A Randomized Controlled Trial of Rectal Indomethacin for the Prevention of Post-ERCP Pancreatitis.

B. J. Elmunzer, James M. Scheiman, Glen A. Lehman, Amitabh Chak, Patrick Mosler, Peter D. Higgins, Akbar K. Waljee, Rodney A. Hayward, Joseph Romagnuolo, Grace H. Elta, Stuart Sherman, Evan L. Fogel

**Background:** Preliminary research suggests that rectally administered non-steroidal anti-inflammatory drugs (NSAIDs) may reduce the incidence of pancreatitis after endoscopic retrograde cholangiopancreatography (ERCP).

**Methods:** A multi-center, randomized, placebo-controlled, double-blinded clinical trial enrolling subjects at elevated risk for post-ERCP pancreatitis was conducted. High-risk subjects were included on the basis of validated patient and procedure-related risk factors. Enrolled subjects were randomized to receive a single dose of rectal indomethacin or placebo immediately after ERCP. The primary outcome was post-ERCP pancreatitis, defined as new upper abdominal pain, pancreatic enzyme elevation at least three times the upper limit of normal 24 hours after the procedure, and hospitalization of at least two nights.

**Results:** Six hundred and two subjects were enrolled and completed follow-up. The majority of enrolled subjects (82%) had a clinical suspicion of sphincter of Oddi dysfunction. Fifty-two of 307 (16.9%) patients in the placebo group developed post-ERCP pancreatitis compared with 27 of 295 (9.2%) patients in the indomethacin group (p=0.005). Twenty-seven patients (8.8%) in the placebo group and 13 patients (4.4%) in the indomethacin group developed moderate to severe pancreatitis (p=0.034).

**Conclusions:** Among patients at high risk for post-ERCP pancreatitis, rectal indomethacin significantly reduced the incidence of the condition. (ClinicalTrials.gov number, NCT00820612)

Algorithms Outperform Metabolite Tests in Predicting Response of Patients with Inflammatory Bowel Disease to Thiopurines

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**Background & Aims:** Levels of the thiopurine metabolites 6-thioguanine nucleotide (6-TGN) and 6-methylmercaptopurine commonly are monitored during thiopurine therapy for inflammatory bowel disease despite this test’s high cost and poor prediction of clinical response (sensitivity, 62%; specificity, 72%). We investigated whether patterns in common laboratory parameters might be used to identify appropriate immunologic responses to thiopurine and whether they are more accurate than measurements of thiopurine metabolites in identifying patients who respond to therapy. METHODS: We identified 774 patients with inflammatory bowel disease on thiopurine therapy using metabolite and standard laboratory tests over a 24-hour time period. Machine learning algorithms were developed using laboratory values and age in a random training set of 70% of the cases; these algorithms were tested in the remaining 30% of the cases.

**Results:** A random forest algorithm was developed based on laboratory and age data; it differentiated clinical responders from nonresponders in the test set with an area under the receiver operating characteristic (AUROC) curve of 0.856. In contrast, 6-TGN levels differentiated clinical responders from nonresponders with an AUROC of 0.594 (P < .001). Algorithms developed to identify thiopurine nonadherence (AUROC, 0.813) and thiopurine shunters (AUROC, 0.797) were accurate.

**Conclusions:** Algorithms that use age and laboratory values can differentiate clinical response, nonadherence, and shunting of thiopurine metabolism among patients who take thiopurines. This approach was less costly and more accurate than 6-TGN metabolite measurements in predicting clinical response. If validated, this approach would provide a low-cost, rapid alternative to metabolite measurements for monitoring thiopurine use.

View this article’s video abstract at www.cghjournal.org.
Bowel Dysfunction Symptom Characteristics and Patient-Physician Communication Concordance Questionnaires in the Spinal Cord Injured Population
Baker, Jason MS, Kalpakjian, Claire Phd, Schutt, William BS, Rodriguez, Maria M. Gianna MD

Background: The spinal cord population tends to experience medical issues concerning several physiological and anatomical systems in the body. Bowel dysfunction including constipation and fecal incontinence affects the majority of individuals with a spinal cord injury. Altered bowel patterns in spinal cord injured patients lower quality of life and interrupts lifestyle. Bowel management, suchlike scheduled defecation periods, laxative therapy, suppositories, and digital manipulation, become time consuming and difficult for this injured population. Spinal cord injuries are growing in number in the United States with the majority of the injuries occurring between the ages of sixteen and thirty. Thus, spinal cord injured individuals are force to adapt concerning their bowel dysfunction for a larger percentage of their lives. Since spinal cord injuries are becoming more prevalent, the importance of effective communication between patient and physician is vital. Communication adherence between the spinal cord injury individual and their physician will limit the possibility of scheduling unnecessary diagnostic studies and enhance the efficacy of the overall medical treatment plan. This study has two objectives. First, it will examine the reliability and consistency of a modified questionnaire related to psychometric bowel characteristics in the spinal cord injured population. Secondly, evaluate the utility of specific questions concerning communication between the spinal cord injured individual and physician. These questionnaires have an impact to influence and guide physicians in making medical decisions relating to bowel dysfunction and awareness of effective communication.

Cannabinoid Modulation of Fear Extinction Learning and Underlying Brain Circuitry in Healthy Humans
Rabinak, Christine, Ph.D., Angstadt, Mike, B.S., Sripada, Chandra, Ph.D., M.D., Abelson, J.L., Ph.D., M.D., Phan, K. Luan, M.D.

Background: Exposure therapy is the treatment of choice for anxiety disorders involving fear-based avoidance. Its therapeutic power could potentially be enhanced (e.g., via greater speed, maintenance and generalization of effects) through basic-science derived tools such as cannabinoid agonists, which, in animal models, enhance fear extinction and its retention through actions within the ventromedial prefrontal cortex (vmPFC) and hippocampus (HPC), brain structures critical to fear extinction. Translation to human use requires testing cannabinoid effects on these neural circuits and retention of extinction memory in human models.

Methods: We conducted an fMRI study using a randomized, double-blind, placebo-controlled, between-subjects design, coupled with a standard Pavlovian fear extinction paradigm and simultaneous skin conductance response (SCR) recording with an acute pharmacological challenge with oral dronabinol (synthetic 9-tetrahydrocannabinol; THC, n = 15) or placebo (PBO, n = 15) 2 hours prior to extinction learning in healthy adult volunteers to assess the effects of THC on vmPFC and HPC activation when tested for recall and maintenance of extinction learning at 24 hours and 1 week after training, respectively.

Results: Compared to subjects who received PBO, those who received THC showed increased vmPFC and HPC activation and reduced fear responding (low SCR) to the extinguished fear cue when extinction memory recall was tested.

Conclusions: The data suggest that THC reduced fear expression at extinction recall testing via increased recruitment of vmPFC and HPC. They provide “proof of concept” that pharmacological enhancement of extinction learning is feasible in humans using cannabinoid system modulators, which may thus warrant further development and clinical testing.
Cognitive Impairment and Medicare Utilization Near the End-of-Life
Lauren Hersch Nicholas, David M. Weir, Theodore J. Iwashyna, Kenneth M. Langa

Introduction: Healthcare utilization near the end-of-life is a controversial topic; aggressive care for patients in the last six months of life are costly to the Medicare program, and it is unknown whether these treatments reflect patient preferences or improve quality of life. Although cognitive impairment may hinder patients’ abilities to assess treatment options at the end-of-life, little is known about end-of-life care for cognitively impaired and unimpaired older adults.

Methods: We use survey data from the Health and Retirement Study linked to Medicare claims for 3,302 respondents who died between 1998 and 2007. Respondent cognitive functioning is assessed using a Telephone Interview for Cognitive Status score and proxy reports of patient functioning. Inpatient hospitalization records are used to assess receipt of life-sustaining treatments including feeding tube placement, mechanical ventilation, hemodialysis, CPR, and intubation, in-hospital death and intensive care unit (ICU) stays. We used multivariate logistic regression to compare treatment of decedents with and without cognitive impairment.

Results: 41% of Medicare decedents were unimpaired, 29% were borderline impaired and 30% were cognitively impaired. Cognitively impaired and unimpaired decedents were equally likely to be hospitalized in the last six months of life, though only 40% of decedents with borderline or full cognitive impairment had written advance directives in place. Compared to unimpaired decedents, cognitively impaired patients were less likely to receive life-sustaining interventions (OR = 0.68, 95% CI [0.57,0.81]); equally likely to die in the hospital (OR = 0.98, 95% CI [0.82,1.16]), and less likely to have an ICU stay (OR = 0.82, 95% CI [0.67,0.99]).

Conclusions: A large proportion of elderly decedents reach the end-of-life without documented treatment preferences or surrogate decision-maker and possible incapacity for informed consent. Although cognitive impairment is a terminal condition, impaired patients face similar odds of receiving many aggressive treatments near the end-of-life. Physician discussions earlier in life are potentially helpful to create awareness, facilitate decision-making while unimpaired.

DASH-Style Diet is Effective in Patients with Treated Hypertension and Diastolic Heart Failure Independent of Change in Body Weight – a Pilot Study
Seymour, E Mitchell, Ph.D., Wells, Johanna M, Hummel, Scott L, Bolling, Steven F

Background: Diastolic heart failure is a leading cause of death in the aged. The effects of diet on diastolic heart failure are poorly understood. The Dietary Approaches to Stop Hypertension (DASH) diet is rich in fruits, vegetables and potassium and is and lower in salt; DASH may also effect diastolic heart failure.

