Gestational age acceleration in neonates predicts NICU course
Knight, Anna K.; Smith, Alicia; Conneely, Karen; Loke, Jane; Cheong, Jeanie; Craig, Jeffery M.; Doyle, Lex W.; Theda, Christiane

DNA methylation changes with age, and can be used to accurately predict chronological age in adults. We have recently developed a methylation-based predictor of gestational age (DNAm GA) for neonates using cord blood or blood spot samples at birth that is highly correlated to clinically-estimated gestational age (GA) based on ultrasound (r=.91; p<2.2E-16) and is accurate within 1.24 weeks in >1,200 samples. DNAm GA increased steadily in longitudinal samples taken from birth to term equivalency in two preterm neonates admitted to the neonatal intensive care unit (NICU). We hypothesized that GA acceleration, which is the residual between clinically estimated GA and DNAm GA, would predict neonates requiring the most intensive interventions in the NICU. The Victorian Infant Collaborative Study (VICS, Victoria, Australia) provides a unique resource to address this hypothesis as preterm infants born before 37 weeks gestation in 1991/1992 were prospectively enrolled in a longitudinal follow-up study. DNA was extracted from dried blood spots used for newborn screening of 183 participants (26.7±2.1 weeks) and was processed on the Human Methylation450 BeadChip. DNA methylation data was used to estimate DNAm GA. Data regarding common NICU interventions (surfactant administration, postnatal steroids, oxygen supplementation) and complications (bronchopulmonary dysplasia) were retrieved from the VICS database. Linear regression models that controlled for cellular heterogeneity and GA were used to evaluate the association of GA acceleration and each NICU outcome. Decreased GA acceleration (lower DNAm GA relative to GA) associates with increased administration of postnatal steroids (31.1% given steroids; p=.002) and surfactant (43.7% given surfactant; p=.02). Similarly, GA acceleration was lower in neonates that required more days on oxygen supplementation (p=.002). Finally, lower GA acceleration associated with the development of bronchopulmonary dysplasia, a chronic lung disorder affecting 36.0% of these neonates (p=.01). This suggests that GA acceleration may be indicative of developmental maturity at birth. Further studies should evaluate DNAm GA and GA acceleration to determine how these measures could contribute to more accurate and individualized predictions of NICU course and short and long-term outcomes.

Development of a Live-Attenuated Vaccine for Respiratory Syncytial Virus with Enhanced Thermostability and Immunogenicity
Rostad, Christina A.; Stobart, Christopher C.; Moore, Martin L.

Respiratory syncytial virus (RSV) is the leading cause of lower respiratory tract infections in infants, and an effective vaccine is not yet available. Although RSV live-attenuated vaccines
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(LAVs) are considered safe to administer to seronegative infants, achieving sufficient LAV immunogenicity and thermostability are ongoing challenges. We first generated an LAV candidate “DB1” which was attenuated by a low-fusion subgroup B fusion protein and codon-deoptimized non-structural proteins. DB1 was broadly immunogenic and protective in mice, but lacked thermostability and stability of the pre-fusion conformation of F. We then identified a chimeric RSV strain A2-line19F which had enhanced thermostability and stability of pre-fusion F compared to parental A2. We hypothesized that substitution of the unique line19 F residues into DB1 would confer thermostability and stability of pre-fusion F to the LAV. We then substituted combinations of four unique line19 F residues into DB1 by site-directed mutagenesis. Using MPE-8 (a pre-fusion F specific antibody) and motavizumab (a pre- and post-fusion F antibody) ELISAs, we found that the DB1 strains with line19 F residues had a significantly increased ratio of pre- to post-fusion F. We then evaluated thermostability of the DB1 mutants at 4°C by measuring the decline in viral titer over a period of 21 days. We found that incorporation of four line19 F residues into DB1 (DB1-QUAD) stabilized the vaccine to the level of A2-line19F at 4°C, whereas incorporation of combinations of two line19 F residues conferred an intermediate thermostability phenotype. We then evaluated the immunogenicity of DB1-QUAD by measuring the neutralizing antibody titers generated by the vaccine in BALB/c mice on day 100 post-infection. We found that DB1-QUAD elicited significantly higher neutralizing antibody titers than DB1 and A2-line19F. Mice vaccinated with DB1-QUAD were also completely protected against RSV challenge on day 100 post-infection. Thus, incorporation of line19 F residues into the heterologous vaccine strain DB1 conferred an increased ratio of pre- to post-fusion F, enhanced thermostability, enhanced immunogenicity, and complete protection against RSV challenge in mice.

Smartphone processing system for non-invasive, quantitative diagnosis of pediatric anemia using only patient-sourced photos
Mannino, Robert; Myers, David; Tyburski, Erika; Boudreaux, Jeanne; Clifford, Gari; Lam, Wilbur

Smartphone-based telehealth is steadily transforming the delivery of medical care worldwide, moving diagnosis of disease from the clinic to the home to potentially anywhere in the globe. Smartphone images alone have recently been used by pediatricians to remotely diagnose a myriad of childhood diseases. However, smartphone telehealth approaches have yet to non-invasively replace blood-based testing, which remains a major cornerstone of disease diagnosis in modern pediatric medicine. While the addition of specialized smartphone attachments and supplemental calibration tools may enable point-of-care diagnosis and analysis of tissue and bodily fluid samples, the additional burden of blood and/or tissue sample collections combined with the additional cost and inconvenience associated with this equipment, prevents worldwide use of these potentially disruptive approaches. Therefore, a smartphone-based system, requiring nothing other than the smartphones native technology and capable of non-invasively replacing blood-based diagnostics, would transform the very nature of telehealth and the
delivery of healthcare worldwide. Towards that end, we specifically focused on anemia, a potentially life-threatening disorder characterized by low blood hemoglobin (Hgb) levels that affects approximately 2 billion people worldwide, including a large percentage of pediatric patients. Despite the high prevalence of anemia, all existing diagnostic approaches to measure Hgb require specialized equipment and represent tradeoffs between invasiveness, accuracy, infrastructure needs, and expense. Aside from being cost-prohibitive, the necessary invasive blood sampling to measure Hgb levels causes discomfort and trauma in younger pediatric patients.

By examining clinical pallor, a common symptom of anemia, we developed a methodology that quantitatively analyzes patient-sourced photos using smartphone-based algorithms to enable a noninvasive, accurate, and accessible anemia diagnostic. Here, a patient or their parent simply takes a picture of their fingernail beds using their smartphone, and the image analysis algorithm analyzes color data and image metadata to measure the corresponding Hgb level. By quantifying clinical pallor, our system non-invasively measures Hgb levels to within a clinically significant and well accepted margin of error (±1 g/dL) of the gold standard Hgb measurement tool with a sensitivity and specificity of 0.90 and 0.82, respectively, of predicting anemia (defined as Hgb < 11.0g/dL) in 100 pediatric patients at Children’s Healthcare of Atlanta with anemia of any etiology mixed with healthy subjects. As additional custom smartphone attachments or calibration equipment are not required, our system enables anyone with a smartphone to diagnose pediatric anemia anywhere and anytime, has significant potential to reduce healthcare costs, and is ideally suited for global health applications.

**Data Driven Post-Operative Appendicitis Care**
Zutty, Jason; Clarkson, Edward; Raval, Mehul

Harnessing the utility of data through data-driven prediction of healthcare outcomes has long been touted as a useful tool for the future of medicine. Unfortunately, there are considerable obstacles to widespread adoption of data-driven prediction models translating research in machine learning and other statistical- and computing-related domains to actual, real world medical care. Surgery represents a finite care experience with three distinct phases within the healthcare continuum. The final postoperative phase involves the recovery from surgically treated disease and the stress induced by the surgical intervention. While a large body of work with machine learning has focused on diagnosis and preoperative surgical care, less attention has been made toward optimizing the postoperative phase. While numerous quality improvement efforts to streamline care in order to decrease length of stay, most of these efforts are based on anecdotal experience and are not data driven.

Appendicitis represents the most common surgical emergency for which children (80,000+ cases) undergo abdominal surgery. Compared to early acute appendicitis, perforated appendicitis is associated with higher rates of complications, such as wound infections and intra-abdominal abscesses, longer hospitalizations, higher readmission rates, and higher costs.
Unfortunately, nearly 40% of children present with perforated appendicitis. The postoperative management of perforated appendicitis is highly variable and any efforts to decrease in hospital length of stay for these complex patients must be balanced with concerns over readmission to the acute care setting. Our objective was to develop a statistical model of case outcomes on which we have built a prototype application for care providers to help create treatment plans for the postoperative management of pediatric appendicitis.

The purpose of our study was to develop a statistical model and interface to provide data driven recommendations for the postoperative management of perforated appendicitis. Specifically, we aimed to identify factors that would optimize length of stay while also providing healthcare providers and patients with information regarding complications including readmission. The result of this work is an initial iteratively-refined data model achieving an accuracy of 87% (88%/59% negative/positive predicted value; 75%/3% false negative/positive error rates), and a prototype smart protocol application under evaluation by pediatric appendectomy care providers. Through this and future work we demonstrate both the utility of such a project and suggest effective mechanisms (both technical and non-technical) for completing projects in similar domains.

**Rapid-Fire Poster and Presentation Abstracts**

*In order of presentation*

**101. Patterns of Visual Engagement Identify Distinct Subgroups of School-Age Children with ASD**
Yurkovic, Julia; Gillespie, Scott; Jones, Warren; Klin, Ami; Shultz, Sarah

Heterogeneity in autism spectrum disorder (ASD) is an obstacle to advancements in identifying and treating causes of the disorder. Eye-tracking measures of atypical visual engagement with the social world provide a promising means for deriving more homogeneous subgroups (Rice et al., 2012; Campbell et al., 2014). Parsing heterogeneity in ASD by measuring visual scanning during dynamic social scenes may contribute to the identification of intermediate phenotypes for genetics research, and to the development of interventions optimized for individuals. We aimed to examine whether subgroups of children with ASD can be reliably identified based on patterns of variability in social visual engagement; and whether the subgroups differ on standardized measures of social disability.

A heterogeneous sample of children with ASD (n=178, age=10.51(3.19)) watched socially-relevant videos while eye-tracking data were collected. The Hopkins index was used to assess whether clusters are reliably identifiable by variability in visual scanning. Unsupervised statistical learning methods were utilized to identify clusters of different visual fixation patterns. A three-cluster solution was achieved through hierarchical clustering of fixations to eyes, mouth, body, and object in each participant pair.
The Hopkins Index indicated the clustering tendency as appropriate (0.16<0.5). Hierarchical clustering analyses identified three clusters of children with ASD. As expected, ANOVA and post-hoc Tukey analyses revealed significantly different fixation patterns between clusters, with Cluster 1 fixating more on eyes, Cluster 2 on mouths, and Cluster 3 on objects. Children in Cluster 1 had lower Vineland communication scores (p=0.051) compared to Cluster 2, suggesting that higher eye-looking may not be associated with greater adaptive skills in this subgroup of children. Consistent with previous reports that higher mouth fixation is associated with lower social disability (Rice et al., 2012) children in Cluster 2 had significantly lower ADOS symptom severity (p=0.051) than those in Cluster 3, and higher Vineland communication scores (p=0.051) than those in Cluster 1. Finally, children in Cluster 3 had higher ADOS symptom severity scores compared to those in Clusters 1 (p=0.098) and 2 (p=0.051), suggesting that high levels of object fixation are associated with greater social disability.

Results demonstrate that variability in visual engagement during dynamic social scenes can be used to identify more homogeneous subgroups of children with ASD. These subgroups displayed distinct patterns of visual attention, and varied by measures of social ability. Future analyses will examine whether the social adaptive value of visual scanning patterns vary for different subgroups of children with ASD.

102. Association analysis identified a novel TPCN2 loci and HLA signals specific to Pediatric Onset Ulcerative Colitis
Venkateswaran, Suresh; Prince, Jarod; Cutler, J. David; Marigorta, Urko M.; Okou, David; Prahalad, Sampath; G. Sauer, Cary; Gibbson, Greg; Denson, Lee; Hyams, Jeffrey; Kugathasan, Subra

Background: The genetic contributions to pediatric onset UC, characterized by severe disease and extensive colonic involvement, are largely unknown. In adult onset disease GWAS has identified numerous loci associated with UC, most of which have a modest susceptibility risk (OR 0.84 to 1.14), with the exception of the HLA region on Chromosome 6 which shows strong association in adults (OR 3.59).

Aim: To perform GWAS/fine mapping exclusively for pediatric onset UC.

Methods: GWAS was performed using the UK Biobank axiom array on a sample of 734 cases and 3,840 disease free controls. The significant SNPs (p<5e-08) were further confirmed by a replication study, performed on a different cohort of 137 pediatric UC cases by using Immunochip genotyping. SNP2HLA was used to impute classical HLA alleles and their corresponding amino acids, and colocalization analysis was performed to compare HLA results with adult onset UC.

Results: We found an interesting, novel SNP rs35264875 (OR=1.86; p=1.19x10-10) on chromosome11, which corresponds to TPCN2 loci. Our study identified 11 other suggestive
SNPs on the same TPCN2 loci in perfect Linkage Disequilibrium (LD) with each other (r2~1). Our replication cohort result further confirmed that the SNP rs35264875 is real and specific to pediatric onset UC. The other established SNPs in adult onset UC loci had similar direction and magnitude in pediatric onset UC while the HLA region dominated the association signals with 191 SNPs (p=5x10-8 to 5x10-10). SNP2HLA imputation identified HLA-DRB1*0103 (OR=6.941, p=1.92*10-13) as the most significant association for pediatric UC compared with adult onset UC (OR=3.59). Further conditioning showed independent effects for HLA-DRB1*1301 (OR=2.25; p=7.92*10-9) and another SNP rs17188113 (OR=0.48; p=7.56*10-9). According to coloc, the two HLA-DRB1 causal alleles are shared with adult onset UC, while at least two other signals are unique to pediatric UC. Subsequent stratified analyses indicated that HLA-DRB1*0103 has stronger association for extensive disease (E4: OR=8.28; p=4.66x10-10) and female gender (OR=8.85; p=4.82x10-13).

Conclusion: This study found a pediatric specific novel SNP rs35264875 correspond to TPCN2 loci. The allelic contributions of other common SNPs to pediatric UC are similar to adult onset UC. The HLA association is approximately twice as strong in pediatric UC, due to a combination of novel and shared effects, confirming the importance of HLA in pediatric UC.

103. YB1 regulates radiation resistance in the medulloblastoma tumor microenvironment
Dey, Abhinav; Malhotra, Anshu; Kenney, Anna

Sonic hedgehog (Shh)-mediated medulloblastoma growth requires IGF2 (Insulin-like Growth Factor 2) and we showed that Yes Associated Protein (YAP1) stimulates IGF2 expression(1) by Y-box protein 1(YB1) in Shh-induced cerebellar granule neural precursors (CGNPs), proposed cells-of-origin for the Shh molecular subclass of medulloblastoma, and mouse Shh-medulloblastoma cells(2). We observed elevated levels of YB1 in tumor cells occupying the peri-vascular niche, a microenvironmental milieu proposed to house so-called tumor re-populating cells that survive radiation and contribute to medulloblastoma recurrence, which is fatal. Due to the absence of standard mouse models to study radiation resistance in the tumor microenvironment, we have developed an ex vivo approach using organotypic brain tumor slice cultures to better understand how YB1 regulates peri-vascular niche cell survival post-radiation. We observed that the perivascular niche cell population expressing stem cell markers increases markedly following exposure to radiation. Additionally, on targeting YB1, using Fisetin/shRNA, we observed increased level of cell death within the niche and compromised cancer stem cell niche expansion post-radiation. Subsequent molecular studies show that YB1 is required for DNA repair post-radiation in medulloblastoma cells. We carried out microarray-based analysis to identify pathways associated with tumor regeneration post-radiation. Using METACORE and Ingenuity Pathway Analysis, we identified GABAergic and Glutamatergic neuronal pathway activation post-radiation. Our bioinformatics based-studies show transcriptional regulation of these pathways by YB1. We have also attempted to ensure that the response to Fisetin treatment correlates with expected responses in the smaller cancer “stem-like” cell population.
by the implantation of neurospheres on a brain slice (NoBS). The NoBS technique is a novel way of mimicking the tumor microenvironment in vitro. These findings strongly indicate that therapeutic approaches intended to impair the function of YB1 could be used to reduce the use of cranio-spinal radiation of medulloblastoma patients, which causes life-long side effects that drastically impair quality of life.

References:

104. Impact on Rotavirus Vaccination: Determining the Effects of Travel Distance and Time on Access to a Rotavirus Vaccine Provider
Brown, Kelly; Churchill, Victoria; Laghaie, Elham; Yan, Fengxia; Immergluck, Lilly

PURPOSE: Rotavirus infection is the most common infection and leading cause of diarrhea in infants and young children throughout the world. The virus is transmitted through the fecal-oral route and infects many children by the age of five. If untreated, rotavirus infection can lead to severe morbidity, namely acute gastroenteritis. Since 2006, two rotavirus vaccines have been marketed for the prevention of rotavirus infections. Travel distance and time from a child’s vaccine provider can be factors that make access to this effective vaccine extremely difficult. We hypothesize that there is an inverse relationship between distance/travel time from a vaccine provider and likelihood for completion of the rotavirus vaccination series in infants.

DESIGN METHODS: This is a secondary data analysis of cross sectional data collected during January 2013 to June 2013 of children who had acute gastroenteritis. Each participant’s immunization records were used to record rotavirus vaccine type, timing of administering vaccine, and number of doses. Geocoding of each participant’s vaccine provider was performed based on information obtained from the Georgia Registry of Immunization Transactions and Services (GRITS). Google Maps and a Georgia public transit planner (MARTA) was used to record travel time and distance at a set time and date in order to record consistent calculations. The distance from participants’ home address to each vaccine care provider was determined in miles and estimates for time were conducted based on walking, car travel, and public transportation.

RESULTS: We have included 325 participants, of whom 201 had complete rotavirus vaccination compared to 124 who did not. Among the included participants, 73.2% had public insurance and the average number of vaccine providers was 1.2. We determined that the average distance by car transportation was 10.4 miles for those with incomplete vaccinations compared to 10.5 miles for those with complete vaccinations.

DISCUSSION: This research will be able to explore the relationship between access to a primary care provider (defined by distance and travel time) and rotavirus vaccination completeness. Our findings may assist public health policy makers and health facilities to address potential barriers
that hinder access to vaccine providers. An increased level of access can in turn increase the likelihood of receiving a complete series of a vaccine and reduce the risk of contracting the rotavirus infection among children.

105. Drug Library Screening and Identification of Novel Targets to Promote the Proliferation of Cardiomyocytes Derived from Human Pluripotent Stem Cells
Jha, Rajneesh; Gentillon, Cinsley; McCormick, Louise; Shepard, Caitlin; Singh, Monalisa; Rampoldi, Antonio; Kim, Baek; Xu, Chunhui

Human heart has limited capacity to regenerate cardiomyocytes lost from myocardial injury and heart failure, contributing to the leading cause of death globally. The therapeutic use of human pluripotent stem cell (hPSC)-derived cardiomyocytes for cardiac repair has generated a great deal of interest. However, it is still challenging to produce large quantities of enriched hPSC-derived cardiomyocytes. In this study, we performed a high throughput screening using Selleck Customized Drug Library to identify drugs with the ability to promote differentiation and proliferation of cardiac progenitors. Human induced pluripotent stem cells were induced to differentiate into cardiomyocytes by growth factors activin A and bone morphogenetic protein 4. Cardiac progenitors were treated with drugs at a final concentration of 10 µM from differentiation days 6 to 8. At day 8 of differentiation, proliferation of cardiac progenitors was examined by co-staining NKX2-5 (a cardiac marker) with Ki-67 (a proliferation marker) and fluorescence signals were detected using high-content imaging by the Cytation 3, Gen5 3.0. Out of 2196 drugs screened, we identified 154 primary hits promoting either or both differentiation and proliferation of cardiac progenitors. These primary hits were further evaluated by the treatment of cardiac progenitors with each drug at 4 concentrations (0.08, 0.4, 2 and 10 µM) in a secondary screening. This study allows us to identify novel and potent inducers of differentiation and proliferation of hPSC-derived cardiac progenitors.

106. Postnatal Zika virus infection causes persistent neurologic abnormalities in infant macaques
Mavigner, Maud; Raper, Jessica; Gumber, Sanjeev; Wrammert, Jens; Suthar, Mehul; Zhang, Xiaodong; Alvarado, Maria; Chahroudi, Ann

The Zika virus (ZIKV) epidemic is associated with fetal brain lesions and other serious birth defects. However, the neurologic consequences of in utero ZIKV infection in infants born without overt anomalies are unknown and, while cases of postnatal ZIKV infection in children have been reported, data on long-term neurologic outcomes are absent.

To address this gap, we developed a model of postnatal ZIKV infection in infant rhesus macaques (RM). Six RM infants were challenged subcutaneously at a median age of 37.5 days with 105 plaque forming units of ZIKV PRVABC59. Two ZIKV-infected infants and two age-
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matched, uninfected controls were followed until six months of age. The four additional ZIKV-infected infant RM were euthanized during the first two weeks after infection for tissue analysis. Viral loads in plasma and tissues were measured by qPCR. Binding and neutralization antibody responses were quantified by ELISA and focus reduction neutralization test. Central and peripheral nervous system tissues (CNS and PNS) were subjected to histopathological analysis and immunohistochemistry. At three and six months of age, infant RM underwent structural T1-weighted magnetic resonance imaging (MRI), resting-state functional MRI (rsfMRI), and Diffusion Tensor Imaging (DTI). At six months of age, the emotional behavioral response to an acute stressor was tested using the Human Intruder Paradigm.

ZIKV RNA in plasma peaked at day 2-3 post infection (p.i.) and cleared by day 7p.i. Postnatal ZIKV infection resulted in the rapid generation of humoral immune responses as shown by ZIKV Env-specific IgM and IgG as well as neutralization activity in plasma. ZIKV RNA was detected in lymph nodes and in the spleen at day 3 and 14-15 p.i. Additionally, at day 14-15 p.i., ZIKV RNA was quantified in CNS and PNS tissues including cauda equina, trigeminal ganglion, frontal cortex, parietal cortex and occipital cortex. ZIKV neuroinvasion caused histological abnormalities in the CNS and PNS including inflammatory infiltrates, astrogliosis, and Wallerian degeneration. MRI/rsfMRI with DTI showed persistent enlargement of the lateral ventricles, microstructural changes in the frontal corpus callosum, and altered functional connectivity between brain hemispheres in ZIKV-infected RM infants several months after clearance from peripheral blood. ZIKV infection also resulted in a distinct alteration in the species-typical emotional reactivity to acute stress.

