate cartilage was open in 10 patients (20 hips, Group 1), and closed in 5 patients (10 hips, Group 2). Congruency between the femoral head and acetabulum (scale 1-4, 4=most congruent) was 3.4 ± 0.5 in Group 1 and 2.6 ± 0.8 in Group 2 ($p=0.024$). Acetabulum-head index (percent coverage of femoral head by acetabulum) was 80 ± 11.1 in Group 1 and 77.7 ± 8.5 in Group 2 ($p=0.509$). Trochanteric height above (+) or below (-) the femoral head center was -4.2 ± 4.7 in Group 1 and 6.3 ± 7.3 in Group 2 ($p<0.001$). SF-36 Physical Composite was 46.9 ± 10.2 in Group 1 and 26.5 ± 2.3 in Group 2 ($p<0.001$). Patient-reported hip pain (scale 1-10, 1=no pain) was 2.2 ± 2.5 in Group 1 and 8.5 ± 0.6 in Group 2 ($p<0.001$). Patient-reported hip function (scale 1-10, 10=best function) was 8.2 ± 2.5 in Group 1 and 2.5 ± 0.6 in Group 2 ($p<0.001$).

Conclusion: With increasing age in MED, significant declines are observed in patient-reported physical health and hip function; significant increases are observed in hip pain. Radiographically, significant increases are observed in trochanteric height, significant declines are observed in joint congruency, and downward trends are observed in acetabulum-head index. This study suggests that declines in joint congruency and femoral head coverage, and increases in trochanteric height, may be related to changes in hip pain and function. It may also inform MED patients about age-related quality of life.

#42: Natasha Gupta, MS2

Mentor: Dorry Segev, M.D., Ph.D

Identifying barriers to living kidney donation

Background: Despite improved graft function and longevity, live donor transplants comprise a moderate proportion of kidney transplants (KT) performed in the U.S. We hypothesized that this is partly due to challenges transplant candidates face in finding living donors. To explore this potential mechanism, we sought to identify key barriers that transplant candidates face in identifying a living kidney donor.

Methods: We developed and piloted a survey that assessed barriers to identifying a live donor and factors associated with previously asking someone to consider donation. Over four months, we administered the survey to patients on the Johns Hopkins KT waiting-list and patients being evaluated for the waiting-list. We quantified the independent association of demographics, social support indicators, KT knowledge, and patient comfort in discussing their disease with our primary outcome (previously asking someone to consider donation) using multivariate logistic regression.

Results: Respondents included 249 of 381 patients (65.4% response rate) from the KT waiting-list and 63 individuals undergoing evaluation. Of respondents, 54.6% were male and 43.6% were Caucasian. Only 43.9% of respondents had previously asked someone to consider donation. Perceived KT knowledge (adjusted OR [aOR] 40, 95% CI 1.10-1.78, p-value 0.006) and patient comfort with telling family and friends about their kidney disease (aOR 1.39, 95% CI 1.08-1.78, p-value 0.01) were both independently associated with previously asking someone to consider donation, whereas a high degree of perceived social support, being married, and having children were not.

Conclusion: The majority of patients on the Johns Hopkins KT waiting-list had never asked someone to consider donation. Patients who were comfortable telling others about their kidney disease and felt knowledgeable about KT were significantly more likely to have pursued living donation. Improving KT knowledge and comfort discussing kidney disease may help patients overcome barriers associated with identifying a live donor, increase live donor KT, and improve patient outcomes.

#43: Kurt Herzer, MSc, MS3
MSRD Poster Competitor

Mentor: Evan Mayo-Wilson, DPhil

Vitamin A supplements for preventing mortality, illness, and blindness in children aged under 5: systematic review and meta-analysis

Background: Vitamin A deficiency increases vulnerability to illnesses such as diarrhea, measles, and respiratory infections, which are leading causes of mortality among children in developing countries. The objective of this study was to determine if vitamin A supplementation is associated with reductions in mortality and morbidity in children aged 6 months to 5 years.

Methods: The design was a systematic review and meta-analysis. Two reviewers independently assessed studies for inclusion. Data were double extracted; discrepancies were resolved by discussion. Meta-analyses were performed for mortality, illness, vision, and side effects. Databases were searched through April 2010 and included the Cochrane Central Register of Controlled Trials, Medline, Embase, Global Health, Latin American and Caribbean Health Sciences, metaRegister of Controlled Trials, and African Index Medicus. Eligibility criteria for selecting studies included: randomized trials of synthetic oral vitamin A supplements in children aged 6 months to 5 years. Studies of children with current illness, hospitalization, and food fortification or β carotene were excluded.

Results: 43 trials with about 215,633 children were included. Seventeen trials including 194,483 participants reported a 24% reduction in all-cause mortality (rate ratio=0.76, 95% confidence interval 0.69 to 0.83). Seven trials reported a 28% reduction in mortality associated with diarrhea (0.72, 0.57 to 0.91). Vitamin A supplementation was associated with a reduced incidence of diarrhea (0.85, 0.82 to 0.87) and measles (0.50, 0.37 to 0.67) and a reduced prevalence of night blindness (0.32, 0.21 to 0.50) and xerophthalmia (0.31, 0.22 to 0.45). Three trials reported an increased risk of vomiting within 48 hours of supplementation (2.75, 1.81 to 4.19).

Conclusion: Vitamin A supplementation is associated with large reductions in mortality, morbidity, and vision problems, and these results cannot be explained by bias. Further placebo controlled trials of vitamin A supplementation in children between 6 and 59 months of age are not required.

#44: Kevin Hur, MS2
MSRD Poster Competitor

Mentor: Gedge Rosson, M.D.

Patient-Reported Assessment of Functional Gait Outcomes Following Superior gluteal artery perforator (SGAP) Reconstruction

Background: The superior gluteal artery perforator (SGAP) flap is upper buttock adipocutaneous tissue used for breast reconstruction. Dissection of the SGAP flap involves exploration of perforating vessels through the gluteal muscle, which might potentially compromise gait and ambulation. The deep inferior epigastric perforator (DIEP) flap utilizes abdominal adipocutaneous tissue. This study compares patient-reported gait and ambulation problems between SGAP flap and DIEP flap reconstruction patients.

Methods: Forty-three patients who underwent bilateral flap reconstruction (17 SGAP, 26 DIEP) between March 2009 and August 2010 participated in the study. The Lower Extremity Functional Score (LEFS) was administered with a supplementary section evaluating issues of gait, balance, fatigue, and pain. During the survey, patients evaluated how they felt at 2-months postop and at time of survey administration. Multivariate regressions were fit to assess the association between type of reconstruction and self-reported lower extremity function, controlling for potential confounding factors.

Results: The SGAP patients had a mean difference in overall LEFS by 4.29 points (95% CI: -8.10 - 16.67) at 2-months after surgery compared to the DIEP patients. Multivariate regression analysis of individual questions controlling for age, BMI, and subsequent reoperations indicated that the SGAP patients reported higher difficulty performing the following activities at 2-months after surgery: usual hobbies ($p < 0.05$), walking a mile ($p < 0.01$), and sitting for an hour ($p < 0.05$). There was no significant difference in LEFS between the two cohorts on the date of survey. The SGAP patients also reported easier fatigue ($p < 0.01$) and more pain in the buttocks or legs ($p < 0.01$) during the postoperative period and on the date of survey compared with DIEP patients.

Conclusion: SGAP flap surgery causes statistically significant patient-reported donor site morbidity during the early postoperative period with eventual recovery to a certain degree. Thus, we feel that patients should be educated appropriately and undergo physical therapy during the early follow-up period.

#45: Melissa Hutchinson, MS2

Mentor: Margaret Chisolm, MD

The efficacy of five weeks of escalating and fixed contingency management reinforcement on illicit drug use in opioid-dependent pregnant patients

Background: Even brief substance use during pregnancy can lead to devastating consequences. Contingency management (CM) (reinforcing target behaviors with vouchers) is known to improve treatment adherence and decrease use in substance-using pregnant women. The Drug Abuse Incentive Systems (DAISY) Study compared the relative efficacy after 13 weeks of escalating and fixed CM schedules in methadone-maintained opioid-dependent pregnant patients. No difference in efficacy by CM schedule was noted, but there was concern that flaws in study design, including delays in receiving the reinforcement voucher and failure to reset the escalating condition's vouchers to baseline after missed urine samples, compromised the internal validity of the study. Other studies have shown CM to be efficacious after just 1 week. The present study's objective was to determine treatment efficacy after a shorter interval, and to examine how failure to reset the escalating condition's vouchers impacts efficacy.

Methods: Data were analyzed from 90 patients (escalating CM, n=52; fixed CM, n=38) who completed the DAISY study. Drug abstinence variables at 5 weeks were analyzed using t-tests. Missing data from the escalating and fixed conditions were analyzed using t-tests.

Results: No statistically significant difference in drug abstinence variables was found between the escalating and fixed conditions after 5 weeks: mean (SD) number of drug negative urines were 8.1(4.5) and 7.4(4.3), for the escalating and fixed conditions, respectively (p=0.46). Assessment of missing data showed no difference between escalating and fixed conditions. No difference was found between number of missed urine samples at 5 versus 13 weeks.

Conclusion: Study results do not support the hypothesis that lack of findings in 13 weeks was attributable to not resetting the escalating group after missed urine samples. The results extend the hypothesis that time-to-reinforcement is more critical to CM efficacy, suggesting that delays weaken the voucher's ability to compete with the immediate positive reinforcing effects of drug use.

#46: Khalda Ibrahim, MS2

Mentor: Angela Guzzetta, MD

Survival following lung metastasectomy for soft-tissue sarcomas

Background: Over 10,000 cases of soft-tissue sarcoma (STS) are diagnosed annually in the US. Up to 50% of patients experience metastasis, with the lungs as the primary site of metastasis. Resection of pulmonary metastases from STS has been shown to increase both disease-free and overall survival.

Methods: We identified all patients with primary non-lung soft-tissue sarcoma and pulmonary metastases treated by resection at JHH between 1996 and 2009. The following data were collected: demographics, stage at diagnosis, recurrences, treatments, and last known vital status. Data were examined with Kaplan-Meier curves and multivariate analysis.

Results: Fifty-six eligible patients were identified (46% male, 89% Caucasian). Mean age at diagnosis was 51.4 ± 16.7 years. Median disease-free survival and median overall survival from first lung metastasectomy were 0.7 years and 2.5 years, respectively.

Conclusion: Median overall survival and median disease-free survival following pulmonary metastasectomy in the selected patient population appear to be less than has been previously reported in other cohorts of STS patients. Patient selection may be responsible for this difference.

#47: Sebastian Jara, MS2

Mentor: Ralph Tufano, MD

The diagnostic and financial implications of BRAF mutation testing of fine-needle aspiration biopsy samples ‘suspicious for papillary thyroid cancer’

Background: Although fine-needle aspiration biopsy (FNAB) is the mainstay for diagnosing thyroid malignancies, management of patients with suspicious thyroid nodules has proven difficult. The purpose of this study was to determine whether detection of the BRAF, the most common genetic mutation in papillary thyroid carcinoma (PTC), is correlated with a higher likelihood of malignancy in patients with suspicious FNAB results.

Methods: We reviewed all records of patients with FNAB results “suspicious for papillary carcinoma” who subsequently underwent thyroidectomy at the Johns Hopkins Hospital from 2001 to 2011. Archived FNAB cytological samples of these patients will be tested for the BRAF mutation using the MutectorR assay. Results from the assay will be correlated with final histopathological data and used to investigate whether BRAF mutation detection is correlated with a higher likelihood malignancy. Medicare reimbursement data will be used to construct a cost analysis to determine the financial feasibility of BRAF detection.

Results: 61 patients with initial FNAB samples that were “suspicious for papillary carcinoma” that underwent thyroidectomy were identified. Of those 61 patients, 16 (26.2%) had benign final histopathological diagnoses and 12 of those patients (75%) underwent a total thyroidectomy. 43 patients (70.5%) were diagnosed with PTC upon final histopathology and 2 patients (3.3%) were diagnosed with follicular thyroid carcinoma. Of the 43 patients diagnosed with PTC, 35 (81.4%) underwent total thyroidectomies and 4 (9.3%) underwent an initial lobectomy and required a completion thyroidectomy due to the presence of malignancy. We await the results of the BRAF assay.

Conclusion: Over one-quarter of the patients in our cohort underwent thyroidectomy for benign lesions due to suspicious-appearing lesions on initial cytopathology. BRAF testing may help better direct therapy for patients with these initially suspicious findings. Estimates from Medicare data show that testing may substantially reduce the financial burden imposed by excessive treatment.

#48: Christine Johnson, MS2

Mentor: Steve Sozio, M.D.

The Relationship of Preoperative ASA Score to Complications Following Total Shoulder Arthroplasty

Background: Studies of lower joint extremity arthroplasty have identified a high American Society of Anesthesiologists (ASA) score as a risk factor for developing postoperative medical and surgical complications, including prosthesis dislocation, infection, and prolonged length of hospital stay. Whether the ASA score predicts complications following total shoulder arthroplasty (TSA) and reverse total shoulder arthroplasty (RTSA), however, has not been described. The purpose of this study was to assess the relationship between the ASA score and surgical and medical complications following total shoulder arthroplasty.

Methods: We conducted a retrospective cohort study of 484 consecutive shoulder arthroplasties (235 TSA, 192 RTSA, and 57 revision operations) performed at Johns Hopkins Hospital. Data was collected on patient demographics, comorbidities, length of hospital stay, and postoperative medical and surgical complications. The chi-square test, linear regression analysis, and univariate and multivariate logistic regression analyses were used to evaluate the ASA score and the probability of developing postoperative complications.

Results: Increasing ASA scores were significantly associated with the development of a surgical complication, with each unit increase in the ASA score significantly increasing the likelihood of any single surgical complication (OR 3.09, 95%CI[1.54, 6.20], $p=0.001$). There was a strong relationship between the ASA score and component failure (defined as prosthesis dislocation or hardware failure), as patients with ASA score >2 were 2.12 (95%CI[1.37,3.27], $p=0.001$) times more likely to have component failure than patients in ASA class <2 . The ASA score also had a significant relationship with length of hospital stay ($p<0.001$). No significant relationship was identified between the ASA score and medical complications.

Conclusion: This study demonstrates that the ASA score is strongly associated with surgical complications and length of hospitalization following TSA and RTSA. The ASA score may be a valuable tool to stratify patients for preoperative risk assessment and for comparison of surgical outcomes in shoulder arthroplasty.

#49: Andrea Jonas, MS2
MSRD Poster Presenter

Mentor: Scott Blackman, MD PhD

Effect of impaired fasting glucose on lung function in cystic fibrosis related diabetes

Background: Blood glucose control in patients with cystic fibrosis related diabetes (CFRD) correlates with improved lung function. Patients with impaired fasting glucose (IFG) on an oral glucose tolerance test (OGTT) are predicted to have worse clinical status. A recent study demonstrates improved survival in IFG patients compared to normal fasting glucose controls, with no increased risk of developing fasting hyperglycemia (Frohnert, 2010). We attempt to replicate this unexpected result in another patient population.

Methods: We conducted a retrospective case-control analysis of 1,767 patients taken from the Cystic Fibrosis Foundation's CFRD and Twin-Sib studies. 586 patients with valid OGTT data were selected. Patients under the age of 7.5 years or who had fasting hyperglycemia (FH) at their first clinic encounter were excluded. We used Fisher's Exact and Student's t-test for our analysis.

Results: For our population of 586 patients, 32% had IFG (56% normal glucose tolerant (NGT), 19% impaired glucose tolerant, 25% CFRD). There was no increase in mortality in IFG cases over an average 17.4-year follow-up. Within the NGT subset, IFG patients had an increased risk of developing FH (4.7% vs. 1.1%, $p < 0.05$, OR = 0.23 [95% CI 0.04-1.21]). Baseline lung function tests and demographics were comparable. On follow-up, IFG cases had worse percent predicted FEV1 (73% vs. 78%, $p < 0.03$) and percent predicted FVC (85% vs. 89%, $p < 0.03$).

Conclusion: We found the prevalence of IFG roughly similar to that in the comparison study (32% vs. 22%, respectively), though the breakdown by glucose tolerance did not follow similar trends. We found no difference in mortality between cases and controls. We also found significantly worsened lung function at follow-up in IFG cases and increased risk of developing FH for patients who were NGT. This counters previous findings that link IFG with improved clinical outcomes, and encourages further study of IFG and lung function in other populations.

#50: Brian J. Lee, MS2
MSRD Poster Competitor

Mentor: Misop Han, MD

External validation of postoperative nomogram for early prostate cancer recurrence following radical prostatectomy.

Background: Background: A quarter of prostate cancer patients who undergo radical prostatectomy experience biochemical recurrence (BCR), as determined by a detectable serum PSA. BCR is a significant predictor of metastatic progression and cancer specific mortality, and up to 75% of BCRs has been shown to occur within 2 years of surgery. Recently, Walz et al developed a nomogram that predicts biochemical recurrence within 2 years, based on tumor grade (Gleason score) and stage. While this model has the potential to guide adjuvant or salvage therapy, there have been no attempts to validate it with a large independent dataset.

Aim: To validate a predictive nomogram of BCR following radical prostatectomy using a large independent dataset.

Methods: Methods: We applied this nomogram to 18,846 of the 19,704 patients at Johns Hopkins Medical Institutions who underwent radical prostatectomy between 1982 and 2011. We excluded those who received neoadjuvant hormonal therapy, or had incomplete data on nomogram parameters. Using a receiver operating characteristic analysis, we then compared actual outcomes against the predicted probability of early BCR, defined as a PSA measurement greater than 0.2 ng/ml within 2 years of surgery.

Results: Results: With a median follow-up duration of 6.5 years, 931 men (4.9%) experienced early BCR, representing 47.8% of BCRs in the cohort. Analysis of the receiver operating characteristic curve yielded a c-index of 0.883 (95% CI 0.871-0.894), which is comparable to the results of the internal validation performed by Walz et al.

Conclusion: Conclusions: Our analysis indicates that this nomogram is a robust prediction model that accurately predicts the risk of early biochemical recurrence, and supports its use as a clinical guideline for individual patients in planning adjuvant or salvage therapy and follow-up monitoring.

#51:

#52: Anne Leonpacher, MS2

Mentor: Fernando Goes, M.D.

Depressive Episodes of Unipolar Relatives in Bipolar and Unipolar Pedigrees

Background: Although unipolar depressive disorder is common in families of individuals with bipolar disorder, it is unclear whether depressive episodes in unipolar relatives from bipolar families differ from those in unipolar relatives from families with major depression. We hypothesized that depressive episodes from unipolar subjects in bipolar pedigrees would more closely resemble depressive episodes seen in subjects with bipolar disorder when compared with depressive episodes of unipolar subjects in major depression pedigrees.

Methods: Using data from separate family studies of bipolar disorder and recurrent major depression, we compared clinical correlates and symptoms of a subject's most severe depressive episode in unipolar relatives from bipolar pedigrees (N=228) and in unipolar relatives from major depression pedigrees (N=686). Regression analysis was used to compare variables across both groups.

Results: Several symptom differences were found between unipolar subjects from bipolar pedigrees compared with unipolar subjects from major depression pedigrees. Unipolar relatives from bipolar families had greater odds of feeling incapacitated while depressed, while unipolar relatives from major depression families were more likely to have poor concentration, feelings of worthlessness, and passive death wishes. We found no evidence of differences in appetite changes, difficulty sleeping, or the presence of psychotic symptoms. Analyses of clinical correlates showed a greater likelihood of having alcoholism in unipolar relatives from bipolar families; unipolar relatives from major depression families had more anxiety disorders (panic and OCD), longer depressive episodes, and more frequent hospitalizations. We are currently performing more sophisticated modeling analyses to determine whether these differences can be diagnostically useful.

Conclusion: Our ongoing work suggests that there may be important phenotypic differences in cases with unipolar depression and a family history of bipolar disorder compared to cases with a family history of unipolar depression. These results may help to simplify the heterogeneous category of unipolar depression and may have potential diagnostic and treatment implications.

#53: Carol Li, MS2

Mentor: Martha A. Zeiger, MD

BRAF V600E Mutation and its Association with Clinico-pathologic Features in Patients with Papillary Thyroid Cancer: A Meta-analysis

Background: Since its discovery, BRAF V600E mutation has emerged as a promising prognostic indicator in patients with papillary thyroid cancer (PTC). However, existing literature is inconclusive regarding the association of BRAF mutation and aggressive clinico-pathologic features. Despite this, some propose that BRAF mutation status be incorporated in the risk stratification and management of PTC. This meta-analysis examines the relationship between BRAF V600E mutation and clinico-pathologic features in patients with PTC.