Purpose: We hypothesized that three weeks of a controlled DASH diet would reduce blood pressure, arterial stiffness, and oxidative stress in hypertensive patients with diastolic heart failure.

Methods: Subjects (n=13, age 71±12 y, mean BMI 33.6±7.9 kg/m2) were instructed to maintain their hypertensive medications. Baseline dietary habits were measured by the 96-question Block Food Frequency questionnaire (FFQ). DASH diet prepared by a metabolic kitchen was administered for 21 days. Menu analysis confirmed DASH guideline concordance. Body weight was strictly maintained by regular assessment and menu adjustment. Paired, two-tailed t-tests examined treatment effects versus baseline values.

Results: DASH diet reduced clinic systolic BP (155±29 to 138±22, p=0.02) and diastolic BP (79±15 to 72±8, p=0.04) and 24-hour systolic BP (130±4 to 123±4, p=0.02) and diastolic BP (67±3 to 62±3, p=0.02), all values in mmHg. DASH diet decreased pulse wave velocity (12.4±3.0 to 11.0±2.2 m/s, p=0.03) and increased six minute walk distance (313±86 to 337±91 m, p<0.01). Finally, DASH diet reduced urinary 8-isoprostane (209±84 to 144±46 pmol/mmol Cr, p=.02). In patients with diastolic heart failure, three weeks of DASH diet intake reduced systemic blood pressure, arterial stiffness, and oxidative stress. This pilot study may guide expanded studies in this patient population.
Hox6 Genes are Important Niche Factors that Play Critical Roles in the Proper Formation and Maintenance of the Pancreas
Hrycaj, Steven PhD, Larsen, Brian BS, Gong, Ke-Qin MD, Wellik, Deneen PhD

Despite significant advances in our understanding of endocrine pancreatic development, the function of the pancreatic mesodermal niche in this process is less well understood. However, niche factors are necessary for proper endocrine development and are likely to be of critical importance in designing successful regenerative therapies aimed at replacing lost islet cells in diabetic patients. Preliminary data generated in our laboratory demonstrates a critical role for Hox6 genes in pancreatic organogenesis. Hox6 genes are expressed exclusively in the pancreatic mesenchyme (and not epithelium) and suggest a primary role for Hox6 genes in proper development of the pancreatic niche. The pancreatic phenotypic abnormalities observed in our Hox6 triple mutants confirm this, as total pancreatic volume in mutants is reduced compared to littermate controls and there is a drastic reduction of hormone producing cells. Finally, while triple mutants die shortly after birth, surviving compound mutants exhibit hyperglycemia and impaired responses in glucose tolerance tests. Moreover, these defects are exacerbated with age and, as Hox6 genes remain expressed in the pancreas through post-natal and adult stages, suggest that Hox6 genes may contribute to post-natal endocrine maintenance as well. Overall, these data suggest that Hox6 genes are critical pancreatic niche factors, necessary for the proper development and maintenance of pancreatic organogenesis.

Indirect Effect of Inhibitory Control Deficit on Body Mass Index Through Tasty-Unhealthy Food Choices: A Structural Equation Model.
Jasinska, Agnes, PhD, Yasuda, Marie, BS, Burant, Charles, MD, PhD, Falk, Emily, PhD.

Background: Impairment in inhibitory control is increasingly recognized as a risk factor for overeating and obesity, but the processes through which inhibitory control deficits affect eating behavior are not fully understood.

Methods: Participants were 172 healthy undergraduates recruited from the Communications Studies subject pool at the University of Michigan. Participants were instructed to refrain from eating and drinking (except water) for at least two hours prior to the study in order to induce hunger and heightened reactivity to food-related stimuli. All participants completed a food-distracter Go/NoGo task to assess the efficiency of inhibitory control in the presence of food cues, and a Food Choice task to assess decision-making about food, as well as other tasks and questionnaire measures as part of a larger study of cognitive control and health behavior. The data were analyzed using structural equation modeling.

Results: We demonstrate that inhibitory control deficits are associated with elevated body mass index (BMI) in part through increased tendency to choose tasty but unhealthy foods, controlling for the effects of hunger. Importantly, the indirect effect is specific to tasty-unhealthy food choices, hypothesized to involve inhibitory control, and is not observed for tasty-healthy or untasty-healthy food choices. These results add to our understanding of the role of cognitive control and decision-making processes in unhealthy eating and may have implications for the treatment and prevention of obesity.
Mirror Neuron Function and Theory of Mind in Patients with Amyotrophic Lateral Sclerosis.
Laura Jelsone-Swain & Robert C. Welsh, Department of Radiology, University of Michigan

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder of the upper and lower motor neurons, with an average survival time of 3-5 years from symptom onset. It has recently become clear that ALS is a multimodal disease also involving cognitive dysfunction. Motor mirror neurons, which are related to cognitive functioning, are bimodal neurons located in the premotor cortex and inferior parietal lobe of the human brain that respond to motor actions of self and others. This double specificity allows for the ability to recognize and understand the actions of others, which is a component of the complex and high-level cognitive behavior called theory of mind. Therefore, the goal of our study is to examine this mirror neuron system (MNS) and theory of mind processing in patients with ALS. Because the MNS has never been directly investigated in ALS, we first aim to identify whether ALS affects the underlying neural substrate of this system. This will be investigated during an action execution and observation task. Our second aim is to examine the relationship between cognitive dysfunction and MNS processing during a theory of mind task. MNS processing will be measured by blood oxygenated level dependent (BOLD) signal activity in the brain between patients with ALS and healthy controls, using functional magnetic resonance imaging (fMRI). Clinically, the MNS is important during social behavior; thus any alteration of this capacity (behaviorally, cognitively, or physiologically) in ALS may be important in disease management and for planning effective therapeutic intervention.

Motivation for Reward in Parkinson’s Patients: Potential Association with Behavioral Addictions
Taylor, Jennifer, PhD, Aldridge, Wayne, PhD, Persad, Carol, PhD, Patil, Parag, MD, PhD, and Chou, Kelvin, MD.

Background: Some Parkinson’s patients develop behavioral addictions when treated with dopamine replacement therapy. Basic science studies suggest that this behavior may be related to an amplified motivational response to reward-related cues triggered by dopamine receptor stimulation.

Purpose: We investigated whether cue-induced motivation for reward (“incentive salience”) is related to the severity of behavioral addictions in Parkinson’s patients.

Methods: We used a human version of the Pavlovian Instrumental Transfer (PIT) task to measure incentive salience in Parkinson’s patients (n=13). During the training phase, participants earned quarters by squeezing a handgrip device. They separately learned that one audiovisual conditioned stimulus (CS+) predicted the delivery of quarters, while a control stimulus (CS-) did not. In the experimental “transfer” phase, we measured the motivational value of the reward-associated cue was by comparing the number of handgrips made in response to the CS+ compared to the CS-. We hypothesized that the difference between the CS+ responses and the CS- responses would positively correlate with scores on a behavioral addiction scale (QUIP-RS).

Results: Contrary to our hypothesis, we have not found a significant relationship between behavioral addictions and number of handgrips made in response to the CS+ compared to the CS- (R2=.15, ns) in the transfer phase of the task. Interestingly, however, the QUIP-RS scores positively correlated with the absolute number of responses to the CS+ (R2=.47, p<.01) and to the CS- (R2=.65, p<.01). This may indicate that those Parkinson’s patients who experience addictive behavior may have a generalized heightened motivation for reward.
Neural Responses to Reward Associated with Oxytocin (OXT) Gene Polymorphisms

Love, Tiffany (PhD), Scott, David (PhD), Goldman, David (MD), Hodgkinson, Colin (PhD), Enoch, Mary-Anne (MD), Zubieta, Jon-Kar (MD, PhD)

Background: Oxytocin is a neuropeptide principally known to play important roles in the regulation of affiliative and reproductive behaviors but is hypothesized to be influential in the expression of motivated behavior in general. Oxytocin and its receptors have been observed in regions associated with rewarding and motivated behavior, including within the nucleus accumbens.

Methods: Given the possibility that oxytocin may be influential in motivational processing, we examined the association between genetic variation at the oxytocin gene and anticipatory responses to reward using functional magnetic resonance imaging (fMRI).

Purpose: Six hundred and two subjects were enrolled and completed follow-up. The majority of enrolled subjects (82%) had a clinical suspicion of sphincter of Oddi dysfunction. Fifty-two of 307 (16.9%) patients in the placebo group developed post-ERCP pancreatitis compared with 27 of 295 (9.2%) patients in the indomethacin group (p=0.005). Twenty-seven patients (8.8%) in the placebo group and 13 patients (4.4%) in the indomethacin group developed moderate to severe pancreatitis (p=0.034).

Method: Four haplotype tagging single nucleotide polymorphisms (SNPs) located in noncoding regions just upstream/downstream of the oxytocin gene (OXT) were identified and, together with 186 ancestry informative markers, were genotyped using the Illumina GoldenGate platform (Hodgkinson et al, 2008) in a sample of twenty-six women and nineteen men. Each subject subsequently underwent fMRI scanning where they performed the monetary incentive delay task which has been previously described to robustly activate reward circuitry (Knuston et al 2001). Data was subjected to GLM analysis then coregistered and normalized into MNI space using SPM.

Results: We observed an association between OXT genotype and BOLD signal change in the nucleus accumbens during the anticipation of reward. Oxytocin has been previously shown to influence motivated behavior in regards to maternal and affiliative behavior. These results in combination with previous research suggest oxytocin may play a more generalized role capable of modulating motivational and reward processing outside of social and reproductive contexts.