In summary, we demonstrate for the first time that postnatal ZIKV infection of infants disseminates into the CNS and has structural and functional neurologic consequences, suggesting that long-term clinical monitoring of pediatric and asymptomatic congenital cases is warranted.

107. KPT-350 ameliorates Duchenne muscular dystrophy symptoms in dystrophic zebrafish and mice
Alexander, Matthew; Hightower, Rylie; Wang, Yimin; Tamir, Sharon; Gibbs, Devin; Kunkel, Louis

Objective: This study evaluated the effectiveness of the Selective Inhibitor of Nuclear Export (SINE) compound KPT-350 in a zebrafish and mouse models of Duchenne muscular dystrophy (DMD).

Background: DMD is an X-linked disorder that affects approximately 1:5000 live male births, making it the most common form of muscular dystrophy worldwide. The nuclear export protein XPO1/CRM1 is a promising target for the treatment of neurological disorders with inflammatory pathology such as DMD. KPT-350 induces dramatic nuclear retention of IkBα, a protein cargo of XPO1. This nuclear retention of IkBα is associated with nearly complete inhibition of binding of pro-inflammatory transcription factor NF-κB to DNA. KPT-350 is a potent, small molecule, orally
available, slowly reversible inhibitor of XPO1, and KPT-350 administration increases the amount of endogenous IKB, thus inhibiting NFKB’s function in a myonucleus.

Design/Methods: In order to assess short-term effect of KPT-350 treatment on dystrophic disease phenotype and muscle architecture, sapje zebrafish (severe model of DMD) embryos were treated from 1 to 5 days post-fertilization (dpf) with vehicle, 1.25 µM KPT-350, 2.5 µM KPT-350, or 2.5 µM aminophylline (positive control). In order to assess the effects of long-term KPT-350 treatment on survivability, sapje zebrafish were treated 3x/week for 24 hrs/dose with vehicle, 0.1 µM KPT-350, 1.0 µM KPT-350, or 2.5 µM aminophylline for 21 dpf. For murine studies, we tested oral KPT-350 (5 mg/kg body weight) given to adult mdx (DBA2J) and control WT mice 3 times a week for 8 weeks in a blinded fashion.

Results: In short-term treatment studies, KPT-350-treated sapje zebrafish showed significant prevention of the muscle degeneration pathology associated with dystrophin-deficiency and improved overall muscle architecture as determined by histological analysis of myosin heavy chains. With long term treatment, KPT-350 extended the lifespan of the sapje zebrafish, with a significant number of KPT-350-treated sapje mutants surviving well past 10 dpf, and reduced overall dystrophic pathology. In the mdx (DBA2J) mice KPT-350 blocked muscle inflammation, improved movement distance and velocity before forced treadmill running and reduced overall dystrophic symptoms compared to vehicle controls. The mdx (DBA2J) KPT-350-treated mice showed increased myofiber size and decreased areas of necrosis.

Conclusions: Our studies demonstrate that KPT-350, IND-ready compound, can improve or block the symptoms associated with muscular dystrophy, and is a promising small molecule compound for the treatment of dystrophin-deficiency.

108. Neural Mechanisms of Asthma
Han, Liang; Limjunyawong, Nathachit; Mitzner, Wayne; Undem, Bradley J.; Canning, Brendan J.; Dong, Xinzhong

Asthma, accompanied by lung inflammation, bronchoconstriction, and airway hyperresponsiveness, affects 10% of the children in the United States. Current investigations of the pathogenesis of asthma have been largely focused on the immune responses. However, anti-inflammatory treatment only partially controls asthma symptoms, demonstrating the urgency to understand the involvement of non-immune systems in the disease. The lung is densely innervated by sensory nerves, most of which are derived from the vagal sensory neurons. These sensory nerves play an important role in regulating the physiological functions of the respiratory system, such as controlling the breathing pattern and maintaining bronchomotor tone. They are also responsible for evoking airway nocifensive reflexes including coughing, cholinergic bronchoconstriction, and mucus secretion, all of which can contribute to asthma symptoms under pathological conditions. Here we report that MrgrprC11, a sensory neuron specific gene, is expressed in a subset of vagal sensory neurons innervating the lung and...
mediates cholinergic bronchoconstriction. Mice lacking Mrgrp genes showed reduced
anaphylactic bronchoconstriction and diminished influenza virus-induced airway
hyperresponsiveness. Conversely, stimulation of MrgrpC11-expressing vagal sensory neurons
enhances airway responsiveness in the absence of lung inflammation. These findings highlight
the critical role of vagal sensory neurons in asthma and suggest a novel therapeutic target for
asthma treatment.

109. Virtual transcatheter pulmonary valve replacement to optimize patient outcomes in
pediatric patients
Hashemi, Sassan; Parks, W. James; Sallee III, Denver; Bauser-Heaton, Holly D.; Kim, Dennis W.;
Petit, Christopher J.; Vincent, Robert N.; Slesnick, Timothy C.

Background: Pulmonary regurgitation (PR) is common as a result of surgical repair of several
types of congenital heart disease, most commonly tetralogy of Fallot. Over time, PR causes right
ventricular (RV) dilation and ultimately dysfunction. In the past, repeat surgical intervention
was needed to replace the pulmonary valve, but recently transcatheter pulmonary valve
replacement (TPVR) has been increasingly used for some patients. However, it is crucial to
ensure that coronary arterial flow will not be compromised when undergoing TPVR. Currently,
this requirement can only be tested during invasive cardiac catheterization (cath), wherein a
test balloon is inflated across the proposed location of the prosthetic valve to assess the
coronary flow. We seek to predict coronary obstruction in these patients before cath by
modeling of pertinent patient specific anatomy and virtual TPVR placement.

Methods: Cardiac magnetic resonance imaging data of potential TPVR candidates were
prospectively obtained. RV outflow tract, main pulmonary artery (MPA), aorta (AO) and
coronary arteries were segmented and their 3 dimensional meshes were created. After Mesh
optimization, the narrowest section of the MPA was dilated to fit a stent mesh with exact
dimensions used for TPVR. When this technique resulted in overlap of the expanded MPA with
the coronary arteries, this was defined as coronary compression (and thus a contraindication to
TPVR). Patients subsequently underwent invasive cath for possible TPVR. Results from virtual
modeling and cath balloon dilation were compared.

Results: Two patients were studied. In the first patient (15 year-old female), dilation of
narrowest part of MPA to the desired 22mm resulted in overlap of MPA and left coronary
artery mesh (Figure 1A, B). Balloon dilation of MPA during cath also resulted in left coronary
artery compression in the exact same location (Figure 1C, D). Therefore, TPVR was not
performed and she was referred for surgical valve replacement. In the second patient (15 year
old male), dilation of narrowest part of MPA to 22mm did not cause overlap with coronary
arteries. Subsequent MPA dilation during cath did not result in coronary flow compromise and
TPVR was successfully performed.
Conclusion: This is the first proof-of-concept virtual modeling technique for prediction of coronary flow compromise with TPVR. If this non-invasive technique can be further validated, it would allow selected patients to avoid invasive catheterization if they are not an appropriate candidate for TPVR.

110. The Emory 3q29 Deletion Project: Profiles of Neurodevelopmental and Neuropsychiatric Phenotypes
Pollak, Rebecca M.; Boddu, Sherly; Park, Joy; Zwick, Michael E.; Saulnier, Celine A.; Mulle, Jennifer G.

3q29 deletion syndrome (3q29) is an extremely rare (~1 in 30,000) genetic disorder characterized by a 1.6 Mb deletion on chromosome 3 and is associated with developmental delay, intellectual disability, and a significantly increased risk for neuropsychiatric disorders including Autism Spectrum Disorder (ASD) and schizophrenia. The clinical presentation of these phenotypes is highly variable, which combined with the low frequency of the deletion has resulted in a poor understanding of the syndrome. To improve the current understanding of the phenotypic and molecular characteristics of 3q29, Emory University has launched a comprehensive 3q29 deletion syndrome project, including the 3q29 deletion registry (3q29deletion.org), an IRB-approved, HIPPA-compliant patient ascertainment website. The registry was launched in November 2013 and we have since registered over 100 patients; thus, Emory’s cohort is the largest sample of 3q29 deletion patients ever assembled. We have implemented a combination of custom and standardized questionnaires to assess demographic information, medical history, patient outcomes, and neuropsychiatric symptomology. Standardized questionnaires include the Social Responsiveness Scale (SRS), Social Communication Questionnaire (SCQ), Child Behavior Checklist (CBCL), and the Autism Spectrum Screening Questionnaire (ASSQ). These data show an elevated prevalence of neuropsychiatric phenotypes in 3q29 deletion patients. For example, 24% report a diagnosis of ASD, a 16-fold increase as compared with the general population. We also find increased rates of anxiety disorder and panic attacks. A point of specific concern is that multiple registry patients scored in the “severe” range on the SRS, a research tool that has strong correlation with the presence of ASD, but do not report a clinical diagnosis of ASD, suggesting that the true prevalence of ASD among individuals with 3q29 deletion may be underestimated. We will report on the full range of neurodevelopmental and neuropsychiatric manifestations as ascertained by registry instruments. Future directions for this project will include direct in-person clinical evaluation for ASD, anxiety, and additional neuropsychiatric and medical phenotypes. The results from the Emory University 3q29 deletion registry suggest that internet-based registries are an effective means for characterizing rare genetic disorders.
111. Visualization of Racial Disparities in Surgical Outcomes among Children via Network Analysis of Pre-Operative Risk Factors

Akbilgic, Oguz; Langham, Max; Davis, Robert

Despite a dramatic decline in surgical mortality of children in the United States over the past 30 years, racial disparities in adverse surgery outcomes persist. African American (AA) children have more than a two-fold higher risk of death within 30 days after surgery (D30). Understanding the causes and associated risk factors for racial disparities in surgery outcome is necessary to develop interventions to reduce racial health disparities. Our goal is to improve our understanding on racial disparities among children in surgical outcome using network analysis based data visualization.

We used the National Surgical Quality Improvement Program (NSQIP)-Pediatric participant use file (Pedi-PUF) data covering 2012-2014 with a total of 183,233 (with 621 deaths) surgical operations in children <18 years of age at time of operation, including a total of 130,437 operations on Caucasian and 23,263 on AA children. Among the 300-perioperative variables in Pedi-PUF, we considered fourteen preoperative variables as risk factors of D30, based on previous studies. These risk factors were: do-not-resuscitate status, ventilator dependency, receipt of oxygen support, previous cardiac intervention, cerebrovascular injury, wound infection, bleeding disorder, hemodisorder, sepsis, receipt of inotropic support, transfusion, malignancy, case type, and neonatal status.

We used network analysis to visualize the prevalence of risk factors and their association with D30. In the network, nodes were risk factors of D30, while edges represented the type and the strength of relationship between these risk factors. Four different node sizes represented the prevalence of risk factors (small: prevalence <1%, medium: 1%< prevalence <5%, size 3: 5%<prevalence<10%, and large: prevalence>10%) and node color codes represented the risk of death (green: risk<1%, yellow: 1%< risk<5%. orange: 5%<risk <%10, red: risk>10%). A similar color code was applied to edges (the risk of death for co-occurring risk factors) (green: risk<1%, yellow: 1%<risk<5%. orange: 5%<risk<%10, red: 5%<risk<25%, black: risk>25%).

Our risk factors networks for AA and Caucasian children showed that the node sizes for oxygen support, transfusion, and hemodisorder were larger for AA, indicating higher prevalence. In addition, the color of the ventilator node indicates a stronger association with death among AA on ventilator support compared to Caucasian children. A similar observation is shown for the risk factors of sepsis, neonate, emergent case, and malignancy.

Our study suggests that the prevalence of risk factors and their association with D30 are different for AA and Caucasian and these disparities can be visualized using a network of risk factors.
112. Patient reported long-term outcomes in children with gastroschisis
Arnold, Hope; Baxter, Katherine; Short, Heather L.; Travers, Curtis; Bhatia, Amina; Durham, Megan; Raval, Mehul

PURPOSE: The goal of this study is to determine long-term outcomes for patients with gastroschisis including quality of life measures, surgical reoperation rates, and residual gastrointestinal symptom burden.

METHODS: Retrospective chart review of patients who underwent surgical repair of gastroschisis between January 1, 2009 and December 31, 2012 was performed at a quaternary children’s hospital. Phone surveys of parents were conducted using two validated surveys (PedsQL Pediatric Quality of Life Inventory/PedsQL Gastrointestinal Symptoms Module). We collected additional outcome data including subsequent operations and current health status. Descriptive statistics were compared using chi-square and Wilcoxon Rank-Sum tests.

RESULTS: Of 143 gastroschisis patients identified, 52 families (36.3%) were reached with 45 (87%) agreeing to participate. The median age at follow-up was 4.7 years. Eight (17.7%) had complex gastroschisis. Twelve (26.7%) were closed primarily and 33 (73.3%) were silo closures (mean closure 7 days). Despite differences in short-term outcomes such as longer length of stay for patients with complex gastroschisis, there were no major differences in long-term outcomes when patients were stratified by birthweight, complexity of gastroschisis, or closure timing. Children with complicated gastroschisis experienced abdominal pain/gas/diarrhea more often than those with simple gastroschisis. Five (11.1%) children needed additional surgery after definitive closure and establishment of intestinal continuity. There were no explorations for lysis of adhesions or bowel obstructions identified, and though 10 (22.5%) of children had umbilical hernias, none had undergone repairs at the time of follow-up.

CONCLUSIONS: Although children with complicated gastroschisis were more likely to experience certain gastrointestinal symptoms, overall quality of life scores and surgical outcomes were reassuring for children with gastroschisis.

113. Bioinformatic analysis of gene expression patterns in 22q11.2 deletion syndrome points to dysregulation of ubiquitination pathways
Arth, Annelise; Ousley, Opal; Walker, Elaine; Duncan, Erica; Weng, Lei; Kobrynski, Lisa; Fernandez-Carriba, Samuel; Harwell, Christina; Coleman, Karlene; Cubells, Joseph; Pearce, Bradley

Purpose and Aims. The interaction of genetic and neuroimmune factors in the neurobehavioral sequela of 22q11.2 Deletion Syndrome (22q11DS) is not well understood. These behavioral sequella include autism spectrum disorders (ASD) and schizophrenia (SZ). Considering that 22q11DS is also associated with immune dysregulation, and that B-cell abnormalities are linked
to idiopathic SZ, we used genome-wide microarray analysis to measure differential gene expression in isolated B-cells from individuals with 22q11DS and controls.

Methods: We compared B-cell expression profiles of 12 individuals with 22q11DS and 12 controls in an RNA microarray to i) examine expression of genes in the 22q11 deletion region ii) examine differentially expressed genes using Ingenuity Pathways Analysis (IPA) bioinformatics software to determine significant cellular and metabolic pathways associated with 22q11DS.

Results: IPA analysis revealed that ubiquitination pathways play a central role in molecular networks predicted by our differential gene expression patterns. Disruptions in the ubiquitination pathway have previously been associated with autism spectrum disorders and idiopathic SZ. Our analysis revealed down-regulation of UFD1L, which is in the 22q11.2 deleted region and may be one link to the higher risk of these neuropsychiatric disorders among individuals with 22q11DS. We also found altered expression of genes outside of the 22q11.2 deleted region, which included genes involved in synaptic plasticity (RICH2, BASP1) and Wnt signaling (CHD8).

Conclusions. Our analysis suggests potential mechanisms by which disruption of complex molecular pathways can lead to neuroimmune irregularities and possibly increase the risk of psychiatric sequella in this population. Our findings also suggests possible molecular targets for early intervention to abrogate immune dysfunction and behavioral sequella in individuals with 22q11DS.

114. Preliminary investigation of machine learning on Neonatal ICU feeding transition
Ashouri, Hazar; Cunningham, Tommy; Capilouto, Gilson

In the United States, up to 70% of the infants born prematurely have trouble transitioning to breast or bottle feeding on their own. Difficulty with oral feeding can result in significant health problems that delay discharge from the Neonatal ICU (NICU). Although oral feeding has been identified as a rate limiting factor in discharge delay for this population, it has limited evidence based treatment guidelines using scalable technology and objective data. Nipple movement patterns during feeding collected via nfant Feeding Solution (NFANT Labs, Atlanta GA) are hypothesized to be indicative of neurodevelopment and ability to feed throughout neonatal maturation. Advances in machine learning algorithms, when applied to feeding patterns, present an opportunity to identify infants at risk for delay and enhance guidelines to advance their care.

Nipple movement data from select feedings were extracted from a larger ongoing study being conducted at a major academic medical center in the southeast tracking preterm infants from initiation of oral feeding through discharge, and full-term infants at discharge. Data were categorized binarily as pre-discharge or discharge. Feeding signals were divided into one second windows with 50% overlap between the windows. From each window, 9 short-term time and frequency domain features were extracted. Each of the 10 consecutive windows were then
grouped together and 8 midterm statistics were extracted for each of the 9 short-term features, resulting in a total of 72 extracted features. Training and test sets were created from the feedings with the training set i including instances from all feedings except feeding i, and test set i including the instances from feeding i. Feature selection functions and a random forest decision tree classifier were used to train each training set with the selected features. A threshold of 50% accuracy for each test set was used to determine whether that particular feeding was classified correctly or incorrectly.

Preliminary results indicated that 78% of the feedings were correctly classified into their respective groups. Future work will improve these results by expanding the training pool of feedings, optimizing window lengths for feature extraction and adding new features and classifiers from other variables also collected in the study.

Our goal in the coming months is to improve the classification rate for these trained algorithms and apply results to feeding data collected throughout the NICU stay to help guide feeding readiness and discharge criteria in a “Go”, “No-Go” output.

115. Procollagen III N-Terminal Propeptide (PIIINP) as a Circulating Biomarker for Active Stricture Development in Pediatric Crohn’s Disease
Ballengee, Cortney; Prince, Jarod; Baldassano, Robert; Katz, Jerry; Denson, Lee; Cross, Raymond; Patel, Ashish; Tomer, Gitit; Quiros, Antonio; Kugathasan, Subra;

Background: Up to 40% of Crohn’s disease patients eventually require surgery due to strictures. Extracellular matrix components, including type III collagen, play a vital role in the development of intestinal fibrosis and stricture in Crohn’s disease (J Crohns Colitis 2014;8:1147-65). In previous work, we have shown that genes involved in extracellular matrix accumulation are upregulated at diagnosis in pediatric patients with inflammatory (B1) phenotype who later evolve into stricturing (B2) disease as compared to those who do not develop strictures. There are currently no circulating biomarkers being used clinically to predict the risk for development of strictures in patients with inflammatory (B1) Crohn’s disease.

Aim: To determine if plasma PIIINP concentration is elevated in pediatric patients with inflammatory (B1) Crohn’s disease phenotype at diagnosis who subsequently develop strictures (B1 to B2) as compared to patients who never develop strictures (constant B1 phenotype), patients with B2 disease phenotype at diagnosis and patients with no inflammatory bowel disease (controls).

Methods: 8 patients with B1 disease phenotype at diagnosis, 8 patients with B2 disease phenotype at diagnosis, and 8 patients with B1 disease phenotype at diagnosis who subsequently developed strictures were matched with 16 patients without inflammatory bowel disease (controls). ELISA for PIIINP was performed on the plasma of each group drawn at
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diagnosis (Biomatik EKU06786). Mean plasma PIIINP concentration was compared between each group using ANOVA and adjusting for multiple comparisons (Tukey method).

Results: Plasma PIIINP concentration was significantly higher in the patients who went on to develop strictures (B1 to B2) when compared with controls (1737 vs 737 pg/mL; P=0.009). Without adjustment for multiple comparisons, serum PIIINP was significantly higher in B1 group as compared with controls (1394 vs 737 pg/mL; P=0.032) and B1-B2 groups as compared with B2 at diagnosis (1737 vs 977 pg/mL; P=0.032).

Conclusion: Plasma concentration of PIIINP was significantly elevated in pediatric patients with B1 Crohn’s disease phenotype at diagnosis who subsequently developed strictures (B2 phenotype). These results are consistent with previous work and are supported by the known pathogenesis of excess collagen deposition leading to tissue fibrosis. Our ongoing study involves measuring plasma PIIINP concentration in samples from 2 large cohorts, each with over 1000 pediatric and adult patients with Crohn’s disease. We speculate that circulating serum PIIINP may be clinically useful to predict Crohn’s disease phenotype in individual patients at the time of diagnosis.

116. The Effect of Healthcare Utilization Prior to Presentation on Perforated Pediatric Appendicitis Rates
Baxter, Katherine; Nguyen, Hannah; Raval, Mehul

Purpose: The purpose of this study is to determine whether increased utilization of healthcare prior to presentation is associated with lower complicated appendicitis rates in children.

Methods: A retrospective cohort study was performed using Truven MarketScan national claims database of insured patients. We identified cases of appendicitis in children (1-18 years) from 2010-2013. Utilization of healthcare was defined as ≥1 outpatient encounter in the year preceding presentation with appendicitis. Since visits within one month of presentation may be related to appendicitis, these were excluded. Logistic regression was performed to predict presentation with complicated appendicitis, using healthcare utilization as the key independent variable and adjusting for age, sex, geographical region, and insurance type.

Results: Of 39,740 children identified with appendicitis, 30,940 (77.9%) had an outpatient visit prior to presentation. Of the 12,159 (30.6%) classified as complicated appendicitis, 9060 (74.5%) had an outpatient visit prior to presentation. In the adjusted model, older patients were less likely to present with complicated appendicitis (odds ratio (OR) 0.91 per year, 95% confidence interval (CI) 0.91-0.92). Patients in the Midwest (OR 1.45, 95%CI 1.35-1.56) and Southern regions (OR 1.30, 95%CI 1.21-1.39) had higher odds of presentation with complicated appendicitis. Children with one or more outpatient visits in the year prior to presentation had lower odds of complicated appendicitis compared to children with no visits, OR 0.76, 95%CI 0.72-0.81. This relationship remained protective with increased intervals between outpatient visit and presentation with appendicitis.
Conclusions: Among insured children with access to healthcare, utilization of care within a year prior to presentation was associated with lower rates of complicated appendicitis. This finding highlights the role of utilization of primary care as a metric for quality improvement that is relevant to inpatient and surgical outcomes.