Methods: A systematic literature review was performed within PubMed and EMBASE databases using the following MeSH terms and keywords: “braf,” “mutation,” “thyroid,” “neoplasms,” “tumor,” “cancer,” and “carcinoma.” When multiple studies of the same patient population were published, only the most comprehensive study was included. BRAF status and clinico-pathologic data were extracted from each study. Individual study-specific odds ratios (OR) and confidence intervals (CI) were calculated, as were Mantel-Haenszel pooled odds ratios for the combined studies.

Results: The meta-analysis included thirty-one studies with a total of 6,271 patients. 3,156 (50.3%) patients had BRAF V600E positive PTCs. BRAF V600E mutation was associated with lymph node metastasis (LNM) (OR = 1.78; 95% CI: 1.57-2.02), stage (OR = 1.82; 95% CI: 1.58-2.10), extrathyroidal extension (OR=2.57 95% CI: 2.24-2.95), and tumor size (OR = 1.51; 95% CI: 1.25-1.83).

Conclusion: Based upon this meta-analysis, BRAF V600E mutation is associated with LNM, stage, the presence of extrathyroidal extension, and tumor size in patients with PTC. These associations indicate that BRAF mutation status is useful in the risk stratification of patients with PTC. However, the decision to base the management of PTC on BRAF mutation status is premature due to limitations in the existing literature. Thirty out of thirty-one studies were retrospectively analyzed and biased, as patients did not undergo routine central lymph node dissection. Prospective studies that address these limitations are needed before BRAF mutation status is used to determine management.

#54: Michael Lin, MS2

Mentor: Lawrence Cheskin, M.D.

Tailored Rapid Interactive Mobile Messaging (TRIMM) to Promote Weight Loss

Background: A challenge to achieving and sustaining lifestyle changes among obese, marginalized adults is the cost and intrusiveness of traditional interventions. Text messaging is a low-cost, widely-used technology shown to have potential for prompting behavioral change. We are conducting a randomized controlled trial (RCT) to assess the efficacy of a structured text messaging intervention to induce behavior changes that lead to weight loss.

Methods: We will recruit 150 African-American subjects from churches in Baltimore to participate in a 6-month RCT. Participants are randomized to one of two groups: (1) a traditional lifestyle change approach that involves an initial assessment and prescription with periodic follow-up; (2) the traditional approach enhanced by the TRIMM program of daily text messages tailored to the subjects' weight management challenges. The TRIMM intervention design is based on behavioral change theories and includes messages that are informational, motivational, and "cues to action." In addition, interactive "pull" messages promote accountability and self-monitoring by prompting the participants for their weight and quantifiable measures of healthy eating and exercise.

Results: Enrollment is ongoing and 14 participants have completed 5 weeks of the TRIMM trial. Through the "pull" messages, the group has self-reported mean (SD) weight loss of 2.92 (2.54) pounds after 5 weeks of daily text messages. All participants receive their first follow-up assessment at 3 months, after which we will have our first opportunity to compare weight loss between intervention and control groups.

Conclusion: Self-reported weights from participants randomized to the TRIMM intervention thus far indicate its potential for effectively inducing behavioral change. Although early in the RCT, we hypothesize that the TRIMM intervention will be a cost-effective method to facilitate behavioral change resulting in weight loss.

#55: Susan Lin, MS2
MSRD Poster Competitor

Mentor: Ming Hsien Wang, MD

Vesicoureteral reflux, urinary tract infections, labial adhesion and meatal stenosis are the most common causes of surgical intervention in children with urinary incontinence

Background: Urinary incontinence (UI) is common in childhood and the most frequent cause for referral to a pediatric urologist. Although UI can be behavioral in nature, it may also be associated with anatomical defects. Clinical distinction between behavioral and surgical cases is vital since treatment and management for these two etiologies are vastly different. Our objective was to assess the prevalence of behavioral versus anatomical etiologies, and to identify predictors of surgical intervention in children referred for incontinence.

Methods: We conducted a retrospective cohort study of children referred to the Johns Hopkins Pediatric Urology Clinic between 9/2009 and 6/2011 for UI (ICD code 788.30). Demographic characteristics, urologic history, treatment and outcome data were collected by chart review. Data were analyzed with the statistical software STATA© v10.

Results: Three hundred eleven children met inclusion criteria. The cohort was 75.9% non-Hispanic white, 12.9% African American, and 28.6% male. UI in 274 (88.1%) children was attributed to maladaptive behavioral patterns, including constipation and fecal impaction (n=249). The remaining 37 (11.9%) children required surgical interventions to fix anatomical defects detected during physical exam or on imaging studies. Anatomical causes of UI included meatal stenosis (20), vesicoureteral reflux (VUR, 9), circumcisions (4), labial adhesions (3), and hypospadias (1). We found that a diagnosis of VUR ($p<0.01$), meatal stenosis ($p<0.01$), labial adhesion ($p<0.01$), or urinary tract infections (UTI, $p=0.03$) predicted the need for surgical intervention. However, UTI was a significant predictor of surgery only in patients with simultaneous diagnosis of VUR ($p<0.01$).

Conclusion: In children referred for UI of unknown etiology, only a minority had associated anatomic malformations. Clinical findings of VUR, UTI, meatal stenosis and labial adhesion were most likely to be associated with the need for surgical intervention. The remaining cases, frequently related to poor bladder and bowel emptying, were more appropriately managed with conservative behavioral management.

#56: Timothy Markman, MS2

Mentor: Frederick Lenz, MD/PhD

Examination of functional cortical interactions during attention to and distraction from painful cutaneous laser stimuli

Background: The 'pain network' has previously been studied by EEG techniques focusing on the prestimulus interval or a fixed cognitive task. Our studies have demonstrated that the functional connectivity between somatosensory (S1), parasyllian (PS) and medial frontal (MF) cortex changes dynamically with tasks, such attention to the laser versus distraction from the laser. We now test a novel distraction task while identifying source activity specifically associated with attention and the increased perception of pain.

Methods: Scalp encephalogram (EEG) recordings were acquired from 16 health subjects when performing an attention task (counting laser stimuli) and a distraction task (counting non-nociceptive somatosensory stimuli). A total of 19 electrodes were placed according to the international 10-20 system. Continuous EEG recordings were segmented into 2.0 s epochs (-1.0 to +1.0 s relative to stimulus onset) and separate average event related potential (ERP) waveforms were computed for each subject and stimulus type. Subjects were asked to rate pain intensity, unpleasantness, and saliency of the nociceptive laser as well as unpleasantness and saliency of the somatosensory stimulus. Both stimuli were adjusted to produce the same baseline saliency rating.

Results: The attention task was associated with higher reported pain intensity ($P < .05$), unpleasantness ($P < .05$), and saliency ($P < .05$) as well as larger and longer latency N2-P2 LEP complexes ($P < 0.05$) relative to the distraction task.

In this study, the results from source analysis implicate MF and specifically identify midcingulate cortex generators of laser evoked potentials (LEP). [N.B. Preliminary results]

Conclusion: We validated the use a novel distraction task involving non-nociceptive somatosensory stimuli, permitting further direct comparisons between the processing of painful and salient non-painful stimuli. Additionally, the present results suggest the widespread functionally discrete subunits in MF subserve pain and attention, and therefore that MF areas may be an effective stimulation target for the treatment of pain.

#57: Joseph Molenda, MS2

Mentor: Judy Huang, M.D.

Dural Arteriovenous Fistulae at the Craniocervical Junction: A Systematic Review and Analysis of Clinical Features and Treatment Outcomes

Background: Dural arteriovenous fistulae (DAVF) are potentially life-threatening vascular abnormalities, but the presenting features and optimal treatment have not been established. The goals of this study were to characterize the clinical, radiological, treatment, and outcome data for DAVFs at the craniocervical junction, with specific comparison of embolization and microsurgery.

Methods: A retrospective chart review of 6 cases at Johns Hopkins Hospital was included into the analysis. For the analysis, a MEDLINE search was performed for all case reports of DAVFs at the craniocervical junction between 1970 and the present. Potential abstracts were reviewed by one of two reviewers. Overall demographics were calculated from these reports. These case reports were used to compare embolization and microsurgery, by evaluating success and failure rates, as well as functional outcome.

Results: A total of 48 articles were identified which included 109 cases of DAVF. The patients ranged in age from 35 to 78 years (mean 57.5 years) at the time of diagnosis, with men outnumbering women 79 to 29. The most common clinical presentations were SAH (42.2%) and myelopathy (35.8%). Surgery was used as the initial treatment in 67 cases (70%) while embolization was used as the initial treatment in 27 patients (28%). Definitive obliteration of the dural arteriovenous fistulae was achieved in 100% of patients treated with microsurgery, and 55.6% of patients treated initially with embolization. Embolization was described as “not possible” in 8 patients (safety concerns or not technically feasible). In 7 cases, surgery was utilized as a second treatment after embolization failure.

Conclusion: Microsurgery seems to be the best option to definitively treat DAVFs at the craniocervical junction due to the potential risk of recurrent fistulae with embolization, as well as embolization failure. Further prospective studies are needed to identify specific populations that may respond differently, as well as long-term risks of fistula recurrence with newer embolic agents such as ONYX.

#58: Shalini Moningi, MS2

Mentor: Stephanie Terezakis, MD

The Role of Adjuvant Therapy in the management of low-grade pediatric spinal cord tumors

Background: There is scarce literature on the management and treatment of low-grade spinal tumors; specifically those seen in children. The purpose of this study is to evaluate the outcomes of pediatric patients with low-grade spinal tumors and specifically address the role of adjuvant therapy in the management of this unique entity.

Methods: We conducted a retrospective chart review including 42 pediatric patients with WHO grade 1&2 spinal tumors treated at Johns Hopkins Kimmel Center between 1993-2010. The primary outcome was the local recurrence rate and secondary outcomes included overall survival, distant recurrence and disease free survival. Statistical analysis included univariate and multivariate analysis using the Cox proportional hazards and Kaplan-Meier models.

Results: Our patient population consisted of 27 males and 15 females; with a median age at diagnosis of 7.21 years (0.33–21.17) and a predominance of astrocytomas (64.28%). Astrocytoma patients had a lower median survival (35 months) compared to non-astrocytoma patients (68 months) and underwent more interventions; including chemotherapy, radiation therapy (RT) and/or surgical tumor removal. Astrocytoma patients receiving RT had a trend towards better progression free survival (PFS) compared to astrocytoma patients not receiving RT ($p=0.67$). Astrocytoma patients receiving chemotherapy had a 20% PFS at 5 years while astrocytoma patients who did not receive chemotherapy had a 54.26% 5 year PFS ($p=0.037$). Overall, low-grade patients receiving chemotherapy had an 18.18% PFS at 5 years while patients that did not receive chemotherapy had a 60.87% 5 year PFS ($p=0.0045$).

Conclusion: Pediatric low-grade spinal astrocytoma patients had a lower median survival compared to non-astrocytoma patients and adjuvant RT contributed to improvements in their PFS. Negative effect of chemotherapy on astrocytoma patients might reflect the overall poorer prognosis of patients who are referred for systemic treatment. Astrocytoma patients should be managed in a multi-disciplinary manner in order to offer the optimum combination of therapy.

#59: Amanda Morris, MS4
MSRD Poster Competitor

Mentor: Stephen Yang, MD

A comparison of patient outcomes after repeat and first-time thoracotomies

Background: To compare perioperative patient outcomes after repeat and first-time thoracotomies given that repeat thoracotomies may be more technically challenging because of tissue adhesions.

Methods: We performed a retrospective cohort study on patients, who were at least 18 years of age and had undergone repeat thoracotomy between 1994 and 2009 at the Johns Hopkins Hospital. Demographics, preoperative data, intraoperative data, as well as postoperative complications, ICU stay, and overall length of hospital stay were collected for both first and repeat thoracotomies.

Results: From a database of 5,124 patients, 60 (1.2%) were identified of having at least one repeat thoracotomy. Of these, 27 had information from both the first and repeat thoracotomies, which occurred during separate hospital admissions. Among these patients, mean age was 58 years at first thoracotomy and 60 years at repeat thoracotomy. For both thoracotomies, the most common surgical indication was lung metastasis (first-time = 48% versus repeat = 41%, $p = 0.58$). Preoperatively, mean percent of expected forced expiratory volume in one second was 91% at both time points. Intraoperatively, mean difference for estimated blood loss was 50 cc greater during repeat thoracotomy ($p < 0.0001$). There was no statistically significant difference in operative time, ($p > 0.05$). Mean length of hospital stay after repeat thoracotomy was 7 days, which was significantly 1 day longer than first-time thoracotomy, ($p = 0.05$). There was no statistically significant difference in ICU duration or complication incidence, (all $p > 0.05$).

Conclusion: Repeat thoracotomy appears to have similar perioperative patient outcomes as first-time thoracotomy with a mean length of hospital stay that is one day longer. These findings may help to reassure patients in need of repeat thoracotomy. Future work may address strategies during preoperative assessment to identify patient risk factors to further mitigate postoperative complications.

#60: Ashley Nieves, MS2

Mentor: Kate Puttgen MD

Surgical outcomes in infantile hemangiomas treated with corticosteroids, propranolol, or expectant management: a retrospective cohort analysis

Background: Infantile hemangiomas (IH) are the most common benign tumor of infancy, with females affected three times more frequently than males. The majority of IH do not need treatment, but a subset require medical and/or surgical intervention. Oral corticosteroids, the mainstay of treatment for 40 years, and propranolol, used since 2008, are options for first line medical management. It is not clear which treatment is superior, though many physicians have adopted propranolol. We examined outcomes in patients treated surgically to determine if there are differences based on treatment received.

Methods: We performed a retrospective cohort analysis of patients with IH who were treated surgically at Johns Hopkins Hospital by a single surgeon from 2004 to 2011. Demographic data, hemangioma characteristics, treatment course, and surgical data including number of surgeries and age at surgery were obtained. For a subset of patients with complete pre- and post-op photos, additional outcome analyses were performed. We used a validated measure of baseline severity and investigators rated the post-op outcome on a scale of 1-5, with 1 being excellent and 5 being unsatisfactory.

Results: We identified 113 patients that were treated surgically for 119 hemangiomas. The cohort was 80% white and 70% female with IH on the face in 52%. Eighty-two patients received no treatment, 21 received corticosteroids only, and 10 received propranolol. The mean age at first surgery was 34.8 months for patients treated with propranolol and 114 months for those not treated with corticosteroids or expectant management.

Conclusion: The earlier age at first surgery for patient treated with propranolol suggests that earlier involution induced by propranolol allowed earlier surgical intervention. Improving the cosmetic appearance of the patient's IH at an earlier age could have psychosocial benefits for the patient.

#61: Jason Norman, MS2

Mentor: Elliott Haut, MD

Prehospital Care, Scene Times, and Signs of Life: A Retrospective Study of Trauma Deaths

Background: Should EMS personnel do what they can to help a victim in need before arriving at the emergency department (stay and play), or should they focus on arriving to the ED as quickly as possible without many interventions (scoop and run)? This is heavily discussed in urban environments, where penetrative wounds occur in higher frequencies. More research needs to be done in order to analyze the benefits and consequences of each emergency tactics in regards to patient outcomes.

Methods: We conducted a descriptive study where we gathered data from deceased trauma patients from 2009-July 2011 (n=205). We collected demographics, transport/scene times, procedures done, mechanism/location/type of injury, signs of life, and autopsy reports of each patient. We analyzed the number of people with signs of life further to whether or not they had such signs at the scene, and if they had recovered or lost them at the ED.

Results: With n=130, 123 were male, 124 aged 50 or younger, with 68 of those 124 aged 25 or younger, 120 were African-American. 116 patients presented with gunshot wounds. 35 patients had signs of life in the field, 12 lost them prior to ED arrival, with 96% of the 35 less than 5 miles away. A scene time of less than ten minutes was associated with a higher probability of maintaining vital signs (94% vs. 35%, p=0.0009). Patients who lost vital signs were more likely to be intubated in the field, although this did not reach statistical significance.

Conclusion: Having signs of life when arriving at the ED may be a field of interest in outcomes research; if more people are arriving to the hospital with signs of life, this may be a benefit for their survival, as they may be able to get the proper care that a paramedic cannot be able to give.

#62: Dare Olatoye, MS2

Mentor: Michael Carducci, M.D

Stepwise examination of prostate cancer clinical trial participation.

Background: The decision to participate in a therapeutic clinical trial results from multiple stepwise patient and physician decisions beginning with trial availability and ending with enrollment. Opportunities for participation may be lost at any one of these steps. Our objective was to examine the association of race, distance from the cancer center, disease severity and age with each stepwise decision.

Methods: We conducted a retrospective cohort study of prostate cancer patients seen for initial consult visits by medical oncology in the Sidney Kimmel Comprehensive Cancer Center (SKCCC) from January to June 2010. Demographic and clinical data were obtained by chart review. The Clinical Research Office provided information about prostate cancer clinical trials enrolling during the study period. We examined 6 enrollment steps including trial availability, patient eligibility, trial discussed, patient interested, patient consent, and trial enrollment.

Results: 132 patients were included in the cohort. Of these, 92 (70%) had a trial available, 72 (55%) were eligible, 57 (43%) had a trial discussed with them, 27 (20%) showed interest, 15 (11%) consented, and 13 (10%) patients enrolled. Analysis by race showed that 8% of whites, and 29% of black patients enrolled ($p = 0.06$). Analysis by disease severity demonstrated that 8% of low-risk, 6% of mid-risk, and 14% of high-risk patients enrolled ($p = 0.40$). Analysis by distance from SKCCC showed that 11% of patients from Maryland and surrounding states and 4% of patients from outside this region enrolled ($p = 0.30$). Finally, 22% of patients aged (50-65), 6% of (66-70), and 4% of patients (>71) enrolled ($p = 0.04$).

Conclusion: The enrollment rate observed in prostate cancer trials at SKCC is low. The most significant drop occurred between physician discussing the trial and the patient showing interest. Adjustment for disease severity, age, and race did not alter these findings. Patient's race and age were significantly associated with enrollment.

#63: Ravi Pandit, MS3

Mentor: Michael Boland, MD PhD

Electronic Health Record (EHR) Deployment in Outpatient Ophthalmology

Background: As of 2008, the adoption rate of Electronic Health Records (EHR) in ophthalmology was less than 15%. To address concerns regarding EHR adoption, we conducted an evaluation of the impact of an EHR on a outpatient ophthalmology clinic.

Methods: We observed patient-physician encounters in a glaucoma clinic for 2-week periods immediately before (n=44), immediately after (n=50), and 6 months after (n=38) deployment of an EHR. An observer recorded electronically the time spent on various activities including talking to and examining the patient, reviewing paper records, and using the computer. Patients completed a survey about their perception of care and attitudes regarding EHR.

Results: Immediately after deployment, physicians spent more time on the computer (0.93 vs. 2.12 min, $p=0.001$) and talking while using the computer (1.43 min vs. 2.08 min, $p=0.04$). These increases remained statistically significant at 6 months. Despite the increase in time spent on the computer, time spent talking to and/or examining patients also increased by 6 months (6.41 vs. 5.06 min, $p=0.03$). Immediately after the transition, patients noted their physicians did not seem as comfortable with the EHR ($p=0.05$). However this effect disappeared by 6 months. At 6 months, patients were slightly more likely to agree that that EHR interfered with communication ($p = 0.04$).

Conclusion: The deployment of an EHR in a glaucoma practice resulted in both transient and permanent changes in the nature of the encounter. Some of these changes were expected – increased time spent on computer-related activities, while some were more concerning – slightly more agreement that the EHR interfered with communication. EHRs have the potential to alter elements of the physician-patient encounter. Given the political and financial imperative to “go digital,” more studies are needed explore these effects.

#64: Ju Park, MS2
MSRD Poster Competitor

Mentor: Ho-Young Song, MD

Benign Anastomotic Strictures after Esophagectomy: Long-term Effectiveness of Balloon Dilation and Factors Affecting Recurrence in 155 Patients

Background: Fluoroscopically guided balloon dilation has been regarded as a safe and effective treatment for anastomotic strictures of the upper gastrointestinal tract. However, the risk factors, prevalence, and clinical history of recurrent strictures have been poorly delineated. This retrospective study aimed to evaluate the long-term clinical results of balloon dilation for anastomotic strictures after esophagectomy and to identify factors associated with recurrence of strictures.