Phenotypic Characterization of Clostridium Difficile Clinical Isolates

Carlson Jr., P.E. PhD, Walk, S. PhD, Bourgis, A.E.T., Liu, M., Young, V.B. MD, PhD, Aronoff, D.M. MD, and Hanna P.C. PhD.

Specific ribotypes of Clostridium difficile (Cd), associated with epidemic spread and increased disease severity, have been characterized as “hypervirulent”. This “hypervirulence” has been associated with enhanced sporulation and toxin production. However, the extent to which ribotype is associated with specific virulence phenotypes in vitro or predicts clinical disease severity in patients remains unknown. We sought to determine whether there is a correlation between multiple Cd phenotypic characteristics and either strain ribotype or clinical disease severity. More than 100 Cd strains, representing 13 different ribotypes and isolated from symptomatic patients, were analyzed. Detailed clinical information was available for 89 of the cases, which were diagnosed at the University of Michigan. Severe infection was defined according to 2007 CDC definitions. All strains were tested for germination efficiency, sporulation, spore viability, and growth rate. The tested isolates exhibited a wide range of phenotypes. All were capable of full germination within five minutes of exposure to bile salts. In contrast, the ability of isolates to sporulate was variable, with greater than a 100 fold difference observed across these strains. Even greater differences were observed in spore viability, with 1-83% of observed spores being capable of outgrowth. Although significant differences were observed in each of these assays, these results could not be correlated to a strain ribotype or clinical disease severity. Interestingly, a significant correlation between Cd growth rate and clinical disease severity was observed. Strains associated with severe disease exhibited faster growth than those associated with non-severe infection (p > 0.0001). We speculate that differences in growth rate will correlate with differences in toxin production (currently under assessment). We have newly identified a link between bacterial growth rate in vitro and clinical disease severity that is independent of ribotype. This study represents one of the first reports correlating a specific phenotype of Cd isolates and disease severity.
Plagiarism: Are you at Risk?
Ellen M. Lavoie Smith, PhD, APRN, AOCN® - Assistant Professor, University of Michigan School of Nursing

Problem: Plagiarism comprises 66% of scientific misconduct allegations investigated by the National Science Foundation. It is defined by the national Office of Research Integrity as theft or misappropriation of intellectual property, substantial unattributed textual copying of one’s own or another’s work, or unauthorized use of ideas obtained by a privileged communication. Plagiarism and duplicate/redundant publications accounted for 14.4% and 15.8% respectively of all article retractions occurring from 2000 - 2010. Close collaboration within scientific teams, “cut-and-paste” technology, and the significant pressure to “publish or perish” places academics at increased risk. Plagiarism can result in a variety of negative consequences ranging from loss of credibility to debarment for receiving federal funding. In addition, plagiarism falsifies the truth regarding the originator of an idea or the facts, strains the publication review process, and can lead to human harm.

Strategies: Several web- resources can be used to detect plagiarism. A few examples include iThenticate®, wCopy-find, and Turnitin. If plagiarism is suspected, authors can ask for assistance from their institutional Office of Research Integrity, funding agencies, and journal editors. International resources include the European Union and the Committee on Publication Ethics (COPE). Yet, despite these resources, there is ambiguity regarding how to interpret and operationalize the definition of plagiarism, and as a result, policies are not consistently enforced.

Conclusions: Academics are at increased risk to plagiarize, and to be plagiarized. Raising awareness regarding high-risk environments and available resources may help to prevent devastating personal, professional, and societal consequences of plagiarism.

Positive and Negative Emotional Expression Predict Poor Longitudinal Drinking Outcomes Among Alcoholics Interviewed about Drinking and it’s Consequences

Higher levels of positive affect have been associated with good health outcomes and health-protective factors in the general population. This study investigated whether positive and negative emotions expressed during the baseline interview of a longitudinal survey of alcohol-dependent individuals might predict drinking outcomes over time. We hypothesized that positive emotional expression would predict better outcomes and negative expression worse outcomes.

Results: 364 alcohol dependent individuals were asked open-ended questions about their drinking (e.g., What made you seek help for your alcohol problem right now?) Interviews were recorded and 56 were randomly selected and transcribed. Transcripts were analyzed by the Linguistic Inquiry and Word Count program to identify high content positive- and negative-emotion words. Partial correlations (controlling for age, gender, and baseline drinking severity) determined associations between affect expressions and percent days abstinent (PDA), drinks per drinking day (DDD), and percent heavy drinking days (HDD).

Results: Some positive emotions, such as joviality and well-being, as well as some negative emotions, such as guilt and stress, were associated with poor drinking outcomes. Some emotional states, such as anxiety, depression, anger, fatigue, fear, hostility, sadness, calmness, and serenity had no association with drinking.

Conclusions: While it is reasonable for alcoholics to express negative emotion while describing their drinking, it is noteworthy that both positive and negative emotional expressions were associated with poor longitudinal outcomes. These results suggest that affect examined as a predictor of outcomes for individuals with alcohol use disorders may be more complex than for individuals with other health challenges.
Preoperative and Intraoperative Predictors of Postoperative Acute Lung Injury in a Low-Incidence Surgical Population

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Background: Acute Lung Injury (ALI) is a devastating condition with an estimated mortality between 30 and 40 percent. There are data suggesting risk factors for ALI development in high risk populations, but few data are available in lower incidence populations. Using propensity-matched analysis and a combination of clinical and research datasets, we determined the incidence and risk factors for the development of ALI in this unstudied population.

Methods: We conducted a review of all adult non-cardiothoracic, non-transplant procedures performed between January 1, 2006 and July 1, 2009 using an anesthesia information system. This dataset was merged with an ALI registry and an institutional death registry. Preoperative variables were subjected to multivariate analysis. Propensity matching was then used to determine if there of intraoperative risk factors associated with the development of ALI.

Results: 53,910 separate patient admissions were identified and 102 (0.2%) of these patients developed ALI. Preoperative risk factors for ALI development after multivariate analysis included ASA status (OR 19.95), emergent surgery (OR 6.42), vascular or trauma surgery (OR 3.46), renal failure (OR 1.7), and number of anesthetics during the admission (OR 1.17). After matching, intraoperative risk factors included number of epochs with peak inspiratory pressure >= 30cm H2O (OR 1.063) and packed red cell transfusion (OR 5.53).

Conclusions: ALI is a rare condition postoperatively in the non-cardiothoracic, non-transplant population and is exceptionally uncommon in low ASA status patients undergoing scheduled surgery. Analysis after propensity matching suggests ALI development is associated with peak inspiratory pressures >= 30 cm H2O and transfusion.

RNA-seq Defined Glomerular Cell-Lineage Enriched Transcripts in Human Glomerular Disease

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To perform their specialized functions, glomerular endothelial, epithelial and mesangial cells have developed unique structural and molecular components. For a comprehensive survey of cell lineage-enriched transcripts, deep-sequencing (RNA-Seq) was employed on conditionally immortalized human endothelial and podocyte cell lines and microdissected glomeruli. Transcript abundance was determined using Affymetrix U133plus and RNA-Seq with 30 million reads per experiment(Illumina Genome Analyzer), yielding an average expression correlation of 0.80 for transcripts detected on both platforms. On NGS, a total of 17441 transcripts were detected above noise for podocytes, 17305 for endothelial cells, and filtered against 18244 transcripts in glomeruli to confirm in vivo expression. Cell lineage enrichment was defined by the absolute difference in normalized expression exceeded by 2 standard deviations across all transcripts and yielded 449 podocyte and 283 endothelial transcripts. The podocyte-enriched transcripts were interrogated for protein-protein interactions and the resulting networks analyzed for shared transcriptional responses using promoter models (Genomatix Modellnpector). Comparative promoter analysis defined a model containing transcription factor matrices VSZBP and VS$EGRF (including WT1) in TNRB, CAMK2B, COL4A4, MATN2. Among the 656 human genes containing the promoter model, 264 were present on Affymetrix HGU133A microarrays and investigated for their ability to classify expression profiles from 34 patients with glomerular diseases. These could also segregate glomerular transcriptional profiles of MGN from FSGS. Functional analysis of this gene set revealed significant overrepresentation of the Wnt canonical pathway and PI3K signaling events.
The Danforth’s Short Tail Mouse Phenotype is Due to a Retrotransposon Insertion Affecting Expression of the Ptf1a Gene

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Department of Pediatrics1, Center for Translational Pathology2, Department of Pathology3, Biological Chemistry Department4, University of Michigan DNA Sequencing Core5, Center for Computational Medicine and Bioinformatics6, Department of Human Genetics7, University of Michigan, Ann Arbor, MI USA

The semidominant Danforth’s short tail (Sd) mutation arose spontaneously in the 1920s. The homozygous Sd phenotype includes severe malformations of the axial skeleton with an absent tail, kidney agenesis, anal atresia, and persistent cloaca. The Sd mutant phenotype mirrors features seen in human caudal malformation syndromes including urorectal septum malformation sequence, VACTERL association and persistent cloaca. We hypothesize that identification of the Sd mutation will provide a model for understanding the etiology behind these human syndromes. The Sd mutation was previously mapped to mouse chromosome 2qA3. We performed Sanger sequencing of exons and intron/exon boundaries mapping to the Sd critical region and did not identify any mutations. We then performed DNA enrichment/capture followed by next generation sequencing (NGS) of the entire critical region. Standard bioinformatic analysis of paired-end sequence data did not reveal any causative mutations. We then interrogated reads that had been discarded because only a single end mapped correctly to the Sd locus. Using this novel technique, we identified an early transposon (ETn) retroviral insertion at the Sd locus, mapping 12.5 kb upstream of the Ptf1a gene. We further show that Ptf1a expression is significantly upregulated in Sd mutant embryos at E9.5. Although ETn sequences are predicted to affect expression of nearby genes when they insert intergenically, the Sd ETn is the first reported mutant phenotype due to this type of mechanism. Currently, work is underway to determine the role of Ptf1a in proper caudal development in mice and humans.