117. Ethnic Differences in Age of Concern, Age of Diagnosis, and Parental Report on the M-CHAT-R
Beacham, Chloe; Lambha, Meena

Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by social communication deficits and restricted/repetitive behaviors. Studies have shown ethnic differences in parental report of age of concern (AOC), age of diagnosis (AOD), and attainment of treatment (Mandell, Levy, & Pinto-Martin, 2007; Herlihy et al., 2014; Mandell et al., 2009; Burkett et al., 2015). Rosenberg et al. (2011) concluded that ethnic differences in the perception of atypical behaviors can contribute to reports of AOC and AOD. Studies investigating ethnic differences regarding parental reports on screeners, specifically the M-CHAT-R (Modified Checklist for Autism in Toddlers- Revised, Robins et al., 2014), found ethnic differences in the endorsement of items (Scarpa et al., 2013); however, ethnic differences on the M-CHAT-R between African American and Caucasian families, specifically, have not been investigated.

Objectives: This study examined parent report of AOC, AOD, as well as overall scores and individual M-CHAT-R items between African American and Caucasian families. It was hypothesized that the AOC and AOD would be significantly older in the African American sample, and that the African American and Caucasian samples would differ in their overall scores and endorsement of items on the M-CHAT-R.

Methods: Data was collected from 103 Caucasian families (ages 16 to 44 months) and 35 African American families (ages 20 to 42 months) at a regional clinic. Data included the age for Caucasian children (AOD: M = 29.42), gender (male N=87, female N=16), and AOC (M =16.22). Similar information was obtained for the African American sample: AOD (M = 30.17), gender (male N=30, female N=5), and AOC (M= 15.00). Data from the two sample groups was compared for children diagnosed with ASD using independent samples t-tests.

Results: There were no differences in AOC or AOD between the two groups. Analyses of M-CHAT-R items indicated no differences in overall scores between the two groups; however, significant differences in seven out of 20 M-CHAT-R items were found, with fewer African Americans families endorsing more culturally normed questions.

Conclusions: These findings show that African American and Caucasian families are reporting similar AOC and AOD. These results are encouraging because they suggest that African American families are endorsing red flags of ASD sooner. Differences noted on certain items
indicated by African American families (behaviors found to vary among cultures) suggest that clinicians should be cognizant of the impact of culture on the endorsement of items on the M-CHAT-R.

118. Early Neuromotor Abnormalities in Infants at Risk for Autism Spectrum Disorder
Beacham, Chloe; Carpenter, Sydney; Evans, Lindsey; Bradshaw, Jessica

Background: Deficits in motor performance are often seen in individuals with autism spectrum disorder (ASD), a neurodevelopmental disorder characterized by social-communication impairments and restricted interests and repetitive behaviors. Studies have shown a strong relationship between ASD and atypical neuromotor development, including increased rates of hypotonocity (Brian et al., 2008; Bhat, Galloway, & Landa, 2012; Serdarevic et al., 2017). There is currently little evidence identifying the earliest age at which these motor abnormalities emerge. Infants who have an older sibling with ASD are at an increased risk of developing ASD and have been shown to exhibit early developmental abnormalities (Ozonoff et al., 2011). The current study explored early motor abnormalities in these high-risk (HR) infants.

Objectives: This study sought to explore neuromotor profiles of HR from birth through six-months. Additionally, neuromotor profiles for those infants who presented with ASD red flags at a 12-month follow-up visit were explored.

Methods: Data was collected from 38 HR infants (male N= 23) and 34 low-risk (LR) infants (male N= 20) in a longitudinal, federally funded study. Infants were assessed monthly from 1-week to six months of age on measures of motor development with the NICU Network Neurobehavioral Scale (NNNS; Lester & Tronick, 2004) and the Bayley Scales of Infant and Toddler Development. Additionally, we investigated patterns of motor development among participants who displayed red flags at a 12-month follow up visit (N=10).

Results: Results showed comparable muscle tone between HR and LR infants from 1-week to 6-months. Infants with ASD red flags did not show significant differences on scores of muscle tone on standardized measures. However, individual review of the 10 infants who exhibited ASD red flags revealed that eight infants displayed increased hypertonicity at the 1-month, 2-month, and 3-month visit. At the 6-month visit, infants either remained hypertonic (N=4), became hypotonic (N=2), or abnormalities dissipated (N=4).

Conclusions: Our present data shows that HR and LR infants do not differ in their early motor presentation, in contrast to previous research (e.g., Serdarevic, 2017). Those that presented with ASD red flags showed patterns of early neuromotor abnormalities. Notably, these abnormalities were not captured in the summary scores but were noted in examiner observations, which suggests the need for improved standardized assessments to quantify muscle development in infants.
119. Inhaled Corticosteroids do not improve Lung Function in Young Cystic Fibrosis Patients
Beaty, Timothy; Gillespie, Scott; McCracken, Courtney; Stecenko, Arlene;

Background: Inhaled corticosteroids (ICS) are frequently prescribed for Cystic Fibrosis (CF) patients despite the failure of several placebo-controlled studies to show efficacy for pulmonary outcomes. These studies were limited by relatively small patient populations (7-171 patients) and short study periods (3 weeks – 2 years). In addition, these studies enrolled older children and adults who are capable of performing spirometry maneuvers as a measure of pulmonary function. Other anti-inflammatories, notably ibuprofen, have been noted to be most effective in CF when started chronically in younger ages, presumably because it slows the rate of irreversible lung damage from uncontrolled inflammation. This study tests the hypothesis that chronic ICS use started early in life is associated with improved lung function in early age.

Methods: Data were obtained from the Emory+Children’s CF Center patient registry. All patients born after newborn screening in Georgia (Jan 1st, 2007) with at least one year of data were included in the study. Baseline Forced Expiratory Volume in 1 second as a percent predicted (FEV1) was used as the measure of lung function outcomes. Student’s T test was used to compare FEV1 between groups.

Results: The study population included 252 subjects, 72 prescribed ICS during follow up (ICS+) and 80 with no ICS prescription (ICS-). ICS+ subjects were 1.0 (0.5, 2.0) month old and had follow up time of 6.3 (4.4, 7.8) years vs ICS- subjects at 1.2 (0.8, 2.4) months at study entry with follow up 4.2 (2.2, 7.5) years. Duration of ICS use was 3.1 (1.1, 4.8) years. There was no difference between the two groups in terms of weight-for-length or genotype at study entry. There was no difference between FEV1 between ICS+ and ICS- (98.94 ±13.15 vs. 98.60 ±10.01, p-value 0.27). FEV1 at each year of the study similarly had no difference (data included in poster).

Conclusions: These data suggest that even prolonged ICS use in very young CF patients does not result in improved FEV1 at school age. As this is an observational study we cannot rule-out that treated subjects may have had worse outcomes if not treated, however they did not appear to be less healthy at study entry (measured by weight-for-length). This result is consistent with previous clinical trials which did not demonstrate improvement in FEV1 over shorter periods of treatment. This may be because ICS are less effective in other diseases dominated by neutrophilic inflammation such as CF.
120. Effect of frequency on whole body movement control in children with and without Down syndrome during two-legged hopping in-place
Beerse, Matthew; Wu, Jianhua

It is unknown if children with Down syndrome (DS) are able to hop continuously outside of their preferred frequency, like their typically developing (TD) peers. This study aimed to assess the whole-body control strategies employed to modulate hopping frequency by children with DS compared to TD children.

Fifteen children with DS and 16 TD children aged 6-11 years were recruited for this study. Six children with DS were unable to coordinate continuous two-leg hopping in place. We age- and sex-matched 9 TD children corresponding to the remaining 9 children with DS. Each subject completed three self-selected 20-second hopping trials to calculate the subject’s preferred frequency. We randomly presented four frequency conditions: their preferred frequency (preferred), 20% decrease (slow), 20% increase (moderate), and 40% increase (fast). Only two DS subjects completed the fast condition so this condition was removed from analysis. We calculated absolute and normalized whole-body vertical stiffness. We calculated COM range and toe displacement in both anterior/posterior (AP) and medial/lateral (ML) directions.

Similar to TD children, children with DS were able to modulate their whole-body vertical stiffness across frequencies. Children with DS hopped at a faster preferred frequency (DS: 2.65 Hz, TD: 2.29 Hz), but with a similar whole-body vertical stiffness (no group effect for absolute and normalized stiffness). Both children with DS and TD children increased whole-body vertical stiffness when increasing hopping frequency (condition effect for absolute: p<0.001, normalized: p<0.001). Both groups increased hopping frequency across conditions, but not from preferred to moderate.

Children with DS did not effectively coordinate hopping at the moderate frequency condition. At the moderate frequency children with DS increased AP and ML toe displacement, flight time, and hopping height, while TD children decreased. This result is similar to previous studies where children with DS, when asked to tap on a pad faster, incorrectly tapped with greater force. Furthermore, children with DS did not display as much balance control as TD children. TD children reduced AP COM range of motion (p=0.005) to increase hopping frequency. Children with DS were unable to modify AP COM range of motion at the moderate frequency.

Our results suggest that children with DS modulate whole-body movement similar to TD children during two-leg hopping in place. However, children with DS demonstrate ineffective control strategies and greater horizontal movement when required to hop at a faster frequency.
121. Reovirus Infectivity is Modulated by Interactions with Bacteria and Bacterial Components.
Berger, Angela; Yi, Hong; Mainou, Bernardo

Mammalian orthoreovirus (reovirus) was isolated from stool specimens of children. Although most humans are exposed to reovirus during childhood, infections are usually asymptomatic. Reovirus infection of mice with depleted intestinal microbiota leads to impaired viral replication in the intestines and reduces viral-induced pathology. How the microbiota affect reovirus infectivity is not known. To investigate how bacteria and bacterial membrane components lipopolysaccharide (LPS) and peptidoglycan (PG) affect reovirus infection, we assessed viral infection of prototypical reovirus strains Type 1 Lang (T1L) and Type 3 Dearing (T3D) in the absence or presence of gram positive and gram negative bacteria, LPS, and PG. In the absence of bacteria or bacterial membrane components attachment and infectivity of T1L and T3D was impaired following environmental assault. In contrast, incubation of T1L and T3D with increasing concentrations of LPS, PG, gram negative, or gram positive bacteria during environmental assault provided a dose dependent protection against loss of infectivity. Reovirus virions were observed to associate with gram positive and gram negative bacteria by confocal and electron microscopy. Incubation of virions with LPS and PG did not alter cellular receptor usage or cell entry kinetics. Interestingly, incubation of reovirus with LPS or PG enhances the neutralization efficiency of reovirus-neutralizing antibodies. Based on these observations we conclude that reovirus virions are stabilized by bacterial membrane components as a consequence of small conformation changes in outer capsid proteins.

122. Functionalization of Flexible Polyvinyl Chloride Tubing for Medical and Industrial Application
Beveridge, Jennifer; Geoghan, Allison; Chenot, Haley; Crich, Alexander; Jacob, Alexis; Finn, M.G.

Bacterial colonization and biofilm formation on medical tubing presents a significant risk for infection for hospitalized patients. Currently, tubing with silver nanoparticles is the only FDA approved product to reduce bacterial adhesion for endotracheal tubing, however this is not approved for pediatric use as it relies on leaching heavy metals for its activity. To develop tubing intended to reduce bacterial adhesion for both pediatric and adult use, covalent modifications were made to endotracheal and catheter tubing. These tubing types are often made of polyvinyl chloride, which can be subject to a substitution reaction with small nucleophiles, including azide, in the presence of a phase transfer catalyst. These modifications provide convenient handles for covalent click chemistry linkages that allow for diverse functionalization at the surface. A variety of alkyne partners have been attached to azide modified tubing and assessed for material changes to the tubing, as well as for function in reducing bacterial adhesion.
123. Development and Technical Implementation of a No Show Predictive Model at Outpatient Pediatric Clinics
Braykov, Nikolay

Reducing the frequency of appointment No Shows (NS) is a key component in the transition to Value Based Care. No shows limit patient access by reducing the efficiency of care delivery, and increase healthcare costs due to missed revenue. Known approaches to counter these effects include 1) additional reminders and patient education, and 2) scheduling template optimization and double booking. Both strategies can be improved and targeted through the use of predictive analytics.

The Outcomes Center at Children’s Healthcare of Atlanta is developing a predictive model to identify NS appointments at 12 Children’s Physician Group clinics. Predictors include 3 years of individual-level data on encounter history and patient demographics sourced from custom schemas in EPIC’s Caboodle Data Warehouse, and merged with external data on Fulton County school calendar, weather conditions and projected driving times between patient and clinic zip codes. The model is trained on an R server using an ensemble of machine learning algorithms, including boosted logistic regression, neural networks, extreme gradient boosting (XGBoost) and support vector machines. Model hyperparameters are tuned through repeated cross-validation.

During the training period (01/2014 to 12/2016), the pooled NS frequency (including last minute cancellations) in the departments of interest was 23.24%, ranging from 18.47% for Pediatrics to 33.92% for Gastroenterology. No shows were associated with higher rate of prior no shows and cancellations, new patient status, longer interval between referral and appointment date, shorter time between current and prior appointment, self- or Medicaid-paying financial class, unconfirmed appointment 5 days prior to appointment, lower parent age at birth, below-freezing temperatures, heavy precipitation or snow conditions, driving time > 20 mins. When testing on a 20% holdout sample that was not used in model training, the current ensemble of predictive models has an ROC of 0.735, accuracy of 78.6%, positive predictive value (precision) of 80.1% and recall rate (sensitivity) of 96.3%, assuming a probability cutoff of 50% for assigning a class.

The NS predictive model has reasonable statistical performance. Further refinements, integrating the scores in the EPIC Hyperspace environment and operationalizing the model are forthcoming.

124. Measuring Sucking Performance to Identify Infants at Risk: What Big Data Can Tell Us
Capilouto, Gilson; Giannone, Peter; Cunningham, Tommy

Successful infant feeding is a complex neonatal behavior that requires integration of physiologic function and neurobehavioral ability. In our lab, we have focused on neonatal sucking as a
marker for later neurodevelopment since it is considered the most precocious purposeful motor skill of the newborn and an early window into the overall integrity of the central nervous system. We present results from an ongoing study investigating neonatal sucking as a marker of risk for adverse neurodevelopmental outcomes. The purpose of the current study is twofold: (1) compare metrics of sucking performance between preterm infants and healthy term infants at initiation of feeding and at discharge; and, (2) investigate changes in sucking performance longitudinally among preterm infants from initiation of oral feeding through post discharge. Our methods for collecting sucking data address the limitations of previous approaches. Here, we relied on automated analyses of elements of sucking to provide a set of summary statistics. Moreover, our present methodology uses a scalable and noninvasive tool to measure important sucking parameters throughout the course of a feeding so no modification of nipples is required and the moment to moment variability characterizing neonatal sucking is captured.

Healthy term infants (FT) (N = 15) with appropriate weight for gestational age, and healthy preterm infants (PT) (N = 40) with appropriate weight for gestational age were recruited for participation. Infants in the FT had no anomalies or diseases known to interfere with feeding (e.g. cleft lip and/or palate). PT infants had no anomalies or diseases known to interfere with feeding, no congenital disorders, chromosomal abnormalities, or major congenital anomalies, no disorders secondary to known perinatal exposure to toxic substances and no history of intraventricular hemorrhage greater than Grade II. Our measures of sucking performance focused on metrics characterizing movement variability and how variability evolves as movement skill is acquired.

Results showed no significant difference in our measures between healthy term infants (FT) and preterm infants at low risk for developmental concerns (LRPT). However, the coefficient of variation of suck duration (COVD) was found to be significantly different between preterm infants at risk for adverse outcomes (HRPT) and LRPT. For HRPT, results indicated the coefficient of variation of suck smoothness (COVSM) increased from initial feeding to discharge and remained significantly greater than FT at discharge. Results highlight the value of routine evaluation of early sucking as an indicator of relative risk of adverse neurodevelopmental outcomes at discharge.

125. Longitudinal Examination of Head Control in Infants at High- and Low-Risk for Autism Spectrum Disorder from Two to Six Months
Carpenter, Sydney; Evans, Lindsey; Beacham, Chloe; Klaiman, Cheryl; Bradshaw, Jessica

Background: Toddlers with autism spectrum disorder (ASD) show atypical motor and cognitive development in the first two years of life (Landa et al., 2013). Recently, motor delays have been documented in infants at high-risk for ASD as young as 6-months of age, highlighting head control as an area of concern (Bhat et al., 2012, Flanagan et al., 2012). Prospective, longitudinal
measurement of motor milestones, beginning as early as 2-months, will inform early detection methods and support the development of novel interventions for ASD.

Objectives: The goal of this study is to explore differences in the emergence of head control abilities, coordinated with visual and auditory attention, in 2- to 6-month-old infants at high- and low-risk for ASD.

Methods: The Bayley Scales of Infant and Toddler Development was administered monthly to infants at high (HR, N=35) and low-risk (LR, N=32) for ASD at five time points between 2- and 6-months of age. Four items were selected from the Bayley to measure head control in the current analysis: follows-ring, turns-to-sound, shifts-attention, and follows-ball. Each item required head control in conjunction with visual and/or auditory attention. Chi-square analyses were used to identify differences in reaching each of these milestones at monthly time points.

Results: Overall, HR infants appeared to meet each milestone later than LR infants. Milestones were “met” when 100% of infants within a group demonstrated the behavior. LR infants met the follows-ring milestone at 3-months while HR infants met this milestone at 5-months. The turns-to-sound milestone was achieved at 4-months for LR infants and 5-months for HR infants. The shifts-attention milestone was achieved at 4-months for LR infants and 5-months for HR infants. Finally, results revealed that LR infants met the follows-ball milestone at 4-months, while HR infants met this milestone at 5-months. A significant difference was observed at 4-months (p=0.01).

Conclusions: This preliminary study is one of the first to provide evidence for very early delays (starting at 2-months) in HR infants’ use of head control while attending to visual and auditory stimuli. Identification of early differences in head control, especially when paired with measures of attention, can contribute to our understanding of motor ability within the cascade of developmental and social abnormalities observed in children with ASD. These results could have significant implications for early detection of ASD and the development of early intervention.

126. Long Term Outcomes of Children Operated for Anomalous Left Coronary Artery from the Pulmonary Artery (ALCAPA)

Chan, Alice; Thomas, Amanda; Alsoufi, Bahaaldin; Kochilas, Lazaros;

Background: Anomalous left coronary artery from the pulmonary artery (ALCAPA) is a rare congenital cardiovascular anomaly with limited information regarding its long-term outcomes after surgical intervention.

Methods: This is a cohort study from the Pediatric Cardiac Care Consortium, a multi-institutional US-based registry of interventions for congenital heart diseases. We identified 187 patients with the diagnosis of ALCAPA having adequate identifiers for linkage studies. Long
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term outcome data are provided by linkage to the National Death Index (NDI) and the United Network for Organ Sharing (UNOS) up to the latest update of 12/31/2014.

Results: The median age at time of repair was 6 months (range: 9 days-17.2 years). Of the 186 patients, 141 underwent coronary re-implantation (78%), 28 Takeuchi procedure (13.2%), 7 coronary artery bypass grafting (4%), and 10 ligation of the anomalous coronary artery (4.6%). A total of 162 patients survived to discharge (87%). Concomitant procedures at time of repair for these individuals included mitral valve surgery (n=14), interatrial communication closure (n=11), and patent ductus arteriosus ligation (n=3). Twenty-four patients (14.8%) needed subsequent procedures including mitral valve surgery (n=9), coronary artery intervention (n=7), pulmonary angioplasty (n=10), heart transplant (n=4) and other procedures (n=5). There were 8 deaths (two after heart transplant) over 32 years of follow up as provided by linkage to the NDI and UNOS. The 20-year transplant-free survival rate was 94.3% for ALCAPA patients discharged alive, with a median follow-up of 17.9 years (IQR=14.3-23.4). The 20-year rate of freedom from re-operation was 82.8%.

Conclusions: 20-year transplant-free survival after surgery for ALCAPA reaches 94.3%, but there is significant remaining morbidity requiring additional interventions. The most common long-term complications after surgical intervention are mitral regurgitation, Takeuchi tunnel leak or stenosis, pulmonary artery stenosis and heart failure.

127. Gut Microbiome Profiles of Obese vs Lean Children
Chandwani, Vinita; Jabbar, Aysha; Fareed, Shaaz; Lewis, Jeffery; Laghaie, Elham; Stewart, Frank; Reese, LeRoy; Walsh, Stephanie; Immergluck, Lilly

INTRODUCTION: Childhood obesity is a cause of significant public health concern in the United States. The obesity epidemic is driving efforts around the world to identify host and environmental factors that affect energy balance, which in itself is a contributing factor to obesity. Amongst these internal host factors, the different compositions of gut microbiota in humans could provide further insight into the outcomes in human physiology. The phyla of Bacteroidetes and Firmicutes are the two predominant bacterial populations of microbiota.

BACKGROUND: Aims: (1) To determine gut microbiome phenotypical differences between children with obese vs. healthy BMI and to explore the differences in gut microbiota (specifically Firmicutes to Bacteroidetes ratio) in these two population of children. (2) To explore the relationship between a high-fat and high-sugar diet on the gut microbiota composition, taken into account potential influences of socio ecological factors, which are determined by where patients live. Hypothesis: We hypothesize that a difference exists between the gut microbiome profiles of obese children compared to healthy BMI children. We expect an increased ratio of Firmicutes to Bacteroidetes in the obese patients when compared to healthy. Secondarily, we hypothesize there will be a positive correlation to this ratio with those patients who report increased frequency of high-fat and high-sugar dietary intake.
METHODS: This is a pilot epidemiology case-control study. The patient population includes obese and healthy BMI patients between the ages of 8-12 years. Obese patients are defined as those with a BMI >95th percentile for their age, and lean patients were defined as those with a BMI between the 5th and 85th percentile. These patients were recruited at various sites within the Children’s Healthcare of Atlanta health system. An analysis of microbial community taxonomic composition and short chain fatty acid (SCFA) concentration was performed on the stool samples collected from the patient groups. Further, variation in the taxonomic composition of the fecal microbial community between obese and healthy donors and across health categories will be evaluated using high-throughput Illumina sequencing of bacterial 16S rRNA gene amplicons. A survey tool was also administered to parents and participants as a personal interview, regarding demographic information and dietary questions using a validated tool.

RESULTS AND CONCLUSIONS: We have enrolled 6 cases and 4 controls, beginning in October 2016. 70% of study participants have completed the questionnaire and 10 of 10 total stool samples have been collected and sent for analysis.