Methods: From January 1996 to June 2011, a total of 309 sessions of balloon dilation were performed in 155 patients with esophageal strictures after esophagectomy. Long-term clinical effectiveness was assessed using the following variables: technical and clinical success, complications, and patency rates. Technical success was defined as the full obliteration of stricture deformity without a complication. Clinical success was achieved if the patient did not report dysphagia until the last follow-up or death. Patency rates were evaluated with the Kaplan-Meier method. Factors related to recurrence were evaluated with the Cox multivariate analysis.

Results: The mean follow-up period was 37 months. Overall clinical success was achieved in 99% of patients after a single (n = 78) or multiple (n = 75) balloon dilations. During follow-up, stricture recurrence requiring repeated dilation was seen in 50% of patients. Esophageal rupture occurred in 14% of patients. The patency rates at 1, 3, 6 months and 5 years were 88%, 67%, 59%, and 43% respectively. In the multivariate analysis, early development of stricture within 10 weeks after surgery (OR, 2.39; 95% CI, 1.38-4.13) and McKeown esophagectomy (OR, 2.35; 95% CI, 1.38-4.01) were independently related to recurrence after initial balloon dilation.

Conclusion: Balloon dilation under fluoroscopic guidance has encouraging long-term results in the treatment of benign anastomotic strictures after esophagectomy. However, recurrence after balloon dilation was common, with McKeown esophagectomy and stricture development within 10 weeks after surgery associated with recurrent strictures.

#65: Janaki Paskaradevan, MS2
MSRD Poster Competitor

Mentor: Christopher L. Wu, M.D.

Analgesic efficacy of intravenous magnesium infusion: a systematic review and meta-analysis

Background: The efficacy of perioperative intravenous magnesium administration on postoperative opioid use, opioid-related side effects (e.g., nausea and vomiting) and pain are uncertain, as randomized controlled trials on this topic have reported disparate results.

Methods: An electronic search was conducted using the PubMed and EMBASE databases. Included studies were randomized controlled trials in an adult population that compared perioperative intravenous magnesium administration to a control with documented assessment of opioid usage and postoperative pain. The quality of each study was determined by calculating the Cochrane and Jadad scores. Pooled estimates for weighted mean difference (WMD) with 95% confidence intervals (CI) were obtained for our primary outcome (opioid usage) using the Cochrane Collaboration's RevMan version 5.0.25 (Cochrane Collaboration; Oxford, United Kingdom). WMD and odds ratios (OR) were calculated using a random effects model.

Results: The literature search ultimately yielded 23 trials, enrolling 1454 patients, to be included in the analysis. 749 patients were randomized to receive magnesium and 705 to control. A significant decrease in opioid usage by those patients who received magnesium was noted (WMD = -7.15; 95% CI: [-9.09 to -5.22], $p < 0.001$). Perioperative magnesium administration was not associated with a difference in postoperative nausea or vomiting (Odds Ratio = 0.95, 95% CI: [0.68 to 1.31]). The pooled visual analog scores for pain at 4-6 hours and 8-12 hours after surgery were significantly less in those patients who received magnesium (WMD = -0.63, [-0.97 to -0.28] and WMD = -0.70, [-1.17 to -0.24]); however, there was no difference in pain scores at 20-24 hours after surgery (WMD = -0.29, [-0.67 to 0.09]).

Conclusion: Perioperative intravenous magnesium may be a useful adjuvant for the management of postoperative pain, providing analgesia through a different mechanism than opioids. It may be a possible addition to multimodal analgesic treatment plans.

#66: Aymen Rashid, MS2

Mentor: Quan Dong Nguyen, M.D, M.Sc

Reliability and Reproducibility of Optical Coherence Tomography Images in Patients with Age-related Macular Degeneration

Background: Currently, several machines perform optical coherence tomography to follow retinal thickness (RT) and morphology in patients with age-related macular degeneration (AMD), with potentially different results. It is important to understand the impact of change in operator and machine on the accuracy and precision on RT values. We compare intra-observer reproducibility and inter-observer agreement of two Spectral-domain (SD-OCT) and one Time-domain (TD-OCT) device in patients with non-neovascular (NNV-AMD) and neovascular AMD (NV-AMD).

Methods: Fifty eyes of 36 patients at Wilmer Eye Institute were scanned using Spectralis® and Cirrus® SD-OCT, and Stratus® TD-OCT machines. The intra-class correlation coefficient (ICC), coefficient of repeatability (COR), and Bland Altman plots were calculated to determine reproducibility, repeatability, and agreement among machines, respectively. Spectralis® and Cirrus® automated algorithms were corrected manually. Paired t-tests were used to compare the retinal thickness before and after correction.

Results: ICCs were greater than 0.90 for all three machines. Mean (+SD) central 1mm foveal thickness (FTH) was 229+67, 343+119, and 277+94 μm for the Stratus®, Spectralis®, and Cirrus®, respectively. FTH values were significantly greater in NV-AMD, when compared to NNV-AMD ($p < .05$). Bland Altman plots gave the mean FTH difference before [after] correction of 52[55], 63[19], and 120[73] μm for Cirrus® vs. Stratus®, Spectralis® vs. Cirrus®, and Spectralis® vs. Stratus®, respectively. The COR before [after] correction was 18[20], 31[31], and 50[44] μm , for Spectralis®, Stratus®, and Cirrus® respectively. Neither Spectralis® nor Cirrus® had significantly different values before and after correction of boundaries.

Conclusion: Statistically insignificant differences in FTH measurements when correcting images suggests that manual correction for accuracy may not be necessary. ICC values indicate that readings are reliable when scanning a patient on the same machine. Spectralis® had the lowest COR and thus best repeatability. Different scanning technologies had large BA plot intervals, indicating they may not be used interchangeably when scanning a patient longitudinally.

#67: Mona Rezapour, MS4

Mentor: Philip Fleshner, MD

Prospective Evaluation of Risk Factors for Symptomatic Hemorrhoids

Background: While hemorrhoids are common in the general population, risk factors have not been well defined in the literature. We aim to prospectively assess risk factors which predispose to symptomatic hemorrhoids in a cohort of patients evaluated by colorectal surgeons.

Methods: A questionnaire encompassing over 80 factors possibly related to the development of hemorrhoids was completed by patients presenting with anal symptoms to the offices of five colorectal surgeons in an urban setting. The incidence of these risk factors in patients with symptomatic hemorrhoids was compared those without symptomatic hemorrhoids.

Results: Of the 907 patients studied, 646 (71%) were diagnosed with hemorrhoids. Univariate analysis revealed a statistically significant difference between the hemorrhoid and control group in percentage of individuals over 40 years of age (63% vs 55%, $p=0.02$), income greater than \$100,000 per year (50% vs 39%, $p=0.01$), individuals with a Bachelors degree or higher (78% vs 71%, $p=0.02$), family history of hemorrhoids (73% vs 63%, $p=0.04$), moderate or high intake of spicy food (41% vs 31%, $p=0.006$), consumption of 2 or more cups of tea or coffee daily (34% vs 27%, $p=0.04$), one or more episodes of diarrhea weekly (16% vs 25%, $p=0.003$), rushing to toilet with urgency to defecate (24% vs 35%, $p=0.001$), exertion on the toilet (17% vs 12%, $p=0.04$), and pain upon defecation (12% vs 19%, $p=0.02$). On multivariate analysis, the only statistically significant differences were in the percentage of individuals with family history of hemorrhoids ($p=0.01$; OR=2.0, 95%CI=1.2-3.3), and income over \$100,000 per year ($p=0.02$; OR=1.9; 95%CI=1.1-3.2).

Conclusion: This first reported prospective study of patients examined by colorectal surgeons revealed both family history and income greater than \$100,000 per year were independently associated with symptomatic hemorrhoids.

#68: Danielle Rochlin, MS2

Mentor: Julie A. Freischlag, MD

Improvement Following Surgical Intervention for Neurogenic Thoracic Outlet Syndrome is Sustained Over Time

Background: First rib resection and scalenectomy (FRRS) is standard treatment for neurogenic thoracic outlet syndrome (NTOS) that is refractive to physical therapy, where scalene block is used to identify surgical candidates. Previous investigation indicates that quality of life (QOL) improves within two postoperative years, as SF-12 physical and mental component scores (PCS and MCS, respectively) increased over preoperative baseline values. Long-term results are not well studied, though benefits are believed to decrease over time. Our objective was to characterize long-term NTOS outcomes using validated QOL instruments.

Methods: We mailed three surveys [SF-12, Brief Pain Inventory (BPI), Cervical Brachial Symptom Questionnaire (CBSQ)] to 162 NTOS patients aged ≥ 18 treated by FRRS at Johns Hopkins Hospital from 2003-2010. Demographic and clinical data was extracted from medical records, and each FRRS was categorized based on clinical assessment of postoperative course. Analysis of variance and linear regression were used to test associations of variables with survey scores.

Results: Survey yield was 51% (n=83) with a mean 42.8 months follow-up (range 9.8-91.9). Despite no overall trend in QOL with time, there were differences in SF-12 PCS across yearly postoperative intervals ($p=0.0001$) with all mean SF-12 scores above published baseline. Poorer scores on all instruments were associated with comorbid chronic pain and/or neck/shoulder injury, preoperative narcotic use, and clinical assessment ($p<0.05$). Poorer scores on select instruments were associated with smoking (MCS, BPI $p<0.04$), postoperative injections (BPI, CBSQ $p<0.05$), and complications (PCS $p<0.01$). Scalene block exhibited no significant association with most scores.

Conclusion: QOL following FRRS varies over time, but on average represents a sustained improvement over published baseline. Clinical assessment reflects patient-reported outcomes, and can serve as a surrogate method of evaluating improvement. Patient factors, particularly comorbidities, narcotic use, and smoking, are more predictive of long-term scores than scalene block, and should be considered when selecting patients for surgical intervention.

#69: Robert Same, MS2
MSRD Poster Competitor

Mentor: Arik Marcell, M.D. MPH

Young Men's Interest and Experience with Sexual & Reproductive Health Services

Background: Preventing unintended pregnancy is a public health priority for young persons. Men play a significant role in reproductive healthcare decision-making including pregnancy and sexually transmitted infection (STI) prevention but few studies examine males' sexual/reproductive health (SRH) needs and care receipt.

Methods: Cross-sectional survey was conducted among 177 males aged 16-35 from clinics in Baltimore to examine SRH needs and care receipt. Participants were asked about 11 SRH needs, provider preferences to discuss, and past discussions with a provider about each need; SRH issues included STIs, vaccines, condoms, female methods, emergency contraception (EC), sexual function, infertility, fatherhood, relationships, cancer, and acne. We conducted bivariate and multivariate regression analyses.

Results: Participants reported a mean of 1.20 SRH needs (standard deviation=1.60) with most cited needs including STIs (23.7%), testicular cancer (18.1%), and fatherhood (17.5%). Participants reported 3.22 (SD=3.20) past provider SRH discussions with majority reporting discussions about decreasing STI risk (57.1%) but <50% reporting discussions on any other SRH topics. However, participants reported wanting their provider to bring up 6.77 (3.42) SRH topics with majority wanting their provider to bring up STIs (83.1%), testicular cancer (78.0%), and HPV vaccine (72.9%) followed by EC (69.5%), condom use (66.1%), female methods (60.5%), and acne (57.1%). Wanting provider discussions on more SRH topics was associated with greater numbers of past provider SRH discussions (Beta=.24, p=.004) and age with 20-24 year olds more likely to endorse more SRH topics than 16-19 year olds (Beta=1.91, p=.012), after controlling for participants' background characteristics.

Conclusion: Despite low proportions of young males self-reporting SRH needs, the majority had a strong preference that healthcare providers should bring up these topics which was associated with past provider discussions on these topics. Future work is needed to raise males' awareness of SRH issues and providers' delivery of these services.

#70: Claire Sampankanpanich, MS2

Mentor: Barrie Cassileth, Ph.D

Lymphedema may be treatable at early and later stages with acupuncture therapy: a pilot study.

Background: Lymphedema is a chronic condition that impacts many women who are treated for breast cancer and leads to significantly decreased quality of life, recurrent infections, pain, and decreased limb function. Our clinical experience suggests that acupuncture may be a useful treatment for lymphedema. This study was undertaken to determine (1) whether earlier acupuncture treatment leads to better clinical outcomes and (2) whether improvement varies with body mass index (BMI) and/or time since diagnosis of lymphedema.

Methods: In 2011, the Integrative Medicine Service conducted an IRB-approved pilot study of acupuncture treatment for chronic lymphedema in 33 female breast cancer survivors. The pilot study database was queried and Spearman's rank correlation applied to compare relative percent decrease in arm circumference of the affected limb to (1) initial BMI prior to start of acupuncture treatment, (2) time between surgery and start of acupuncture treatment, and (3) time between lymphedema diagnosis and start of acupuncture treatment.

Results: 11 of the 33 patients showed a significant response of >30% decrease in arm circumference of affected versus unaffected limb. Significant responders had a lower median initial BMI (30.59 vs. 26.78), average time since surgery (62 vs. 42 months), and median duration of lymphedema (31 vs. 21 months). Using Spearman's rank correlation, we failed to find a statistically significant correlation between relative percent decrease in arm circumference and initial BMI ($r = 0.182$, $p = 0.31$); time between surgery and start of treatment ($r = 0.253$, $p = 0.16$), or time between lymphedema diagnosis and start of acupuncture treatment ($r = 0.148$, $p = 0.43$).

Conclusion: Initial research suggests that acupuncture is a safe and effective treatment for lymphedema. Initial BMI and lymphedema chronicity do not seem to influence the effectiveness of acupuncture in treating lymphedema. This pilot study suggests that acupuncture may effectively treat both early and longer-term lymphedema.

#71: Patrick Sayre, MS2

Mentor: Kelly Dooley, M.D., Ph.D

Effect of rifampin and rifabutin on the pharmacokinetics of the next generation HIV integrase inhibitor, dolutegravir

Background: Dolutegravir (DTG) is an investigational HIV integrase inhibitor. Among HIV-infected individuals, tuberculosis is the leading cause of death. Rifamycins are the cornerstone of antitubercular therapy and potent inducers of metabolic enzymes, including those that metabolize DTG. Increasing the dose of DTG may overcome the reduction in DTG concentrations by rifamycins.

Methods: This study is a phase 1, open label, two arm, fixed sequence crossover study involving healthy volunteers. In arm 1, subjects received DTG 50 mg daily for 7 days, DTG 50 mg twice-daily for 7 days, then DTG 50 mg twice-daily with rifampin 600 mg daily for 14 days. In arm 2, subjects received DTG 50 mg daily for 7 days, then DTG 50 mg daily with rifabutin 300 mg daily for 14 days. Plasma pharmacokinetic sampling was performed at the end of each dosing period. Plasma DTG concentrations were quantified using LC-MS/MS. Pharmacokinetic analysis was performed using a non-compartmental model. Geometric least squares mean ratios (GMR) were used for treatment comparisons.

Results: In arm 1, 12 subjects were enrolled and 11 completed. Median age and weight were 49 years and 79 kg, respectively. 67% were African-American. 17% were women. Comparing DTG twice-daily with rifampin to DTG once-daily alone, the GMR for the 24-hour area under the time-concentration curve (AUC₀₋₂₄) was 1.33 (90% CI 1.14 to 1.54), for the maximum concentration of DTG (C_{max}) was 1.20 (1.04 to 1.38), and for the trough at the end of the dosing interval (C_T) was 1.22 (1.01 to 1.47). There were no grade 3 or higher adverse events (AE) and no discontinuations for AEs. Arm 2 is ongoing.

Conclusion: DTG given twice daily with rifampin was well tolerated and yielded similar plasma DTG concentrations to DTG once daily alone. DTG may represent an important option for concomitant treatment of HIV and TB.

#72: James Schroeder, PhD, MS2

Mentor: William Baumgartner, MD

MELD Score Predicts Mortality Following Orthotopic Heart Transplant

Background: The Model for End-Stage Liver Disease (MELD) score predicts morbidity and mortality after many surgeries. Orthotopic heart transplant (OHT) candidates often have congestive liver dysfunction and elevated MELD scores. While optimal candidate selection is important, existing risk models do not utilize MELD score.

Methods: MELD score was calculated for patients receiving single-organ OHT at Johns Hopkins Hospital 1996-2011 (n=258). The primary outcome was 1-year survival; secondary outcome was perioperative blood product utilization. Kaplan-Meier survival analysis was performed per quartile of MELD score. Univariate and multivariate Cox proportional hazard regression models were created comparing MELD to other risk factors previously shown to predict OHT mortality. The predictive power of MELD score was compared with two OHT-specific composite risk scores, the IMPACT score and Risk Stratification Score (RSS).

Results: MELD score was highly predictive of 1-year mortality and showed equivalent predictive power to IMPACT and RSS. By Kaplan-Meier analysis, 1-year survival was significantly lower in patients with highest-quartile MELD scores, 57.8% (44.8-68.8%) compared to patients with lower-quartile MELD scores, 87.9% (82.3-91.8%; $p < 0.0001$). Patients in the highest MELD quartile also required more units of perioperative fresh frozen plasma and red blood cells ($p < 0.001$). By multivariate and univariate regression models, each point of MELD increased mortality hazard by 21 and 22%, respectively (both $p < 0.001$).

Conclusion: Preoperative MELD score should be considered in prospective OHT recipients to assist in clinical decision making. Patient preoperative lab data needed to calculate MELD score should be collected in national databases so future OHT composite risk models may incorporate MELD score.

#73: Brett Shannon, MS2

Mentor: Simon Mears, M.D., Ph.D.

Relationship between long-term bisphosphonate therapy and cortical thickness of the proximal femur

Background: Growing evidence suggests that treatment with bisphosphonates is associated with an increased risk for subtrochanteric and atypical femoral shaft fractures. Current management includes “drug holidays” to minimize the risk of subtrochanteric fracture. One radiographic feature noted in patients who experience bisphosphonate-related subtrochanteric fractures is hypertrophied diaphyseal cortices. The relationship between long-term bisphosphonate therapy and hypertrophied diaphyseal cortices is not yet clear, but cortical hypertrophy may be an early sign of alterations in bone remodeling that predispose to subtrochanteric fracture.

Methods: We retrospectively evaluated cortical thickness ratio (ratio of cortical to femoral shaft diameter) in the subtrochanteric proximal femur as measured by dual-energy x-ray absorptiometry in 141 patients. Patients were divided into two groups: unexposed (no history of bisphosphonates, 91 patients) and exposed (history of bisphosphonate \geq 5 years, 50 patients). Cortical thickness ratio was measured at the lower limit of the total femur bone density region. T-tests and multivariate linear regression were used to compare groups.

Results: The cortical thickness ratio (mean \pm standard deviation) was 0.48 ± 0.06 in unexposed patients and 0.46 ± 0.06 in exposed patients ($p=0.1$). In multiple linear regression, younger age ($p<0.04$) and higher bone mineral density scores ($p<0.0001$) were associated with increased cortical thickness ratios. Among those exposed to bisphosphonates, a history of interruption in therapy was associated with a 10% increase in cortical thickness ratio ($p<0.05$).

Conclusion: We found that there was no significant difference in cortical thickness ratio between patients treated with bisphosphonates \geq 5 years and those with no history of bisphosphonate treatment. However, the association between interruption of bisphosphonate therapy and increased cortical thickness ratio suggests that “drug holidays” may not be beneficial to patients. Further investigation is needed to understand the relationship between long-term bisphosphonate therapy, cortical thickening, and subtrochanteric fractures.

#74: Sonal Sodha, MS2

Mentor: Edward McFarland, MD

Clinical Significance of the Gagey Sign for Examination of the Shoulder

Background: A “Gagey sign” or hyperabduction test (an assessment of the range of passive abduction) of greater than 105 degrees was originally proposed to be diagnostic of multidirectional instability (MDI). However, since its description by Gagey and subsequent popularity as a test for examining shoulder instability, the Gagey sign has not been rigorously studied for its clinical utility. The purpose of this study was to examine the clinical significance of the Gagey sign for a variety of pathologic shoulder diagnoses, especially MDI.