The Prevalence of cognitive Impairment in Older Adults with Heart Failure

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Objective: We used a national probability sample to determine the prevalence of cognitive impairment (CI) in older adults with heart failure (HF).

Methods: We used the 2004 wave of the Health and Retirement Study linked to 2002-04 Medicare claims (6,189 respondents ≥ 67 years old). An algorithm was developed using a combination of self- and proxy-report of a heart problem and the presence of ≥ 1 Medicare claim in inpatient, outpatient, and carrier files using standard HF diagnostic codes. On the basis of the algorithm, we created 3 categories to characterize the likelihood of having a HF diagnosis: 1) Moderate/High Probability of HF; 2) Low Probability of HF; and 3) Not a HF case. Cognitive function was assessed using a population-based screening measure of cognitive function or by proxy rating, depending on the respondent’s ability to self-respond. Age-adjusted prevalence estimates of CI were calculated for the highly likely HF cases (including high-moderate probability groups), low probability of HF group and non-HF cases. Multivariate logistic regression models were used to predict the independent association of heart failure with moderate/severe CI.

Results: Table 1-Age-adjusted prevalence estimates of cognitive performance, by heart disease category (n=6,189)

<table>
<thead>
<tr>
<th>Probability of Having Heart Failure (HF); n (%)</th>
<th>Not HF</th>
<th>Low Probability</th>
<th>Moderate/High Probability</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive performance</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>2,698 (0.72)</td>
<td>1,126 (0.67)</td>
<td>411 (0.59)</td>
<td>4,235 (0.70)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Mild impairment</td>
<td>778 (0.20)</td>
<td>419 (0.22)</td>
<td>184 (0.24)</td>
<td>1,381 (0.21)</td>
<td></td>
</tr>
<tr>
<td>Moderate/severe impairment</td>
<td>271 (0.07)</td>
<td>188 (0.09)</td>
<td>112 (0.14)</td>
<td>571 (0.09)</td>
<td></td>
</tr>
</tbody>
</table>

Heart failure was independently associated with moderate/severe cognitive impairment after adjustment for age, education level, net worth and prior stroke (OR: 1.48; 95% CI: 1.10-1.99).

Conclusions: Cognitive impairment commonly co-occurs with heart failure in community-dwelling older adults. Heart failure is an independent risk factor for the presence of cognitive impairment consistent with dementia. A cognitive assessment should be routinely incorporated into HF-focused models of care.
Visual Perception In Depressed Patients: A Behavioral and Brain Imaging Study
Jing Liu, Ph.D.

Abnormal neurochemical levels and neural network functions that underlie mental disorders can affect many brain areas and manifest in a range of measurable behavioral deficits, including visual perceptual deficits. Understanding the interplay between neurochemicals, neural network activity and behavior in the visual system thus can help understanding the neural origin of other deficits in mental disorders. The role of GABAergic inhibitory network in shaping visual perception, as well as its impact on mental disorders, has been receiving increasing attention. Scattered studies have found correlations between GABA level and visual perceptual accuracy in healthy observers. There is also converging evidence that GABA dysregulation (lower level in multiple brain regions, including the visual cortex) plays a major role in Major Depression Disorder (MDD). However, it is not clear how the lower GABA level affects neural network activity that lead to mood and cognitive deficits in MDD. In this study, we examine correlations between GABA level in the visual cortex, visual cortex activity during visual perception, and perceptual accuracy in both healthy subjects and those with MDD. We hope establish a model of GABA functions in the regulation of neural activity and behavior, so as to further investigate its role in the regulation of mood and cognitive functions in MDD. All of our protocols—visual perceptual tests, GABA measurement, brain activity measurement—have been established and we are in the stage of data collection and initial analysis.

Accuracy of Determining Small Renal Mass (SRM) Management with Risk-Stratified Biopsies: Confirmation by Final Pathology
Halverson, Schuyler, B.S., Gadzinski, Adam, B.S., Wolf, J. Stuart Jr.

Background: Tissue biopsy prior to surgical resection of a tumor is standard of care for a large proportion of resectable neoplasms. Renal cancer is an exception to this rule, as small renal mass (SRM) biopsy has classically been considered too inaccurate to be used in clinical decision making, but recent evidence has suggested this is no longer the case.

Purpose: Our algorithm for SRMs (< 4 cm) calls for routine percutaneous biopsy, with management recommendation driven largely by risk stratification of the biopsy result. We assessed the accuracy of biopsy risk stratification in determining treatment versus active surveillance (AS), as confirmed using pathology from the final excision.

Methods: Among 151 patients with SRM who underwent biopsy and subsequent surgical excision, 133 had biopsy results revealing cell type and grade allowing categorization into Unfavorable (U), Intermediate (I) or Favorable (F) risk groups. Management was determined primarily by SRM size and biopsy risk group. U biopsy results lead to treatment regardless of SRM size. I biopsy results prompt treatment for SRM > 2 cm, but AS if < 2 cm. AS is recommended for all SRM with F biopsy results. We compared the management recommendation determined using the biopsy result with the management which would have been recommended based on the surgical pathology.

Results: When comparing predicted management by biopsy with suggested management by surgical pathology, we achieved specificity = 1.0, sensitivity = 0.9, PPV = 1.0, NPV = 0.69, and kappa = 0.768.
Asthma Control In Detroit Children Is Associated With Exposure To Highway Traffic

L. Doan1,2, T. Robins2, S. Batterman2, B. Mukherjee2, G. Mentz2, X. Ren2, S. Grant2, E. Parker3, T. Lewis2, CAAA Steering Committee4

1Touro University California- Vallejo, CA/US, 2University of Michigan - Ann Arbor, MI/US, 3University of Iowa - Iowa City/US, 4Community Organizations- Dearborn and Detroit, MI/US

**Rationale:** Exposure to motor vehicle emissions is known to aggravate asthma symptoms. We investigated whether children with asthma who live very close to highways have poorer asthma control than children who live farther away from major roads.

**Methods:** Our community-based participatory research partnership, Community Action Against Asthma, observed a cohort of 61 school-age children with asthma in Detroit living in three traffic exposure groups: a) within 150 m of highways carrying high volumes of truck traffic, b) within 150 m of highways carrying predominantly cars, and c) more than 300m from major roads. Data on child characteristics and health were collected through a detailed parental questionnaire. The Asthma Control Test (ACT) is a standardized questionnaire scored from 0-25, where scores 19 or greater indicate good asthma control. In a cross-sectional analysis, we conducted multivariable linear regression modeling to determine if there was an association between highway exposure and ACT score.

**Results:** Children with asthma who lived near high-truck and low-truck traffic highways had lower ACT scores than children living farther away from highways (mean (SD): 19.7(4), 18.7(4.5), and 21.4(3.2) respectively). In adjusted models, high diesel highway exposure was associated with a 2.8 point reduction in ACT score relative to children with background urban exposure.

**Conclusions:** Proximity of home residence to high-diesel highways is a strong independent risk factor for poorer asthma control. This finding is important to minimize the health impacts of roadway-associated air pollution and to better understand health disparities within the urban environment.

Behavior of Tissue Plasminogen Activator (tPA) in an Ex-Vivo Lung and Liver Species-Specific Model

Curry-Burns, Jade, Cleopatra Caldwell, PhD

**Background:** Research on communication about sex between resident and non-resident African American fathers and their sons at any age has been understudied.

**Methods:** The purpose of this study is to determine the influence of racial socialization and father involvement on non-resident African American father and son communication about sex.

**Results:** Results of a multiple regression analysis showed that more perceptions of parental monitoring and racial socialization were predictive of increased communication about sex with fathers. While both variables were significant predictors of sexual communication, racial socialization had a greater impact on father-son communication about sex than parental monitoring.
Determining dissection risk in patients with Marfan Syndrome or Bicuspid Aortic Valves: Is size sufficient? Insights from the International Registry of Acute Aortic Dissection (IRAD)

Siddiqi, Hasan, BA, Isselbacher, Eric, MD, Suzuki, Toru, MD, Montgomery, Daniel, BS, Pape, Linda, MD, Fattori, Rossella, MD, O’Gara, Patrick, MD, Jondeau, Guillaume, MD, Misslov, Emil, MD, PhD, Forteza, Alberto, MD, Bossone, Eduardo, MD, PhD, Hirsch, Alan, MD, Rogers, Adam, MD, Nienaber, Christoph, MD, Eagle, Kim, MD

Background: Patients with Marfan Syndrome (MS) or bicuspid aortic valves (BAV) are at increased risk for aortic dissection. Surgical guidelines primarily use the diameter of the ascending aortic (dAA) to assess dissection risk in these patients. We used the International Registry of Acute Aortic Dissection (IRAD) database to retrospectively examine dAA in MS and BAV dissection patients and gauge the effectiveness of size-based guidelines in preventing dissections.