128. Research at the Medical Robotics and Automation (RoboMed) Laboratory
Cheng, Shing Shin; Sheng, Jun; Park, Kihan; Chitalia, Yash; Wang, Xuefeng; Desai, Jaydev

The Medical Robotics and Automation (RoboMed) Laboratory has been actively working in the development of minimally invasive surgical robots and automated medical diagnostic tools, both with potential pediatric applications. We are working in the areas of flexible meso-scale robotic systems for neurosurgery, cancer diagnosis at the micro-scale, as well as our recent efforts in developing steerable guidewire technology for intravascular interventions. In the area of neurosurgery, we are focusing on developing flexible 3-D printed minimally invasive neurosurgical intracranial robot (MINIR-II), that is patient-specific and disposable. It is equipped with electrocautery and suction and irrigation capabilities to electrocauterize and aspirate deep-seated brain tumor. The robot has three segments, the stiffness of which can be independently modulated to improve its maneuverability. An MRI-compatible remote actuation setup with a quick connect module has been developed for the robot. Another meso-scale robot for neurosurgical intracerebral hemorrhage evacuation (NICHE) has also been developed based on smart actuators made of shape memory alloy. By integrating the motion of a torsion joint with a distal bending tip, the end effector of the robot can articulate within the hemorrhage cavity for effective treatment. Additionally, a lightweight skull-mounted headframe is developed to precisely align the NICHE robot with a planned trajectory towards the target.

We have also developed a portable diagnostic device based on the combination of MEMS technology and tissue characterization technique. Since the device is able to capture the changes in physical properties of diseased tissue samples such as mechanical, electrical, or thermal characteristics, it can potentially be used to diagnose a disease by phenotyping a tissue
sample from pediatric biopsy. Finally, in the area of intravascular intervention, we have developed a micro-scale mechanically actuated robotic guidewire with the goal of allowing a clinician access through arterial sections that are hard to navigate, such as in peripheral artery disease procedures (PAD). The guidewire prototype is constructed from a single Nitinol tube by laser cutting asymmetric bi-directional notches to achieve multiple degrees-of-freedom. This steerable Nitinol tube has an outer diameter of 0.78 mm (< 2.4 Fr)!

Coben, Ella; Khan, Alyna; Jones, Warren; Klin, Ami; Shultz, Sarah

Background: Perceived stimulus salience and learning are tightly linked: attending to a particular stimulus at a given moment may result in learning that impacts where one chooses to look in the future. Likewise, not attending to that stimulus may lead to a different pathway of learning, resulting in different future fixations. Despite reports that children with Autism Spectrum Disorders (ASD) attend to social scenes differently than typically-developing (TD) children (Shultz et al., 2011), studies have not examined conditional probabilities of dynamic visual scanning, that is, the probability that viewers will fixate on a particular location given viewers’ previous fixation locations. Investigating the conditional probability of fixations on a moment-by-moment basis may reveal what is learned and what is missed by children with ASD.

Objective: This study characterizes learning pathways in toddlers with and without ASD by identifying on-screen fixation locations that predict future fixation locations.

Methods: Eye-tracking data were collected from 81 toddlers with ASD (mean age=24.1(1.7) months) and 75 TD toddlers (mean age=24.6(0.9) months) while viewing clips of naturalistic peer interactions. Fixation targets were defined as characters or objects perceived as highly salient, identified separately for TD and ASD groups (‘TD targets’ and ‘ASD targets’). Conditional probability ratios were calculated for all target pairs as the proportion of viewers who fixated on initial target X and later target Y relative to those who fixated on Y but not X. Conditionally dependent target pairs had conditional probabilities above 1.0, indicating targets were more likely to be fixated on had viewers looked at specific locations, and were less likely to be fixated on had viewers not looked at those earlier locations.

Results: Conditionally dependent target pairs were identified for TD and ASD viewers, indicating that viewing patterns of both groups are influenced by past viewing experience. Interestingly, TD fixations on TD targets appeared to be more strongly influenced by previous viewing experience compared to ASD fixations on ASD targets: a greater number of conditionally dependent target pairs were identified for TD viewers and the conditional probabilities of identified pairs were higher for TD (mean=5.33(10.40)) than for ASD viewers (mean=3.17(3.15)).
Conclusions: In navigating the social world, current understanding depends on past experiences, as information conveyed in past fixation locations may influence future viewing. Calculating conditional probabilities of dynamic visual scanning provides a novel means of quantifying how learning shapes and is shaped by altered patterns of visual engagement in ASD.

130. Epigenome-Wide Association Study in a Cohort Exposed to Polybrominated Biphenyl (PBB)
Curtis, Sarah; Kilaru, Varun; Terrell, Metrecia; Marcus, Michele; Conneely, Karen; Smith, Alicia

Early-life exposure to chemical pollutants is linked to increased risk for chronic disease in adulthood. In the 1970’s, Michigan residents were exposed to polybrominated biphenyl (PBB), an endocrine disruptor, when it was accidentally added to farm animal feed. Children were exposed during the initial contamination event by directly eating contaminated food products. Additionally, because PBB is highly lipophilic and can pass through the placenta, children of exposed mothers were also exposed, both in utero and through contaminated breastmilk. People who were exposed have numerous health problems, and, in many cases, the people exposed as children have more health problems than people exposed after puberty. However, the underlying mechanism for this remains unknown, but alterations of epigenetic marks may be to blame. Other endocrine-disrupting compounds have been linked to epigenetic differences and causing chronic disease, but no epigenetic studies have been done for PBB. Therefore, DNA from the blood of individuals with current (N = 671) PBB levels was interrogated with the MethylationEPIC BeadChip. Associations between each of the ~850,000 CpG sites and serum PBB levels were tested with a regression that controlled for age, sex, and cell type proportion. After multiple test correction (FDR <0.05), 4736 CpG sites associate with current blood PBB levels. These CpGs are in genes that are associated with immune, developmental, reproductive, and epigenetic regulation. For example, CpGs in DNMT3A, a gene essential for de novo methylation and mammalian development, associate with PBB levels (p = 1.23E-05). Future work will determine whether these CpG sites associate with the development of health problems reported in exposed individuals, and whether these differences in epigenetic marks can explain the more severe health problems in children.

131. THE EFFECT OF DIURNAL SLEEP DURATION AND EXCITABILITY, SELF-REGULATION, AND COGNITIVE ABILITY IN 1- AND 2-MONTH-OLD NEONATES
Evans, Lindsey; Carpenter, Sydney; Beacham, Chloe; Bradshaw, Jessica;

Background: Sleep serves a crucial role in a child’s global development (Spruyt et al. 2007). During the first months of life, neonates sleep an average of 14 hours a day (Bathory & Tomopoulous, 2007). As sleep and feeding cycles mature, sleep needed to sustain the infant decreases (Bathory & Tomopoulous, 2007). Previous research shows that infants exhibit increased durations of nocturnal sleep by six months and require significantly less diurnal sleep.
by 12 months (Bathory & Tomopoulous, 2007). Additionally, studies link sleep disturbances in early childhood with difficult temperament, decreased capacity to self-regulate, and lower cognitive performance (Sedah et al. 2015; Gevea et al., 2016; Turnbull et al., 2013), which could interfere with later social interactions, communication, and learning (Liu et al., 2016; Gomez & Baird, 2005). For this reason, neonates with disrupted sleep patterns may exhibit decreased neurobehavioral organization and consequently may be vulnerable to later lower cognitive performance.

Objectives: This exploratory study considers early associations between sleep and neurobehavioral organization of neonates. Relationships between sleep and self-regulation, attention, excitability, arousal, and cognitive scores of 1-month and 2-month infants were investigated.

Methods: As part of a longitudinal study, participants included 25 1- and 2-month-old infants. A parent-report Infant Sleep Questionnaire was collected to measure the infants’ sleep during 24 hours prior to their clinic visit. Measures of excitability, regulation, attention, and arousal were obtained from the NICU Network Neurobehavioral Scale (NNNS; Lester & Tronick, 2004). The cognitive domain of the Bayley Scales of Infant and Toddler Development was also administered at each visit.

Results: Bivariate correlations were run to assess the relationship between NNNS summary scores and sleep patterns. At 1-month, a significant positive correlation between attention and diurnal sleep duration ($r = .432, p = .045$) was found. At 2-months, there was a significant positive correlation between infant excitability ($r = .397, p = .040$), arousal ($r = .454, p = .025$) and diurnal sleep duration. A significant negative correlation between infant regulation ($r = -.430, p = .025$) and diurnal sleep duration at 2-months was also observed. No significant correlations between NNNS assessment scores, Bayley cognitive scores, and nocturnal sleep duration were found.

Conclusions: Few studies have investigated the relationship between sleep difficulties and behavioral and developmental problems in neonates as young as 1- and 2-months. Findings of this study suggest that even as early as 2-months, increased diurnal sleep duration may be an indication of immature sleep patterns resulting in increased irritability, decreased self-regulation, and lower cognitive capacities.

132. DNA methylation variations in cord blood associated with wheezing or lower respiratory tract infections among infants
Everson, Todd; Karagas, Margaret; Marsit, Carmen

Background: Respiratory conditions such as wheezing and lower respiratory infections (LRI) are some of the most common health issues experienced by infants and young children. The discovery of molecular markers at birth, associated with early life wheezing and LRI, may help clinicians manage higher-risk infants, and contribute to our understanding of the molecular etiology underlying these early life respiratory conditions. To this end, we screened the cord
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blood epigenome for differentially methylated regions (DMRs) associated with wheeze and/or LRI throughout the first 12 months of life.

Methods: We measured DNA methylation in cord blood throughout the genome from 296 infants (94 experienced wheeze and/or LRI within 12 months after birth) from the New Hampshire Birth cohort. DNA methylation was measured in cord blood via the Illumina Infinium EPIC array. Wheeze and LRI status were obtained via medical records abstraction. We clustered nearby loci, then tested for infant wheeze and LRI associated differentially methylated regions (DMRs), while adjusting for potential confounders (infant sex, birth site, and estimated proportions of cell-types).

Results: The top three DMRs included 8 CpGs within 3’UTR of MUC4 (3.4% difference; p-value = 0.0015), 1 CpG within the body of FSTL4 (8.8% difference; p-value = 0.0020), and 2 CpGs within a putative transcription factor binding site in the 5’UTR of SLC17A9 (4.1% difference; p-value = 0.0031). However, these associations did not survive FDR-adjustment (FDR q-value = 0.21-0.31). Though multi-functional, all are involved in T-cell activation and differentiation. We did not observe any associations between infant respiratory outcomes and cord blood proportions of CD4+ or CD8+ T cells, nor with any of the other estimated immune cell types (p-values > 0.05).

Conclusions: We observed modest differential methylation in cord blood at multiple regions of the genome related to immune cell activation and differentiation, associated with infant respiratory outcomes. These may represent differential immune programming at birth among infants are more likely to experience wheeze and/or LRI. We are currently pursuing further investigation of these preliminary results to evaluate the robustness of these associations with additional confounder adjustment, and within subgroups of our sample.

133. Joint kinematics of the pendulum test in children with and without Down syndrome
Ferreira, Diego; Liang, Huaqing; Wu, Jianhua

Previous studies have shown that children with Down syndrome (DS) have reduced movement ability and coordination compared to typically developing children (TD). However, most studies examined differences in walking pattern or upper extremity movements, and compared performance on specific tests between the two groups. The pendulum test is a specific test that has become a common tool to measure spasticity in populations with neurological or physical conditions. Adults with DS have been found to display a different pattern of knee joint kinematics by using the pendulum test. We aimed to compare knee joint kinematic via the pendulum test between children with and without Down syndrome.

We recruited 15 children with DS and 15 TD children aged 6-11 years for this study. Preliminary results are presented here, with 7 subjects in each group. Subjects completed at least 5 pendulum trials with their dominant leg. We presented two weight conditions: without ankle load (no load), and with external ankle load equal to 2% of their body weight (ankle load). We
use a Vicon motion capture system to record 3D movement of the leg and calculated knee joint angles in the sagittal plane. Differences in knee joint kinematics were observed through comparisons of the relaxation index (RI), number of swings or cycles, and range of motion (ROM). Averages from the 5 trials performed were used for each subject. A series of two-way mixed ANOVAs were conducted on these variables.

Results from the pendulum test indicated that TD subjects scored higher than children with DS for the variables measured: RI, cycles, and ROM. The RI score was 1.31 in children with DS and 1.63 in TD children. Visual observation of the plotted knee joint angle throughout the pendulum test showed that TD subjects averaged over 4 swing cycles, but the DS subjects averaged less than 2 swing cycles during testing. TD subjects had a significantly higher ROM than the DS subjects (83.95° vs. 61.17°). There were no differences between the no load and ankle load conditions for any of the variables.

The pendulum test performed in TD and DS children indicated that there is a significant difference in the amount of passive motion during the leg swing of a pendulum test. Further study in the subjects’ muscle activity is warranted to investigate if the decreased passive movement in the DS group may be due to muscle architecture, or from the central nervous system.

134. Metabolic Perturbations in Second-Trimester Amniotic Fluid Associated with Maternal Exposure to Secondhand Smoke
Fischer, Taylor; Lili, Loukia N.; Li, Shuzhao; Tran, ViLinh; Stewart, Kim; Schwartz, Charles E.; Jones, Dean; Sherman, Stephanie L.; Fridovich-Keil, Judith L.

Decades of public health research have documented that active smoking in pregnancy poses significant health risks to both mother and child. More recent studies have revealed that even passive maternal exposure to secondhand smoke associates with negative birth outcomes. However, the mechanisms linking exposure to outcomes have remained obscure. As a first step toward defining the metabolic consequence of passive exposure on fetal development, we conducted an untargeted metabolomic analysis of 81 paired samples of maternal serum and amniotic fluid collected from karyotypically normal pregnancies in the second trimester. We used the level of cotinine, a nicotine derivative, in the maternal serum to classify tobacco exposure and found that even low levels of cotinine consistent with maternal secondhand tobacco smoke exposure associated with distinct metabolic perturbations, particularly in amniotic fluid. In fact, the metabolic effects of passive maternal exposure in amniotic fluid showed greater overlap with perturbations previously observed in the sera of adult smokers than did the perturbations observed in the corresponding maternal sera. Dysregulated fetal pathways included aspartate and asparagine metabolism, pyrimidine metabolism, and metabolism of other amino acids. We also observed a strong negative association between level of maternal serum cotinine and acetylated polyamines in the amniotic fluid. Combined, these results confirm that maternal exposure to low-level nicotine consistent with secondhand
smoke is associated with striking metabolic consequences in the fetal compartment and that the affected pathways overlap those perturbed in the serum of actively smoking adults.

135. Impact of an accelerated discharge pathway on early outcomes and recovery following posterior spinal fusion for adolescent idiopathic scoliosis: A prospective comparative study
Fletcher, Nicholas; Murphy, Joshua; Bush, Patricia; Guerrero, Heather; Habib, Eva; Kusomoto, Hiro; Schmitz, Michael; Miyanji, Firoz

Purpose: Accelerated discharge (AD) pathways following posterior spinal fusion (PSF) for AIS offer earlier discharge home with a modest cost savings and similar complication rates when compared to a traditional discharge (TD) pathway. The impact on post-operative pain scores and recovery have not been well defined.

Methods: A prospective evaluation of patients undergoing PSF for AIS at two spine centers was performed with focus on early post-operative recovery. One center used the AD pathway while the other used a more traditional pathway. Post-operative quality of recovery as determined using the validated QOR9 instrument, last inpatient VAS score, and return to school were collected. Patients were matched for curve magnitude and estimated blood loss (EBL).

Results: 30 patients treated using the AD pathway were matched by curve size and EBL to 33 patients treated with the TD pathway. Length of stay was 2.7 days shorter in the AD group (2.48 ± 1.22 days AD vs 5.0 ± 0.83 days TD, \( p < 0.0001 \)). Age at surgery, number of levels fused (11.4 ± 2.5 AD vs 11.2 ± 2.1 TD, \( p = 0.62 \)), major curve magnitude (59.2° ± 10.6° AD vs 58.6° ± 10.8° TD, \( p = 0.83 \)), percent major curve correction (71.8 ± 15.6% AD vs 72.3 ± 8.3%, \( p = 0.64 \)) and EBL (616 ± 193 cc AD vs 669 ± 264 cc TD, \( p = 0.38 \)) were all similar. Patients treated at the TD center had 30 minutes longer total operating room time (332 ± 54 min TD vs 302 ± 55 min, \( p = 0.03 \)), likely due to a greater number of patients requiring osteotomy (50% AD vs 100% TD, \( p < 0.001 \)). Pain based on the VAS score at discharge was lower in the AD group (2.6 vs 4.5, \( p = 0.001 \)) and patient based quality of recovery scores (QOR9, maximum score 18) were similar at 6 weeks follow up (15.6 AD vs 15.4 TD, \( p = 0.80 \)). Days until return to school was similar between groups (21.4 ± 9.0 days AD vs 18.7 ± 5.7 days TD, \( p = 0.28 \)). 1 patient in the TD group and none in the AD group developed a postoperative infection. No patient was readmitted after discharge for medical issues.

Conclusion: The accelerated discharge pathway resulted in a shorter length of stay with lower pain scores at discharge. No patient required readmission or sustained a wound infection related to early discharge. Quality of recovery and time off of school are likely multifactorial and not as dependent on length of stay.

Significance: An accelerated discharge pathway for post-operative management following PSF for AIS can result in an earlier discharge with no difference in complications and a similar return to school.
136. Newborn Screening for Pompe Disease, MPS-I and X-Linked Adrenoleukodystrophy in Georgia
Foley, Allison; Hall, Patricia; Wittnaeur, Angela; Laney, Dawn; Hagar, Arthur; Wilcox, William

Introduction: Pompe disease, mucopolysaccharidosis type I (MPS-I) and X-linked adrenoleukodystrophy (XALD) are the most recently added conditions to the recommended uniform screening panel (RUSP) in the United States. Emory University, EGL Genetic Diagnostics and the Georgia Department of Public Health have been awarded Pilot Screening Project from the National Institute of Child Health and Human Development of the National Institutes of Health to assist with the implementation of screening for newly recommended disorders. In late 2016, we started screening all Georgia newborns for Pompe disease and MPS-I, and added XALD in 2017.

Materials and Methods: Our initial screening test for Pompe and MPS-I is a two-plex enzyme assay with detection by tandem mass spectrometry, which is interpreted with the assistance of post-analytical tools from the Collaborative Laboratory Interpretive Reports (CLIR). A positive result by the two-plex enzyme assay triggers a second tier test, a 6-plex enzyme assay, which is also interpreted using appropriate post-analytical tools. If the second tier assay is positive for any screened condition, the infant’s provider is contacted and follow-up procedures are initiated.

When screening for XALD was started, the analysis and detection of C20 – C26 lysophosphatidylcholines (LPC) was added to the 2-plex injection for Pompe and MPS-I. The initial screen positive result is based on post-analytical tools, and prompts a second tier chromatography assay, which also does not require additional patient contact.

Results and Discussion: Newborn screening for lysosomal storage disorders and peroxisomal disorders adds complex assays to the screening panel. In order to reduce the burden on follow-up programs and families, false positive screens need to be kept to a minimum. At the time of submission, over 18,000 samples have been tested for two analytes, with 1.5 – 2% referred for 2nd tier testing. The analysis using post-analytical tools allows for comparison of patient samples with both Georgia specific references ranges and ranges from laboratories across the country. This permits quick method validation and access to additional specimens from patients with rare disorders. The increase in reference sample size from collaboration allows for screening values to be corrected for multiple variables, including birth weight, age at collection and potentially gestational age. In addition, the tools may differentiate true positives, false positives, and carriers. Combined, this reduces the burden on follow-up programs and families and improves the overall performance of the screening program.
137. The Pediatric Interview: Are Preschool Aged Children Reliable Sources of Information?
François, Sandy; Lee, Grace; Smith, Shelby; Chen, Kuang-Ho; Roberts, James; Chen, Suephy

Introduction: The pediatric medical interview is distinct from the adult patient interaction. The combination of parent, child and physician creates a particular dynamic with every stage of development of the child. Preschoolers slowly emerge as sources of information for their care, particularly in cases of chronic disease where regular medical visits are expected. Of interest is their understanding of the concept of time.

Methods: Children between the ages of 4 & 5 who experience chronic itching (6 weeks or longer) were recruited from an Emory clinic. A total of 33 children were recruited: Eighteen 4-year-olds (12 girls and 6 boys) and fifteen 5-year-olds (8 girls and 7 boys). The child’s legal guardian reported the race and there were: 11 “African American/black”, 4 “Asian”, 12 “Caucasian/white” and 6 “biracial”. All subjects were enrolled between June 2015 and July 2016. Children were asked: “How many days are in a week?” and “What are the days of the week?” Categorical variables were created for each question. One sample proportion was used to determine quantity of children in each category. Chi Square was used to examine the relationship between gender and naming the days correctly and Pearson’s correlation coefficient was used for the possible difference between 4 and 5 year old naming the days correctly.

Results: Only 10 (30.3%) children were able to state correctly how many days were in a week, 10 (30.3%) were incorrect and 13 (39.4%) did not attempt to answer. Furthermore, 12 (36%) children named all 7 days of the week correctly, 8 (24.2%) named 5-6 days correctly, 2 (6.1%) named 3-4 days correctly, 4 (12%) named < 3 days correctly and 7 (21.2%) did not attempt to answer. The subgroups indicated an insignificant relationship between gender and naming the days correctly X2(1, N=33)=0.43 p>0.05 and a weak correlation between age and naming the days correctly r(31)=-0.35.

Conclusion: The majority of children couldn’t name the days of the week and had no knowledge about how many days were in a week. This provides insight to providers as they foster relationships with their young patients with chronic illnesses. It’s imperative to keep in mind their limited cognition of the concept of time which can affect follow-up appointments when inquiring about how they are coping and doing as recent as the past week. This was a small sample and warrants a larger scaled study.

138. Talk With Me Baby: Training Workforces on the Primacy of Early Language Exposure
Gaines, Tyra; Ryan, Timothy; Williams, Bryan; Darcy-Mahoney, Ashley; Zauche, Lauren; Weldon, Arianne; Costo, Megan;

There is an astounding number of children in the state of Georgia who cannot read proficiently at the close of third grade (77 percent), magnifying their risk of dropping out of high school and facing poor health outcomes and a shorter life expectancy. Mounting research highlights the
mediating effects of early language exposure on young children’s brain development and long-term health outcomes and also reveals that the single strongest predictor of a child’s academic success is in fact the quality and quantity of words spoken to the baby in the first three years of life. The Talk With Me Baby™ (TWMB) public-action campaign aims to ameliorate this epidemic via educating the public on the importance of early language exposure. TWMB is a cross-sector coalition aimed at transforming parents into conversational partners by: 1. training large scale workforces to act as coaches in their interactions with new and expectant parents, and 2. increasing the public’s awareness of the importance of Language Nutrition through publically accessible media. TWMB trainings emphasize the scientific evidence of early language exposure, the importance of meaningful social interactions between adult and child, use of home language, and empowering families of all backgrounds to be their child’s first and best teacher all while providing trainees with strategies to effectively demonstrate and communicate TWMB principles to families. Individuals in workforces that interact with new and expectant mothers, especially nurses, are the primary focus for TWMB. The present investigation is to evaluate the effectiveness of TWMB trainings in teaching Language Nutrition and motivating trainees to implement the principles. During trainings a pretest is given followed by an interactive presentation. Afterwards, a post test and training feedback form are administered. Trainees have included nurses, medical assistants, students, other medical professionals from locations including pediatric offices, hospitals, health centers, etc. A significant increase in scores from pretest to post test was demonstrated ($N= 449, t =-25.28, p= 2.9074E-88$, in a paired $t$ test), suggesting the training was effective in teaching Language Nutrition. The feedback data also suggest trainees were encouraged to implement TWMB (using a Likert scale 1= very unlikely, 2= unlikely, 3= unsure, 4= likely, 5= very likely; the mean score was 4.5 with a standard deviation of 0.9). The preliminary data supports the effectiveness of training workforces on Language Nutrition and mobilizing them to act. With more robust outcome measures TWMB findings can be validated.