Methods: We retrospectively reviewed medical records of 922 patients who were preoperatively examined using the Gagey sign at a Johns Hopkins orthopedic clinic from 2005-2011. We used statistical analysis of variance to correlate the Gagey sign to diagnoses of osteoarthritis, rotator cuff tears, and instability.

Results: In our cohort of patients, the Gagey sign was rarely found to be positive, with only 2 of 922 patients (0.2%) testing positive with greater than 105 degrees in the involved shoulder. Of the patients with MDI (n=7), the Gagey sign was positive in 1 patient (14.3%). The average Gagey sign for a diagnosis of osteoarthritis was 44.1 degrees (range 0-90), for cuff tears was 62.3 degrees (range 0-95), and for instability of any type was 71.0 degrees (range 35-110). For MDI in particular, the average Gagey sign was 79.3 degrees (range 45-110). Our analysis suggests that a more clinically useful indicator of MDI is a Gagey sign greater than 75 degrees, with a sensitivity of 85.7% and specificity of 81.5%.

Conclusion: On average, the Gagey sign is lower in patients with osteoarthritis and higher in patients with MDI as compared to other diagnoses. Although we rarely found the Gagey sign to be positive, it may have better clinical utility for multidirectional instability if the criterion for a positive test is greater than 75 degrees.

#75: Amar Srivastava, MS2
MSRD Poster Competitor

Mentor: Duvuru Geetha, M.D.

Comparisons of features of double-positive disease with anti-GBM disease and ANCA-associated vasculitides

Background: ANCA-associated vasculitides (AAV) and anti-glomerular basement membrane (GBM) disease are two causes of rapidly-progressive glomerulonephritis (RPGN) with distinct laboratory markers and clinical outcomes. However, a rare cohort of patients exhibits markers of both diseases and suffers from “double positive disease.” Clinical features of these patients are disputed, and while studies suggest double-positive patients resemble anti-GBM patients and fare worse than AAV patients, no U.S. cohort has been studied. Therefore, the purpose of this study was to describe the clinical and laboratory features of patients with double-positive disease in the U.S., and compare these characteristics to patients with either anti-GBM-disease or AAV.

Methods: We performed a retrospective cohort study using the Johns Hopkins Hospital/Bayview Medical Center biopsy database. We identified cases of RPGN with crescentic glomerulonephritis on light microscopy and pauci-immune or linear-IgG immunofluorescence staining. Serologies were used to classify patients as ANCA only (c-ANCA or p-ANCA positive), anti-GBM positive only, or double-positive. We compared clinical and laboratory features and outcomes for these patients by serologic classification group.

Results: At presentation, the mean ages of the ANCA (n=20), anti-GBM (n=7), and double positive (n=10) groups, respectively, were 55 ± 3.3 , 54 ± 6.7 , and 57 ± 3.8 years ($P=0.32$). At biopsy, renal involvement was present in 95%, 86%, and 90% ($P<0.01$) of patients by group. Lung involvement was observed in 35%, 71%, and 60% ($P<0.01$) of patients, respectively. Concurrently, mean MDRD glomerular filtration rates were 30 ± 4.6 , 6 ± 0.8 , and 8 ± 2.7 ml/min/1.73m² ($P<0.01$). When these patients were followed up, recovery of renal function was seen in 80%, 28%, and 30% of patients ($P<0.01$), respectively, and patient survival at 24 months was found to be 70%, 60%, and 70% ($P=0.05$).

Conclusion: U.S. patients with double positive disease were found to demonstrate clinical features and laboratory values comparable to patients with anti-GBM disease alone, and less severe than those with AAV.

#76: Erika Tanaka, MS2

Mentor: Jennifer Thorne, Ph.D, M.D.

Analysis of Diagnostic Evaluations and Outcomes in Birdshot Chorioretinitis (BSCR)

Background: Birdshot Chorioretinitis (BSCR) is a chronic posterior uveitis with a remitting and relapsing clinical course. Patients often suffer from significant loss of visual function over time, though central visual acuity may be spared initially. Immunosuppressive treatments have shown favorable clinical outcomes. However, the ideal time to start treatment is not always clear. Therefore, there is a need for testing that is correlated with visual outcomes, reproducible, and non-invasive that can be used for monitoring disease progression and to guide treatment decisions.

Methods: We conducted a retrospective, cross-sectional analysis of patients with bilateral BSCR. Data were collected by chart review on the following tests: optical coherence tomography, fluorescein angiography, color fundus photography, color vision, contrast sensitivity, Goldmann visual field, and Humphrey visual field. We also collected corresponding visit data on the patients' visual acuity and clinical assessment of disease activity.

Results: Twenty-eight patients (56 eyes) were included in the analysis. Nearly 36% were male, 100% Caucasian, and median (IQR) age was 54 (37,76) years. We analyzed results from 128 optical coherence tomography tests, 124 fluorescein angiography tests, 128 color fundus photographs, 173 color vision tests, 18 contrast sensitivity tests, 193 Goldmann visual fields, and 98 Humphrey visual fields.

Conclusion: Conclusions will be drawn upon completion of statistical analysis.

#77: George Tang, MS2

Mentor: Stephen Yang, MD

Does Neoadjuvant Treatment Site Matter? Pathologic Response and Overall Survival Rates Following Esophageal Cancer Resection are Independent of the Treatment Center

Background: To evaluate whether there is a difference in rates of complete pathologic response (pCR) and overall survival between patients who underwent induction chemoradiation therapy at Johns Hopkins Hospital (JHH, a large academic institution) and those who were treated at an outside treatment center prior to esophageal cancer resection at JHH.

Methods: A retrospective analysis of a prospectively kept database was performed on all patients who underwent esophageal cancer resection between 1989 and 2009 at JHH after completing induction chemoradiation treatment either at JHH or at an outside treatment center. We compared our two groups of patients based on their neoadjuvant treatment center, JHH or outside.

Results: A total of 349 esophageal cancer patients were evaluated, 240 of which received neoadjuvant treatment at JHH while 109 received treatment at an outside treatment center. Patients treated at outside centers tended to be younger and female compared to JHH. There were no significant differences between the two groups by chemotherapy regimen, radiation dosage, tumor location, esophagectomy type, tumor histology, pre-neoadjuvant clinical stage, ASA scores, race, or smoking status. The unadjusted pCR rates for the JHH and outside groups were 29.6% and 29.4%, respectively. Multivariable logistic regression model, adjusting for chemotherapy regimen, radiation dosage, esophagectomy type, tumor histology, pre-neoadjuvant stage, age, sex, race, and smoking status, found no association with pathologic response by neoadjuvant treatment institution (aOR=1.06, 95%CI 0.55-2.06). Furthermore, Kaplan-Meier survival analysis showed there was no significant difference in survival between our JHH group and outside group (log rank p=0.897).

Conclusion: For patients undergoing esophageal cancer resection at JHH, receiving induction chemoradiation therapy at JHH versus at an outside treatment center does not improve odds of achieving a pathologic complete response or overall survival. These data are helpful to patients in determining where to get their neoadjuvant therapy for locally advanced esophageal cancer. Although it is highly encouraged that multimodality therapy be performed in a clinical trial, patients often opt to have neoadjuvant treatments outside the surgical institution due to practical and logistical purposes.

#78: Linnan Tang, MS2

Mentor: Sean Berenholtz, MD

ICU Alcohol Withdrawal Syndrome Treatment is Highly Variable at JHH

Background: Nearly 7% of US adults are heavy drinkers, with 10% of academic hospital patients affected by alcohol use disorder. Alcohol withdrawal syndromes(AWS) present with symptoms ranging from autonomic disturbance to delirium and possible death. AWS as a comorbidity is generally treated at the discretion of individual physicians rather than based on standardized protocols. Our objective was to identify the spectrum of AWS evaluation and treatment at Johns Hopkins Hospital(JHH).

Methods: We performed a cross-sectional study of patients at risk of AWS identified by physicians in 7 ICUs at JHH from May 2011 to August 2011. A daily phone survey of ICUs collects patient IDs. Demographic and clinical information, including AWS screening, treatment, and outcomes, were obtained from the electronic medical record(EMR) by chart review.

Results: Twenty-six patients were analyzed. The cohort was 92% male, mean(SD) age 55.1(10.7) years, and 46% African-American. Seventy-seven percent of patient records contained data on daily-drinking-amount, 50% documented time of last drink before admission, and 50% documented blood alcohol level at admission. One record contained Clinical Institute Withdrawal Assessment of Alcohol Scale score. Daily dose of lorazepam ranged from 0.5 to 500 mg; midazolam 1 to 575 mg; chlordiazepoxide 10 to 400 mg. One patient was offered an alcoholic beverage. The overall mean(SD) ICU length of stay (LOS) was 6.6(5.8) days and hospital LOS 12.6(8.9) days. Fifty-percent of patients required restraint for > 2 days. Thirteen-percent of patient-days demonstrated maximum Richmond Agitation Sedation Scale < -1, and 17.5% of the patient-days were delirium positive by Confusion Assessment Method for the ICU.

Conclusion: The assessment and treatment of AWS-prone patients is highly variable within JHH. It would be feasible to systematically evaluate the care of these patients using the EMR at JHH. This survey supports the ongoing effort of implementing an institutional standard protocol for treating AWS.

#79: Ye Tao, MS2

Mentor: Duke Cameron, MD

Risk factors for permanent pacemaker implantation after AVR

Background: Recent studies suggest that trans-catheter aortic valve replacement (TAVR) is a safe technique for aortic valve replacement (AVR) in patients who are high risk candidates for surgical repair of aortic stenosis. Currently, there are multiple prostheses under investigation, including the Edwards-Sapien and Core-Valve devices. Both TAVR and surgical AVR are associated with post-operative arrhythmias that require the implantation of a permanent pacemaker (PPM). Our study examines the incidence of and risk factors for PPM requirement after AVR. In addition we used the exclusion criteria of the CoreValve trial to create a benchmark rate of PPM requirement.

Methods: We conducted a retrospective cohort study of 1,491 patients who received an AVR at JHH from Jan 2001 to Dec 2010 to evaluate the frequency of post-operative PPM implantation. Multivariable logistic regression models were constructed to identify risk factors for PPM implantation.

Results: The overall rate of PPM implantation was 4.02%. There was no difference in 1-year survival between patients who received a PPM and those who did not (83% vs. 88%, $p=0.30$). Concomitant mitral valve (OR 2.46, 95% CI 1.06-5.74, $p=0.04$) and concomitant mitral and tricuspid valve (OR 3.67, 95% CI 1.19-11.29, $p=0.02$) intervention, first degree heart block (OR 2.30, CI 1.28-4.13, $p=0.005$), Right Bundle Branch Block/Left Bundle Branch Block/Bifascicular Block (OR 2.10 CI 1.12-3.95, $p=0.02$), and chronic lung disease (OR 2.06, CI 0.80-5.00, $p=0.03$) were associated with increased risk of PPM requirement. Among the subset of high-risk patients matched to the CoreValve trial criteria, the rate of PPM was 4.51%, which was not significantly different from the entire cohort (4.02%)

Conclusion: Multiple valve operations are associated with increased risk for post-operative PPM. The strongest predictor for PPM is pre-existing conduction system disease. In addition, we found a rate of 4.5% for post-operative PPM implantation for our cohort of high risk patients which is similar to the overall rate. This should serve as a benchmark rate for the CoreValve trial.

#80: Kanika Trehan, MS2

Mentor: Stephen C. Yang, M.D.

Increased/Decreased Smoking Recidivism after Minimally Invasive Surgery for Lung Cancer

Background: Lung resection remains the gold standard of treatment for patients with lung cancer, however the 5-year survival rate is only 60%. Part of this may be attributed to high rates of post-operative smoking; 55% of lung cancer patients who undergo the traditional open lung resection are expected to return to smoking within 2 years. The purpose of this study was to examine the smoking recidivism rate in lung cancer patients undergoing minimally invasive lung resection through video-assisted thoracic surgery (VATS) and to compare that data to smoking recidivism after open thoracotomy resection. We hypothesize that those patients who undergo open thoracotomy will be more discouraged from smoking and therefore will have lower rates of post-operative smoking recidivism due to an expected lower quality of life.

Methods: We conducted a retrospective cross-sectional analysis of 193 patients, all of whom underwent lung resection at Johns Hopkins, were confirmed to have stage IA-III B non-small cell lung cancer (NSCLC), and had a prior history of smoking. Patients were categorized as either having undergone VATS or thoracotomy procedures. Patients will be administered a questionnaire in clinic asking about smoking practices at various time periods, including (1) before meeting with the thoracic surgeon, (2) after meeting a thoracic surgeon but before surgery, (3) 1 month after surgery, (4) 6 months after surgery, and (5) at the current point in time. Information on quality of life will also be collected.

#81: Suzanne van Landingham, MS3

Mentor: Pradeep Ramulu, MD, PhD

Driving Cessation, Driving Restriction, and Driver Preference in Older Adults with Glaucoma

Background: To determine if glaucoma is associated with driving limitation, driving cessation, or driver preference.

Methods: Subjects reported their driving habits via questionnaires. Glaucoma status and severity were defined by chart review and visual field (VF) results.

Results: Driving cessation was noted in 23% of glaucoma subjects and 6.9% of controls ($P=0.01$), and glaucoma subjects had more driving restrictions (2.0 vs. 1.1, $P=0.007$). In multivariable models, driving cessation was more likely amongst glaucoma subjects as compared to controls ($OR=4.0$; 95% $CI=1.1-14.7$; $P=0.03$), and the odds of driving cessation doubled with each 5 decibel (dB) decrement in the better-eye VF ($OR=2.0$; 95% $CI=1.4-2.9$; $P<0.001$). Glaucoma subjects were more likely to report a greater number of driving restrictions ($OR=4.7$; 95% $CI=1.3-16.8$; $P=0.02$), and the likelihood of reporting more restrictions increased with the VF loss severity ($OR=1.6 / 5$ dB decrement in the better-eye VF; 95% $CI=1.1-2.4$; $P=0.02$). Specific restrictions reported more frequently in glaucoma subjects as compared to controls included avoidance of night driving ($OR=5.5$; 95% $CI=1.6-18.7$; $P=0.006$) and avoidance of driving beyond a four-state geographic region ($OR=3.2$; 95% $CI=1.3-7.8$; $P=0.01$). Neither glaucoma nor glaucoma severity was associated with driver preference ($P>0.05$ for all).

Conclusion: Glaucoma is associated with more frequent driving cessation and greater restriction of driving in the elderly, and driving becomes more limited with worsening VF loss. Given the importance of driving for independence and mobility, these data indicate that glaucoma may have a substantial impact on mobility in aging populations.

#82: Kipp Voth, MS2

Mentor: Dr. Mohamad Allaf

Rates of Abdominal Imaging and Complications Following Transperitoneal and Extraperitoneal Prostatectomy

Background: Multiple approaches to radical prostatectomy (RP) exist; traditionally, extraperitoneal (EP) radical retropubic prostatectomy (RRP) has been the gold standard surgical treatment for prostate cancer. In recent years, there has been a paradigm shift toward minimally invasive surgery. However, few studies have compared the short term (<30days) complications among open and minimally invasive surgery techniques and even fewer have compared the results of EP and transperitoneal (TP) prostatectomy. In order to investigate peri-operative morbidity associated with surgical approach we compare transperitoneal (TP) robotic-assisted laparoscopic RP (RALRP), RRP, and EP laparoscopic RP (LRP).

Methods: The Johns Hopkins RP Database (1982-2011) was queried for a recent cohort of consecutive patients undergoing RP, including 501 RALRP, 500 RRP, and 226 contemporaneous LRP patients. Abdominal imaging studies performed within 30 days of surgery, including plain radiography (AXR) and computed tomography (CT), were evaluated. The indications, findings, interventions associated with each imaging study, and overall complications within 30 days of RP were analyzed.

Results: A total of 64 CT and 125 AXR were obtained in 71 patients (5.8%). The rate of imaging was 3.4%, 9.3% and 3.5% for RRP, RALRP and LRP respectively ($p<0.001$). On average, the first imaging study was obtained 6.4 (range 0-28) days from surgery. Common findings on imaging following RALRP were ileus (19, 3.8%) and anastamotic leak (13, 2.6%). Rates of radiographic ileus ($p=0.03$) and anastamotic leak ($p=0.03$) were greater for RALRP than RRP and LRP. Overall 30-day complication rate was 7.3%; 7.8%, 8.8% and 2.7% for RRP, RALRP and LRP respectively ($p=0.01$).

Conclusion: Abdominal imaging rates following RALRP were greater than RRP or LRP. The profile of post-operative morbidity was different based on surgical modality. The majority of abdominal imaging findings and complications following transperitoneal radical prostatectomy were consistent with anastamotic leak and ileus.

#83: Katie Washington, MS3

Mentor: Kelly Gebo, MD, MPH

Demographic and Clinical Outcomes are Different in Transgendered Persons Living with HIV

Background: Gender identity may affect the quality of healthcare received by patients infected with HIV. Few sites have had enough transgendered patients to do comprehensive analyses. This study evaluated whether clinical outcomes and health care utilization within the multisite HIV Research Network differed in male, female and transgender PLWH.

Methods: Clinical and demographic characteristics, inpatient and outpatient utilization, AIDS defining illness rates, receipt of highly active antiretroviral therapy (HAART), opportunistic infection (OI) prophylaxis usage and virologic suppression were compared among patients, using patients followed at 11 sites within the HIV Research Network in 2010 stratified by self reported gender (male/female/transgender). Chi square was performed

Results: Among 19,841 patients in the HIVRN in 2010, 0.7% were transgender, 69.7% male, 29.6% female. Transgender patients were significantly younger (median 41; range 20, 62) than females (44; range 16,83) or males (45; range 16,91) ($p < 0.001$). Transgender patients had significantly higher use of HAART, more frequent use of outpatient and inpatient care, and more frequent mental health visits compared to males and females; however self-reported gender identity did not affect the OI prophylaxis rates, incidence of AIDS defining illnesses, or length of inpatient stay.

Conclusion: Transgendered patients had higher rates of HAART utilization and health resource utilization than other PLWH. In this cohort, transgender identity did not have a negative impact on the quality of care, once engaged within an HIV care system. However, it is possible that significant barriers to entry exist for this population and improved measures should be taken to improve recruitment retention into care.

#84: Aaron Wild, MS3
MSRD Poster Competitor

Mentor: Joseph Herman, M.D., M.Sc.

Effect of chemoradiation-related lymphopenia on survival in patients with unresectable, locally advanced pancreatic adenocarcinoma

Background: Pancreatic ductal adenocarcinoma (PDA) has been shown to elicit antitumor cell-mediated immune responses. In high grade gliomas, treatment-related lymphopenia has been associated with shorter survival. This study was performed to determine if patients with locally advanced PDA treated with definitive chemoradiation therapy (CRT) develop significant lymphopenia and if this affects overall survival (OS).

Methods: Retrospective analysis of patients with locally advanced PDA treated at a single institution with CRT from 1997-2009 was performed. Serial lymphocyte counts were recorded and OS was analyzed as a function of lymphopenia and known prognostic factors.

Results: 99 patients met eligibility criteria (≥ 18 years of age, ECOG performance status 0-2, and baseline/follow-up lab values measured at our institution). Mean age was 61.6 years (SD, 11.6), 55% were male, mean tumor size was 4.1 cm (SD, 1.6), and 97 had stage III disease. Total lymphocyte counts were normal in 87% prior to RT. Mean RT dose was 47.3 Gy (SD, 8.2) and concurrent chemotherapy was 5-FU (67%), gemcitabine (20%), taxotere (7%), or none (6%). Total lymphocyte counts fell to < 500 cells/mm³ in 51% two months after initiating CRT with a median reduction of 66% from baseline ($p < 0.0001$). Median OS of patients with lymphocyte counts < 500 cells/mm³ at 2 months was 7.7 months (95% CI, 6.8-8.7) versus 15.4 months (95% CI, 11.9-19.0) for patients with ≥ 500 cells/mm³ ($p < 0.001$). Univariate analysis additionally revealed that among pre-treatment patient characteristics, only age ≥ 65 was significantly associated with OS (8.8 vs. 11.4 months; $p = 0.043$). Type of concurrent chemotherapy was not significantly associated with OS. Multivariate analysis revealed a significant association between survival and lymphocyte count (< 500 vs. ≥ 500 cells/mm³) at 2 months post-CRT (HR 3.8, $p < 0.001$).

Conclusion: Definitive CRT induced lymphopenia is frequent, severe, and appears to be an independent predictor for OS in patients with locally advanced PDA.