Methods: We used the IRAD database to stratify Type A acute aortic dissection patients from 1996 to 2011 into groups with MS (n=51), BAV (n=64) or neither of these conditions (n=1514). dAA was used to determine the percent of patients with MS or BAV who dissected at various sizes.

Results: Patients with MS and BAV dissected at a younger mean age than those without these conditions (35.3 ±10.3 yrs vs. 51.6 ± 16.0 yrs vs. 62.5 ± 13.2 yrs, P<0.001). The dAA was <5cm in 45.9% of MS patients and in 36% of BAV patients. There were no significant differences in long-term outcomes amongst MS or BAV patients when stratified by dAA at time of dissection.

Conclusions: Analysis of the IRAD database showed a significant proportion of MS and BAV patients dissecting at dAA <5cm. In addition, dAA at time of dissection was not correlated with differences in outcomes. Rather than primarily using size, future development of a personalized risk assessment approach that combines genetics, proteomics and dynamic imaging will allow for better identification of those at risk for dissections.

Differential Metabolic Effects of Dietary Macrocomposition in Bariatric Surgery Candidates with Non-Alcoholic Fatty Liver Disease (NAFLD): Results from a Pilot Study

Germanuel Landfair, Virginia Uhley, Suma Amarnath, Marissa Cooper, Adam Neidert, Jonathan Finks, John Birkmeyer, Charles Burant and Elif A. Oral

Introduction: Enlarged fatty livers present a relevant risk factor for bariatric surgery. Low carbohydrate diets have led to quicker weight loss, and more effective triglyceride reduction. This led to a hypothesis that hepatic fat may be reduced more effectively by low carbohydrate diets.

Objective: Our primary interest was observing the differential effects of two short-term (6 to 8 weeks) dietary approaches before bariatric surgery to reduce hepatic fat and inflammation. Other endpoints of interest were changes in body weight, triglyceride, CRP (marker of systemic inflammation), and incretin levels.

Methods: Thirty patients with nonalcoholic fatty liver disease and approved for bariatric surgery were randomly assigned to equally hypocaloric (1000 cal, 75 gr protein) low carbohydrate (49.0% fat, 18.3% carbohydrates) or low fat (19.8% fat, 53.5% carbohydrates) diets. Diets were provided weekly and continued until the time of surgery (mean duration 6.3 weeks). Study parameters were collected at baseline and within the last week before surgery, after a 10-hour fast. A MRI of the liver was obtained at the end visit to quantify liver fat. A liver biopsy was obtained at surgery and nonalcoholic steatohepatitis (NASH) score was determined by a single pathologist.

Results: Both groups lost clinically significant weight (Table 1). There were trends towards a differential pattern for weight loss and triglyceride levels. Changes in insulin resistance and incretin levels tracked with weight loss. There were no differences in hepatic fat content as measured by MRI right before surgery or in final NASH scores obtained from liver biopsy samples. CRP levels were significantly more reduced with low fat diet (mean: -2.8±2.6 mg/L) compared to low carb diet (mean: -0.2 ±2.2, p=0.017).

Conclusion: While there were no short-term differences between a high fat and low fat diet when attempting to impact hepatic inflammation or fat, a low fat diet improved systemic inflammation significantly.
Effect of Urinary Incontinence Treatment on Depression Symptoms

An association between urinary incontinence (UI) and depression has been previously reported. The objective of this study was to determine which type of UI is most associated with depression and whether treatment-related improvements in UI result in similar improvements in depression.

Methods: Women presenting with a chief complaint of urinary incontinence were consented and enrolled in this prospective cohort study. Assessments at baseline and during follow-up after treatment for UI (pharmacological, behavioural or surgical) ascertained UI symptom severity (using the Incontinence Symptom Index (ISI), a validated, 10-item self-administered questionnaire) and depression severity (using the Patient Health Questionnaire (PHQ-9)). The minimally important difference (MID) of each ISI domain has previously been reported, whereas MID for the PHQ was determined as one half standard deviation of the baseline PHQ levels. Logistic regression models were used to evaluate the baseline association of incontinence severity with moderate/severe depression levels (PHQ>10). Mixed regression models were used to assess the relationship of change in UI with a corresponding change in depression severity at 3, 12, and 24 months post-treatment. All models were adjusted for age, BMI, income and education.

Results: 85 women, with a median age of 57 years, reported baseline ISI scores ranging from 0 to 32 (maximum possible score), with a mean of 16.9. At baseline, 13% of the participants had moderate/severe depression levels; greater UI was associated with higher levels of depression, with the largest impact seen for Urge UI (odds ratio (OR)=1.4) and Bother (OR=1.6). After UI treatment, improvements in UI were associated with corresponding improvements in depression severity. The effect was largest for Pad Use and Urge UI (Table), though the impact for all domains falls much below the estimated PHQ MID of 2.6.

The proportion of women with moderate/severe depression remained stable (range 11.8% - 14.1%) even while incontinence symptoms improved (Figure).

Conclusions: Our data suggest that while there may be a statistically significant association between change in UI symptoms and change in depression symptoms following treatment, the effect may not be clinically meaningful.

Engaging Multiple Communication Strategies to Effectively Disseminate Research Findings
Cooper, Roanna E., MA, Zimmerman, Marc, PhD

The mission of the Prevention Research Center of Michigan (PRC/MI) is to create and foster knowledge resulting in more effective public health programs and policies, particularly in populations with a disproportionate share of poor health outcomes. The PRC/MI does this through a set of community-based participatory research guidelines. An important component of this is the production and dissemination of findings to community members in ways which will be useful for community action. Multiple strategies are employed to accomplish this goal. Three strategies currently under development include: (1) a PRC/MI periodic report, which speaks to the community as well as various governmental and funding agencies; (2) health briefs, which provide community members with important information on a wide range of issues related to individual and community health; and (3) an interactive on-line presence, achieved through various project websites. The PRC/MI's use of these various approaches supports community-based participatory research guidelines, which recognize the importance of drawing on multiple communications strategies to disseminate findings and share information among various partners and affiliates.
Exploratory Study to Evaluate the Utility of Bronchoalveolar Lavage Fluid (BALF) for Metabolite Detection

Odilia Chan1, Chunhai Ruan2, Charles Evans2, Alla Karnovsky3, Charles Burant2, Theodore Standiford4, and Kathleen A. Stringer1

1Department of Clinical, Social and Administrative Sciences, College of Pharmacy, University of Michigan, 2Nutrition Obesity Research Center, University of Michigan, 3Department of Computational Biology and Medicine, School of Medicine, University of Michigan, 4Division of Pulmonary and Critical Care Medicine, School of Medicine, University of Michigan

Background: Metabolomics is an emerging science of biomarker discovery. The BALF has high protein and low metabolite levels. As such, nuclear magnetic resonance (1H-NMR) is insufficient for metabolite detection. The utility of the BALF as a biofluid for metabolomics may be achieved by using liquid chromatography-mass spectrometry (LC-MS) due to its higher sensitivity.

Purpose: To determine if there are LC-MS detectable and biologically meaningful metabolites of acute lung injury (ALI) in BALF.

Methods: Metabolite BALF profiles of ALI (n=8) and healthy volunteers (n=4) were determined by LC-MS. Named metabolites were mapped to metabolic pathways using Metscape. Signal intensities were compared between ALI and control using a Student’s t-test; p-value and false discovery rate <0.05 were considered significant. The primary endpoint was the uniqueness of the BALF metabolite network of ALI patients compared to healthy controls. The utility of BALF was based on linkage of metabolites to biological pathways and differences in signal intensities between ALI and health.

Results: LC-MS identified 26 named metabolites with KEGG ID and two closely associated metabolite networks were constructed. Phosphotidylserine (p=0.0024) and phosphotidylcholine (p=0.0019) were lower and arachidonate (p=0.0007) was higher in ALI compared to control. These preliminary data suggest that by LC-MS, BALF is a viable biofluid for metabolomics since it detected metabolites that distinguished ALI from health. Limitations include the use of existing samples. Future studies will determine if there are unique metabolites in other biofluids such as plasma and urine that can be used to differentiate ALI from other critical illnesses.

Inpatient Surgical Care in Critical Access Hospitals

Gadzinski, Adam J. BS, Dimick, Justin B. MD, MPH, Ye, Zaojun. MS, Miller, David C. MD, MPH

Background: Critical Access Hospitals (CAHs) comprise over 25% of acute care hospitals in the United States. As evidenced by their unique Medicare cost-based reimbursement, policymakers view CAHs as essential healthcare providers for rural communities and other underserved populations.

Purpose: To examine utilization patterns and outcomes of inpatient operations at CAHs.

Methods: We used data from the American Hospital Association (AHA) survey to identify all CAHs in the United States. After linking AHA data with the Nationwide Inpatient Sample (NIS), we used Clinical Classification Software to identify all patients who underwent an operation during admission. We classified all operations by surgical specialty. We compared the type and distribution of all primary operations at CAH versus non-CAHs. We created multivariate models, adjusting for patient characteristics, to compare in-hospital mortality, prolonged length of stay (LOS), and costs of common operations at CAH versus non-CAHs.