139. Whole Blood Transcriptome in Children with Sickle Cell Anemia
Gee, Beatrice; Meller, Robert; Pearson, Andrea; Buchanan, Iris; Darden, Truddie; Simon, Roger

BACKGROUND: Chronic vascular complications of sickle cell anemia (SCA) include stroke, pulmonary hypertension, priapism, renal disease, and retinopathy. Circulating immune cells are in contact with the vasculature and are involved in cardiovascular diseases. Our group has shown distinctive whole blood transcriptome profiles in adults with acute stroke or traumatic brain injury. We used next generation RNA sequencing of whole blood to define the immune cell transcriptome of children with SCA, including a sub-group with high stroke risk, in comparison to healthy African American children.

METHODS: African American children 3 - 21 years old were recruited from Children’s Aflac Sickle Cell Clinics and Morehouse Healthcare Pediatrics Clinic. Subjects with SCA had Hemoglobin SS or S-β0-thalassemia, no transfusions in 3 months or hydroxyurea therapy in 6
months. They were categorized WITH Cerebral Arteriopathy (cerebral infarct, cerebral arterial stenosis or Transcranial Doppler (TCD) velocity > 200 cm/s) or WITHOUT Cerebral Arteriopathy (no clinical event or imaging abnormality, and TCD velocity < 170 cm/s). Exclusions included acute illness, chronic diseases other than SCA, pregnancy, and cardiovascular risk factors.

RESULTS: Samples were collected from 19 Controls and 27 SCA, including 4 WITH Cerebral Arteriopathy. The average age of Controls was 12 years, SCA 8 years, WITH Cerebral Arteriopathy 6 years. We have sequenced 32 patients using the total RNA protocol for the Ion Torrent. Samples were barcoded and sequenced on an S5 Ion torrent using 540 chips. Sequences were aligned to the human hg19 reference genome, and annotated using Aceview transcripts. Samples yielded on average 26 million aligned reads. Three samples failed our sequencing QC, either poor RNA library with evidence of degradation (1), or low number of reads (2). We performed 1 way ANOVA to determine differential expression between patient groups. From this, 2163 genes were differentially expressed between control (12) and SCD patients (17) (±1.5 fold change, FDR p<0.05). Data show a clear delineation by condition using hierarchical cluster analysis or principle component analysis (68.9%). We also determined differential expression between SCD patients WITH and WITHOUT Cerebral Angiopathy (2 vs 15, respectively) (243 genes ±1.2 fold change p<0.05 FDR). These also show a clear delineation on hierarchical cluster analysis and principle component analysis (85.2%). Preliminary modeling suggest 90% accuracy to predict SCD, based on transcriptome patterns.

CONCLUSIONS: Whole blood transcriptome analysis can define actively expressed genes involved in a disease. These genes may be developed as diagnostic biomarkers or investigated as mechanistic mediators.

140. Biomechanical Comparison of Prosthetic Knee Prescription Protocols in Children with Limb Loss
Geil, Mark; Safaeepour, Zahra; Giavedoni, Brian; Coulter, Colleen

A well-established clinical standard dictates that young children with limb loss at or above the knee joint do not receive a prosthetic knee that flexes until they are capable of independent standing and walking. A general assumption has been made that in the development of upright balance and walking, stability is preferred over mobility. Indeed, control of a passive prosthetic knee joint requires balance, coordination, and selective firing of residual limb hip flexors and extensors at appropriate phases of the gait cycle. Recent research has shown that young children are actually capable of crawling and walking with an articulating prosthetic knee and that several gait parameters are improved versus a locked knee. While promising, there is a lack of formal comparison to children in the traditional protocol. This study compared the biomechanical impact of the two protocols.

Instrumented 3-D gait analysis was performed on two groups of children (N=5 in each group) five years of age or younger with unilateral lower limb loss. The Early Knee protocol (EK)
children were assessed at Georgia State University, and children in the traditional protocol, with no articulating knee (TR), were assessed at Shriners Hospitals for Children in Shreveport. The protocol was approved by IRBs at each institution.

Mean results show that the EK group utilized the prosthetic knee for swing phase flexion averaging 66.5 degrees. Bilateral asymmetries are apparent in both groups. The EK group on average was slower but took longer steps.

This study is the first direct comparison of these two protocols, and it establishes that young children who are provided with a flexing prosthetic knee at an early age are capable of using the knee for flexion. It would therefore be expected that clearance adaptations would be reduced in this group. Some in the EK group did, however, exhibit signs of upward pelvic obliquity during swing phase, a measure of hip-hiking, possibly due to the nature of amputation in that group (proximal femoral focal deficiency). The children in the locked knee group exhibited a trend toward a greater hip joint frontal plane motion, especially for hip abduction in the swing phase. Swing phase hip abduction is a measure related to circumduction for clearance. Additionally, maximum ankle plantar flexion in the TR group was larger than the ER knee group. This could be a strategy for swing phase toe clearance.

(This study was funded by a grant from the Gerber Foundation.)

141. Metabolic Approach to Promote the Maturation of Human Pluripotent Stem Cell-Derived Cardiomyocytes
Gentillon, Cinsley; Jha, Rajneesh; Rampoldi, Antonio; Yu, Wen-Mei; Li, Shuzhao; Liang, Bill; Todor, Andrei; Anthony, Neil; Reedy, April; Qu, Cheng-Kui; Brown, Lou Ann

Background—Human pluripotent stem cell-derived cardiomyocytes (hPSC-CMs) represent a viable cell source for clinical application and other purposes, such as disease modeling and drug discovery for cardiovascular diseases. However their immature phenotype limits their utility for these applications. It is widely known that a transition in energy metabolism is implicated in cardiomyocyte differentiation and development. While fetal cardiomyocytes rely on glycolysis to produce most energy, adult cardiomyocytes use predominantly fatty acid oxidation (FAO). Using this metabolic hallmark of cardiomyocyte maturation, we investigated a platform that combines three-dimensional cell cultivation and molecules that target key pathways involved in the energy metabolism of cardiomyocytes. Methods and Results—Cardiac spheres of highly-enriched hPSC-CMs were generated from cardiac-differentiated cultures and treated for one week with a combination of molecules. A Seahorse XF-24 extracellular flux analyzer was performed to assess mitochondrial functions of treated hPSC-CMs in comparison to the control treatment (DMSO), and the expression of various metabolic genes was further examined via qRT-PCR. Altogether these assays showed that a combination of five molecules was the most potent at increasing mitochondrial respiratory capacity and FAO. Metabolic profiling of hPSC-CMs based on the measurement on a Fourier transform ion cyclotron resonance mass
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spectrometer (FTICR) identified more than one hundred metabolites that were altered by the treatment in comparison to DMSO. However, cardiomyocyte purity was comparable among the culture conditions according to immunocytochemical analysis using cardiomyocyte-associated markers, including structural proteins, α-actinin, cardiac troponin I and cardiac troponin T, and cell-cell adhesion molecule cadherin. Conclusions—Treatment of cardiac-differentiated cells with a combination of five molecules increases mitochondrial function, alters metabolic profiles, and potentially improves cardiomyocyte maturation.

142. Examining Parental Sensitivity to Early Social Communication Delay in Autism Spectrum Disorders Using the MacArthur-Bates Communicative Development Inventories
Grosman, Hannah; Klaiman, Cheryl; Richardson, Shana

Background: Early language delays often serve as the first indicator of concern for parents of children later diagnosed with ASD (Coonrood & Stone, 2004) Therefore, parent-report measures of language development that can also highlight ASD red-flags are critical for appropriate referrals and ASD evaluations. Previous studies have found agreement between receptive and expressive language scores on a parental report measure of early language and social communication, the MacArthur-Bates Communicative Development Inventory (MCDI), and standardized developmental assessments in the ASD population (Luyster et al., 2007). The MCDI also includes ratings of early gesture use and play given that gestures are meaningful precursors to language that reveal early social communication intent (Ellawadi & Weismer, 2014). Our study further assesses the accuracy of parent report on the MCDI by evaluating parent’s ability to identify more subtle social communication delays in early play and gesture use.

Methods: 99 children (84 males) who received an ASD diagnosis following gold-standard evaluations. Children were between the ages of 14-31 months (mean = 24.79) and referred based on parental concerns and/or recommendation from pediatricians or early interventionists. Parents completed the MCDI and children were evaluated with the Mullen Scales of Early Learning (Mullen) and the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2, Toddler Module). A gesture and play combined composite score was created from item level responses on the ADOS-2. Data from 24 additional participants is expected to be collected and included in data analysis by June 2017.

Results: MCDI reports of receptive and expressive language were significantly correlated with receptive and expressive language T-scores from the Mullen, respectively (r’s=.389, .572, both p’s<.001). MCDI reports of gesture use were significantly correlated with the ADOS-2 gesture and play composite scores (r=-.639, p<.001). The associations remained significant when splitting the sample based on developmental skills as assessed by the Mullen. Conclusions: Consistent with previous research, parents were accurate reporters of receptive and expressive language skills on the MacArthur-Bates CDI. Findings further show that parents can detect and report on subtleties of early social communication markers beyond speech and word use, such
as early gesture use, participation in social games, functional play and pretend play, as parent report of such skills on the MCDI was consistent with clinical observation. These results provide further support for the use of parent-report measures in assessing children’s early language use and development and their use within multidisciplinary evaluation for ASD.

143. Immunogenicity of VLP-based RSV G vaccines
Ha, Binh; Jadhao, Samadhan; Chen, Xuemin; Spearman, Paul; Oomens, A.G.; Anderson, Larry

Respiratory syncytial virus (RSV) is the single most important cause of serious lower respiratory tract infections in young children and infants worldwide. Symptoms of RSV infections include fever, bronchiolitis, bronchitis, and pneumonia. Unfortunately, there is no vaccines or highly anti-viral drugs available currently. RSV expresses two glycoproteins G and F that mediate viral attaching and fusion, respectively, and have been shown to induce protective immune responses. Antibodies that bind to the central conserved region of G (CCR-G) have also been shown to have an anti-inflammatory effect and decrease disease and, therefore, might improve an RSV vaccine. In this study, we hypothesized that a G protein construct could be designed to focus on induction of anti-CCR-G antibodies. We designed four G protein constructs that included CCR-G and used them to immunize mice in the form of virus-like particles (VLPs). Our data show that G protein constructs were immunogenic and that the CpG plus Poly IC or adjuvant system 04 (AS04) significantly boosted the immune response with AS04 being more potent. Preliminary results show with either adjuvant plus full length G or aa 155-206 construct that includes Gs central conserved region were most effective at inducing antibodies that bind to Gs central conserved region-derived peptide. These result suggest it should be possible to include G peptides in a vaccine to enhance induction of anti-G antibodies are associated with disease prevention.

144. Improving the use of the NPASS tool: using “Big Data” helped to confirm the need for staff education
Hardin, Barbara; Darr, Mary Rose; Hensley, Natalie; Hixson, Megan; King, Kaitlin; McElreath, Marjorie; Sims, Shaniqua; Murray, Eileen; Coughlin, Mary; Davis, Tod; Jo, Mingyoung

Background/Purpose: According to the pain guidelines posted by the National Association of Neonatal Nurses, “Repeated noxious stimuli experienced during a critical period of key brain development results in unique pain behaviors, sensory cortex activation, and neuroendocrine and physiological stress responses.” “Pain assessment is an essential prerequisite to pain management.”

The Neonatal ICU at Children’s Healthcare of Atlanta (CHOA) adopted the NPASS (Neonatal Pain Agitation and Sedation Scale) tool in order to improve staff assessment skills and documentation of pain. NPASS was chosen because it is a widely validated tool that incorporates behavioral, physiologic, and bio-behavioral measures--one of which is variance
from baseline vital signs--to assess neonatal pain, stress, and agitation. The tool was introduced in the CHOA NICU as part of annual competency-based education. During education follow up, a knowledge gap was identified specific to the baseline vital sign component of the (NPASS) tool. In collaboration with CHOA information technology specialists, we were able to validate this finding by comparing the NPASS vital sign scores with stored vital sign data from patient monitors “big data”. Review of big data showed no real correlation between the NPASS vital sign score and the actual stored vital signs, confirming the need for further education. The unit developmental care team launched an initiative to improve staff competency in establishing valid vital sign baselines for each patient and applying these baselines when assigning NPASS vital sign scores.

IV. Program, Materials, or Methodology: One-to-one education for all NICU staff nurses was provided, covering the process for establishing valid vital sign baselines for a patient by evaluating vital sign trends and individual patient history and condition, as well as directions on initiating or modifying baseline vital sign orders and then using the ordered baselines to assign appropriate NPASS scores.

V. Impact and Results: Follow up review of big data comparing NPASS vital sign scores and the actual stored vital signs in 2016 showed overall improvement over time. We have observed an increase in staff confidence and competence in applying the principles of the education provided. A chart audit of the NPASS VS score and charted VS is also being conducted.

The experience of using of using big data to confirm opportunities for performance improvement has opened our eyes to the possibilities of it’s use in future projects, including the evaluation of the effectiveness of clinical practice changes and education.

145. Revisiting the Bernoulli Equation in Coarctation Following Norwood Procedure
Hashemi, Sassan; Petit, Christopher J.; Sachdeva, Ritu

Background: In patients with hypoplastic left heart syndrome (HLHS), determination of coarctation (CoA) can be difficult by echocardiography (echo) due to caliber changes around the aortic arch. We sought to determine the relation between the peak gradient obtained by simplified Bernoulli equation in the descending aorta (DAo) and peak-to-peak gradient by catheterization (cath) following the Norwood. Our goal is to determine the best formula for accurately predicting presence of CoA.

Methods: HLHS patients with Norwood procedure between 2003 and 2014 who had a cath and an echo ≤ 5 days prior were included. CoA was defined as arch intervention in the cath lab. Diameter at the proximal transverse arch (D1) and narrowest region of native descending aorta (D2) were measured by echo. Based on the best fit quadratic curve, multiple polynomial regression curves were generated and their predictive values tested.

Results: The study included 96 patients, of whom 26 (27.1%) had CoA. Comparison of patient characteristics, echo and cath parameters, in those with and without CoA is shown in table 1.
Echo peak DAo velocity <2 m/s has a negative predictive value of 96% and that ≥2 m/s has a positive predictive value of only 51%. Echo peak DAo velocity, D1 and D1/D2 ≥3 were significantly association with CoA in multivariate analysis. No more than 56% of changes in cath gradients could be predicted by echo peak DAo velocity alone, with 4V2 having the weakest correlation and systematically overestimating the cath gradient (Figure 1). Similarly, no more than 52% of CoA could be predicted by any other models. However, D1/D2 ≥3 and proximal arch diameter significantly increased predictive value of all models from 65-68%.

Conclusion: Prediction of recurrent CoA by models based on echo peak DAo velocity remains challenging, with simplified Bernoulli equation having the weakest correlation with cath gradients. Morphologic factors such as size discrepancy between reconstructed arch and native DAo could improve echo diagnosis of CoA following Norwood.

146. Changes in Spatiotemporal Gait Parameters Following Treadmill Training in Children with Agenesis of the Corpus Callosum: A Case Study
Henderson, Gena; Beerse, Matthew; Wu, Jianhua

Objective: To investigate the effect of a treadmill-based training program on spatiotemporal gait parameters in children with agenesis of the corpus callosum (ACC).

Design: Single case study, before-after trial.

Setting: Treadmill training occurred at the participant’s home during physical therapy sessions. Before and after training, gait data of overground barefoot walking were collected at Georgia State University.

Participants: Single subject. 13-year-old female with ACC and secondary diagnoses of cortical visual impairment and deafblindness. At baseline the subject ambulated with modified independence using a reverse walker but was not a functional community ambulator secondary to poor efficiency of gait, poor endurance, and significantly slowed walking speed.

Interventions: Weekly bouts of a treadmill-based training program for three months. Protocol consisted of 10 minutes forward walking (0.94-1.12 m/s) and 5 minutes backward walking (0.27-0.31 m/s), with 3.0-3.5% incline during forward walking and 0.5% incline during backward walking.

Main Outcome Measures: Spatiotemporal gait parameters were collected with a Vicon motion capture system and analyzed with a customized MATLAB program.

Results: Participant completed 10/12 recommended training sessions, with two sessions missed due to illness and travel. The protocol was tolerated well and no adverse effects were reported. After training, the subject increased walking speed (0.28 to 0.37 m/sec, 31.6%) and cadence (88 to 98 steps/min, 11.9%), decreased step length (21.0 to 16.7 cm, 20.4%), and maintained step width (about 7.5 cm). Additionally, cycle time decreased (1.3 to 1.0 sec, 23.9%), with similar
percentages of stance phase (69%), swing phase (31%), and double support phases (19%) maintained. Furthermore, the subject decreased foot toe-in/toe-out angle (34.2° to 26.6°, 17.9%) and decreased the asymmetrical pattern in step width (asymmetry index of 14.2% to 4.2%).

Conclusions: A clinically significant increase in walking speed was seen post-training, indicating improved walking ability. This was achieved through increased cadence but decreased step length. No changes noted in step width and temporal parameters. Decreased out-toeing and step width asymmetry index indicate improved balance control. These pilot data indicate that treadmill training can be an effective, well-tolerated rehabilitation technique to improve functional walking of children with ACC.

147. Development of new molecules to treat pediatric glaucoma
Huard, Dustin; Qi, Min; Crowley, Vincent; Suntharalinam, Amirthaa; Tomlin, Moya; Du, Yuhong; Dickey, Chad; Fu, Haian

Defects in the protein myocilin are causal in 10-33% of juvenile open angle glaucoma cases. Nearly 70 different gain-of-function mutations in the myocilin olfactomedin domain have been documented, resulting in early-onset blindness in populations worldwide. Mutant myocilin readily aggregates and its toxic intracellular accumulation hastens the predominant glaucoma risk factor, elevated intraocular pressure (IOP). We have shown that the endoplasmic reticulum-resident chaperone Grp94, in its effort to triage misfolded myocilin, enhances its aggregation and intracellular retention. Upon Grp94 knock down or pharmacologically inhibition, aggregated myocilin is cleared. Since the absence of myocilin does not cause glaucoma, strategies aimed at eliminating myocilin could be therapeutic. We recently developed a high-throughput aggregation assay to identify new small molecules that target the myocilin-Grp94 interaction in different ways. The availability of a novel disease-modifying therapy for myocilin-associated glaucoma would represent personalized medicine for this prevalent ocular disease and would motivate genotyping in the clinic to identify patients who would benefit from this treatment.

148. Development of Enzyme Linked Immunosorbent Assays to Measure Antibody Response to Respiratory Syncytial Virus Infection in Children
Jadhao, Samadhan; Ha, Binh; Ayanoglu, Muhammet Mert; Chirkova, Tania; Rosas-Salazar, Christian; Hartert, Tina; Anderson, Larry

BACKGROUND: Respiratory syncytial virus (RSV) is a leading cause of lower respiratory virus infections in infants, immunocompromised individuals and the elderly. Despite many decades of research and development, licensed RSV vaccines are not available. Making availability of RSV antibody assays to detect and quantify antibodies to RSV infection is important to not only assessing response to infection but also to RSV vaccines. The EIA assays are particularly of
interest to screen children for detecting past infection and assessing primed versus naïve status to accurately assess the impact of RSV vaccination on RSV disease severity and outcome.

METHODS: We developed and are evaluating EIA using RSV lysate antigens from strains representing the two major antigenic and genetic RSV groups, A and B, and expressed RSV F and G protein antigens and RSV G protein central conserved region synthetic peptides as antigens to detect anti-RSV antibodies in human plasma. RSV lysate antigens were produced in HEp2 cells, RSV F, and G protein antigens were expressed in 293T or 293F cells. Plasma samples from more than 80 RSV infected children were tested using different EIA assays. The EIA data was analyzed using reference RSV positive serum standard curve and tests on single dilution of patients plasma using in-house developed excel regression analysis.

RESULTS: We will present results on evaluation of 6 RSV antibody EIA assays using RSV lysate, RSV F protein, two synthetic G protein peptides (one from group A and one from group B strains), and two secreted G proteins (one from group A and one from group B strains). The lysate and F protein EIAs gave good sensitivity and specificity. The peptide EIAs are less specific but do help to differentiate group A from group B infections. The G protein EIAs are being evaluated.

INTERPRETATION: This study will inform decisions about which RSV antibody EIAs are best for defining RSV primed and naïve state and infecting strain.

149. The Effect of Patient Weight on Trampoline Injury Patterns
Jones, Nicholas; Kelleman, Michael; Little, Wendalyn; Agarwal, Maneesha

Background: Pediatric trampoline injuries are common and increasing in frequency. The rate of obesity in children is also increasing. Given the mechanics involved in these injuries, a patient’s weight may have an impact on the type and severity of the injury sustained.

Objective: To determine if overweight or obese patients have a higher rate of fracture, need for sedation, admission to the hospital, or difference in extremity fractured in trampoline injuries.

Methods: This was a retrospective chart review of trampoline injuries from 1/2010 through 6/2014 at a level 1 pediatric trauma center. Charts were abstracted for type of injury, demographics, weight, need for sedation, and disposition. Patients were classified into underweight (<5th), normal weight (5th-<85th), overweight (85th-<95th), and obese (>95th) based on weight for age percentiles from CDC growth charts. Odds ratios with 95% confidence intervals were then calculated for each endpoint.