#85: Wendy Ying, MS2
MSRD Poster Competitor

Mentor: Ephraim Fuchs, MD, MBA

Low incidence of severe mucositis after myeloablative, HLA-matched bone marrow transplantation and high dose, post-transplantation cyclophosphamide

Background: Oral mucositis is a debilitating and frequently encountered consequence of bone marrow transplantation (BMT). We compared mucositis measures among patients receiving post-transplantation cyclophosphamide (PT/Cy) with historical controls receiving cyclosporine A and methotrexate (CsA/MTX) as graft-versus-host disease (GVHD) prophylaxis after BMT.

Methods: We performed a retrospective review of 142 patients who underwent myeloablative, HLA-matched BMT and received busulfan (Bu) and cyclophosphamide (Cy) for pre-transplant conditioning and PT/Cy for post-transplant GVHD prophylaxis. We also examined a historical group of 15 patients who also received conditioning with Bu/Cy, but subsequently received CsA/MTX for GVHD prophylaxis. Mucositis was graded on a scale from 0 to 4, where 0 indicates normal oral mucosa and 4 represents hemorrhagic ulcerations. Total parenteral nutrition (TPN) use, IV narcotics administration via patient-controlled analgesia (PCA), and oral pain have been associated with mucositis incidence and were also analyzed.

Results: Recipients of PT/Cy experienced a significantly lower incidence of severe (grades 3-4) mucositis than did recipients of CsA/MTX (25.3% vs. 93.3%, $p < 0.001$). The peak mucositis severity among PT/Cy recipients was 2.2, compared to 3.4 for patients receiving CsA/MTX ($p < 0.0001$). Incidence of TPN use was significantly lower among patients receiving PT/Cy than among recipients of CsA/MTX (8.4% vs. 33.3%, $p = 0.012$). PT/Cy recipients also had a lower incidence of PCA use than CsA/MTX recipients (41.5% vs. 80%, $p = 0.006$). The maximum oral pain rating experienced by PT/Cy and CsA/MTX recipients, respectively, were 4.5 and 7 ($p = 0.004$).

Conclusion: The incidence and severity of mucositis among patients receiving BMT with PT/Cy are low compared to those of patients receiving CsA/MTX for GVHD prophylaxis. Measures of TPN, PCA, and oral pain were significantly lower among recipients of PT/Cy than among recipients of CsA/MTX. Thus, GVHD prophylaxis with PT/Cy can significantly reduce mucositis and associated clinical sequelae after transplant.

#86: Xun Zhou, MS2

Mentor: John Conte, MD

The Fate of Driveline Infections: Outcomes in Patients on Ventricular Assist Device Support

Background: Driveline infections are a common and difficult-to-treat complication of ventricular assist device (VAD) implantation that may affect quality of life and jeopardize successful heart transplantation. We undertook this study to identify risk factors, examine transplant outcomes, and determine effective treatments for driveline infections.

Methods: We conducted a retrospective review of all adult patients receiving a continuous flow VAD from 2004-2011 at Johns Hopkins Hospital, analyzing each episode of VAD-specific infection. Primary outcomes included mortality, survival-to-transplant, and re-infection. We analyzed Kaplan-Meier survival and multivariate Poisson regression of risk factors.

Results: Of the 131 patients studied, 51 (39.4%) developed at least one driveline infection, and 33 (25.1%) developed multiple infections. Among the 76 patients awaiting transplant, there was no difference in 4-year survival-to-transplant (67.0% vs. 74.5%, $p=0.94$) or post-transplant survival (59.6% vs. 64.6%, $p=0.46$) between individuals that had never had a driveline infection and those that did. Diabetes (Poisson coefficient [PC]: 1.2, $p<0.001$), younger age (PC: -0.30, $p<.01$), destination therapy designation (PC: 1.1, $p<0.001$), and decreased pre-operative acuity ([INTERMACS score: PC: 0.27, $p=0.01$], [APACHE score: PC: -0.11, $p<0.001$]) were associated with an increased risk of developing multiple infections. Of the patients receiving treatment, 39 (76.5%) received at least one course of antibiotics, 33 (64.7%) had at least one driveline debridement, 12 (23.5%) required device pocket debridements, and 3 (5.9%) needed a device exchange. Some patients received multiple treatments for recurrent infections. Overall, 24/61 (39.3%) courses of antibiotics and 19/92 (23.5%) driveline debridements resulted in no re-infections. When used to treat first-time infections, 13/34 (38.2%) courses of antibiotics alone and 5/13 debridements (38.5%) prevented re-infection.

Conclusion: Driveline infections did not affect transplant outcomes. Diabetes, young age, destination therapy, and decreased pre-operative acuity increased the risk of multiple infections. Although rates of re-infection were high, approximately one-third of patients were successfully treated with antibiotics or surgical debridement.

HISTORY OF MEDICINE

Listed Alphabetically

#87: Michael Baxter, MS2

Mentor: Randall Packard, PhD

Dengue's Rise in the Philippines 1900-1950

Background: Dengue fever is the most important vector borne viral illness in terms of breadth of distribution and the morbidity and mortality it causes. In the early 20th century, the Philippines was a hub of research on the etiology and epidemiology of dengue due primarily to the large number of American military service members and medical personnel deployed there. In this milieu that has been so significant in the modern history of dengue, there is surprisingly little information available comparing rates of dengue in natives and foreigners and contrasting it with rates of other diseases prevalent during this era. This following reports aims to demonstrate how dengue fever grew in relative importance in the Philippines when compared to other diseases prevalent at the time. Furthermore, it explores the disconnect between the recognition of dengue as an important illness and the lack of a public health effort to control its spread.

Methods: Research was conducted at the U.S. National Archives, National Library of Medicine, Welch Library and Maryland Library of the Health and Human Services. Quantitative data of disease rates came primarily from U.S. Army reports with Filipino troop data serving as proxy for the experience of native Filipinos and American troop data serving as the experience of foreigners.

Results: Dengue admissions and time lost due to dengue in the U.S. Army in the Philippines for this time period were typically only exceeded by the combination of all venereal disease and malaria. Even as malaria decreased drastically as a cause for hospital admissions among Filipino, colored, and white soldiers in the period 1905-1915, dengue's high numbers persist. At least with respect to venereal disease, malaria, dengue seems to have increased in relative importance. Despite its greater share of disease burden, dengue is only intermittently a priority for public health authorities.

Conclusion: Dengue fever, though very rarely a fatal disease in this era, assumes a greater role in causing morbidity thanks to the decline of several other diseases.

#88: Laura Beth Kaplan, MS2

Mentor: Graham Mooney, Ph.D.

Dissecting Birth: A Case Study in Anatomy, Obstetrics, and Newborn Care in the Early United States

Background: Although historians have long recognized that the study of anatomy helped physicians to justify their expansion into obstetrical care, the existing literature leaves room for a deeper consideration of what anatomical knowledge meant to individual medical practitioners. This study explores the way in which an emerging trans-Atlantic focus on anatomy and dissection – especially involving fetuses and newborns – impacted the career of a popular Bostonian physician at the turn of the nineteenth century.

Methods: This study relied upon careful textual analysis of archival resources, including medical essays written by John Jeffries (1745–1819), the physician under consideration; his diaries; correspondence; patient records; and catalogues of medical instruments and textbooks. Other sources included lectures on anatomy given in the early United States and textbooks about midwifery published during the time period.

Results: Three main trends emerged. First, within the published midwifery tracts of the late eighteenth century, physicians increasingly focused on the anatomy of the fetus and infant in addition to the anatomy of the childbearing woman. Second, lectures and essays on the utility of dissection emphasized the exclusive knowledge of the human body that dissection offered physicians. As a local medical practitioner, Jeffries repeated these claims and continued his anatomical studies despite community resistance. Third, both published and unpublished primary sources placed particular emphasis on the fetus and the infant, thereby transferring a field of traditional maternal expertise to the physician's purview. Understanding early human development became a cornerstone of physicians' claims to understanding the human body.

Conclusion: Existing scholarship has underemphasized the spotlight placed upon the fetus and the infant in physicians' anatomical studies in the late eighteenth century. By focusing on a community doctor like Jeffries, it becomes possible to connect trans-Atlantic intellectual trends to the provision of daily local care.

Public Health Perspective of Traffic Injuries in the Developing World

Background: Traffic injuries are one of the leading causes of morbidity and mortality worldwide. According to the WHO, traffic injuries were the ninth leading cause of mortality in 2000 and are expected to be the fifth in 2030. The problem of traffic injuries is exacerbated by insufficient infrastructure and increased traffic in the developing world. Over the past fifty years, road safety has received increasing attention from the WHO, UN, World Bank, and NGOs.

Methods: In order to understand the evolution of the public health movement, I looked at meetings, reports, recommendations, and resolutions from the WHO, UN, and World Bank. I also looked at publications and presentations from NGOs and health care professionals. I conducted a case study of Cambodia and looked at their transportation, law enforcement, and medical services. In order to understand the safe systems approach, I looked at Dr. William Haddon's publications and interviews.

Results: The public health movement started with the WHO, which passed its first resolution in 1966. The WHO created the Department of Injuries and Violence Prevention in 2000. Over the last decade, the UN and World Bank have gotten involved. The UN passed its first resolution in 2003 and the World Bank created the Global Road Safety Facility in 2005. Recently, NGOs have gotten involved and held a conference in 2010 to increase their global presence. The relationship between these organizations is complex and constantly evolving.

Conclusion: There is a dichotomy in the road safety movement. When the movement first emerged, the responsibility was placed on individual road users and the focus was on behavioral interventions. After Dr. Haddon's work, there was a shift towards sharing the responsibility between those who designed the roads and those who used them. Here the focus is on more comprehensive systems based interventions.

#90: Gino J. Scalabrini, MS2
MSRD Poster Competitor

Mentor: Graham Mooney, Ph.D

Tactical Emergency Medicine (TEMS): A Historical Overview

Background: Since the late 1960s, American law enforcement agencies have used special weapons and tactics (SWAT) teams to handle dangerous operations including high-risk warrant service, hostage rescue and extrication of barricaded suspects. In recent years, police departments have begun to provide their tactical teams with embedded tactical emergency medical support (TEMS). This paper outlines the history and development of medicine in the law enforcement tactical setting.

Methods: Documentary research was conducted using a wide variety of primary and secondary sources. In addition to the development of tactical medicine, the genesis of emergency medicine, paramedic service and SWAT were also explored. This research was supplemented with personal interviews of pivotal figures in the development of tactical medicine.

Results: The first TEMS program appears to have been created in Tucson, AZ during the late 1980s as the brainchild of trauma surgeon and police officer Richard Carmona. A former United States Army Special Operations soldier, Carmona approached his police superiors with the idea of emulating the military model, where high risk operations are never conducted without direct medical support. There is also documented evidence of direct medical support being integrated with tactical operations by the Montgomery County, MD police during this time period as well.

Conclusion: Tactical emergency medicine (TEMS) medicine appears to have a dual genesis on the East and West coasts. There is no solid data on the exact prevalence of TACMED programs today, indicating a good avenue for future study. The future is likely to bring about a national certification program, getting the field out in front of law enforcement as a whole.

MEDICAL HUMANITIES, BIOETHICS, and the HEALING ARTS ABSTRACTS

Listed Alphabetically

#91: Catherine Bennet, MS4

Mentor: Sarah Clever

The Student Preceptor Program (SPP): Teaching 4th year medical students to be effective clinician educators in preparation for residency

Background: To investigate the efficacy of a novel program training MS4 medical students to teach during residency

Methods: In 2010 and 2011, 26 MS4 students participated in SPP, which included a student-run seminar series and a teaching practicum using MS1 volunteers. MS4s completed surveys before and after participating in SPP. Paired t-tests compared pre- and post- self-ratings of their ability to plan lessons, present material, provide feedback, and evaluate students using a 5-point scale. M1s used a 5-point scale to rate their preceptors after each practicum session based its effectiveness, clarity, format, engagement, interest, and relevance. We emailed surveys to all 2010 JHSOM graduates during their internship and used independent t-tests to compare ratings of teaching skills between SPP and non-SPP participants.

Results: Among 2011 MS4 participants, 81% (13/16) completed pre- and post-SPP surveys. Average self-ratings significantly increased for planning lessons, presenting material, providing feedback, and evaluating students (range of increases: 0.81 to 1.67 points; all $p < 0.01$). The 69 participating MS1s gave preceptors a median rating of 5/5 across all practicum sessions. Sixty interns (51%) responded to our survey; 15 (25%) were former SPP participants. Of responding SPP participants, 93% (14/15) felt the program prepared them to teach in residency. They gave higher average ratings for planning lessons ($p=0.001$), presenting material ($p=0.001$), providing feedback ($p=0.026$), and evaluating students ($p=0.300$) on the first day of internship versus non-SPP participants.

Conclusion: A student-run program in which MS4 students train one another to be effective teachers is well received by all participants and results in higher self-ratings of preparedness to teach during internship. The SPP may be a useful model to prepare medical students to enter internship as effective educators.

#92: Yishan Cheng, MS2

Mentor: Lixing Lao, Ph.D.

Developing a Protocol: How to rigorously study Traditional Chinese Medicine without deconstructing a holistic system.

Background: Traditional Chinese Medicine is a holistic system with vastly different disease definitions (differentiations) and treatments from conventional medicine. Though rising use has spurred greater research interest, methods for conducting TCM clinical trials remain controversial. Double screening is a technique where trial participants are required to meet two sets of criteria. This project aims to model a novel research method, using double screening, that is at once scientifically rigorous and stays true to the TCM conceptual framework.

Methods: I reviewed textbooks and recent literature in English and Chinese to select a disease entity with dual definitions in TCM and conventional medicine, which is necessary for double screening; find standard acupuncture and herbal treatments for each differentiation; and identify outcome measures and ways to minimize the placebo effect.

Results: Diarrhea-predominant irritable bowel syndrome was identified as the model. Two-out-of-four TCM differentiations (“Liver qi-stagnation” and “Kidney qi-asthenia”) were chosen for this protocol. Trial participants will be screened for D-IBS using the ROME-III criteria and further subcategorized into “Liver” or “Kidney.” Each differentiation will be randomized into 5 groups: usual care, usual care+placebo acupuncture+herbal placebo, usual care+acupuncture+herbal placebo, usual care+placebo acupuncture+herbal, and usual care+acupuncture+herbal. This factorial design can assess synergism of the treatments. Separating the diagnostician assessing the participant from treatment delivery allows for blinding. Additionally, the diagnostician will be allowed to add select herbs and/or acupuncture points to the standard treatment, depending on the participant’s condition that day. Room for personalization, along with the factorial design, allows the trial to mimic, in a controlled setting, real-life TCM practice.

Conclusion: A randomized, double-blind placebo controlled trial for TCM requires more intricate planning than conventional trials because it involves taking into account concepts of a different medical system. Here, with D-IBS as a model, I offer a novel protocol design that can be used in future TCM research.

#93: Alexander Cole, MS2

Mentor: Albert Wu, MD

Ethical Reasoning and Error Disclosure

Background: Open and honest communication about medical errors is vital for error reduction but remains elusive in practice. Deciding to speak up about a medical error involves weighing a variety of conflicting practical and ethical concerns. This may be especially difficult for trainee physicians who are under evaluation and who have been shown to be less likely to discuss medical errors with patients. Data suggests that ethical reasoning is a measurable skill, which can be taught and enhanced. The purpose of our study is to determine whether trainee physicians' skill in ethical reasoning is associated with more open communication about errors.

Methods: We conducted a cross-sectional, IRB-approved survey of 29 Medicine house officers at Johns Hopkins Hospital. Residents were recruited during monthly house staff meetings and via email.

Our instrument consisted of three-part written survey adapted from existing instruments: The DIT-2 measures ethical reasoning. The safety attitudes questionnaire (SAQ) measures communication attitudes. An error scenario asked residents their likely response to a common error. All three have been previously validated in large studies. The DIT-2 is a proprietary test, which is being scored at the Center for Ethical Development at the University of Alabama.

Our primary analysis consists of a student's T test to compare mean DIT-2 scores of residents based on whether they would "definitely disclose" the error.

Results: Twenty nine individuals (of 129 contacted) completed our survey. In the standardized error scenario 53% said they were "Extremely Responsible" but only 39% reported that they would "Definitely Disclose" the error to a patient. We are awaiting scores from the DIT-2.

Conclusion: We are unable to make any conclusions on our primary outcome since we do not yet have DIT-2 scores. The limited sample size may prevent generalizability but a p value < 0.20 will be suggestive of a trend to investigate further.

#94: Nick Cuneo, MS2

Mentor: Chris Beyrer, MD, MPH

Exculpation and Equivocation: The Scientific Depoliticization of the Zimbabwean Cholera Outbreak

Background: In August 2008 an outbreak of cholera erupted in Zimbabwe that ultimately claimed more than 4000 lives. The epidemic resulted from the politicization of water and health services under Robert Mugabe's regime, epitomized by the dumping of raw sewage into Lake Chivero, the capital city's primary water source. Mortality was further exacerbated by Mugabe's early denialism, which undermined the international response effort. Physicians for Human Rights sent an investigatory team of physicians and scientists to Zimbabwe that documented the disaster's political underpinnings in a published report.

Methods: To determine the extent to which the scientific discourse included discussion of the political roots of the epidemic, we performed a literature review using the PubMed database, with the input "cholera AND Zimbabwe" spanning from 2008 onward. We were able to identify 32 articles in the search, of which 31 were accessed. These articles were reviewed both qualitatively for their rights-based content (both political and civil as well as economic, social, and cultural) as well as quantitatively using key words (Mugabe, ZANU-PF, election, politics) as proxies for political discussion.

Results: Robert Mugabe's impact on the epidemic was widely ignored within the articles—only 5 of the 31 articles (19.4%) made any mention of his name. A greater portion of the articles referenced the political circumstances surrounding the epidemic at 32.2%, with less than half of the articles making reference to any one of the terms searched (41.9%).

Conclusion: The Zimbabwean epidemic serves as a case study in the failure of the scientific community to publicly address the political and broader human rights realities of those it ultimately aims to serve. Such realities are understudied determinants of human health and will remain neglected so long as we enable the continued depoliticization of anthropogenic public health catastrophes like the Zimbabwean outbreak within the literature.

#95: Matthew Molloy, MS2
MSRD Poster Competitor

Mentor: Debra Roter, DrPH

Factors Associated with Patient-Provider Concordance in Prenatal Genetic Screening

Background: Prenatal genetic screening presents a complex communication challenge. Ethical issues relate to the adequacy of informed consent. At a minimum, informed consent requires the patient and provider to be aware that a decision conversation has occurred. This study assessed providers' and patients' shared awareness of prenatal genetic screening informed consent discussions and the factors associated with shared awareness.

Methods: Secondary analyses were performed using data collected as part of an IRB-approved study of communication in the prenatal setting in which each participant audio-taped a visit with her provider; both provider and patient completed post-encounter questionnaires. We assessed shared awareness of screening discussions by measuring the concordance of 121 patient-provider dyads on post-encounter reports. Using multinomial logistic regression analyses controlling for gestational age, we identified variables associated with concordance. We conducted a content analysis of 59 transcripts with a screening conversation.

Results: 50.9% of dyads agreed that they had a conversation about screening, and 10.0% agreed that they had not. In 2.7% of visits, the physician indicated that a conversation had occurred but the patient did not. Patients who agreed with their providers that a conversation did not occur were more likely to have lower literacy skills (N=98, p=.053) and to have been in a less patient-centered encounter (N=109, p=.011) than those who agreed that a conversation did occur. Patients who indicated that they had a conversation about screening but whose providers did not were more likely to have lower educational status (N=98, p=.053). While a majority explained the testing and presented it as a choice, only 25.4% covered associated advantages and disadvantages.

Conclusion: While concordance was high, there were instances of discordance. Of greatest concern is the minority of women who did not report a conversation about screening that the provider believed had occurred. Many conversations did not include suggested informed consent elements.

#96: Neil M. Neumann, MS2

Mentor: Jeremy Sugarman, MD, MPH, MA

Assessing Patient Attitudes Towards Induced Pluripotent Stem Cell Research

Background: Although there has been considerable discussion of the ethics of induced pluripotent stem cells (iPSC) in the popular and academic literatures, there is a paucity of data regarding the attitudes of patients regarding the donation of biological materials for this research. Furthermore, while informed consent plays a central role in research with human-subjects, the informational needs of patients and potential research participants regarding iPSC donation are unclear. The purpose of this project is to gather such information to inform the development of appropriate policies for the consent, collection and use of tissues being procured to create induced pluripotent stem cells.