Results: Among the 1,292 CAHs and 3,760 non-CAHs reporting to the AHA, 35% and 36%, respectively, had at least one year of data in the NIS. From 2005 through 2009, these centers had 6,587,713 operative admissions; only 1% occurred at CAHs. Operations from general surgery, obstetrics & gynecology, and orthopedics comprised 96% of cases at CAHs versus 78% at non-CAHs (p<0.01). Patients treated at CAHs had a lower risk of experiencing a prolonged LOS in 4 out of 8 common operations compared to non-CAHs (p<0.01 for each). Medicare beneficiaries undergoing hip fracture repair at CAHs had a greater risk for in-hospital death relative to non-CAHs (p<0.05). CAHs had higher adjusted costs for all common operations (p<0.01).

COI: None
Investigating the Association between Seborrheic Keratoses and UV-Light Exposure: the Seborrheic Keratoses Tissue Bank Project

Aravind, Maya, MA, Sachs, Dana MD, Helfrich, Yolanda MD, Wang, Frank MD, Fisher, Gary PhD, Patel, Rajiv MD, Nair, Rajan PhD, Elder, James MD, PhD, Voorhees, John MD

Background: Seborrheic keratoses (SKs) are benign skin tumors commonly seen in the adult population. Although well described clinically, the etiology remains unknown. We aim to investigate the role of UV-light exposure in the development of SKs by molecular analysis, personal and family history of SKs, and history of sunlight exposure.

Methods: We will enroll up to 200 adults with SKs. Subjects will complete a 49-question survey, undergo photographic assessment of predominant SK subtype and undergo comprehensive clinical evaluation. Punch biopsies (6 mm) will be performed on lesional and surrounding normal skin. Biochemical, immunohistochemical and histopathologic evaluation will be performed. Statistical analysis will include descriptive statistics, including means, standard errors and ranges. Laboratory findings will be assessed using paired t-test, using SAS analytic software v. 9.2. (SAS Institute Incorporated; Cary, NC).

Results: Eight subjects have been enrolled. Preliminary analysis of data reveals that all subjects have evidence of photoaging, with Hamilton/Griffiths’ scores ranging from 4 (moderate damage) to 8 (severe damage). The majority of subjects have common subtype SKs located on the face, neck, chest, abdomen, arms, back and thighs, all of which are single-covered areas; of note, only two subjects had SKs on their buttocks, a double-covered area that is rarely sun-exposed. All subjects also report having had sunburns in their lifetime, with 76% reporting more than 10 lifetime-sunburns.

Conclusions: No conclusions can be drawn at this time. Subject enrollment is currently underway.

Localized Compliance and Vaginal Wall Movement Direction in Women with Pelvic Organ Prolapse: A Pilot Study

Cheney DS, MS; Newcomb L, BA; Ashton-Miller JA, PhD; Chen L, PhD; DeLancey, JOL, MD.

Objectives: Establish methods to determine the localized compliance and direction of movement of the vaginal support and determine differences in the anterior and posterior support of women with normal support, cystocele and rectocele.

Methods: Mid-sagittal MRIs were obtained during Valsalva while abdominal pressure was monitored via a bladder catheter. The anterior vaginal wall (AVW) and posterior vaginal wall with perineum (PVW) were traced for 5 subjects with cystocele, 5 with rectocele and 5 with normal support. The tracings of each MRI were divided into 10 equally-spaced points. The vector of vaginal wall displacement was ascertained for each location and compliance was calculated as the linear relationship between displacement (mm) and pressure change (mmHg).

Results: In patients with cystocele, both the AVW and PVW support systems have increased compliance while in rectocele, only the PVW support shows increased compliance compared to normal. Women with cystocele had the most compliant support system (AVW and PVW). Both anterior and posterior supports in the upper vagina (point 6-10) are more compliant than in the lower vagina (1-5). The 3 groups also differed with regard to the direction of vaginal wall movement. The cystocele and rectocele patients exhibited more downward movement of the AVW than normal, while only rectocele patients exhibited more downward movement of the PVW. The direction of movement differed most from normal in the lower vagina for both rectocele and cystocele patients.

Conclusions: Movement and compliance at discrete points of the vaginal wall can be determined and vary along vaginal length. Although compliance is greatest in the upper vagina, in women with cystocele the vectors diverge most prominently from normal in the distal vagina. The anterior vaginal wall in women with cystocele demonstrates the most compliance.
Parent and Adolescent Attitudes Towards Mental Health Help-Seeking in an Arab-American Community

Jaber, Reda, BS, Farroukh, Mona, BA, CFLE, Ismail, Marriam, BS, Najda, Jehad, BS, Hammad, Adnan, PhD, Dalack, Gregory, MD

Background: Depressive illness affects approximately 1 in 10 adults in the United States, however depression rates have been found to vary significantly by ethnic group. Several studies have shown that Arab-American adults in particular have been found to have significantly high rates of depression. In addition, young people from cultural minority groups may be even less likely to seek professional help when needed.

Purpose: We are exploring rates of depression, presence of other mental health issues and willingness to seek help among adolescents in a Metro Detroit Arab-American community. Since stigma associated with mental health care is a major factor in the decision to seek out and engage in treatment, we are assessing whether viewing an educational video about mental health stigma will decrease ratings of stigma towards help-seeking.

Methods: We are conducting a survey of adolescents (12-17 years). Participants will be recruited from ACCESS’ Child & Adolescent Health Center, a local outreach organization in Dearborn, MI. The adolescent survey includes the PHQ-9 Depression Scale, the Self-Stigma of Depression Scale (SSDS) and questions about body image, cigarettes, drugs, guns, violence, physical and sexual abuse. The adolescent surveys are randomized for subjects to view an educational video about mental health stigma vs. a control video about childhood obesity prevention before responding to questions about help-seeking for mental health conditions. An optional, linked parent survey includes the SSDS, allowing us to compare the parent responses to their child’s.

Results: In progress.

Phase Ib Pilot Study to Evaluate Reparixin in Combination with Chemotherapy with Weekly Taxol in Patients with HER-2 Negative Metastatic Breast Cancer: Assessment of Biomarker Assay Data

Ashley Amick

Background: Mounting evidence suggests that breast cancer and other solid tumors may be driven by a small population of self-renewing cells known as cancer stem cells (CSCs). This study examines the effects of Reparixin, a small molecule inhibitor of the IL8 receptor CXCR1, which is postulated to be a CSC targeting agent. The aim of this study is to determine if Reparixin effects downstream pathway targets, and if Reparixin successfully reduces the CSC population in treated patient tumors.

Methods: Patients received one of 3 doses of oral reparixin in combination with weekly taxol for treatment of HER2 negative metastatic breast cancer. We measured human cytokines IL1B, IL8, IL6, and TNFa on plasma samples collected at days 1, 7, 14, 21 of cycle 1, and days 21 of each subsequent cycle. In addition we also analyzed the CSC and pathway biomarkers CD44, ALDH1, P-AKT, P-FAK, and FOXO3A in tissue biopsy taken at enrollment and time of progression.

Results: Pending

Discussion: Pending

Conclusions: Pending
Procarbazine and Antidepressants: A Retrospective Evaluation of the Risk of Serotonin Toxicity
Julia Carpenter, College of Pharmacy, University of Michigan, Nicki Baker, College of Pharmacy, University of Michigan, Shawna Kraft, PharmD, Department of Pharmacy, University of Michigan, Jolene Bostwick, PharmD, Department of Pharmacy, University of Michigan

Background: The actual risk of developing serotonin toxicity due to the combination of procarbazine and an antidepressant is unclear. The concern about an interaction appears to be based solely on procarbazine’s classification as a monoamine oxidase inhibitor with no supporting clinical accounts. There is a lack of available clinical information regarding the use of procarbazine concurrently with antidepressants resulting in inconsistent information between interaction-checking programs. As a result, practitioners are left with conflicting information and no evidence-based guidance for treating depression in patients on procarbazine. Because the incidence of depression is at least four times greater among cancer patients than that of the general population, the clinical significance of the interaction between procarbazine and antidepressants warrants further investigation.

Purpose: To determine the degree of risk of serotonin toxicity associated with specific antidepressants concurrently administered with procarbazine and to provide evidence-based recommendations for the safe utilization of antidepressants in patients being treated with procarbazine.

Design: A retrospective chart review of lymphoma patients was conducted at the University of Michigan. Charts of patients who were treated with both procarbazine and an antidepressant were examined to determine if signs and symptoms of serotonin toxicity existed based on Hunter’s Serotonin Toxicity Criteria and Sternbach’s Diagnostic Criteria.

Results: We expect to find that procarbazine and antidepressants can safely be used together.

Psychosocial Care of Adolescent and Young Adult (AYA) Cancer Patients and Survivors
Isaacson, Sinead BS, MPH Candidate
Zebrack, Brad PhD, MSW, MPH

Background: The delivery of quality care for adolescent and young adult (AYA) cancer patients and survivors requires understanding the unique qualities of this population – the shared norms, attitudes, and beliefs that determine their behavior, as well as the unique stresses they face on a day-to-day basis. Adolescents and young adults have characteristic concerns about being comfortable with who they are and who they want to become (identity development, including sexual identity). They are acutely aware of their bodies (body image) and intent upon initiating intimate and emotional relationships, separating from parents, and making independent decisions about future goals (autonomy). Yet, AYA cancer patients’ and survivors’ efforts to develop and mature are often confounded by restrictions and limitations placed on them by their disease and treatment.

Purpose: The aim of this paper is to summarize evidence of the needs of AYAs with cancer and effective interventions to support these needs. Recommendations for clinical care are made based upon these findings.