Results: 429 charts met inclusion criteria. The average age of patients was 7.8 years (SD =3.6 years). There was an even split between males (n=223, 52%) and females (n=206, 48%). A total of 215 (50.1%) patients had a fracture. The odds of fracture in obese children was lower than that of normal weight children (OR 0.48, [0.27-0.85], p=0.012). The odds of fracture in the
underweight (OR 0.64, [0.22-1.88], p=0.414) and overweight (OR 0.74, [0.43-1.30], p=0.295) patients was not different when compared to normal weight patients. The overall rate of sedation was 12.1% and admission was 18.9%; there was no statistical difference between weight categories for either of these outcomes. Of the patients with fracture, 151 (70.2%) were of the upper extremity, 56 (26.0%) were of the lower extremity, and 8 (3.7%) were of the axial skeleton. The odds of fracturing the upper extremity, lower extremity, or axial skeleton were not different between weight groups.

Conclusion: Underweight and overweight children do not have higher odds of fracture in trampoline injuries when compared to normal weight children. Obese children have a statistically significant lower odds of a fracture when compared to normal weight children. There was no difference in the anatomic location of the fractures, rate of sedation, or rate of admission between groups when compared to normal weight children. The overall emergency department outcomes and resource utilization for pediatric trampoline injuries are similar regardless of patient weight.

150. The Role of Immune Factors in Recurrent Childhood MRSA Infections
Kahf, Sebastian; Newman, Gale; Chu, Jane; Laghaie, Elham; Mohammed, Anaam; Immergluck, Lilly

Background: Recurrent methicillin-resistant Staphylococcus aureus (MRSA) infections in children are a well-documented occurrence in the United States. However, there are currently gaps in scientific knowledge regarding why some children develop recurrent skin and soft tissue infections (SSTIs) due to community-associated MRSA. Although there is evidence that strain specific virulence factors may be responsible for this observation, it is unclear whether there are also host immune factors responsible. Impaired macrophages have been known to be activated in response to infection by S. aureus and play a significant role in the innate immune response to S. aureus skin infections. In addition, toll-like receptors play an important role in the innate immune response and facilitating the adaptive immune response. Specifically, TLR2 is known to have a binding site for staphylococcal peptide glycan, so it is believed that this toll receptor plays an important role in the host defense against staphylococci. We therefore hypothesize that impaired macrophages and resulting levels of immune factor releases (such as IL-17/Th-17) will have altered responses in patients with recurrent S. aureus SSTIs compared to patients with non-recurrent MRSA infections. We also hypothesize that there are unique TLR2 genetic polymorphisms in children with recurrent MRSA infections that are not present in otherwise healthy children.

Methods: This is a prospective, case control study, which followed enrolled patients for more than 1 year from the time of enrollment. We used the CDC case definition for community associated MRSA infection. Recurrent infection was defined as two or more SSTI infections separated by 28 days or more. To test for these differences in immune profiles, wound and colonization swabs were obtained to determine carriage, and a follow-up blood draw was
scheduled for immune factor testing. Blood will be tested for IL-17 immune markers, TLR2 density, and TLR2 genotypes.

Results: We have enrolled 15 patients who met our definition for recurrent skin and soft tissue infection. Eight patients’ wound cultures confirmed MRSA; half of these patients’ colonization swabs did not reveal MRSA. Study participants have been prospectively followed for 24 months since the time of enrollment. Data analysis will include an ANOVA comparison of mean inflammatory marker levels, non-parametric ANOVA comparisons of TLR2 surface expression, and genotype prevalence comparisons via X2 analysis.

Conclusions: Our results will help to explain host factors contributing to the risk of recurring SSTIs in children and further the understanding of the overall innate immune response to S. aureus infection.

151. Engaging Community Systems to Enhance Early Screening and Identification of Autism
Kaiser, Eileen; Costa, Megan; Gaines, Tyra; Stapel-Wax, Jennifer

Early signs of autism spectrum disorder (ASD) include delays in social communication that appear in the first 2 years, but most children are not diagnosed until 4-5 years of age. Underserved families are identified later and significantly underrepresented in research. It is important to build the capacity of community members to recognize the early signs of ASD in order to connect children to early intervention services before age 3 when services can have the greatest impact on child and family outcomes. Community Based Participatory Research (CBPR) is used increasingly to address health issues and disparities for children by focusing on social, structural, and environmental inequities through involvement of community members, organizational representatives, and researchers in all aspects of the research process (Israel et al 2001). CBPR can be used to address challenges to translational research including limited external validity, poor community trust in research, and lack of sustainability of practice change in community settings (Dankwa-Mullan et al, 2014).

Community Service Providers (CSPs) from primary care practices, early learning centers and faith-based organizations were recruited to participate in this study. CSPs were provided with a tablet containing an interactive web platform that includes an automated screening tool linked to family resources on social communication development and early signs of autism. Prior to initiating screening, participants were asked to complete an 8-hour web-based course to increase the ability to recognize early signs of autism, understand how to share screening results with families, and provide direction for next steps to families. The course includes extensive video footage to rapidly build the capacity for early detection. Feedback from CSPs is used to make improvements to the screening process and potentially improve access to screening, diagnosis, and early intervention for all children.
To date, 75 CSPs have been recruited in one state of this four site project. Participants have screened 1,200 children by 20 months of age. Demographic information will be provided about the CSPs in each of the service systems.

Barriers to screening experienced by CSPs and solutions to help CSPs incorporate change into their busy workflow will be reported.

These findings will have important implications for bridging the research-to-practice gap and lowering the age of early detection of ASD. Screening by different community service systems will provide the opportunity to study strategies to address health disparities in access to early screening, diagnosis, and care.

152. Health Literacy- An Unaccounted Factor in Transplant Recipients’ Adherence and Outcomes
Kamel, Margret; Liverman, Rochelle; Pirani, Farha; Morris, Nneka; Gazmararian, Julie; George, Roshan

Introduction: Transplantation is the treatment of choice for children with End Stage Renal Disease. Successful long-term transplant outcomes depend largely on the patients’ and their families’ strict adherence to immunosuppressive medication regimens and stringent monitoring protocols, to avoid rejection. An adequate level of functional health literacy is essential to comprehend information given by healthcare providers and to generate sustained behaviors needed for successful adherence and favorable long-term outcomes. There is limited data about health literacy in the pediatric solid organ transplant population. The purpose of this project is to study prospectively the association between health literacy, adherence and outcomes in pediatric kidney transplant recipients.

Methods: Health literacy in patients and caregivers was assessed in adolescents, post renal transplant, using short test of functional health literacy (S-TOFHLA) and Newest Vital Signs (NVS). Barriers to adherence was assessed utilizing Adolescent and Parent Medication Barriers Scales (AMBS and PMBS) which is a validated measure of perceived adherence barriers. Allograft outcome was assessed using data from indication and protocol biopsies at 6 months, 1 year and 2 years.

Results: A total of 25 people including 9 parents/caregivers and 16 patients (ages 15-21 years; median age 17; 7 females, 9 males; 7 African American, 5 Caucasian [including 1 Hispanic Caucasian], 4 other/not reported) who are ≥ 6 months post-transplant with a stable, functioning allograft were enrolled. Patient NVS scores ranged from 0-6 (average = 3.4) and parent/caregiver scores ranged from 1-6 (average = 3.6) indicating limited health literacy. Patient S-TOFHLA scores ranged from 21-36 (average = 31.1) and parent/caregiver S-TOFHLA scores ranged from 22-36 (average = 32.3) indicating adequate functional health literacy. Three patients (18.75%) indicated a perceived adherence barrier (a total endorsement score of ≥3 for AMBS), while 4 parents (44.45%) endorsed perceived adherence barriers (endorsement scores
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≥2 for PMBS). Six patients (37.5%) experienced rejection (N=3 borderline, N=2 1A, N=1 2A cellular rejection) and of these, 3 patients (50%) had a low NVS score.

Implications: Patients experiencing rejection have adequate health literacy but limited numeracy literacy and have a parent/caregiver who endorsed perceived adherence barriers on PMBS. Although enrolled patients numbers are currently limited, this is an ongoing study and these preliminary findings indicate the importance of assessing health literacy as a screening tool. Health literacy, especially numeracy literacy, in patients with complex medical conditions is a hidden barrier, which needs to be recognized and overcome to improve long-term outcomes.

153. Developmental Trajectories of the Attunement of Visual Salience in Infants at High-Risk for ASD with Varying Levels of Affectedness at Outcome
Kreuzman, Andrew; Micheletti, Megan; Jones, Jessica; Klin, Ami; Shultz, Sarah; Jones, Warren

Background: Infants actively shape their environment by directing their attention towards content that they perceive to be most salient. From birth, typically developing (TD) infants selectively attend to socially adaptive signals. In contrast, reduced interest in the social world—a hallmark of autism spectrum disorders (ASD)—may lead to increasingly atypical development. The current study dynamically assesses group allocation of visual resources over the first two years of life to examine how deviations from typical norms may yield increasingly divergent schemas of salience during infancy across the spectrum of social ability to disability.

Objective: Use data collected at a millisecond timescale to map developmental trajectories of attunement of visual salience across the first years of life in infants with varying levels of social disability.

Methods: Longitudinal eye-tracking data were collected from children at high-risk for ASD at 10 time points by 24 months of age. Participants watched naturalistic videos of caregivers and toddler interactions. Diagnostic evaluations at 24 and 36 months identified infants who: were clinically unaffected (HR-UA; N=33), exhibited subthreshold symptoms of ASD (BAP; N=19), or received a diagnosis of ASD (N=24). Allocation of visual resources was quantified by kernel density analysis at each movie frame in a sample of 24-month-old TD toddlers (N=79) to create moment-by-moment maps of normative salience in relation to movie content. The salience maps of TD toddlers were used as a baseline and compared to HR-UA, BAP, and ASD infants at each longitudinal time point.

Results: Results showed graded effects by outcome, with HR-UA infants displaying the greatest attunement to features perceived as salient by TD 24-month-olds and infants with ASD showing the least attunement to such features. Preliminary results indicate that HR-UA infants’ deployment of dyadic attention to eyes and mouths is synchronized with that of TD 24-month-olds by as early as 7 and 9 months of age, respectively. By contrast, BAP infants showed
consistent delays in reaching similar milestones, and ASD infants failed to reach almost all milestones.

Conclusions: This research demonstrates the power of moment-by-moment sampling of viewing patterns in constructing developmental trajectories across the first years of life. Deviations from typical trajectories of visual attention are associated with greater social disability at outcome in infants at high-risk for ASD. By deploying attention in ways that are less conducive to social learning, BAP and ASD infants are learning about the world in very different ways, leading to increasingly atypical developmental trajectories.

154. Exploration of the clinical profile for children and adolescents who experience persistent concussion symptoms following a mild traumatic brain injury (mTBI).
LaPlace, Michelle; Heggs, Akilah; Antonucci, Lauren; Weissman, Barbara;

Children and youth have the highest incidence of Mild Traumatic Brain Injury (TBI) or concussion and emergency department visits in the US making this condition a significant public health burden. A recent Institute of Medicine (IOM) report indicated there is limited reporting of mild TBI/concussion data for young children and adolescents, and even less research on younger children who persist with concussion symptoms, which has led to a gap in the clinical evidence related to their course of recovery and the impact on health and educational outcomes (IOM, 2013). The goal of this project is to develop an exploratory study to specifically examine the natural history of children with chronic persistent symptoms following a mild brain injury. Because of our interest in persistent symptoms as related to injury mechanism, we have included the expertise of biomedical engineering. This specialty can provide a perspective on the biomechanics from mechanism of injury and how that may contribute to persistent symptoms.

Aim 1: What are the demographic trends in young children and adolescents with a history of mild brain injury who report persistent concussion symptoms? Aim 2: Is concussion history predictive of persistent symptoms in type and/or duration? Aim 3: Is mechanism of injury predictive of persistent symptoms in type and/or duration?

Retrospective data has been extracted from the medical records of children treated in a clinical neurology clinic at Children’s Healthcare of Atlanta for children aged birth to 17 with a history of mild brain injury (N=200). Demographic and injury variables will be collected from clinical records. Variables collected will include initial site of injury care, date of injury, injury mechanism, location of injury, symptoms reported, imaging findings, medical and concussion history, injury complications and date cleared for activity (return to school and play). The results of this project have the potential to provide novel evidence related to the predictive factors that contribute to the chronic persistent concussion symptoms in children and adolescents with a history of mild brain injury. Data from the study will also uncover information about the role of the mechanism of injury in sports and non-sport related activities
and how they impact the type and duration of persistent symptoms. Furthermore, we hope to better understand the predictive value of a history of brain injury and any mediating factors that may place children at increased risk for repeat injuries.

155. Non-invasive optical monitoring of cerebral oxygen metabolism during therapeutic hypothermia in neonatal hypoxic-ischemic encephalopathy
Lee, Seung Yup; Sun, Yu-Yo; Sanders, Bharat; Ledwig, Patrick; Kuan, Chia-Yi; Buckley, Erin

Neonatal hypoxia-ischemic encephalopathy (HIE) occurs in 1-4/1000 live term births and can cause significant neurodevelopmental impairments. Therapeutic hypothermia (TH) is the only clinically-available treatment for HIE with proven efficacy. It is reported that a reduction of core temperature to 33-34°C reduces mortality and long-term disability. However, many questions still exist regarding the selection of candidates for TH and the optimal degree and duration of hypothermia. Since successful treatment with TH is associated with decreased cerebral metabolism and cerebral blood flow (CBF), a noninvasive modality capable of assessing these parameters at the bedside may be an invaluable tool for therapy monitoring and prognosis of HIE. Current imaging techniques such as MRI that are commonly used to detect brain injury associated HIE might not be suitable for an early screening tool either prior or during TH. In contrast, our novel optical techniques – diffuse correlation spectroscopy (DCS) combined with frequency-domain near infrared spectroscopy (FDNIRS) can provide non-invasive measures of bedside cerebral blood flow index (CBFi) and cerebral oxygen metabolism index (CMRO2i).

The goal of this project is to determine sensitivity of FDNIRS/DCS measures of CBFi and CMRO2i during TH and investigate the relationship between optical measurements and outcomes (infarct volume and neurocognitive outcomes). For this purpose, the well-established Vannucci neonatal rat model of hypoxic ischemia (HI) has been employed to demonstrate the feasibility of FDNIRS/DCS in a controlled environment. This rat model has been selected because longitudinal assessments and functional (long term) outcomes can be easily assessed. We have performed FDNIRS/DCS measurements prior to any intervention (baseline) and at 0, 4, 8, 12, 24 and 48 hours post-HI in three separate groups; HI treated with hypothermia (in a cooling chamber with 29 ~ 30°C during 4 hours), untreated with normothermia, and controls. Our preliminary results show that the TH led to significant decreases in CMRO2i and CBFi compared to the normothermic group. These initial results of our pilot study demonstrate that our novel optical techniques have potential as a non-invasive, bedside monitoring tool of cerebral blood flow and oxygen metabolism to determine efficacy of therapeutic hypothermia for individualized patient management.
156. Timed up-and-go (TUG) test in children with and without Down syndrome
Lelko, Michael; Beerse, Matthew; Wu, Jianhua

The Timed Up-and-Go (TUG) test consists of functional tasks of daily living. Specifically, the test requires the participant to stand up from a chair, walk, turn-around, and sit down. The TUG test has been shown to be a valid tool to assess functional mobility in children with DS. The purpose of this study was to compare the biomechanical pattern of the TUG test between children with and without DS, particularly during the sit-to-stand and walk-out phase. Fourteen children with DS aged 6-11 years (4M/10F) and 14 sex- and age-matched TD children participated in this study. Subjects sat on a chair without side arms, feet in contact with the floor, hip and knee flexed at about 90 degrees and ankle at neutral. Subjects were instructed to stand up from a chair, walk as quickly as possible towards a target 3m away, touch the target, turn around, walk back to the chair, and sit down. Subjects completed five trials. We used an 8-camera Vicon motion capture system and a full-body marker set to record these five trials. We visually separated each trial into five phases: (1) sit-to-stand, (2) walk-out, (3) turn around, (4) walk-in, and (5) stand-to-sit. We conducted t-tests to compare various variables between two groups. Our results showed that on average, children with DS completed the TUG task in 9.35 seconds compared to 4.59 seconds for TD children (p<0.001). When broken down to each phase, children with DS required more time across each phase, except sit-to-stand. During sit-to-stand regarding the vertical direction, the DS group showed a slower peak center-of-mass (COM) velocity (p=0.021) and reached peak velocity earlier in the phase (p=0.046). The DS group exhibited slower peak hip and knee extension velocities than the TD group (p<0.001 and p=0.046), respectively. During the walk-out phase, children with DS walked with a spatiotemporal gait pattern typically seen in children with DS at this age range. Children with DS took shorter but wider steps and walked at a slower speed. This group difference may suggest a lower capacity for children with DS to modify gait pattern for a specific task, or achieve quicker walking speed comparable to TD children. Overall, our results demonstrated that children with Down syndrome have a lower level of functional mobility than TD children, and displayed less motor ability in each phase of a TUG test.

157. Use of GIS to map patterns of pediatric community infection
Leong, Traci; Waller, Lance; Rust, George; Edelson, Mike; Giarrusso, Tony; Immergluck, Lilly

Healthcare costs associated with treating and preventing antibiotic resistant staphylococcal infections (MRSA) have continued to rise in the US and worldwide. Paramount to improving the healthcare delivery to those who are infected with MRSA is efficient identification of those who might be at highest risk for infection so that correct and appropriate antibiotic therapy can be given when they present with symptoms of infection. We propose to use geographic information system tools (GIS) and geo-spatial statistical modeling to identify specific socio-environmental and -economic conditions, which may be associated with MRSA infections in Atlanta area children. Identifying those children who have risk factors for MRSA infection based
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on characteristics found in a particular geographic community (e.g., median household income, housing condition, density of neighborhood, etc.) can improve the delivery of preventive or empiric treatment.

There were 10,647 community-associated S. aureus infections and 50.6% were the antibiotic resistant form, MRSA at two pediatric hospitals in Atlanta, Georgia (Scottish Rite Children’s Hospital and Egleston Children’s Hospital) from 2002-2010. We plan to apply two space-time models using a log-Gaussian Cox process and a non-homogeneous Poisson process to analyze our dataset. By using GIS, we geocode each patient’s place of residence in order to obtain US Census tract data. We are then able to evaluate these patient's profiles for potential covariates such as crowding and housing conditions by census tract. Using multi-level analyses will allow us to better understand how the patterns of staph infection have changed in metro Atlanta over time.

The results generated by this research will indirectly impact the delivery of healthcare and assist with the development of health policy guidelines as it pertains to infection control, quality of healthcare delivery for those who may be at increased risk for MRSA and save healthcare dollars by improving the efficiency of diagnosing and managing those infected.

158. Improving the assessment on risk factors for unplanned extubation in pediatric intensive care
Li, Zihao; Vats, Atul; Keskinocak, Pinar; Pyreddy, Alekhya; Mukharya, Vardaan

Objective: Risk assessment score (RAS) is a scoring tool developed by Children’s Healthcare of Atlanta to identify patients at risk of unplanned extubation. RAS classifies critical care patients into groups of low, moderate, high and extreme risk and was used for appropriate monitoring patients with risks of unplanned extubation. The objectives of this study are to 1). analyze whether the RAS successfully correlates with incidences of unplanned extubation in pediatric patients and 2). to update the scoring tool by using predictive modeling techniques.

Method: Data of intubations, RAS, and unplanned extubation events for patients at five intensive care units between July 2014 and February 2017 were collected. Extubation outcomes and severity levels (with maximum RAS of each intubation) are compared across demographic groups. Logistic regression models are developed using RAS and demographic information to classify extubation outcomes.

Results: For intubations with maximum RAS falling in risk categories of low, moderate, high, and extreme, the incidence rates were 4%, 8%, 15%, and 17%, respectively. For the logistic regression model, the incidence rates were 2%, 4%, 10% and 34%, respectively. The logistic regression model identifies the weight, age, and whether the patient has a history of unplanned extubation as the most significant predictors. The logistic regression model captures 70% unplanned extubation in the high and extreme risk categories while the RAS-based model captures 40%.
Conclusion: Higher risk assessment scores are strongly associated with incidences of unplanned extubation. The logistic regression model outperforms the RAS-based model. The updated scoring tool is simplified due to less variables in the logistic regression model.

159. Motor Strategy and Locomotor Adjustments in Children with and Without Down Syndrome
Liang, Huaqing; Wu, Jianhua

Children with Down Syndrome (DS) often show impaired motor control and ability compared to typically developing (TD) children. When negotiating an obstacle, children with DS often stop for a longer duration in front of it, tend to choose a more conservative crawling strategy, and display a smaller toe clearance than their TD peers. In comparison, stairs negotiation is another setting to study adaptive locomotion in children, but requires moving the center-of-mass up constantly. The purpose of this study was to understand motor strategy and gait adaptation in children with and without DS while transitioning from level surface to stairs.

Fourteen children with DS (mean age 8.6 years) and fourteen age- and gender-matched TD children (mean age 8.2 years) participated in the study. Thirty-five markers were placed on the subjects and an eight-camera Vicon motion capture system was used for data collection. Subjects walked along a five-meter walkway, and then ascended a three-step staircase without handrails. Custom wooden staircases with three riser heights were provided: 17cm (LS), 24cm (MS), or 31cm (HS). There were two loading conditions: without load or with load equaling to 2% of the bodyweight on each ankle. Motor strategies were categorized as avoidance, crawling, or walking. The proportion of each strategy was calculated for each group. The placements of the leading and trailing foot (toe-to-stair distance), the stance time before ascending, and vertical toe clearance at the edge of the stair were calculated.

Results showed that all the TD subjects walked up the stairs in all conditions. However, the DS subjects primarily walked up the stairs in the LS condition but crawled up in the HS condition. Both groups displayed a longer toe-to-stair distance, a shorter stance time, and a higher toe clearance of the leading foot than that of the trailing foot. When preparing for the ascent, the DS group placed their feet closer to the stairs, and took longer time compared to the TD group. When negotiating the stairs without ankle load, the DS group tended to produce a higher toe clearance in the LS condition and a lower toe clearance in the HS condition compared to the TD group. However, the addition of ankle load resulted in a similar toe clearance between the two groups across three stair-height conditions. All the results suggest that the DS group had reduced motor ability and coordination when adapting to stairs with different heights.
160. Online Calculator Predicting Adverse Outcomes after Red Blood Cell Transfusion after Cardiac Surgery in Neonates and Young Infants
Locandro, Christopher; Guzzetta, Nina; Leong, Traci

Little is known about the incidence of red blood cell (RBC) transfusion in neonates and infants undergoing cardiac surgery, specifically concerning the appropriate amount of RBC's to transfuse and how transfusions affect in-hospital and overall mortality. We first sought to predict complications from cardiac surgery and then provide an online tool for clinicians to assess the risk of complications post surgery. We performed a retrospective review of all congenital cardiac surgical patients from 1/1/2011 to 7/31/2013.