Methods: The study was conducted using 3-5 focus groups, each lasting two hours, with 8-10 participants per focus group discussion. Participants for the focus groups are patients receiving outpatient care at Johns Hopkins, recruited by their Hopkins physicians. Informed consent was obtained prior to each focus group. A trained focus group moderator lead the focus group discussions. Additionally, the medical student assisting in conducting this research study gave a brief, 5-minuted background presentation on iPSCs. Audio recordings from the focus groups were transcribed and then checked for accuracy. Digital recordings were maintained securely and will be destroyed after the study has been reported in the peer-reviewed literature. The text was coded inductively to account for themes that emerge from the discussions. Data was analyzed using ATLAS.ti, a software package designed to facilitate qualitative analysis, to summarize output according to the final set of domains and codes.

Results: There are no results at the time of this submission.

Conclusion: There are no conclusions at the time of this submission.

#97: Max Romano, MS2

Mentor: Lisa Cooper, MD, MPH

Overcoming barriers to quality hypertension care: A qualitative study of health system leaders

Background: Hypertension is a prevalent and poorly controlled disease in the United States. Despite recent innovations in hypertension treatment, prevalence rates continue to rise. While most research describes isolated problems with hypertension care, little is known about the full scope of individual and organizational barriers to successful treatment. This study explores the ways that healthcare systems can provide better treatment to patients with hypertension.

Methods: Through purposive sampling we identified 21 key informants in an ambulatory healthcare system located in Baltimore, MD. We interviewed senior staff from six clinics including medical directors, practice administrators, and executive leaders. The semi-structured interviews assessed each administrator's knowledge and attitudes regarding hypertension treatment. Two investigators conducted grounded thematic analyses of verbatim transcripts to identify and classify emergent themes using NVivo 9 software.

Results: The interviews focused on the themes of: problems with existing hypertension care, characteristics of successful interventions, and systemic barriers to change. Analysis of these three themes revealed opportunities for improvement at the patient, provider, organizational, and health-system levels. Most participants stated that patient adherence is essential for hypertension control, although suggested strategies to improve adherence varied widely. Participants stated that providers require more time with patients, improved motivational interviewing training, and more accurate blood pressure measurements. Participants stated that healthcare delivery organizations should expand patient outreach, set population-level hypertension control as a management objective, and directly respond to community-expressed needs. On a healthcare-systems level, participants stated that interventions should target cost-reduction for patients, accurate outcomes data for insurers, and better incentives for primary care trainees.

Conclusion: Population-level improvement in hypertension control will require action by patients, clinicians, healthcare delivery organizations, and the healthcare system as a whole. Policymakers hoping to enhance patient adherence to existing treatment regimens should focus on improving the delivery of primary health care through multi-pronged interventions.

#98: Vivian Wang, MS2
MSRD Poster Competitor

Mentor: L. Ebony Boulware, MD, MPH

Highlighting Health Disparities: a Photo-Essay to Illustrate Highlandtown Clinic Patients Beyond the 15-Minute Interview

Background: Baltimore is a city with significant health disparities, especially in certain ethnic/racial and lower socioeconomic groups. Many factors influence health disparities, including the patient-physician relationship. When the patient and physician have differing backgrounds, communicating in a 15-minute visit can be especially challenging, a potential disadvantage for achieving health. Storytelling combined with visual media can be a powerful way to understand a patient's background, and may improve physician cultural competency and communication skills. This is a photo-essay, a form of social documentary employing visual and descriptive methods. My subjects are two patients who participate in the Healthy Beats walking program at the Highlandtown clinic of Baltimore Medical System (BMSI). Each participant has racial and/or socioeconomic characteristics associated with a lower health status. My goal is to illustrate the lives of patients beyond the symptoms or diseases they present in clinic, in order to enhance the medical student's understanding of various factors influencing a patient's health status.

Methods: This project involved three methods: (1) photo-voice, where participants were given a disposable camera to photograph personal health influences, (2) individual one-hour audio-recorded interviews about their photo-voice pictures, their daily lives, and their health experiences, and (3) environmental portraiture, a form of photography that captures the subject in his/her natural environment. The project was reviewed by JHSOM IRB and determined exempt from approval. I conducted the interview and took the environmental portraits. Interviews will be transcribed.

Final Product/Dissemination: Based on the interview, an exhibit will be created, consisting of 6-12 photographs of each participant and captions. Aliases will be used. This will be displayed in the Armstrong Medical Education Building for 2 weeks, and will be pre-approved by the participants. Viewer reactions will be solicited through anonymous feedback forms. An electronic format of the exhibit will be made for dissemination to future students.

#99: Shira G. Ziegler, MS3

Mentor: William Gahl, MD PhD

From Bench to Bedside Through Visual Art: Enhancing Empathy for Patients with Undiagnosed Diseases

Art can be used as a medium to help understand the human experience and develop empathy and compassion for patients. Indeed, art can help connect what might be frustratingly disjointed in clinical practice and in research. Anatole Broyard remembers “My initial experience of illness was a series of disconnected shocks, and my first instinct was to try to bring it under control by turning it into a narrative... Stories are antibodies against illness and pain.” Narratives, poetry, and visual art can be created to help conceptualize a disease process and facilitate greater understanding. Patients with undiagnosed diseases are often neglected in clinical medicine and research. Because of the novelty and complexity underlying their disease processes, these patients often do not receive the medical care or research commitment their conditions necessitate. In the National Institutes of Health's Undiagnosed Diseases Program, a team of physicians and scientists work together to evaluate these patients both in the clinic and in the laboratory with the intention of discovering new diseases, mechanistic pathways, and potential treatments. This program provides the unique framework to observe a disease process in both the clinical and research settings. Unfortunately, empathy for these patients can often be lost to the healthcare professional or laboratory researcher. Art can be used as a medium to help all those involved (directly or indirectly) appreciate the complete disease process --- from bench to bedside --- and has the potential to elicit empathy and compassion to promote better patient care and research interest.

I interviewed and formed relationships with patients during their stay at the NIH Clinical Center. I created an art piece to embody their experiences which was informed by my perspective both in the clinic and in the laboratory. All patients provided written informed consent; photographs and letters are used with their permission.

**PUBLIC HEALTH and COMMUNITY
SERVICE
POSTER ABSTRACTS**

Listed Alphabetically

#100: Andrew Bissonette, MS2
MSRD Poster Competitor

Mentor: David S. Friedman, MD, MPH, PhD

Simple Solutions for Big Problems

Background: National monitoring and evaluation projects pose significant obstacles, especially in developing countries where challenging environments, limited resources, and little external review can hinder progress or lead to inferior data collection. The purpose of this study was to identify ways to increase the efficiency and quality of research in these settings.

Methods: A seven-week, qualitative review of the standard operating procedure utilized by the Notre Dame Haiti Program was conducted in Leogane, Haiti. This program is leading an effort to eliminate filariasis from Haiti. I reviewed the processes employed by the research site and surveyed the literature on monitoring and evaluation in order to develop a set of recommendations for improving research quality at the site.

Results: Multiple oversights resulted in poor quality data collection and research implementation. Better management of the research site can be achieved through a substantial overhaul of current management procedures. Specific recommendations include: developing detailed plans for the shipping and storage of research materials (to avoid wastage and inaccurate results), instituting regular review of depot management, insuring comprehensive lab technician training with ongoing quality assessment through observation, and implementing technician checklists. Because the center has research projects that run for relatively long periods and receive funding from multiple sources, the center needs to set intermediate deadlines ahead of larger project deadlines and meet those deadlines or revise the timeframe. Finally, more thorough review of research objectives requires secondary review by an external reviewer to insure that funds are spent wisely.

Conclusion: Concerns about limited resources among researchers in the developing world are often valid. It seems that the implementation of relatively low-cost strategies aimed at enhancing efficiency, such as those outlined here, might prove an invaluable adjunct to fundraising efforts in some research settings. In addition, such strategies may also yield the added benefit of higher quality data collection.

#101: Rachel Blair, MS2

Mentor: Susan Hutfless, Ph.D

Limited Availability of Industry-Sponsored Inflammatory Bowel Disease Trial Results on ClinicalTrials.Gov

Background: The International Committee of Medical Journal Editors required clinical trials to register in a database such as ClinicalTrials.Gov in 2005 and the Food and Drug Administration required reporting of trial results in 2007, which was intended to decrease selective reporting. The purposes of our study were to describe the availability of results of registered clinical trials on treatments of inflammatory bowel disease (IBD) and to examine whether study funding is associated with availability of trial results.

Methods: We searched ClinicalTrials .Gov for Phase II and III clinical trials in IBD, ulcerative colitis, and Crohn's Disease. Two reviewers independently reviewed and included randomized trials that tested biologics, immunomodulators, steroids, or aminosalicylates. We excluded trials that did not conduct interclass or intraclass medication comparisons or were not placebo-controlled. We extracted data on intervention, funding source, and study result availability. The funding source was classified as industry, government, academic, or other. We specified if results were provided via a link to a peer reviewed publication, a table of results in ClinicalTrials.Gov, or on an outside website (ClinicalStudyResults.org).

Results: 134 trial records met the inclusion criteria from the 513 trials identified in ClinicalTrials.Gov. 48 (35%) of the included trials reported results; 38 (28%) provided links to peer reviewed publications. 113 (84%) trials were funded exclusively by industry. 24% (27) of industry funded trials provided links to peer reviewed articles and 9% (10) reported non-peer reviewed results (ClinicalTrial.Gov table or outside website). In contrast, 57% (8/14) of trials with exclusively non-industry funding provided results, all as links to peer reviewed articles. Links to peer reviewed articles were more common in non-industry funded trials (Mantel-Haenszel p-value=0.009).

Conclusion: Industry sponsorship of Phase II and III clinical trials for IBD is associated with decreased accessibility to peer reviewed articles in ClinicalTrials.Gov. Industry sponsored trials are more likely to selectively report results.

#102: Martha Brucato, MS2
MSRD Poster Competitor

Mentor: Beth Marshall, MPH, CHES

Community Adolescent Sexuality Education (CASE) Program Needs Assessment and Curriculum Update

According to the Maryland Department of Health and Mental Hygiene, since 1997 the African American teen birth rate of Baltimore City has consistently been approximately twice that of Maryland on average. Yet despite the high teen pregnancy rate, the Baltimore City Public School System has no funding for sexual education before high school. Community Adolescent Sexuality Education (CASE) is a program developed by the Hopkins chapter of the Student National Medical Association to address this disparity. The curriculum is targeted to 8th grade students, and covers topics ranging from decision-making, goal-setting, sexually transmitted infections (STIs), contraception, and anatomy. The aim of my project was to revise and update the curriculum of CASE. I first conducted a needs assessment, soliciting feedback from previous volunteers, school administrators, and the students themselves. Pre- and post-course surveys were given to the students, testing their factual knowledge of common consequences of sex and attitudes with regards to sexual norms. Analysis of these surveys shows that the course significantly improved scores on a 10-question factual test (average value of 4.95 correct answers pre-intervention, 7.93 correct answers post-intervention, p -value 2.9×10^{-7}). However, despite this encouraging data, qualitative feedback from school staff, students, and previous volunteers suggests the curriculum needs to be more participatory, to engage the students and enable them to personalize the information. More activities focused on role-playing and practicing healthy decision-making were requested. There is also a need for standardized teaching materials, such as PowerPoints accompanying the lessons; as part of this goal, an Alumni Association grant has been submitted to fund the purchase of STI and contraception displays. I have begun to restructure the curriculum to implement the changes suggested by my needs assessment, and will analyze the impact of these changes on the effectiveness of Fall 2011 CASE classes.

#103: Jina Chung, MS2

Mentor: Linda Chang, MD, Susumu Mori, Ph.D

Studying the effects of nicotine on HIV+/- adult brains using Diffusion tensor imaging

Background: Prevalence rates of smoking among HIV+ individuals surpass 50%, but how smoking contributes to the neurologic progression of HIV has been rarely investigated. The purpose of our study was to use diffusion tensor imaging (DTI) to examine the independent or combined effects of HIV and nicotine on the brain.

Methods: We used DTI data to evaluate the brain microstructural integrity of HIV and non-HIV patients with and without a history of nicotine use. We analyzed images from 216 subjects (49 HIV-Nonsmoking, 59 HIV-Smoking, 64 Control-Nonsmoking, 44 Control-Smoking) using Large Deformation Diffeomorphic Metric Mapping, and two DTI metrics (Fractional Anisotropy and Trace) were calculated in 176 sub-regions. The resulting data were analyzed using 2-way ANOVA to assess for the HIV effect, the Nicotine effect and the HIV-by-Nicotine interaction effect. Repeated Measures ANOVA was used to evaluate data from 11 “super-regions”.

Results: HIV+ patients had significantly lower FA in many regions compared to controls, especially in the left and right bodies of corpus callosum ($P=0.0002$ and 0.0003), and higher Trace in many regions also including the corpus callosum ($P=0.0004$). Grouping by “super-regions” showed lower FA and higher Trace in HIV+ subjects in many regions. Nicotine alone did not have significant effects on FA and Trace. Only trends for interactive effects (normalization) between HIV and nicotine were observed on FA and Trace in several regions.

Conclusion: The abnormal diffusion measures in the corpus callosum may explain the cognitive and motor deficits associated with HIV progression. Lower FA and higher Trace than normal in many super-regions of HIV+ patients suggest that HIV infection may disrupt the microstructural integrity of these areas. The relatively normal measures in smokers suggest that nicotine has little effect on brain microstructures. The trends for normalization in HIV subjects with nicotine exposure suggest a possible neuroprotective effect of nicotine.

#104: Mariyam Faiz, MS2

Mentor: Gerard Anderson, Ph.D

Mortality Burden of Behavioral Risk Factors in Bangladesh

Background: Modifiable behavioral risk factors are leading causes of mortality and morbidity worldwide. Quantifying the effect of these risk factors using country specific data will provide insight into the specific effects of recent behavioral trends on each country's population. In this study, we quantified the effect of tobacco use and underweight/obesity (by BMI) on population mortality in Bangladesh.

Methods: Through a Medline and Cochrane database search complemented by personal communications, we identified epidemiological prospective studies that examined the association between tobacco use or BMI and all-cause mortality in large South Asian cohorts. We identified relative risk data that demonstrate the association of tobacco use or BMI with all-cause mortality from two published prospective studies with the greatest statistical validity. Prevalence data from the WHO STEPS/Bangladesh data 2010 were used along with these relative risks to calculate the population attributable fraction. Subsequently we calculated the absolute number estimates for all-cause mortality by multiplying the population attributable fraction with the total mortality data from Bangladesh.

Results: Tobacco use (smoked and smokeless) accounts for approximately 173237 deaths (PAF = 19.6%). Being underweight (BMI < 18.5) accounts for an average of 123175 deaths (PAF = 13.6%). However, overweight/obesity (BMI > 25.0) does not account for a significant number of deaths. This is because elevated BMIs currently have not been found to be significantly associated with an increased risk of death in South Asians according to our identified studies.

Conclusion: Tobacco use and low BMI account for a large number of deaths in the Bangladesh population. However, elevated BMIs currently do not appear to be associated with a significant number of deaths. This highlights the need to further investigate the effects of behavioral risk factors specifically on the South Asian population and to establish prevention efforts aimed at reducing the prevalence of tobacco use and low BMIs.

#105: Rebecca Greene, MS2

Mentor: Peter Winch, MD, MPH

Learning how to assess the “world of drugs” related to malaria in Ghana

Background: Chloroquine is no longer effective in treating malaria in Ghana due to widespread resistance, so artemisinin combination therapies (ACTs) have taken its place. As part of a project evaluating the Global Fund’s program to make ACTs available in Ghana at competitive prices, we sought to develop instruments to understand local perceptions of antimalarials.

Methods: We designed a preliminary set of data collection instruments based on a similar protocol used in Mali and then revised them based on the situation in Ghana and discussions with Ghanaian counterparts. The instruments used qualitative research methods including free listing, semi-structured interviews, pile-sorting, and ranking to assess the understanding of antimalarials among three different groups: caregivers of young children, healthcare providers, and licensed chemical sellers.

Results: The first set of instruments included exercises intended to elucidate local terminology for antimalarials, discrepancies in local terminology and technical names for antimalarials, and how perceptions of drug names and purposes affect the success of the Global Fund program. The informal drug market in Ghana was not as disorganized as we expected and there were unforeseen concerns about the availability of pediatric medicines, so the data collection instruments were edited to reflect this. The final set included: (1) Ranking of and semi-structured interview about pediatric drugs, (2) Structured listing of and semi-structured interview about drug names, (3) Matching: ACT generic and trade names, and (4) Ranking of and semi-structured interview about combination therapies. The instruments were designed to assess participants’ perceptions of the relationships among antimalarials, preferences for different drugs, as well as the scope of combination drugs known to participants and the words used to refer to them.

Conclusion: We combined existing literature with observations of local antimalarial use and collaboration with stakeholders to improve the content validity of our data collection instruments to assess local perceptions about antimalarials in Ghana.

#106: Jennifer Im, MS2
MSRD Poster Competitor

Mentor: Diana Do, MD

Retreatment Decision-Making in Treating Age-Related Macular Degeneration: A Comparison of Optical Coherence Tomography and Fluorescein Angiography

Background: Choroidal neovascularization (CNV) in age-related macular degeneration (AMD) is currently diagnosed using a combination of clinical exam, fluorescein angiography (FA), and optical coherence tomography (OCT). While FA is the gold standard, this study compares both imaging modalities to see if the less invasive OCT can diagnose CNV activity as reliably as FA.

Methods: The study population consisted of 159 patients with AMD-related CNV who received monthly anti-VEGF injections over one year. The seven ophthalmologists who saw these patients recorded whether they would retreat based on the OCT. This decision was then re-evaluated once FA was done to see if the FA would alter the original decision. Cases with vague imaging results were marked accordingly as questionables. A prospective review focusing on concordance among OCT, FA, and final treatment decision was done.

Results: The overall frequency (crude agreement) with which OCT and FA yielded the same retreatment recommendation was 72%. The kappa value for OCT and FA was 0.548, which suggests moderately strong agreement. Concordance between OCT and final treatment decision was seen in a kappa value of 0.748. Notably, the concordance between FA and final treatment decision was higher, with a kappa of 0.923. Sensitivity/specificity were also superior for FA than OCT (95%/100% vs. 84%/96%). Approximately 48% of cases with questionable OCT resulted in decision to retreat because the FA was positive. Conversely, about 9.7% of cases with questionable FA resulted in treatment because the OCT was positive.

Conclusion: There is moderate agreement between OCT and FA in detecting CNV activity. FA, more so than OCT, has higher concordance with final treatment decision along with superior sensitivity and specificity. Despite being less invasive, OCT is not on par with FA in diagnosing CNV activity. Although both modalities complement each other, FA is the more crucial factor in driving retreatment decision making.

#107: Alexander Jenson, MS2
MSRD Poster Competitor

Mentor: Sheila West, Ph.D

Gender and performance of Community Treatment Assistants in Tanzania

Background: Mass drug administration of azithromycin for trachoma requires high rates of distribution to achieve effective control and prevent spread. Previous research in Tanzania found that villagers given drugs by male community treatment assistants (CTAs) were 1.75 times more likely to refuse treatment the following year. This is the first study evaluating the role of gender on CTA performance.

Methods: Thirty-two villages underwent mass drug administration with azithromycin for trachoma control using paid CTAs. Two to three CTAs were working per distribution site, with 2 to 10 sites per village. Nine villages were chosen for the study based on previous performance. Sites were randomly chosen for audio-recording during each day of drug distribution. Audio recordings were coded using both the Roter Interaction Analysis System (RIAS) for interaction description, and a separate system for CTA performance.

Results: Fifty-eight (32 male, 26 female) CTAs from 24 drug distribution sites were chosen at random for audio recordings, comprising 3115 interactions. Assessing CTA performance, only 6.22% of interactions included mentions of cleanliness and trachoma prevention, and 22.5% included polite greetings. No correlation was observed between CTA gender and either metric. RIAS analysis showed that, at mixed-gender sites, female CTAs spoke less than males (5.89 vs. 6.85 utterances/interaction $p=0.021$). Female CTAs at mixed gender sites also spoke less than females at all-female sites (5.89 vs. 9.87 utterances/interaction $p<0.000$). CTAs at all-female sites spent more time per interaction than CTAs at all-male sites (80.1 vs. 104.9 sec/interaction $p<0.001$).