Methods: Information and conclusions are based upon a literature review of evidence-based psychosocial support interventions for AYAs with cancer and other life-threatening or chronic diseases, with particular attention to the positive effects of peer support, technology-based interventions, and skill-based interventions.

Results: The manuscript describes the psychosocial needs of AYA cancer patients and survivors, evidence-based interventions to meet these needs, and concludes with recommendations for clinical care that are intended to promote AYA’s abilities to cope with cancer.
Racial and Ethnic Differences in Shared Decision Making in Cancer Treatment: 
A Systematic Literature Review

Mead, Erin L., MHS, Doorenbos, Ardith Z., PhD, RN, FAAN, Flum, David R., MD, MPH, Morris, Arden M., MD, MPH

Background: Shared decision-making (SDM) has emerged as the ideal model of patient-centered care in the U.S., but may vary substantially between cultures. We developed a conceptual framework to more fully describe SDM for cancer treatment among racial/ethnic minority patients and include the role of other stakeholders.

Purpose: To conduct a systematic literature review of SDM in cancer treatment among minority groups.

Methods: In July 2011, a systematic search of literature published in PubMed, PsycInfo, CINAHL and EMBASE retrieved 246 articles.

Results: 23 articles (11 quantitative, 12 qualitative) met the inclusion criteria. Most focused on breast cancer (8 quantitative, 9 qualitative), followed by prostate (1 of each), lung (1 qualitative), multiple sites (2 quantitative), and not reported. African Americans were represented in the most studies (n=14), followed by Latina (n=9), Asian (n=5), and Jewish (n=1) populations. Overall, quantitative studies found that 33-40% of most minority groups engaged in SDM for cancer treatment. However, per qualitative studies, they often did not feel fully engaged in decision-making (DM) and frequently reported ineffective physician communication. Preferred decisional role varied substantially by race/ethnicity and acculturation level. Minority groups experienced high decisional dissatisfaction and regret, which were associated with decisional role conflict or ineffective physician communication. Family and friends played an important role in treatment DM for some groups, but not others. Although the community could be a source of support, stigma was a significant concern of African American and Asian patients.

Psychosocial Care of Adolescent and Young Adult (AYA) Cancer Patients and Survivors

Isaacson, Sinead BS, MPH Candidate
Zebrack, Brad PhD, MSW, MPH

Background: The delivery of quality care for adolescent and young adult (AYA) cancer patients and survivors requires understanding the unique qualities of this population — the shared norms, attitudes, and beliefs that determine their behavior, as well as the unique stresses they face on a day-to-day basis. Adolescents and young adults have characteristic concerns about being comfortable with who they are and who they want to become (identity development, including sexual identity). They are acutely aware of their bodies (body image) and intent upon initiating intimate and emotional relationships, separating from parents, and making independent decisions about future goals (autonomy). Yet, AYA cancer patients’ and survivors’ efforts to develop and mature are often confounded by restrictions and limitations placed on them by their disease and treatment.

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Results: The manuscript describes the psychosocial needs of AYA cancer patients and survivors, evidence-based interventions to meet these needs, and concludes with recommendations for clinical care that are intended to promote AYA's abilities to cope with cancer.

Conclusions: The new conceptual framework can provide policymakers and healthcare professionals greater insight into SDM for cancer treatment among minority patients.
Risk Factors for Candida dubliniensis Bloodstream Infections
Veltman, Katherine B.S., Carver, Peggy Pharm.D

Candida dubliniensis appears to be a newly emerging pathogen in Candida bloodstream infections (BSIs) that had previously been associated primarily with oral candidiasis in HIV-infected patients. Previous small case series (1-4 patients) have shown that the characteristics of these patients are varied but may include GI disease, liver disease, immune system dysfunction and the use of certain medications. We reviewed clinical data from the charts of 20 patients with C. dubliniensis bloodstream infections and compared them to the characteristics of 73 control patients with either C. glabrata or C. albicans BSIs. Preliminary data has shown that the average time at risk (in hospital before C. dubliniensis infection) is 15 days, among other significant results. Determining the association of certain conditions with C. dubliniensis infection may lead to decreased time to proper diagnosis and care, as well as more information about the pathogenicity of this species.

The Association of Having Sexual Intercourse with Pubertal Development and Age Among Chilean Adolescents
Serrano, Katrina J., MS, Delva, Jorge, PhD, Andrade, Fernando A., PhD(c)

Background: Disparities exist in adolescent sexual health behaviors between developed and developing countries. In Chile, approximately 51 out of 1000 girls ages 15-19 become pregnant, a higher rate than that of the U.S. Studies of antecedents to sexual behaviors in adolescence have examined the significance of pubertal development in comparison to chronological age with mixed results.

Purpose: This study examined the association of having sexual intercourse with pubertal development and age among Chilean adolescents while controlling for numerous factors.

Methods: Cross-sectional data were obtained during 2007-2010 from the Santiago Longitudinal Study (SLS), a NIDA-funded study of youth and their families from Santiago, Chile. A total of 1064 youth were included (mean age 14 years, 51% male). The dependent variables, ever had sex and number of partners, were combined and recoded into 0=never had sex, 1=had sex with one person and 2=had sex with two or more persons. The independent variables were pubertal development and age, controlling for behavioral, parental, peer, and neighborhood factors. Pubertal development was based on the Tanner stages of development, assessed by a nurse. Multinomial logistic regression was used to analyze these data; the base outcome was individuals who never had sex.

Results: Approximately 15% (n=158) of adolescents had sex of which about 5% had sex with two or more partners. For males, pubertal development and age were not statistically significant predictors of sexual intercourse but pubertal stage was significantly associated with multiple sexual partnering. For girls, pubertal stage, but not age, was significantly associated with ever having coitus. Pubertal stage and age did not predict having multiple sexual partners.

Discussion: This study shows that sexual behaviors differ between adolescent boys and girls living in Santiago, Chile. Boys are more at risk for multiple sexual partnering based on their pubertal development than are girls. However, girls are at a higher risk of ever engaging in sexual intercourse based on their development. Some implications include introducing sexual health education at an earlier age, and that tailoring these programs might be effective in decreasing the rates of unintended pregnancies or other health complications associated with risky adolescent sexual behaviors.
The Prevalence and Natural History of Conservatively Treated Chiari 1 Malformations in Adults

Brandon Smith, BS, Cormac Maher, MD, Jennifer Strahle, MD

**Background:** Despite being a commonly managed neurological and neurosurgical disease, little is known about the prevalence and natural history of Chiari 1 Malformation (CIM). Current information on CIM prevalence is based on small cohorts of patients selected for surgical treatment and is not representative. The surgical outcomes have been extensively investigated; however, the natural history of those managed without surgery is unknown. Asymptomatic or minimally symptomatic CIMs are often treated without surgery. However, the lack of natural history knowledge in these patients makes it difficult for surgeons to make evidence supported decisions in their management.

**Purpose:** The authors will attempt to better define the prevalence and natural history of CIM in adults. Specifically, the authors will determine the age-based prevalence of the CIM, complete with normative descriptive data for cerebellar anatomy in separate age cohorts. Additionally, the authors will define the natural history of conservatively managed CIM in adults.

**Methods:** The authors will analyze a database of approximately 50,000 patients who have had MR imaging of their brains. An electronic search engine will be utilized to identify patients within this database who have been diagnosed with CIM. Statistical analysis will be performed to determine the age-based prevalence of CIM in 10-year cohorts. To control for a possible radiologic bias, the investigators will then examine MRIs of 300 randomly chosen subjects within each cohort and will record their radiographic findings. Clinical history and radiologic findings will be gathered for analysis in patients initially selected for non-surgical management of CIM.

**Results:** Pending.

Association of Plasma Omega-3 and Omega-6 Lipids with Burden of Disease Measures in Bipolar Subjects

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**Background:** Objectives: Omega-3 (n-3) fatty acids have been implicated in mood disorders, yet clinical trials supplementing n-3 fats have shown mixed results. However, the predominant focus of this research has been on the n-3 fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). We used an unbiased approach to assay serum n-3 and omega-6 (n-6) species that interact at the level of biosynthesis and down-stream processing, to affect brain function and, potentially, mood.

**Methods:** We used lipomic technology to assay plasma levels of n-3 and n-6 fatty acids from 31 bipolar and 18 control subjects to investigate differences in plasma levels and associations with the burden of disease markers, neuroticism and global assessment of function (GAF) and mood state (Hamilton Depression Scale (HAM-D)).

**Results:** We found the levels of dihomo-gamma-linolenic acid (DGLA) to positively correlate with neuroticism (r=0.428, p=0.001) and HAM-D scores (r=0.468, p<0.001) and negatively correlate with GAF scores (r=-0.582, p<0.001). We also found linoleic acid (LA) and alpha linolenic acid (ALA) to negatively associate with neuroticism (r=-0.398, p=0.002; r=-0.30, p=0.025, respectively) and LA to positively associate with GAF scores (r=0.329, p=0.021) and negatively associate with HAM-D (r=-0.450, p<0.001). Finally, we found the activity of fatty acid desaturase (FADS) 1 to positively associate with GAF (r=0.389, p=0.006) and FADS2 to positively associate with neuroticism (r=0.294, p=0.03).