The data set included clinical information from 605 patients aged 6 months or less who underwent cardiac bypass surgery. These patients underwent 666 surgeries. The most common procedures conducted were: Norwood, VSD repair, Glenn, and TOF repair. Data collected included sex, age, preoperative diagnosis, procedure performed, risk adjustment for congenital heart surgery (RACH and STAT) scores, hospital length of stay (LOS), amount of RBC transfused intra-operatively and 24 hours post-operatively (mL/kg), in-hospital mortality, and overall mortality within the study period. Additionally, we define 'complication' as the occurrence of any of the following: mortality, infection, thrombosis, renal failure, or ECMO.

We investigated three models including logistic regression (LR), decision trees, and random forests. The dataset was randomly divided into a training set of 466 subjects, and a test set of 200 subjects. The proportion of data from patients with complications was kept similar in both sets using a randomization algorithm, which preserved initial outcome frequencies in each. The test set was excluded from training and used only for cross validation (n1/n2 method). We compared the performance of each binary classifier by examining receiver operating characteristic curves (ROC curves) and computing area under the curve (AUC) as a performance metric. A random forest model had the best fit with an ROC area of .718 for predicting complication. A prognostic calculator using this model can be deployed for availability on the Internet, allowing input variables to be entered and calculating the odds of complication. This computational model uses multiple variables including amount of RBC's transfused to improve individualized prediction of complication with almost 72% accuracy. This work is based on preliminary data. Additional blood bank and clinical data will be added to improve the accuracy of this prognostic calculator in order for this tool to be useful in predicting individualized complication following RBC transfusion for infant cardiac surgery.

161. Utilizing the Electronic Medical Record to Identify Rare Genetic Disease, Mabry Syndrome as an Example
Logan, Rachel; Shankar, Prabhu; Foley, Allison; Li, Hong

Rare diseases individually are uncommon, but when considered collectively, affect millions of people worldwide. Mabry syndrome (also known as Hyperphosphatasia with Mental
Retardation Syndrome, HPMRS) is a rare inherited neurometabolic condition that manifests with developmental delays, intellectual disability, seizures, and constitutively high serum alkaline phosphatase (ALP) as a unique biomarker. This rare condition only has about 55 reported cases in the literature; the prevalence of this disease is unknown. Due to lack of provider knowledge about ALP as a biomarker and the heterogeneous nature of this condition, persons with Mabry syndrome have the potential to go undiagnosed. The purpose of this study is to use a retrospective chart review approach to understand how common Mabry syndrome is in the Children’s Healthcare of Atlanta (CHOA) patient population and to improve medical care by identifying undiagnosed persons. Utilizing this approach, 2823 children with ALP above 500 IU/L from 2012-2016 were identified. Given elevation of ALP often occurred in patients with bone or liver disease, after initial exclusion of children with such disease, 2162 were evaluated. Iterative evaluation of the remaining data was constituted on ALP levels, clinical presentation, and diagnostic codes. Of this cohort, 158 were found to have predominant neurological presentation and unexplainable elevation in ALP, especially persistently elevated. 12 children highly suspect for Mabry syndrome were ultimately identified. Recruitment is prioritized based on level of clinical suspicion. Referral to genetics clinic for evaluation is done in collaboration with the primary care physician or neurologist responsible for care of the child. A diagnosis of Mabry syndrome can be beneficial to both clinician researchers and patients as it provides a unifying diagnosis for the patient and an opportunity to learn more about this heterogeneous condition. This information can provide prognosis information for families and recurrence risks for future children. Additionally, there is some evidence to suggest that treatment with pyridoxine (vitamin B6) may be beneficial in seizure control in a subset of these patients. One person has been evaluated as a part of this study and recruitment is ongoing.

162. Enhanced Protective Immunity and Increased Th1 Cytokine Level Achieved By Cloning Cpg Motifs into RSV Fusion Glycoprotein Plasmid Backbone
Ma, Yao; Yu, Yunzhou; Jiao, Yueying; Hua, Ying ; Fu, Yuanhui; Anderson, Larry; He, Jinsheng

Respiratory syncytial virus (RSV) is the most significant cause of acute lower respiratory infection among children and infant hospitalization. Despite more than 50 years of research, yet there is no licensed vaccine available. Previously, vaccine trials using formalin-inactivated RSV caused enhanced respiratory diseases in children due to poor neutralizing antibody responses and the release of Th2-biased hypercytokines. Recent studies have demonstrated that CpG oligodeoxynucleotide (ODN) can promote Th1-biased or balanced immune responses.

In the current study, we use the CpG motif cloned into RSV fusion (F) glycoprotein plasmid to modulate the bias from Th2 to Th1 response and enhance the weak immunogenicity of DNA vaccine. Vaccination with our reconstructed DNA vaccine candidate generated more serum antibody and neutralizing antibody in Balb/c mice. In addition, after challenge with RSV, we detected increased Th1 cytokine levels and decreased cytokine ratio between Th2 and Th1. Furthermore, we found reduced viral RNA in homogenized lung supernatant in CpG-vaccinated
group and weaker lung pathology post challenge. This study suggests that cloning CpG motifs into RSV F glycoprotein backbone may be desirable for DNA vaccine against RSV disease.

163. Sonic Hedgehog and Reactive Oxygen Species interact to regulate mitochondrial morphology in Medulloblastoma
Malhotra, Anshu; Potts, Chad; Dey, Abhinav; Kenney, Anna

Sonic hedgehog (Shh) signaling is closely coupled with the bioenergetics of medulloblastoma, the most common malignant pediatric solid tumor. We have reported earlier that Shh causes deregulation of mitochondrial biogenesis by suppressing mitofusins, leading to fragmented mitochondria in vitro as well as in SmoA1 mouse medulloblastomas (MB) in vivo. Ectopic expression of mitofusins restored mitochondrial fusion accompanied by a rescue in proliferation to the non-proliferative phenotype. In the present study, we report that a rescue in proliferation is also observed in organotypic slice cultures implanted with mitofusin overexpressing SmoA1 neurospheres. When mitofusin overexpressing tumor cells were injected into the cerebella of postnatal day 2 mice, tumor development was significantly delayed. We have significant evidence indicating that Shh induces high increases levels of Reactive Oxygen Species (ROS) in Cerebellar Granule Neuron Precursor cells (CGNPs). When total ROS in a cell was scavenged by treating with N-Acetyl Cytosine (NAC), the fragmented mitochondrial morphology was rescued to their fused morphology. NADPH Oxidase 4 (NOX4) is a known producer of ROS in cells. When we treated CGNPs with apocynin, an NADPH oxidase inhibitor, a significant reduction in proliferation was observed. NOX4 was also found to localise in the peri-vascular niche in SmoA1 tumors. This could have possible implications for a role of ROS in promoting the proliferation of tumor re-populating cells post irradiation. Our goal is to determine if manipulating ROS-mediated mitochondrial dynamics can restore the metabolic profile of tumor cells to that of non-transformed, non-proliferating cells. This would suggest a potential novel treatment paradigm for medulloblastoma that may reduce the requirement for high dose radiation.

164. Tumor-Associated Macrophages Associated with Better Survival in Sonic Hedgehog Medulloblastoma Patients
Maximov, Victor; Chen, Zhihong; Wei, Yun; Robinson, M. Hope; Hambardzumyan, Dolores; Kenney, Anna M.

Medulloblastoma is the most common malignant solid tumor of children and a leading cause of pediatric mortality. Current treatment includes surgery, chemotherapy, and cranio-spinal irradiation, resulting in a 70% 5-year overall survival rate, but survivors are frequently left with life-long side effects, including cognitive impairment, seizures, premature aging, and susceptibility to other cancers. MB was classified based on molecular and genetic profiles and resulted in four distinct subgroups. The most common subclass of MB is SHH, which accounts
for approximately 30% of cases. This class has been successfully modeled in vivo in murine models, which have been shown to closely recapitulate human disease, providing a convenient and relevant model system for analyzing the SHH MB subclass in vivo.

To better understand the mechanisms of tumor growth and recurrence, recent attention has been focused on determining the composition and role of non-tumor cells comprising the tumor microenvironment (TME). Tumor-associated macrophages (TAM) are a key component of the TME that could have two opposite effects on tumor. TAMs can help tumors to evade the immune system by suppressing other immune cell functions, and contribute to tumor growth by promoting angiogenesis. On the other hand, pro-inflammatory activated TAMs could suppress tumor growth and delay tumor development. Recently, it was reported that of the subgroups, human SHH MB has the greatest number of TAMs, as well as increased expression of macrophage-associated genes. However, to date, there are no studies covering the functional role of TAMs in SHH MB.

In this work, we demonstrate functional role of TAMs in both in vitro and in vivo models. We determine that bone marrow derived macrophages are capable of promoting tumor cell apoptosis and inhibiting their proliferation in vitro. We show that reduction of macrophage numbers leads to increased animal mortality in a murine model of SHH MB. Determination of tumor cell interactions with immune cells will provide a better understanding of tumor growth and maintenance and could lead to novel treatment options exploiting the host immune system.

165. From Milliseconds to Months: Long-term Developmental Change in Moment-by-Moment Attention to Social Stimuli in Infants with ASD
Micheletti, Megan; Kreuzman, Andrew; Klin, Ami; Shultz, Sarah; Jones, Warren

Background: Attention bridges the gap between the environment and an individual’s subjective experience: on a moment-by-moment basis, and throughout development, children devote attention to features of the environment perceived to be most relevant. Existing research suggests that children with autism spectrum disorder (ASD) look less at other’s eyes and faces than typically developing (TD) peers. However, little is known about how these looking patterns differ on a millisecond timescale and how they emerge or change over the course of development. One way to examine the longitudinal development of these looking patterns is to compare the way that younger infants dynamically scan social scenes to how older infants scan the same content. Objective: Quantify the developmental attunement of time-varying visual salience between 2 and 24 months in infants with and without ASD. Methods: From 2-24 months of age, children at low- and high-risk for ASD viewed video scenes of naturalistic social interactions while eye-tracking data were collected. TD and ASD outcome groups were identified by diagnostic evaluations at 24 and 36 months. Analyses focused on low-risk TD males (n = 79) and males with ASD (n = 24). For both groups, time-varying kernel density estimation was used to quantify moment-by-moment visual attention to eyes, mouth, body and
object regions, quantifying the extent to which younger infants looked at the same content at the same moments in time as older infants. Results: By 7 months, TD infants time their eye and mouth fixations in a manner that is not significantly different from that of TD 24-month-olds. Likewise, by 18 months, TD infants time their body and object fixations in a manner not significantly different from TD 24-month-olds. In contrast, ASD infants do not time their fixations in a typical manner for eye, body or object looking at any time in the first 24 months of life. Only fixations on the mouth are timed in a manner similar to TD infants, and this occurs 5-6 months later than is typical. Conclusion: During the first two years of life, TD infants time their fixations in a manner that is increasingly similar to that of older TD children, reflecting a developmental progression in attention to dyadic eye and mouth cues, bodies and objects. In contrast, children with ASD deploy their attention differently across timescales short and long, creating a uniquely different experience, one which is likely to have cascading effects on social and cognitive development.

166. Analyzing Query Logs in Pediatric Clinical Data Mart to Identify Trends and Common Interest among Basic Science, Clinical and Translational Researchers
Mudunuri, Rahul; Viangteeravat, Teeradache; Ajayi, Oluwaseun; Smith, Ebony; Ruchi, Ruchi; Huang, Eunice

Background: At Le Bonheur Children’s Hospital, the Pediatric Research Database (PRD) serves as the pediatric clinical data mart for feasibility assessment and cohort discovery. Researchers enter cohort eligibility criteria into the PRD user interface and results are returned as aggregate counts and descriptive statistics without identifiers. These search logs are stored in PRD and offer an interesting opportunity for data mining to discover existing trends and common interests among researchers at the level of clinical data elements (diagnoses, medications, labs, etc.).

Methods: We extracted the user search history of 2692 queries between January 2014 and March 2017, and converted each query written in Structured Query Language (SQL) into the set of codes that represent specific clinical data element values used in a query. We performed quantitative analysis on these converted queries to identify the most commonly sought clinical data elements based on query frequency and grouped them into diseases.

Results: Our preliminary results show that search terms related to Embolism and Thrombosis (ICD9: 453.*, ICD9: V12.51, ICD9: 415.*), Asthma (APRDRG: 141, ICD9: 493.*) and Diabetes (APRDRG: 420, ICD9: 250.*) were the most dominant queries between January 2014 and March 2017, 15%, 11% and 5%, respectively. Further breakdowns by years revealed that, in 2014, search terms related to Asthma and Diabetes were the most dominant queries, 18% and 11%, respectively. In 2015, search terms related to Operations On Penis (ICD9 Procedure:64.*) and Asthma were the most dominant queries, 11% and 8%, respectively. In 2016, Embolism and Thrombosis and Asthma were the most dominant queries, 43% and 8%, respectively. In
addition, in 2016, the medications Warfarin, Enoxaparin and Heparin were also very commonly searched in conjunction with Embolism and Thrombosis.

Conclusion: These results identified Asthma as the diagnosis of greatest interest to our researchers across the three years evaluated, followed by Embolism and Thrombosis and Diabetes. Analysis of data query logs can help identify areas of interest for all researchers within a research community, which can be used to prioritize areas of focus for data harvesting. By further applying clustering and networking graph analysis techniques in machine learning applications, we may also identify users who might share common interests and help facilitate multidisciplinary research collaborations to address specific pediatric diseases. Furthermore, results from mining of these query logs can be linked to larger knowledge database resources such as PubMed and open access scientific literature, which can improve user search experience.

167. Outcomes of Surgical Fixation with a Titanium Alloy Intramedullary Screw for the Treatment of Adolescent Clavicle Fractures
Murphy, Joshua; Menapace, Bryan; Guerrero, Heather; Malkami, Camelia; Broda, Samuel; Willimon, Clifton; Busch, Michael

Purpose: Review the use of a titanium alloy intramedullary clavicle screw for the treatment of mid-shaft clavicle fractures in the adolescent population.

Methods: An IRB approved retrospective chart and radiographic review was performed on patients who underwent operative treatment with the Acumed Dual-Trak intramedullary clavicle screw between January 2008–May 2016. Pre-operative and post-operative radiographs were measured using previously defined radiographic measurements. Patients were contacted by phone to complete DASH and DASH Sports questionnaires and a subjective questionnaire to document any subsequent procedures or pain associated with the injury or implant.

Results: Twenty-three patients (20 males, 3 females) met inclusion criteria for this study with an average age of 15.5 years. Average time to surgery was 9 days (2-50 days) and average radiographic follow-up 89 days (37–192 days). A total of 16/23 (70%) patients completed the follow-up questionnaires 2 years (146–1305 days) after surgery. Pre-operative radiographs showed mean shortening 1.6 cm, mean angular deformity 17 degrees, mean displacement 1.9 cm, and mean displacement 146% of clavicular width. At the time of final radiographic follow-up all patients were clinically asymptomatic and 22/23 (96%) had bridging periosteal bone. The average time to bridging periosteal bone was 59 days (31-105 days). The average DASH score was 4.4 (0-22.5) and DASH Sports score 7.6 (0-50). With subjective questioning, 5/16 (31%) patients reported pain with carrying objects on their shoulder, 1 (6%) patient complained of chronic pain, and 1 (6%) patient underwent screw removal secondary to hardware prominence. All patients that completed the DASH Sports questionnaire had returned to sports: 11/14 (79%) had no difficulty, 1/14 (7%) with mild difficulty, and 2/14 (14%) with moderate difficulty.
secondary to pain. Of the 1 patient that did not have bridging periosteal bone at final radiographic follow-up, they completed the questionnaires at 434 days after surgery and scored a 0 on the Dash and Dash Sports Questionnaires with no subsequent procedures or pain.

Conclusion: A titanium alloy intramedullary clavicle screw is a viable option for the treatment of adolescent clavicle fractures with low complication rate. After operative treatment, some patients may continue to have pain, but little disability. The majority of patients can return to sports without difficulty.

Significance: This is an early, critical review evaluating radiographic and clinical outcomes of a titanium alloy intramedullary clavicle screw in the adolescent population.

168. Percutaneous Transhepatic Portal Vein Angioplasty for Portal Vein Stenosis after Pediatric Liver Transplantation: A Single Center Experience
Naik, Kushal; Hawkins, Matthew; Gill, Anne; Gupta, Nitika

Background: Stenosis of the portal vein (PV) is a rare complication after liver transplantation (LT) in pediatric patients but it has been shown to adversely affect graft outcomes. With increased lifespan of the pediatric patient after transplant, it is important to take proactive measures to ensure long-term graft survival. In this study we reviewed the safety and efficacy of percutaneous transhepatic balloon angioplasty (PTBA) as a treatment for post-LT portal vein stenosis (PVS).

Methods: Between January 2001 and July 2016, 318 pediatric patients received a liver transplant at this tertiary referral transplant center. 21 children were evaluated post-LT for PVS using percutaneous transhepatic portal venography (PTPV).

Results: Of the 21, 19 patients (7F:12M) with median age 12 years (IQR: 7-15) were diagnosed with PVS using PTPV and were treated with PTBA. Two patients were excluded from the analysis: one did not have PVS; other received surgical shunt surgery instead of PTBA. 7/19 patients (36.8%) also underwent intravascular ultrasonography. Median time between LT and PTBA was 83 months (IQR: 49-138). 58% patients were transplanted due to biliary atresia. Transhepatic approach was used in most patients. Mean pre-procedural PV pressure gradient was 6.3 mm of Hg (SD: 5.0) for the veins that did not have complete occlusion (n=9). Mean post-procedural PV pressure gradient was 0.9 mm of Hg (SD: 1.2). Mean percentage improvement in the pressure gradient across the stenotic region was 86.2% (SD: 15.9%; p<0.01). Average fluoroscopy time was 21.4 minutes (SD: 17.5). Median platelet, bilirubin, AST, ALT and GGT levels at the time of PTBA were 95x109/L (IQR: 75-178), 0.6mg/dL (IQR: 0.5-1), 49.5U/L (IQR: 29-124), 61U/L (IQR: 36-216) and 60.5U/L (IQR: 31.8-145) and those post-PTBA at their 12-month follow-up visit were 175x106/L (IQR: 137-252), 0.4mg/dL (IQR: 0.3-1.2), 27U/L (IQR: 22.5-34.5), 26U/L (IQR: 22-40) and 28U/L (IQR: 17-64). One year after PTBA, the mean percentage increase in platelet levels was 58.7% (SD: 58.3) and the mean percentage decreases
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in AST, ALT, GGT and Bilirubin were 31.5% (SD: 42.3), 40.7% (SD: 28.9), 26.5% (SD: 65.5) and 
40.9% (SD: 30.45). All the patients required no further intervention or stenting, with portal 
venous patency being maintained for a median 16 months (IQR: 5-35).

Conclusion: Percutaneous transhepatic angioplasty of portal vein stenosis after pediatric liver 
transplantation is a safe and effective treatment with long-term patency and improved clinical 
outcomes. This leads to increased longevity of the graft and improved quality of life.

169. Duplicate/Removed

170. Computational Approach to Classification of Emergency Department Notes using Natural 
Language Processing on Unstructured Data
Norman, Brittany; Davis, Tod; Quinn, Shannon; Massey, Robert; Hirsh, Daniel

Introduction: The goal of this project was to evaluate the use of novel techniques such as 
Natural Language Processing (NLP) and Machine Learning (ML) on a previously solved task, in 
order to compare the new methods with existing methods. The task of this proof-of-concept 
(POC) project was to detect which electronic Emergency Department (ED) notes contained 
features of Pediatric Appendicitis Score (PAS). This task had previously been achieved through 
the use of Regular Expressions (RE). The challenge was due to the unstructured nature of the 
dataset and the fact that the same concept could be expressed many different ways in the 
notes (e.g., right lower quadrant could be expressed “RLQ” or “R Lower Quadrant”, among 
other possibilities).

Methods: The dataset included 15,074 electronic ED notes, dated between July 2011 and 
August 2016. Notes were labeled positive for having features of PAS (PAS+) or negative for 
lacking PAS features (PAS-). The dataset was split into 60% for training the computational 
model, 20% for validation, and 20% for testing. Natural Language Processing techniques were 
used to clean and preprocess the notes, extract features, and convert the unstructured data 
into a machine-readable form. Machine Learning techniques were used to build a model which 
could automatically learn which features were relevant or irrelevant to the concept of PAS. 
Three models were compared: Support Vector Machine (SVM), Naïve Bayes (NB), and Logistic 
Regression (LR). The three models were evaluated using the F-Score metric, and a single model 
was chosen for receiving the highest score.

Results: Due to highest performance on the validation set, the Logistic Regression (LR) model 
was chosen. When evaluated on the hand-labeled testing set of unstructured data, the LR 
model received an F-Score of 0.8391, which outperformed the previous RE technique on this 
task (0.3435 F-Score).
Discussion: The new NLP & ML techniques (which made use of an LR model) demonstrated an improvement over the previous technique. The F-Scores were calculated on a hand-labeled dataset, and thus represent a comparison to human performance on the same task.

Conclusion: The new method performed well when compared to human performance and to the previous method on the same task. This new method can be used to expedite manual chart review for identification of PAS features within ED notes.

171. Pediatric Epilepsy Epidemiology: 50 States and D.C.
Oh, Ahyuda; Thurman, David; Kim, Hyunmi

Objectives. To estimate the prevalence and incidence of epilepsy in a U.S. commercially insured pediatric population, using a large nationwide database.

Methods. We performed a retrospective cohort analysis using commercial claims and encounters data from Truven MarketScan® database (1/1/2009-12/31/2013). Our study cohort included an annual average of >8 million subjects (aged 0-19 years) in 50 states and DC. Epilepsy cases were defined by a combination of ICD-9-CM codes (345.xx and 780.39) and antiepileptic drug claims. Epilepsy prevalent cases were subjects who met the case definition, either in the year of interest or in any previous year. Incident cases were determined among prevalent cases with neither epilepsy codes nor antiepileptic drug claims for at least 2 years before epilepsy diagnosis. Yearly epilepsy prevalence (2009 through 2013) and incidence (2011, 2012, and 2013) were estimated. Age-, sex-, and residence-specific estimates were calculated. Standardized prevalence and incidence rates of epilepsy across states and regions were computed using the age distribution of 2010 U.S. Census as the standard.