Conclusion: Interactions between CTAs and villagers indicate that CTAs are not conveying key messages, such as respectful greetings and measures for trachoma prevention, irrespective of CTA gender. However, CTA gender did affect both time and number of utterances, with males dominating conversation or spending less time per villager. These results have important implications for training protocols and site-development in mass drug administration.

#108: June-Ho Kim, MS2

Mentor: Felicia Knaul, Ph.D

Avoidable Cancer Deaths in the Developing World

Background: Cancer has emerged as a major global health problem with opportunities for immediate intervention. Many of these cancers are amenable to prevention, early detection, and treatment. In this study, we seek to identify the current mortality rate of avoidable cancer in the developing world compared to the developed world.

Methods: The analysis is based on incidence and mortality data from the most recent GLOBOCAN 2008 of the International Agency for Research on Cancer. 12 potentially avoidable cancers were identified, and avoidable cancer mortality was analyzed using three scenarios of life expectancy: (1) age 65, often used in literature, (2) the highest average life expectancy for each cancer within each income region, and (3) age 75, which approximates the life expectancy of high income countries.

Results: Overall, about a third of all cancer deaths are considered avoidable globally, with low-and-middle-income countries (LMICs) accounting for approximately 80% of total avoidable cancer mortality in the world. With a minimum attainable standard of 65 years, 47% of cancer deaths in low income countries are avoidable compared to 19% in high income countries. By fixing the life expectancy relative to what is attainable in each income region, the disparity rises to 52% avoidable cancer deaths in low income countries compared to 21% in high income regions. Applying a life expectancy of 75 years, 60% of cancer deaths are considered avoidable in low-income, 57% in lower middle, 48% in upper middle, and 35% in high income countries.

Conclusion: Our analysis of avoidable cancer mortality presents significant opportunities for immediate interventions in prevention, early detection, and treatment to reduce cancer mortality around the world. In particular, LMICs suffer a disproportionate burden of such cancer deaths—many of which are addressed through low-cost prevention or treatment in high income countries—and thus present promising targets for policy and action.

#109: Mimmie Kwong, MS2

Mentor: Kent Stevens, MD, MPH

Exploring Trauma Care Services in India: A Systematic Review of Pre-Hospital, Hospital, Clinical, and Operational Components for the Care of the Injured Patient.

Background: 14000 people die due to injuries each day, accounting for 12% of the global burden of disease. A large portion of this burden falls on low and middle-income countries where the greatest injury mortality and morbidity rates have been observed. In India, the growing population and rapid urbanization rate have made trauma management a uniquely challenging public health concern.

Methods: To develop an understanding of the existing trauma care system in India, a systematic review of peer-reviewed and grey literature was conducted between March and August, 2011. GRADE recommendations were utilized to evaluate the quality of the studies in the review.

Results: A total of 22 studies were included in this review. 18 articles addressed pre-hospital care, 13 addressed in-hospital care, and 12 articles addressed clinical and operational components of trauma care. Our findings indicate concerns regarding pre-hospital care, including a lack of centrally coordinated emergency response, inadequate provision of on-site first aid, and wide variations in transport times. Further, many articles addressed problems pertaining to in-hospital care, including issues with patient volumes and trauma protocols, inadequate physical and human resources, and a lack of trauma education, training, evaluation and research. Finally, our findings indicate a dearth of post-hospital care and rehabilitation. There was much inconsistency with regards to definitions of trauma care and outcomes measured.

Conclusion: Care of trauma poses an important and growing issue in India. There remains no unity among currently available trauma and emergency care services, resulting in system inefficiency and the inability to access timely essential medical care. The studies in our analysis indicate that standardize trauma care systems and protocols need to be addressed and made a national priority. This is a call to action to develop universal methods to implement and ensure the provision of trauma care services to the population of India.

#110: HeeWon Lee, MS4
MSRD Poster Competitor

**Mentors: Peter Pronovost, M.D. Ph.D.,
Bradford Winters, M.D. Ph.D.**

The Effect of Public Reporting on Central Line Associated Blood Stream Infections

Background: Central line associated blood stream infection (CLABSI) is a common, costly, and fatal cause of hospital-related deaths. In a pilot in the state of Michigan, the multifaceted ‘On the CUSP (comprehensive unit based safety program): Stop BSI (blood stream infections)’ program led by Johns Hopkins has demonstrated that CLABSIs are not only preventable but the reduction sustainable over 3 years. Despite the nationwide spread of the program, however, CLABSIs remain a significant source of mortality in hospitalized patients, and factors related to the success of CLABSI reduction remain unknown. The purpose of this study was twofold—one, to determine whether mandatory public reporting of CLABSIs to the National Healthcare Safety Network (NHSN) was a motivator in hospitals’ participation in the CLABSI prevention project and two, whether NHSN reporting was a factor in successful CLABSI elimination.

Methods: In the first part of our study, percent hospital participation in the Stop BSI project was analyzed in NHSN versus non-NHSN reporting states. In the second part, baseline and the last 6 months mean CLABSI rates were analyzed using Poisson regression. Successful CLABSI reduction was defined as $RR < 1$.

Results: NHSN reporting states had 19.15%, while non-NHSN states had 15.12% participation. In the second part of the study, while both NHSN and non-NHSN reporting states as two distinct groups had $RR < 1$, NHSN-reporting states had a lower RR of 0.7091 than non-NHSN-reporting states of 0.7983.

Conclusion: Our data suggest that public reporting to the NHSN was a motivator in hospitals’ joining the Stop BSI program. Secondly, our data demonstrate that public reporting to NHSN may be a factor in successful CLABSI elimination. Given that public reporting and disclosure of infection rates seem to be important factors in CLABSI reduction, our study suggests that changes in public policy could significantly hasten CLABSI reduction in the United States.

#111: Kimberley Lee, MS2
MSRD Poster Competitor

Mentor: Madhav Goyal, M.D.

Stress and stressors in a low-income inner-city out-patient population.

Background: The purpose of this study was to measure the perceived stress levels and evaluate the associations among specific life events, mindfulness, demographic factors, substance use, pain, and perceived stress in a sample of urban uninsured and underinsured patients. Despite all the data that has been accumulated concerning associations between psychosocial stress and decreased health outcomes, there is limited data examining the factors that contribute to perceived stress for blacks living in the inner-city.

Methods: After obtaining permission from the Johns Hopkins IRB, consecutive patients over 18 years of age (n=174) presenting to an inner-city community clinic in Baltimore, MD were asked to participate in the study. Perceived stress, life events, mindfulness, and pain were assessed by the Perceived Stress scale, Life events scale, Mindfulness Attention Awareness scale, and Pain Catastrophizing scale respectively. The CAGE questions and drug abuse screening test were used to screen for substance abuse.

Results: Among all 174 patients surveyed, the mean PSS score was 18.03 +/- 7.81. Paired t-tests indicate that the mean PSS score of black clinic patients 18.08 +/-7.83 was significantly higher than that of black persons in the general population 14.7+/- 7.2; $p<0.001$. Spearman rank-order correlations indicated that perceived stress negatively correlation with higher mindfulness scores. T-test showed that change in number of arguments, living conditions, sleep habits, eating habits, financial state or residence were the factors most associated with higher PSS stress scores ($p<0.001$). Imprisonment, being dismissed from work and divorce in the past year shows no correlation with PSS scores ($p=0.07$; $p=0.14$; $p=0.92$).

Conclusion: This sample of patients had a mean PSS score that was higher than that of the general population, even when accounting for racial differences. These results along with the association of higher mindfulness with lower stress suggest that a mindfulness-based stress reduction intervention would be beneficial for this population.

#112: Lorena Leite, MS2
MSRD Poster Competitor

Mentor: Kathleen R Page, MD

Dial, Text, or Browse: Improving Access to HIV Education & Testing in Baltimore
Latinos

Background: Latinos are the fastest growing demographic in Baltimore but their access to healthcare is limited. Latinos with HIV tend to present very late to care, often after developing AIDS-related complications. The Baltimore City Health Department (BCHD) Latino Outreach Team has improved access to HIV testing among Latinos, but has not implemented strategies using cell phones or internet that have been successful in other U.S. cities to reach vulnerable populations.

We aimed to determine the frequency of text, internet and email use among Baltimore Latinos and evaluate the acceptability of receiving health information by text or e-mail.

Methods: Cross-sectional survey study of Latinos living in Baltimore identified through a stratified sampling scheme, using formative research to determine venues frequented by Latinos. When surveying, every third unit (i.e. family, single person) to walk by was invited to participate. Eligibility included self-identification as Latino, age ≥ 18 , ability to communicate in Spanish or English, and oral consent. \$5 gift card was offered for survey completion. The survey included 21 questions which were reviewed by a community advisory board and sensitive questions were asked last.

Results: The all-venue response rate was 34.8%. The majority of the patients (73%) had previous HIV test. Out of 134 participants, 95% used a cell phone and 42% had not changed their cell number in the past 2 years. 72% used text messaging, 52% used internet and 36% used email. More participants were interested in receiving health information via text compared to internet or e-mail (72% vs 45% vs 32%, $p \leq 0.0001$). Likewise, participants preferred to receive HIV education or HIV results by text (68%) compared to internet or e-mail (42% vs 38%, $p \leq 0.0001$).

Conclusion: Our data suggests text message is the furthest reaching and best received modality for a health intervention targeting Baltimore Latinos. Measuring the efficacy of a text intervention is desirable.

#113: Melissa Liu, MS2

Mentor: Neil Bressler, MD

Assessment of time-domain and spectral-domain ocular coherence tomography in the management of diabetic macular edema with anti-VEGF therapy

Background: Aim/Hypothesis: This study evaluated the impact of time-domain (TD) followed by spectral-domain (SD) ocular coherence tomography (OCT) on treatment decision-making in the management of diabetic macular edema (DME) with anti-vascular endothelial growth factor (anti-VEGF) therapy. We hypothesized that SD-OCT might alter the management decisions.

Background: Standard care for DME involving the center of the macula with vision impairment includes intravitreal anti-VEGF therapy, with injections repeated as often as every 4 weeks, based predominantly on OCT measurements of changes in edema since the last treatment. Clinical trials that proved the benefits of anti-VEGF therapy had utilized TD-OCT, but the impact of SD-OCT, with greater resolution, software to register past with current measurements, and denser sampling, has not been evaluated.

Methods: Methods: Following IRB approval, a prospective study evaluated patients previously treated for DME with anti-VEGF among 4 retina specialists at the Wilmer Eye Institute. After obtaining consent, the managing retina specialist recorded whether additional anti-VEGF was recommended, the follow-up time interval, and the level of certainty, first after performing the clinical examination and reviewing a TD-OCT, and then again after reviewing a SD-OCT.

Results: Results: Data were collected for 129 treatment decision pairs involving 67 eyes from 46 subjects. Non-concordant decisions occurred in 9 (7.0%) treatment decision pairs. In 7 (78%) of these 9, the addition of SD-OCT changed the ophthalmologist's decision from not recommending to recommending retreatment. The addition of SD-OCT increased the certainty of the ophthalmologist in 35.7% of all treatment decision pairs.

Conclusion: Conclusions: SD-OCT may increase the certainty and change the treatment decisions of ophthalmologists relative to TD-OCT. It also may occasionally lead to an increase in recommending retreatment. Further investigations are needed to determine whether there are certain factors which led to the discordant decisions and whether such changes in management lead to improved visual outcomes.

#114: Susan Matesanz, MS2

Mentor: Roxanne Jamshidi, M.D., MPH

Adherence to Recommended Follow-up Care after Abnormal Cytology in Paracentral El Salvador

Background: El Salvador has a cervical cancer rate 3 times that of the United States, and reports a coverage screening rate of 19%, the lowest of Latin American countries with screening programs. A major barrier to effective screening is loss to follow-up. This study sought to identify follow-up rates in women diagnosed with cytologic high-grade lesions (HGL) in the Paracentral region of El Salvador.

Methods: A retrospective chart review of 205 charts was conducted to determine follow-up within one year of diagnosis with cytological HGL. Charts were reviewed at 15 local health units, which provide free primary care services to all residents. For women who qualified for study inclusion, records were then examined at five referral hospitals, which provide diagnosis and treatment after abnormal cytology. Factors associated with adherence were collected including age, marital status, number of children, history of abnormal cytology, and location of referral. Women who did not complete follow-up were contacted to determine reasons for non-adherence. Multivariate logistic regression was conducted to determine factors associated with completion.

Results: Records were available in 72% (148/205) and 89% of these (132/148) qualified for study inclusion. Average patient age and number of children was 39.8 and 3.71, respectively. 46.9% (62/132, CI 38.66%-55.45%) completed adherence to follow-up. The mean time between abnormal cytology and colposcopy referral was 73.4 days. Multivariate regression showed time to referral for colposcopy was significantly related to adherence ($p < 0.05$), but there was no effect of other demographic factors.

Conclusion: Nearly 50% of women with HGL did not complete treatment. High loss to follow-up, both through record keeping issues and clinically, was observed. A longer time to get a referral for colposcopy is associated with a lower likelihood of a woman successfully completing treatment. The data supports the need for systemic interventions to decrease wait time for colposcopy referral.

#115: Rebecca McKibben, MS2

Mentor: Dr. Eric Bass

Reducing Surgical Site Infections Associated with Cesarean Sections: A Review of Reviews

Background: Surgical site infections (SSI) are one of the leading causes of re-hospitalization among women undergoing cesarean section (C-section). Prevention of these infections is important to minimize patient morbidity and healthcare costs. The purpose of this comprehensive review is to synthesize the data from published reviews on the effectiveness of interventions to reduce SSI among C-section patients, assess the quality of these reviews, and identify evidence gaps that require additional research.

Methods: The database search included the Cochrane Database of Systematic Reviews, PubMed, MEDLINE, and EMBASE. Studies were included if they were published after 2000, in English, and focused on interventions to reduce SSI in women undergoing C-section, or included and reported separately on women undergoing C-section. A reviewer extracted the main findings from each review, and assembled the findings in a table format organized by type of intervention. Interventions were classified as pre-operative, intra-operative, post-operative, or a combination of pre-, intra-, and post-operative based on the primary intervention studied in the review. AMSTAR is a measurement tool that was used to assess the quality of reviews, based on criteria such as study inclusion criteria and the risk of bias. A meta-review of multiple reviews conducted on the same intervention was conducted to assess consistency and note discordant findings.

Results: Twenty-eight interventions designed to reduce SSI associated with C-section were identified through literature searches. Surgical technique interventions include the sub-categories of abdominal incision type and closure, uterine incision type and closure, subcutaneous tissue closure, drain use, placenta delivery, and peritoneum closure. Surgical environment interventions include the sub-categories of surgical team hand/forearm hygiene, surgical gloves, surgical masks, and drape use.

Conclusion: A comprehensive synthesis of interventions to reduce SSI among C-section patients is necessary to make evidence available to clinicians and obstetrical programs and to indicate evidence gaps to guide future research.

#116: Matthew Mesias, MS2

Mentor: Stephen Bowman, Ph.D

The Role of For-profit Hospital Status in Traumatic Brain Injury

Background: For-profit hospitals have higher variability in care than not-for profit hospitals, but the data are conflicting about whether for-profit hospital status is associated with increased inpatient mortality. The role of for-profit hospital ownership has not been previously studied in traumatic brain injury (TBI). We assessed the relationship of for-profit hospital ownership status with outcomes in patients with TBI, including: (1) in-hospital mortality, (2) total hospital charges and length of stay (LOS), and (3) procedural intensity (intracranial pressure monitoring (ICP) use).

Methods: Multivariable regression was performed with data from the Nationwide Inpatient Sample (NIS) for years 2006-2008. The NIS reflects approximately a 20% stratified sample of United States Community hospital admissions. Adults (18-64 years) hospitalized with serious, severe, and critical TBI were included (N = 22,425). Regressions controlled for age, sex, payer, injury severity, procedures and hospital factors (region, rural location, and teaching status). Mortality regressions stratified by payer were also performed.

Results: Overall, there was no significant difference in mortality between patients seen at for-profit and not-for-profit hospitals. Hospital charges for TBI, regardless of payer, were significantly greater in for-profit hospitals than in not-for profit hospitals. Patients with serious TBI were more likely to receive ICP monitoring [odds ratio (OR), 2.56; 95% confidence interval (CI) 1.17-5.64] than those seen at not-for-profit hospitals. Patients with Medicaid seen at for-profit hospitals were more likely to die [OR, 2.64; CI, 1.39-4.99] than patients seen at not-for profit hospitals. We did not find a statistically significant difference in mortality in patients with private insurance in regards to for-profit ownership.

Conclusion: In comparison to not-for-profit hospitals, for-profit hospitals appear to provide more expensive care to patients with TBI, and lower quality care to Medicaid patients with TBI.

#117: Luis A Murillo, MS2

Mentor: Charlotte Gaydos DrPH, MPH, MS

Influenza sub-typing analysis of a patient population at Johns Hopkins Hospital during the 2010-2011 influenza season

Background: The 2009 H1N1 pandemic highlighted the need for accurate, rapid tests to subtype influenza isolates. A broad range assay shown to be adaptable to novel influenza specimens is the RT-PCR/electron spray ionization mass spectrometry (ESI-MS) Influenza Typing Assay (Abbott Molecular). We present the performance characteristics of RT-PCR/ESI-MS and analyze the genetic variation of influenza strains detected by spectrometry data in patients presenting to the Johns Hopkins Hospital, January-May, 2011.

Methods: Nasopharyngeal (NP) samples were obtained from patients presenting to the Hospital with a suspected respiratory infection. A portion of each virology positive and negative sample was sent to the Maryland State Laboratory for confirmation via the Center for Disease Control (CDC) RT-PCR protocol. Before testing, a separate 300 ul aliquot of sample was provided for nucleic acid extraction and analysed by the ESI-MS protocol using the PLEX-ID instrument. The assay included primer sets targeting 8 genes (PB1, NP, M1, PA, NS1, NS2, H and N).

Results: A total of 77 NP samples were processed. According to reference testing (CDC RT-PCR), 41 samples were identified as swine H1N1, 24 as H3N2, 10 were negative and 2 were of insufficient quantity to be tested. The RT-PCR/ESI-MS assay identified 32 samples as pandemic swine H1N1, 2 mixed pandemic H1N1 phenotypes, 5 seasonal H1N1, 24 H3N2, and 14 negative samples. The most prevalent pandemic H1N1 strain was Influenza A/New York/15/2009 pandemic-H1N1 (16) followed by Influenza A/California/05/2009 pandemic-H1N1 (7). The most prevalent H3N2 strain was Influenza A/Thailand/CU-B1697/2009 (9) followed by Influenza A/ Kentucky/UR07-0148/2008 (7).

Conclusion: The RT-PCR/ESI-MS protocol is a tool for surveying influenza and discovering new genotypes. The advantage of RT-PCR/ESI-MS over the current gold standard RT-PCR protocol is that it provides rapid genomic characterization, which is important for monitoring the variability of viral strains in real time for rapid surveillance purposes.

#118:

#119: David Narotsky, MS3

Mentor: Julius Pham, M.D./Ph.D.

Are Marathons Dangerous? A Review of Mortality Data over 10 years

Background: To determine if the increase in marathon participation from 2000-2009 has affected mortality and overall performance

Methods: Observational study using publicly available data for number of marathon races, finishing race times, and deaths from 2000-2009

Results: The total number of marathon finishers has increased over this decade from 299,018 in 2000 to 473,354 in 2009. The average overall marathon finishing time is unchanged from 2000 to 2009 (4:34:47 vs 4:35:28, $p=0.85$). Out of 3,718,336 total marathon participants over the 10 year study period, we identified 28 people (6 females & 22 males) who died during the marathon race and up to 24 hours after finishing. The overall, male, and female death rate for the 10-year period was 0.75 (95% CI: 0.38, 1.13) deaths/100,000 finishers (p -value for trend, 0.860), 0.98 (95% CI: 0.48, 1.36) deaths/100,000 finishers (p -value for trend, 0.533), and 0.41 (95% CI: 0.21, 0.79) deaths/100,000 finishers (p -value for trend 0.238), respectively.