**Conclusions:** These data suggest that specific n-3 and n-6 fatty acids and the enzymes that control their biosynthesis, may be a useful biomarkers in measurements of bipolar disorder and burden of disease.
Genetic Variation of the 5-HT2C Receptor Modulates Human Striatal Dopaminergic Activation to Stress
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Serotonin 2C (5-HT2C) receptors mediate the inhibitory effects of serotonin on mesoaccumbal and nigrostriatal function in experimental animals. Accordingly, preclinical findings have implicated 5-HT2C receptors in motor function, motivated behaviors, and psychotropic drug mechanisms. In humans, a common single nucleotide change (rs6318, Cys23Ser) in the 5-HT2C receptor gene (HTR2C) has been associated with greater constitutive activity in vitro and with mood disorders. Methods. We examined the effects of this HTR2C variant on striatal dopaminergic function in 54 healthy humans using positron emission tomography and the displaceable D2/D3 receptor radiotracer [11C]raclopride. Binding potential (BPND) was quantified before and after a standardized stress challenge consisting of 20 minutes of moderate deep muscular pain, and BPND change served as an index of dopamine release. The Cys23Ser variant was genotyped on a custom array, and ancestry informative markers were used to control for population stratification. Results. We found greater stress-induced dopamine release in the nucleus accumbens (p=.003), caudate nucleus (p=.037), and putamen (p=.034) among Ser23 carriers, after controlling for sex, age, and ancestry. Genotype accounted for 12% of the variance in dopamine release in the nucleus accumbens. There was no effect of Cys23Ser on baseline BPND. Conclusions. These findings indicate that a putatively functional HTR2C variant (Ser23) causes greater striatal release of dopamine during stress. Mesoaccumbal stress sensitivity may mediate the effects of HTR2C variation on risk of neuropsychiatric disorders.

High-Throughput Screening for Chemical Modulators of Small Heat Shock Proteins
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Small heat shock proteins (sHsps) are molecular chaperones which help prevent the aggregation of misfolded proteins. One sHsp, B-crystallin, is highly expressed in the eye lens. The well-characterized R120G mutation in B-crystallin causes hereditary cataracts by promoting the aggregation of B-crystallin into amyloid fibrils, resulting in a loss of lens transparency. The conformational changes conferred by the R120G mutation result in a change in thermal stability relative to the wild-type protein. Thus, we hypothesized that a molecule capable of recovering the wild-type stability may also recover the R120G-related disease phenotype. To address this hypothesis, we utilized high-throughput differential scanning fluorimetry to identify a class of small molecules that partially rescue the wild-type thermal stability of R120G B-crystallin. These small molecules bind to R120G B-crystallin with low micromolar affinity. We determined structure-activity relationships from a library of 32 closely related structural analogs, the most active of which was c29. Transmission electron microscopy revealed that c29 prevents R120G fibril formation and dramatically disrupts preformed aggregates, while an inactive structural analog does not. Finally, c29 dissolves cataracts when administered to R120G knock-in mice as an ophthalmic solution. These results suggest that c29 is a “pharmacological chaperone” for the R120G mutant and that this strategy can counteract congenital cataracts. Our current work aims to identify the binding site of c29 and understand its effect on the conformation of R120G. Further, we plan to extend this screening strategy to rescue other sHsp mutants responsible for disease.
**Maternal behaviors at 6 months are related to infant attachment classification at 15 months.**
Broderick, Amanda, BA; Busuito, Alexandra, BS, Alfafara, Emily, BA; Stark, Lori, MA; Richardson, Patricia, BA; Muzik, Maria, MD, MS

Early patterns of infant attachment to the mother have been associated with later child outcomes. In attempts to determine correlates of infant attachment classification, prior research has demonstrated a link between maternal behaviors and attachment, both longitudinally (Seifer, Schiller, Sameroff, Resnick, & Riordan, 1996) and concurrently (Kennedy, 2008). However, this research has been limited to a focus on maternal sensitivity. The objective of the present study was to investigate the relationship between early maternal behaviors and later attachment classification in a high-risk community sample of mothers and infants. Dyads were videotaped interacting when the infants were 6 months old and were coded for positive (e.g., affect sensitivity, warmth, positive affect) and negative behaviors (e.g., intrusive, hostile). When the infants were 15 months old, dyads completed the Strange Situation Procedure. Results indicate that both maternal positive and negative behaviors at 6 months were significantly related to infant attachment classification at 15 months. These results suggest that early maternal behaviors may play an important role in the development of infant attachment.


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**Maternal psychopathology, infant sleep quality, and early childhood outcomes**
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**Background:** The prevalence of sleep problems in infancy and early childhood ranges from 10% to 40% (Fricke-Oerkermann, Pluck, Schredl et al., 2007). Parental factors may contribute to the development of sleep problems during infancy, such that infants of mothers with psychopathology (e.g. depression or posttraumatic stress disorder) are more likely to develop sleep problems. For example, Armitage et al. (2009) found that infants of mothers with current or a history of depression had more sleep problems than infants of healthy mothers. Furthermore, research suggests that sleep difficulty during infancy predicts emotional and behavioral problems later in childhood (Gregory, Caspi, Moffitt & Poulton, 2009; Lam, Hiscock & Wake, 2003).

**Purpose:** The present study seeks to examine the relationship between infant sleep quality, maternal PTSD, and child behavior problems.

**Methods:** The current sample is drawn from the longitudinal MACY study (PI: Muzik), which follows high-risk women and their children across the first 3 years postpartum. Result: Analyses revealed a significant association between infant sleep difficulty at six months and childhood behavior problems at 3 years, and between maternal PTSD at six months postpartum and childhood behavior problems at 3 years. Maternal PTSD moderated the association between infant sleep problems and later behavior problems (r = .43, p < .05). Importantly, this study highlights the critical role of infant sleep quality and maternal PTSD in the development of negative child behavior outcomes. Results contribute to the growing body of literature on early risk markers of child behavioral problems.
Pre-clinical studies of the efficacy of PD132301 in adrenocortical carcinoma

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Background: Adrenocortical carcinoma (ACC) is an aggressive cancer originating in the cortex of the adrenal gland. Currently, ACC has poor prognosis and few treatment options. PD132301 is a compound developed by Parke-Davis Pharmaceutical Research. Toxicology studies demonstrate that PD132301 selectively ablates the adrenal cortex cells in many species.

Purpose and Methods: To explore the potential utility of PD132301 for the treatment of adrenocortical carcinoma (ACC), we investigated the effects of PD132301 on a cultured human ACC-derived cell line (H295R) in vitro and H295R xenografts in SCID mice.

Results: PD132301 rapidly depleted the MTS reducing activity of H295R cells at low µM concentration. PD132301 selectively inhibited the enzymatic activity of cytochrome C oxidase (Complex IV) in situ in frozen ACC xenograft sections. Oral administration of PD132301 caused transient regression of H295R xenografts in SCID mice.

Conclusion: These results demonstrate that PD132301 selectively inhibits respiration in ACC-derived cells and counteracts the growth of ACC xenografts in mice. These results support further development of PD132301 for the treatment of adrenocortical carcinoma.

Social Rejection Activates Endogenous Opioid Systems


Background: Endogenous opioids, which alleviate physical pain, are also thought to regulate the effect of social pain (the distressing experience arising from a threat to social relationships). Although there is some evidence of this from animal studies, it is not known if endogenous opioids perform this function in humans.

Purpose: To test the hypothesis that the endogenous opioid system responds to social rejection (an explicit declaration that one is not liked).

Methods: Thirteen healthy volunteers (9 females; mean age, 32 ± 11 years) were clear of active medical illness, current or past psychiatric disorders, and had no history of medication at the time of study. [11C]carfentanil, a selective and specific µ-opioid receptor radioligand, was intravenously administered during positron emission tomography. During the scan, participants viewed feedback from others that they were not liked. Baseline blocks contained no feedback. Blocks were presented in a randomized, counterbalanced design.

Results: Self-report measures indicated that participants felt significantly more “rejected” during rejection compared to baseline blocks. Significant reductions in µ-opioid binding potential (indictative of endogenous opioid release and µ-opioid receptor activation) was found during rejection compared to baseline blocks in the ventral striatum, amygdala, midline thalamus, periaqueductal gray, anterior insula, and anterior cingulate cortex.

Conclusions: This is the first demonstration in humans that the endogenous opioid system responds to social rejection. Endogenous opioid release may function to regulate activity along a pathway that links social rejection to the development of psychiatric illnesses such as major depressive disorder, social anxiety disorder, and substance abuse disorders.
The Stability of Maternal Social Support and Parenting Efficacy Across the First 5 Years Postpartum
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Purpose: Prior research has demonstrated that social support is an important factor in parenting satisfaction in the early years postpartum. The present study aims to examine: 1) the stability of a mother’s report of social support and her perceived parenting efficacy across infancy and early childhood; and 2) how the absence of such perceived support may act as a risk for parenting efficacy.

Method: The current sample is drawn from the longitudinal MACY study (PI Muzik) which follows mothers and their young children across the first 5 years postpartum. Participants completed telephone interviews with relevant questionnaires at two timepoints: 1) 6 months postpartum; and 2) 3-5 years postpartum.

Results: Key study findings include: 1) maternal report of social support at 6 months was significantly related to report of social support at 3-5 years postpartum; 2) maternal parenting efficacy at 6 months was related to parenting efficacy at 3-5 years; 3) parents classified as ‘low-social support’ versus ‘high social support’ at 3-5 years postpartum report significantly decreased parenting efficacy at the same timepoint.

Conclusion: Results from the present study highlight the stability of maternal social support and parenting efficacy over time in a sample of high-risk mother-child dyads. Furthermore, results suggest that low social support may act as a salient risk for a mother’s perceived feelings of efficacy in the parenting role.