Conclusion: Participation in marathons has increased without any change in mortality or average overall performance from 2000-2009

#120: Angeline Nguyen, MS2
MSRD Poster Competitor

Mentor: Jocelyn S. McGee, M.S.G., Ph.D

Impact of home- and community-based service use on nursing home placement in persons with probable Alzheimer's disease

Background: Home- and community-based services (HCBS), which provide respite to caregivers of persons with dementia, may be associated with delaying nursing home placement (NHP) in persons with Alzheimer Disease (AD).

Methods: Using a longitudinal database from the Alzheimer Disease and Memory Disorders Center, we conducted an event-history analysis that includes log-rank tests and a Cox proportional hazards model to compare the time to NHP 1) amongst participants who first utilized HCBS at different stages of disease (mild, moderate, or severe based on MMSE score), 2) participants who had different preprogression rates (slow, intermediate, or rapid based on change in MMSE score per year), and 3) the interaction between disease stage at first HCBS utilization and preprogression rate on delaying time to NHP while controlling for age, sex, race, functional status, and cognitive status.

Results: The population (n=684) consists primarily of Caucasian patients with AD living in Texas. After adjusting for covariates, disease stage at first utilization of HCBS is only significantly associated with delayed time to NHP for those who began utilizing HCBS at the moderate stage (HR=0.40, CI = (.17, 0.97)) as compared to those utilizing HCBS at the severe stage. Preprogression rate is significantly associated with a shorter delay in time to NHP (p=0.001) for those who have intermediate and rapid preprogression rates as compared to those with a slow preprogression rate (HR=4.78, CI=(2.03,11.27) and HR=6.62, CI=(1.88,23.40), respectively). The interaction between timing of HCBS utilization and preprogression rate is not significant (P=0.20).

Conclusion: Utilization of HCBS before reaching the severe stage of disease is significantly related to delaying time to NHP, suggesting that there may be a critical time period in which to utilize HCBS. Additionally, having a more rapid preprogression rate is associated with a faster time to NHP, and this association is independent of HCBS utilization.

#121: Ralph J Passarella, MS2
MSRD Poster Competitor

Mentor: Mark Dredze, Ph.D

Capturing Patient Input on Patient Safety via Novel Machine Learning Tool

Background: A major problem in patient safety today is the effective incorporation of patient input. The WHO formally declared the need for patients to take an active, participatory role in improving their well-being. However, currently no large-scale, immediate mechanisms exist to capture patient health dialogue. Recent studies have demonstrated the potential for social media sites to do so. Here, we used a machine learning algorithm to mine Twitter for self-reported patient safety incidents.

Methods: A machine learning algorithm used twenty keywords to search 1.6 million health tweets from Twitter.com for patient safety events. From an initial 11,000 candidate patient safety tweets, three independent researchers manually identified the first 150 patient safety tweets. These 150 tweets were descriptively analyzed for content including: tweet source, error source, error type, and emotional response. Search and description criteria were generated by patient safety experts.

Results: Patients and their family and friends generated 87% of patient safety tweets analyzed with the remaining 13% from unknown sources. Medication errors were the most frequently stated error type at 45%. Physicians were noted 54 times as the error source and surgeons 33 times. Users expressed a broad range of emotions regarding patient safety events including sadness, anger, prayer and humor. Notably, 18 tweets stated intent to sue a hospital or provider, some noting specific names of physicians and hospital systems.

Conclusion: Our results suggest that patients and patients' friends and family report patient safety events on Twitter. Our results present significant implications for hospital systems and medical providers covering issues from patient satisfaction to medical liability. In the future we will perform quantitative analyses of patient safety tweets, assessing such phenomena as the "July Effect". While limited to the Twitter-user demographic, this study demonstrates the potential novel use of social media to capture patient input and inform healthcare processes across all domains.

#122: Michelle Peng, MS2

Mentor: David Friedman, M.D., Ph.D.

Visual Disturbances Following Laser Peripheral Iridotomy

Background: Glaucoma is the second leading cause of blindness worldwide, with angle closure glaucoma accounting for up to half of all cases. Laser peripheral iridotomy (LPI) is the current standard of care for angle closure glaucoma. Addressing the harms as well as the benefits of LPI is essential for determining whether it is appropriate for all cases of angle closure.

Methods: Eighteen months following treatment, LPI cases underwent digital iris photography and photogrammetry to characterize the LPI, Lens Opacity Classification System III cataract grading, and measurement of retinal straylight in treated and untreated eyes, prior to inquiry about visual complaints. Controls answered a glare questionnaire, underwent straylight measurement, and received cataract grading.

Results: Among 230 cases (121 [58.8%] with LPI totally covered by the lid, 43 [19.8%] partly-covered, 53 [24.4%] uncovered), 217 (94.3%) completed all testing, as did 250/268 (93.3%) controls. Age, gender, prevalence of visual complaints, and cataract grades did not differ between cases and controls, though nuclear ($p < 0.01$) and cortical ($p = 0.03$) cataract were more common among LPI cases. Neither presenting visual acuity nor straylight score differed between the treated and untreated eyes among all LPI cases. Prevalence of subjective glare did not differ significantly between cases with totally-covered (6.61%), partially-covered (11.6%) or totally-uncovered (9.43%) LPI. In regression models, only worse cortical cataract grade ($p = 0.01$) was significantly associated with higher straylight score, with no potential predictors for subjective glare.

Conclusion: Taken together, these results suggest that LPI is safe with regard to measures of straylight and visual complaints. This randomized study provides the best evidence yet that large-scale screening and treatment programs for narrow angles are unlikely to result in important visual disability in the mid-term.

#123: Ellie Souganidis, MS2

Mentor: Richard Semba, MD/MPH

Determinants of Anemia Clustering Among Mothers and Children in Indonesia

Background: Anemia is a significant public health problem among women and children in developing countries. Clustering of anemia, defined as hemoglobin < 12g/dL in the mother and < 11 g/dl in the youngest child (aged 6-59 months), suggests the effects of a shared environment, including similar access to nutrition, sanitation, and health care. The purpose of our study was to describe the clustering of anemia among mothers and children from rural areas and urban slums of Indonesia. Additionally, we examined the potential role of associated risk factors in developing effective prevention strategies targeted at reducing anemia in those specific populations.

Methods: The study subjects consisted of families from rural areas and urban slums of Indonesia that participated in the National Surveillance Survey from 1999 to 2003. For each family, demographic, socioeconomic, and health-related information was collected. Chi-square tests were used to compare categorical variables between groups. Multivariate logistic regression models were used to examine the relationship between risk factors and anemia clustering.

Results: Anemia clustering occurred in 4,907 (18.3%) of 26,809 urban families and 12,756 (15.5%) of 82,291 rural families. Maternal overweight/obesity, older child age, consumption of fortified milk by the child, use of iodized salt, vitamin A supplementation, and greater expenditure on animal and plant source foods were associated with lower odds of anemia clustering. Older maternal age, maternal underweight, ≥ 2 children in the family, and >4 individuals eating from the same kitchen were associated with greater odds of anemia clustering.

Conclusion: Use of fortified milk, iodized salt, vitamin A supplementation, and greater expenditure on plant and animal source foods are among modifiable risk factors associated with lower risk of anemia clustering in Indonesia and could serve as the basis for the continuation and modification of food fortification and micronutrient supplementation programs targeted at both mothers and children.

#124: Yong Suh, MS2
MSRD Poster Competitor

Mentor: Dr. Eric Bass, MD, MPH

Comparative Effectiveness of Insulin Delivery and Glucose Monitoring Methods for Improving Weight Management in Diabetes Patients

Background: Studies on new technologies for improving the management of diabetes mellitus have come to mixed conclusions about the comparative effectiveness of continuous subcutaneous insulin infusion (CSII) versus multiple daily injections of insulin (MDI) and of real-time continuous glucose monitoring (rt-CGM) versus self-monitoring of blood glucose (SMBG). The purpose of this systematic review was to compare new technologies (CSII or rt-CGM) with the corresponding standard care (MDI or SMBG) in terms of their effects on a particularly important outcome, weight management, in patients with type 1 (T1DM) or type 2 diabetes (T2DM).

Methods: We identified relevant studies through PubMed, EMBASE, and Cochrane CENTRAL. Two reviewers independently reviewed titles and abstracts to identify original reports of randomized controlled trials (RCTs) or observational studies comparing the interventions of interest. Each included article underwent dual review by a pair of investigators to extract data on study characteristics and outcomes, and to assess study quality.

Results: Eleven RCTs and two observational studies were in the final review. In children with T1DM, two studies found no difference in weight change between the two interventions. In adults with T1DM, four studies showed no significant weight change in either intervention group. Similarly, neither of the 2 studies conducted in adults with T2DM and neither of the 2 studies in pregnant women with preexisting T1DM showed a statistically significant difference in weight gain between the two intervention arms. Finally, there was no statistically significant difference in weight gain between the sensor-augmented pump and the MDI/SMBG groups. Overall strength of evidence was low for these comparisons because the studies were small and had limited weight data.

Conclusion: Neither CSII nor rt-CGM helps to improve weight management in comparison with standard care for diabetes mellitus. Clinicians and patients should not expect the use of these new technologies to be sufficient for improving weight management.

#125: Christine Sailer, MS2

Mentor: Petros Karakousis, MD

Multiplex Allele-Specific PCR for Detection of MDR-TB in Panama

Background: Multidrug-resistant tuberculosis (MDR-TB), defined as resistance to the two first-line drugs isoniazid and rifampin, threatens to reverse recent gains in TB control worldwide. The use of currently available culture-based methods in Panama and other developing countries significantly delays detection of MDR-TB cases, resulting in continued transmission throughout the community. MDR-TB requires the use of second-line drugs, which are much less effective, more expensive, and more toxic. It is associated with higher mortality and treatment failure rates, as well as increased transmission of infection. Compared to other molecular tests, Multiplex Allele-Specific Polymerase Chain Reaction (MAS-PCR) is a simple and rapid assay to detect isoniazid and rifampin resistance in *M. tuberculosis* clinical isolates based on PCR of relevant genetic regions and agarose gel electrophoresis without the need for subsequent sequence analysis. Wider use of MAS-PCR would allow for the simultaneous detection of the most common isoniazid and rifampin resistance-associated genetic mutations at relatively low cost and with reduced need for technical expertise.

Methods: Between the period 2002-2009, the Gorgas Institute in Panama collected 69 culture-proven clinical isolates of MDR-TB. We performed DNA sequencing and MAS-PCR on these isolates, as well as on 40 additional non-resistant isolates that served as negative controls.

Results: Preliminary sequencing shows that the mutations our protocol was designed to detect account for 82% of the isoniazid-resistant strains and 93% of the rifampin-resistant strains. Among these isolates with detectable mutations, the MAS-PCR technique has 100% specificity and 97% sensitivity in identifying isoniazid and rifampin resistance.

Conclusion: MAS-PCR has high sensitivity and specificity in detecting isoniazid and rifampin resistance among Panamanian MDR-TB isolates. Furthermore, the prevalence of genetic mutations associated with isoniazid and rifampin resistance among MDR-TB isolates in Panama is similar to that in other areas of the world.

#126: Ruth Tamrat, MS2

Mentor: Dr. Madhav Goyal

Hospitalist Unit Sleep Hygiene (HUSH) Project

Background: Sixty-three percent of inpatients report trouble sleeping through the night, and many inpatients have a sleep quality similar to that of insomniacs. Sleep deprivation has been reported to have harmful health effects, including declines in immune function and wound healing as well as increases in pain and mortality. We sought to design an intervention to improve sleep among medical inpatients on a Hopkins ward that could be tested experimentally for its efficacy in improving inpatient sleep as well as health outcomes.

Methods: A multi-faceted approach was used to design this intervention. An extensive literature review identified previously attempted in-hospital sleep interventions. A 10-hour observation of the ward at night was used to assess which of these interventions were most applicable to Halsted 6. Finally, a meeting with the Nurse Manager allowed for further fine-tuning of the protocol.

Results: Common sleep interventions that have been cited include: noise interventions, rescheduling of procedures, aromatherapy, and massage. The night of observation and interview identified noise and procedural interventions as particularly applicable to Halsted 6. The current design of the pilot study involves: procedural and noise interventions, patient caffeine consumption modifications, and clustering of nursing activities. The entire unit will alternate between the usual protocol and the sleep protocol, adhering to each for 60 days each with a 2-week washout period separating them. The primary outcome to be measured is symptom distress. Secondary outcomes include: sleep quality and quantity, pain, delirium, patient satisfaction, blood pressure, frequency of arrhythmias, and electrolyte disturbances.

Conclusion: Based on our review, interview, and observations, we have designed a multi-component approach to improving sleep on the medical ward that can be tested experimentally using a variety of objective and subjective measures. Such a study could help inform sleep hygiene practices on the medical ward, and possibly improve inpatient experience and health outcomes.

#127: Julia Thorn, MS2
MSRD Poster Competitor

Mentor: Roma Vasa, M.D.

Effects of manipulating attention on the neural response to threat stimuli in children with and without anxiety disorders

Background: Anxiety disorders are the most prevalent childhood psychiatric conditions, yet their pathophysiology remains poorly understood. This study examines whether children with and without anxiety disorders differ in their behavioral and brain responses when viewing facial expressions of emotion under two different attentional conditions.

Methods: Twenty control and 24 anxious 8 to 12 year-olds underwent functional magnetic resonance imaging (fMRI). During the scan, subjects viewed 8 blocks of faces with 32 faces per block (8 per emotion type: angry, fearful, happy, neutral). Each block was preceded with one of two questions, either "Are you afraid of the face?" (Afraid task), or "Is the face a female?" (Non-emotional task); subjects responded "Yes" or "No" accordingly after viewing each face. Diagnostic group x face type repeated measure ANOVAs were conducted on the behavioral data.

Results: For the Afraid task, there was a significant group x face type interaction on the percent Yes responses ($p = 0.047$). Anxious children provided more Yes responses than controls for angry (38% vs. 11.4%, $p = 0.004$) and fearful (25.7% vs. 4.4%, $p = 0.003$) faces. For the Non-emotional task, a main effect of face type was observed on percent correct responses ($p = 0.005$), indicating that all children had more correct responses to happy (91.8%) and neutral (91%) faces than angry (88.5%) and fearful (87.4%) faces ($p < 0.05$ for all relevant t-tests).

Conclusion: Anxious children report greater levels of fear when viewing angry and fearful faces compared to control children. This exaggerated response in anxious children reflects heightened sensitivity of the neural circuits mediating the fear response. Interestingly, both groups made more errors when evaluating the gender of angry/fearful faces vs. happy/neutral faces. This suggests that all children implicitly process threat stimuli when performing a non-emotional task. Analyses of fMRI data corresponding to these behavioral responses are underway.

#128: Beth Vrabel, MS2

Mentor: Bradley Herring, Ph.D.

Projected Effects of Medicaid Reimbursement Rates on Primary Care Physician Participation and Perceptions

Background: The expansion of Medicaid eligibility under the Patient Protection and Affordable Care Act raises concerns about a shortage of primary care physicians willing to accept new Medicaid patients. To address this potential shortage, Medicaid reimbursement rates for primary care services will be increased to no less than 100% of Medicare rates in 2013 and 2014. The purpose of this project is to examine the projected effect of increasing Medicaid reimbursement rates on primary care physician participation and perceptions.

Methods: Using the Urban Institute's Medicaid-to-Medicare fee indices and office-based primary care MD responses to national Health Tracking Surveys administered in 1998-1999, 2004-2005 and 2008, we performed multivariate logistic regression analyses to examine whether changes in Medicaid reimbursement rates over time were associated with changes in primary care physician participation, physician perceptions regarding their ability to provide high quality care and spend adequate time with patients, and/or overall career satisfaction among primary care physicians.

Results: Increases in Medicaid reimbursement rates over time were marginally associated with increased willingness of office-based primary care MDs to accept new Medicaid patients (odds ratio [OR] 2.2, 95% confidence interval [CI] 0.89-5.30, $p=0.09$) and significantly associated with decreased importance of inadequate reimbursement as a reason not to accept new Medicaid patients (OR 0.89, 95% CI 0.82-0.98, $p=0.01$). Increases in reimbursement rates were significantly associated with an increase in perceived ability to provide high quality care (OR 6.6, 95% CI 1.50-28.8, $p=0.01$), but not associated with an increase in perceived ability to spend adequate time with patients (OR 1.3, 95% CI 0.27-6.08, $p=0.75$). Increases in reimbursement rates were also significantly associated with increased overall career satisfaction (OR 3.1, 95% CI 1.20-8.23, $p=0.02$).

Conclusion: We found that increased Medicaid reimbursement rates were significantly associated with several important factors that may affect the willingness of primary care physicians to accept new Medicaid patients.

#129: Sharon Weeks, MS2
MSRD Poster Competitor

Mentor: Kent Stevens, MD, PhD

Is the Kampala Trauma Score An Effective Predictor of Mortality In Low-Resource Settings? A Comparison of Multiple Trauma Severity Scores

Background: Injury results in an estimated 5.8 million deaths worldwide annually, with the majority in developing countries. Multiple severity scores have been developed and validated for the developed world, but few studies support the effectiveness of these scores in the developing world. The Kampala Trauma Score (KTS) was developed for resource-limited settings and has been shown to be a robust predictor of death. However, evidence supporting its utility over other tools is limited. This study evaluates trauma scores as predictors of mortality in a large prospective patient cohort in Cameroon.

Methods: This prospective study was conducted in the emergency ward of the Central Hospital of Yaoundé, Cameroon. Collected information included patient demographics, clinical presentation and outcome. We calculated KTS, Injury Severity Score (ISS), Revised Trauma Score (RTS), Glasgow Coma Scale (GCS) and Trauma Injury Severity Score (TRISS) for each patient. We evaluated scores as predictors of mortality and compared areas under ROC curves.

Results: We enrolled 2855 patients. 73% of patients were male; 60% presented after a road traffic injury. 60% of patients had mild injuries (ISS<9), 29% moderate (9-15), 8% severe (16-24) and 3% profound (> 24). The mortality rate was 0.6%. Logistic regression analysis showed each score to be a statistically significant predictor of mortality ($p<0.05$). The area under the ROC for KTS as a predictor of mortality was 0.7748 (95% CI: 0.6285 - 0.9212). No pairwise difference between AUROC's was statistically significant. Similar results were found when analysis was limited to severe injuries.

Conclusion: This comparison analysis of KTS to developed world trauma scores supports the adoption of KTS for injury surveillance and triage in resource-limited settings. The Kampala Trauma Score is as effective as other scoring systems in predicting patient mortality. As KTS is simple to administer and record, it is therefore a valuable tool available for resource-limited settings.

#130: Carla Williams, MS2
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Mentor: Sean Tunis, MD

Evaluation of Stakeholder Engagement in Comparative Effectiveness Research

Background: Involving patients, providers, payers, policymakers, and industry representatives in comparative effectiveness research (CER) is gaining national attention. The goal of involving stakeholders throughout the research process is to produce findings that are more closely aligned with the information needs of real-world decision-makers. To test this concept, input from 13 stakeholders was used to prioritize research conducted by the Center for CER in Cancer Genomics (CANCERGEN). To determine the project's success and to identify areas for improvement, we initiated an evaluation of engagement practices in CANCERGEN.

Methods: First, we conducted a literature review of evaluation practices. 140 articles were identified; 46 were relevant to evaluation of stakeholder or public engagement and were read in full. In parallel, we performed an evaluation of stakeholder engagement in CANCERGEN, which consisted of a 29-statement, Likert-scale survey and one-on-one semi-structured phone interviews. A conventional content analysis of the interviews was performed. Data was independently coded by two investigators and evaluation participants reviewed the findings to provide further validation.

Results: Six meta-criteria for evaluation were identified in the literature: respect, trust, legitimacy, fairness, competence and accountability. We defined each meta-criterion and matched domains to each to serve as a guide for developing an evaluation tool. Eleven stakeholders completed the CANCERGEN evaluation. Survey results showed that stakeholders were satisfied with their experience, with the majority agreeing or strongly agreeing with the questions. Interview results confirmed that the stakeholder group was well balanced and successfully facilitated. Areas for improvement include creating a standardized selection process and clear role descriptions, increasing technology usage, accelerating the priority setting process, and including more feedback from investigators about how stakeholder input informs clinical research.

Conclusion: Evaluation of stakeholder engagement is important and should assess for respect, trust, legitimacy, fairness, competence and accountability. Methods for engagement in CANCERGEN worked well although areas for improvement were identified.