Results. The crude prevalence of epilepsy was estimated at 3.62/1000 in 2009, rising in subsequent years, up to 6.94/1000 in 2013. From 2011 to 2013, the crude annual incidence rate declined from 135 to 122 per 100000 populations. Average annual prevalence steadily increased with ages. Incidence rate was highest in subjects <2 years of age. Age-adjusted annual prevalence rate per 1000 was highest in Vermont (10.15), followed by West Virginia (9.53), New Jersey (8.48), Georgia (8.39), and New Mexico (8.39). Epilepsy incidence cases were most frequent in Vermont (205/100000), New Hampshire (166), Wyoming (163), and Alabama (153). By region, both prevalence and incidence rates were lowest in West (6.47/1000, 102/100000), followed by Midwest (7.41/1000, 114/100000), South (7.57/1000, 124/100000), and Northeast (7.75/1000, 128/100000).

Conclusion. Epilepsy prevalence and incidence estimates using commercial claims and encounters data are consistent with results from previous population-based epidemiologic studies. This study finds variation in estimates across states and/or regions.
172. Prevalence and Incidence of Pediatric Epilepsy: Geographic Differences in Georgia
Oh, Ahyuda; Thurman, David; Kim, Hyunmi

Objectives. To estimate the prevalence and incidence of pediatric epilepsy in Georgia, compare the estimates with findings from the analysis of the States, and evaluate differences in the estimates by place of subjects’ residency.

Methods. We conducted a retrospective cohort analysis using commercial claims and encounters data from Truven MarketScan® database (1/1/2009-12/31/2013). Our study cohort included an annual average of >300,000 subjects (aged 0-19 years) in Georgia. Epilepsy cases were defined by a combination of ICD-9-CM codes (345.xx and 780.39) and antiepileptic drug claims. Epilepsy prevalent cases were subjects who met the case definition, either in the year of interest or in any previous year. Incident cases were determined among prevalent cases with neither epilepsy codes nor antiepileptic drug claims for at least 2 years before epilepsy diagnosis. Annual epilepsy prevalence (2009 through 2013) and incidence (2011, 2012, and 2013) were calculated. Place of residency were categorized into metropolitan statistical areas (MSAs) and non-MSAs. By place of residency, average annual rates and age-adjusted rate ratio were computed.

Results. Crude annual epilepsy prevalence gradually increased from 4.15/1,000 in 2009 to 8.02/1,000 in 2013. Epilepsy annual incidence decreased from 146/100,000 in 2011 to 134/100,000 in 2012, and then slightly increased to 137/100,000 in 2013. The prevalence and incidence rates were higher in GA than the estimates of the States throughout the years. Epilepsy prevalence increased with ages. Incidence was highest at the earliest age of life, decreasing until the early teenage and increasing afterwards. Average annual prevalence rate per 1,000 was highest in Chattanooga (9.39), followed by Brunswick (8.68), Valdosta (8.20), Albany (8.19), and Rome (8.17). Epilepsy incidence cases were most frequent in Columbus (254/100,000), Albany (217), and Augusta-Richmond County (216). Epilepsy prevalence and incidence rates in Atlanta-Sandy Springs-Marietta (with a population of ≥1 million) were 5.97/1,000 and 128/100,000, which was lower than those in non-MSAs (6.58/1,000 and 141/100,000, respectively).

Conclusion. Trend of epilepsy prevalence and incidence in GA are parallel to estimates from the analysis of the States, but the magnitude of estimates in GA is greater than that in the States. Pediatric epilepsy is most frequent in non-MSAs.

173. Healthcare Burden of Epilepsy in a U.S. Commercially Insured Pediatric Population
Oh, Ahyuda; Thurman, David; Kim, Hyunmi

Objectives. To measure neurobehavioral comorbidities in children with epilepsy compared to those without epilepsy, and examine the pattern of comorbidities by age, using a large nationwide database.
Methods. We performed a retrospective cohort analysis using commercial claims and encounters data from Truven MarketScan® database (1/1/2009-12/31/2013). Our study cohort included an annual average of >6.7 million subjects (aged 0-18 years) in 50 states and DC. Epilepsy cases were defined by a combination of ICD-9-CM codes (345.xx and 780.39) and antiepileptic drug claims. Based on literature review, 12 neurobehavioral comorbidities of epilepsy were evaluated, including psychiatric/behavioral disorders (hyperkinetic syndrome of childhood, conduct disorder, behavioral problem, anxiety & emotional disturbance, depression, and autism), intellectual disability (mental retardation, specific delay in development, delayed milestones, and problem with learning), and headache (headache and migraine). Average prevalence of comorbidities was computed, which was compared between children with and without epilepsy. Age distribution of comorbidities was depicted as well.

Results. The neurobehavioral comorbidities were at least 3 times more likely to occur in children with epilepsy compared to those without epilepsy, even more than 11 times in delayed milestones and autism. The most common single comorbidity in children with epilepsy was headache (23.4%), followed by specific delay in development (21.0%), hyperkinetic syndrome of childhood (18.7%), and delayed milestones (17.2%). Considering a group of comorbidity, psychiatric/behavioral disorders were most frequent in children with epilepsy (32.9%). The biggest discrepancy was found in the prevalence of intellectual disability between children with and without epilepsy (31.0% vs 4.9%). In the psychiatric/behavioral disorders group, hyperkinetic syndrome appeared to be diagnosed around 3-4 years of age and increased remarkably up to 9 years of age. Anxiety disorders and depression increased gradually with ages. Depression showed a sharp increase at early teens. In the intellectual disability group, delayed milestones and specific delay in development were coded at an early age. Problem with learning began to be coded in preschool age and mental retardation increased with ages. Headache and migraine continuously raised with ages. During the teenage years, the age distribution of headache prevalence looked to be parallel to one of depression.

Conclusion. Neurobehavioral comorbidities are highly prevalent in children with epilepsy compared to children without epilepsy. The comorbidities present a various pattern by age.

174. Incorporating Community Engagement into a Clinical Research Study – Lessons Learned from a Study of the Determinants and Consequences of Secondhand Smoke Exposure in African American Children
Olorundare, Elizabeth; Nellum, April; Ahart, Lauren; Hearn, Kendra; Foreman, Marilyn; Gee, Beatrice; Reese, LeRoy; Quarells, Rakale

BACKGROUND: Despite a significant decline in the prevalence of secondhand smoke (SHS) exposure in the United States over the last two decades, there are persistent racial and socioeconomic disparities seen among children exposed to SHS. Elimination of these disparities among African American children requires a better characterization of the factors influencing SHS exposure within this population, and the development of culturally and contextually relevant strategies to address these factors. However, the role of genuine and purposeful
community engagement in effective implementation of such research among traditionally marginalized populations is often overlooked. The Determinants and Consequences of Secondhand Smoke Exposure in African American Children is a clinical study that incorporated community engagement activities in characterizing the social determinants and effects of SHS exposure on cardio-metabolic disease risk among Black youth in southwest Atlanta.

METHODS: This research study was a cross-sectional analysis of the determinants and effects of SHS exposure in a community-based, convenience sample of African American children aged 7 – 15 years old, residing in Metro-Atlanta. There were two components – parent surveys and clinical evaluation of their children. We encountered several noteworthy methodological challenges in the implementation of the study. We present the initial strategies used to conduct the study, and also discuss the adaptive strategies employed to incorporate community engagement and improve recruitment and retention of study participants.

RESULTS: We learned several important lessons while adapting our study to maximize community participation. Concerted efforts with local community advocates were instrumental to successfully engaging the community. Recruitment via techniques such as telephone surveying heightened community members’ sense of distrust regarding the research, while personal interactions with the community in their familiar environment better demonstrated the investigators’ commitment to invest in the community’s health. Community partners’ input in development of recruitment materials led to better acceptability and more interest in the study. Consideration of the level of health literacy among the population was crucial to ensuring that study findings were disseminated to families in ways that were easily understood.

CONCLUSION: A variety of stigmas and barriers pose unique challenges to the successful recruitment and retention of minority participants for research studies. Engaging community members as equal partners at every stage of the research process is crucial to obtaining increased participation and to achieving diverse representation in academic research. The lessons learned from this study may have important implications for investigators seeking to conduct effective clinical research with medically underserved children.

175. Essential Elements of Successful Transition among Adolescents and Young Adults with Sickle Cell Disease who Participate in a Transition Program: A Mixed-Methods Study
Pack-Mabien, Ardie; Bakitas, Marie; Landier, Wendy; Haynes, Johnson

Sickle cell disease (SCD) is a hereditary hematological disorder characterized by the presence of sickle hemoglobin, severe anemia, intermittent vaso-occlusive pain episodes, and acute and/or chronic end organ damage. The medical management of SCD includes utilization of penicillin prophylaxis, folic acid, hydroxyurea, transfusion therapy, and oral iron chelators. As a result of mandatory universal newborn screening and early access to medical management, life expectancy of infants born with SCD in the United States extends into adulthood. With this increase in life expectancy, the successful transition to adult care is crucial. However, this process remains elusive for many adolescents and young adults with SCD. As a result, a limited
number of sickle cell centers have developed transition programs to facilitate a more effective transition process. One such program is the Pediatric to Adult Care Transition Program at the University of South Alabama Comprehensive Sickle Cell Center (USA-CSCC). This program educates and prepares adolescents and young adults with SCD, beginning at 13 years of age, in order to facilitate the transfer to adult care at 19 years of age. However, research findings regarding efficacy of such programs in this population are sparse and anecdotal or limited to transition pilot programs and only two components of transition: disease knowledge scores and transfer of care to an adult hematologist. Questions remain relative to the longitudinal impact of transition programs and factors that may influence adaptation to the transition process. Likewise, less is known about how and why participation in such programs impact the successful transition to adult care from the perspective of adolescents and young adults with SCD who are current or recently transitioned participants of a transition program. This descriptive, observational, cross-sectional, concurrent quantitative + qualitative study, currently in progress, is designed to address this gap. This approach provides a conceptual guide to examine, measure, analyze and promote a more contextual understanding and in-depth description of the successful transition relative to participation in a transition program with well-defined disease-specific indicators and outcome measures. Interim results will be presented during this session. Findings from this study will be utilized to inform the development of new strategies to facilitate a more effective transition process and refine the current transition program to meet the transition needs of the adolescents and young adult with SCD at the University of South Alabama Comprehensive Sickle Cell Center and plausibly larger centers to improve continuity of care and health outcomes.

176. HPV Vaccine Acceptability and African American Males: An Examination of Parental Attitudes and Perceptions
Paige, Asia; Reese, LeRoy; Martin, Nicolle; Haynes, Venice; Churchill, Victoria

Introduction: The human papillomavirus (HPV) is the most common sexually transmitted infection worldwide. Adolescents are more susceptible to this infection given their increased involvement in risky sexual behavior, putting males, the focus of the present study at a higher risk of genital warts and related cancers should they contract HPV. The HPV vaccine currently recommended by APIC offers benefits in reducing these risks among and parents play a critical role in helping their adolescent sons make informed decisions about their health. This study utilized the constructs of the Health Belief Model (HBM) to examine the perceptions of African American parents with adolescent sons regarding HPV vaccine acceptability for their unvaccinated sons.

Methods: This quasi-experimental mixed-methods study was funded by the National Cancer Institute that identified and examined factors that influence HPV vaccine acceptability in low-income African American and Hispanic males adolescents and the parents of male adolescents who had not been vaccinated with the HPV vaccine. The study inclusion criteria relevant here
for parents were that they self-identified as African American, had an adolescent son who not received the HPV vaccine and that they qualified for Medicaid children’s insurance program or one of its corollary insurance programs for low income families. Data were collected from a convenience sample that were recruited through multiple media and from pediatric clinics serving a low income patient census. Although not reported here, participants also included African American and Latino adolescent males and Latino parents. African American parents were the focus of these analyses.

Results: One hundred parents completed author constructed surveys. Demographically, 69% of the participants were female and 75% were between the ages of 36 and 55. In terms of educational attainment 63% reported having attending college without graduation and 26% reported they had completed college and had participated in some graduate training. Multiple regression analysis were conducted to evaluate the ability of the independent variables to predict the dependent variable i.e. vaccine acceptability or Likelihood to Act. A stepwise regression was conducted and showed that perceived benefits was the best predictor and explained 45% of the variance p<.001. Analyses of these data is on-going

Conclusion: Parents play an important role in the health choices of their sons. The preliminary analyses of these data indicates that it is parents perceptions of the benefit of the HPV vaccine that most influences vaccine acceptability reflected here as the Intent to Act construct.

177. Hypertension Knowledge among Black College Students
Powers, Makia; Ford, Bette; Stephen, Shanna; Gee, Beatrice

Introduction: Hypertension and elevated Body Mass Index (BMI) have been closely studied in young African American adults. Despite the number of awareness programs, research demonstrates that blacks continue to have risk factors associated for cardiovascular disease. We believe that health knowledge is a contributing factor that may affect elevated blood pressure in this group. Few studies have sought the level of hypertension knowledge among adolescent and young adult populations. Our goal is to evaluate the association between hypertension knowledge and prevalence of prehypertension and hypertension amongst adolescent and young adult African American males.

Methods: One hundred twenty Black male college students were recruited from a student health center in a southeastern United States college. Inclusion criteria were that participants were 18 years or older, full-time college students, and self-identified as Black or African descent. Participants completed a 70-item survey tool and a research clinical visit. Survey variables included questions on lifestyle behaviors (i.e fruit and vegetable intake, moderate/vigorous exercise, alcohol intake, and cigarette use) and a 14-item validated hypertension knowledge tool (the Hypertension Evaluation of Lifestyle and Management Scale).
During the clinic visit blood pressure, height and weight were obtained in a standardized manner. Descriptive statistics, Chi-square and ANOVA were performed using SAS 9.4.

Results: The mean age of participants was 20 years. Approximately 43% had blood pressures in the prehypertensive range, and 46% were overweight or obese. The mean BMI was 24, 25, and 30 among participants with normal blood pressure, prehypertension and hypertension, respectively. Mean hypertension knowledge score was 7. The majority of participants had moderate knowledge scores (67%), compared with low (9%) and high scores (23%). Students had overall lack of knowledge related to identifying hypertension risk factors and prevention measures. Sixty-eight percent of respondents were unable to identify risk factors for developing hypertension. Only 15% were able to correctly identify secondary effects of uncontrolled hypertension. Knowledge scores were similar between students with science majors vs non-science majors. Scores were not significantly different among students with normal blood pressure (7), prehypertension (6.9) or hypertension (7.6).

Conclusion: The low rates of hypertension knowledge among young African American males is concerning. With the increasing rates of prehypertension among young adult males, it is imperative that they have the knowledge of the healthy lifestyle changes that can decrease their risk of developing hypertension. Future studies should evaluate educational interventions that would improve knowledge and prevention of hypertension in this population.

178. Cardiovascular Health Beliefs among Young Adult Black College Men
Powers, Makia; Stephen, Shanna; Ford, Bette; Gee, Beatrice

Introduction: The health belief model is a construct used to evaluate a person’s ability to change their behaviors based on their perceived risk and benefits of a particular disease. This model has been used in a variety of research areas. However, there are limited studies using a validated cardiovascular health belief model scale, especially in young adults. Our goal is to evaluate the cardiovascular health beliefs among healthy Black college males.

Methods: One hundred twenty Black male college students were recruited from a student health center in a southeastern United States college. Inclusion criteria were that participants were 18 years or older, full-time college students, and self-identified as Black or African descent. Participants completed a 70-item survey tool. Survey variables included demographic information, lifestyle behaviors (i.e fruit and vegetable intake, moderate/vigorous exercise, alcohol intake, and cigarette use) and a 25-item validated health belief scale (Health Beliefs Related to Cardiovascular Disease Scale). This Likert scale consisted of 4 subscales (Benefits, Susceptibility, Barriers and Severity). Descriptive statistics, Chi-square and non-parametric analysis were performed using SAS 9.4.
Results: The mean subscale scores for Benefits, Susceptibility, Barriers and Severity were 21.9, 8.6, 21.7, and 13.7. Likert scale responses ranged from 1 (Strongly Disagree) to 4 (Strongly Agree) Responses for the benefits subscale revealed high item means of 3.6(3.4 -3.8) on the 1-4 scale, suggesting that most students agreed that exercise and diet were good for them. Item means for the susceptibility and severity subscales were low: 1.7 and 2.2 respectively, which is expected among a young healthy population. The perceived barriers item means were low (2.4) relative to the benefits item means, but higher than the susceptibility and severity. There were no significant associations between reported exercise and dietary habits with the benefits subscale scores. There was also no difference of total benefits, susceptibility, barriers and severity scores with students with normal blood pressure, prehypertension, and hypertension.

Conclusions: This study demonstrates that while college students may know the benefits of healthy lifestyles in preventing cardiovascular disease, they may have barriers to implementing these lifestyles in their daily practice. It is important to further evaluate these barriers and implement interventions that can decrease or eliminate them.

179. Protective role of Indoleamine 2,3 dioxygenase in Respiratory Syncytial Virus associated immune response in airway epithelial cells
Rajan, Devi; Chinnadurai, Raghavan; Keefe, Evan O.; Shamayeen, Zayan; Galipeau, Jacques; Anderson, Larry

RSV is a major cause of severe lower respiratory infection in infants and young children and causes disease in persons with compromised cardiac, pulmonary, or immune systems and in elderly. There is no vaccine or effective treatment available despite high incidence of RSV disease. Indoleamine-2,3-dioxygenase (IDO) is an enzyme that catalyzes the degradation of the essential amino acid L-tryptophan and generates a family of catabolites known as kynurenines. IDO is an immunomodulatory enzyme produced by activated macrophages and other immunoregulatory cells. To understand the effect of IDO in the immune response associated with RSV infection, we used IDO siRNA knock down approach and analyzed the levels of various cytokines and chemokines using multiplex luminex assays. Our results show that IDO knock down in airway epithelial cells followed by RSV infection and IFN-γ treatment resulted in increased levels of IL-6, IL-8, IL-13, RANTES, TNF-α, VEGF, IL-7, MIG, HGF, MCP-1 and MIP-1 β. Interestingly, there was an increase in virus replication in IDO knock down airway epithelial cells. In addition, we also noticed a decrease in the levels of IP-10 upon knock down of IDO in A549 cells. Thus, our results indicate that knock down of IDO induces various levels of host inflammatory and immune response which shows that IDO has a protective role in RSV infection and immunity.

180. Targeted Elimination of Tumorigenic Human Pluripotent Stem Cells Using Suicide-Inducing Virus-Like Particles
Human pluripotent stem cells (hPSCs) have the ability to differentiate into a variety of cells and unlimited self-renewal capacity, and they are potential candidates for cell-based regenerative medicine. An important issue after direct differentiation of hPSCs to a desired cell type is the presence of residual undifferentiated cells which if transplanted could proliferate and produce tumors. A promising strategy to eliminate potential tumorigenic hPSCs is to make the cells sensitive to prodrugs via expression of suicide genes, however transgenic modifications have a safety risk due to the possible development of deleterious mutations in the differentiated cells. We developed a safer alternative method to deliver suicide-inducing macromolecules and specifically eliminate undifferentiated cells in vitro based on virus-like particles (VLPs). VLPs are protein structures with similar organization and conformation of viruses but lacking their viral genome. A Qβ bacteriophage capsid was engineered to contain a cytosine deaminase enzyme (CD) which enables the conversion of the pro-drug 5-fluorocytosine (5-FC) into the cytotoxic 5-fluorouracil (5-FU). VLPs with IgG binding ZZ domains were labeled with antibodies against hPSC-specific surface marker SSEA-5. The anti-SSEA-5-labeled VLPs selectively killed hPSCs in co-cultures of hPSC colonies with mouse embryonic fibroblasts or hPSC-derived cardiomyocytes following incubation of pro-drug 5-FC. The treatment did not cause cytotoxicity to differentiated cells; cardiomyocytes maintained beating activity after the treatment. Treatments with the VLPs and 5-FC on immature cardiac progenitors were also effective in killing residual hPSCs without impeding the ability of the progenitors to differentiate into beating cardiomyocyte at late stages. This technology is expected to be a useful tool in the prospective removal of undifferentiated cells in hPSC-based therapies without the disadvantages of genetic modifications.

181. Inhibition of Ileal Bile Acid Uptake Protects Against NAFLD in Mice: Identification of Candidate Mechanisms Using Untargeted High Resolution Metabolomics Analysis of Liver
Rao, Anuradha; Uppal, Karan; Jones, Dean; Karpen, Saul; Dawson, Paul

Background: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in children, and effective medical therapies for NAFLD are limited. Blocking intestinal bile acid (BA) absorption with a luminally-restricted Apical Sodium-dependent BA transporter (ASBT) inhibitor (ASBTi) protects against development of NAFLD in high-fat diet (HFD)-fed mice, however the molecular basis of the efficacy is not understood. Objective: To use untargeted high-resolution metabolomics to identify individual metabolites and metabolic pathways associated with the anti-steatotic and hepatoprotective effects of ASBT inhibition in HFD-fed mice. Methods: Male C57Bl/6 mice were fed for 16 weeks with chow, HFD composed of 45% fat, 0.2% cholesterol, 4% sucrose water (HFD), and HFD plus ASBTi (SC-435; 60 ppm; HFD/ASBTi). Body weight, food intake, glucose and insulin tolerance, liver histology, and liver lipids (bile acids, cholesterol, triglyceride) were measured. Liver gene expression changes were
examined by RNA-seq. Ultra-high-resolution metabolomics analysis of liver samples was performed on a Thermo Fisher Q Exactive mass spectrometry system, coupled with C18 reverse phase liquid chromatography. Metabolite differences between groups were determined by independent t tests using LIMMA. Untargeted pathway analyses were performed using Mummichog. Metabolome-wide associations with the NAFLD Activity Score (NAS) were identified using Partial Least Squares Regression in the mixOmics R package. Results: ASBT inhibition restored glucose tolerance, reduced hepatic triglyceride and total cholesterol concentrations, and improved the NAS in HFD-fed mice. Metabolomics analysis of livers from chow versus HFD-fed mice identified 6,662 m/z features for statistical pair-wise comparisons. Of these metabolites, 959 were altered at P < 0.05. Mummichog pathway analysis revealed HFD-feeding significantly altered pathways for amino acid metabolism and urea cycle/amino group metabolism. Metabolomics analysis of livers from HFD/ASBTi versus HFD-fed mice identified 6,613 m/z features for statistical pair-wise comparisons. Of these metabolites, 454 metabolites were altered at P < 0.05. Mummichog analysis revealed that similar amino acid metabolism and urea cycle/amino group pathways were altered by HFD versus HFD/ASBTi-fed mice. In addition, HDF/ASBTi vs HFD also altered pathways for squalene and cholesterol metabolism. The Metabolome wide association analysis identified 299 metabolic features that were highly correlated with NAS. Significant pathways associated with the NAS included bile acid synthesis. Conclusions: Metabolic pathways for amino acid metabolism and urea cycle/amino group metabolism are significantly altered in HFD-fed mouse models of NAFLD. Changes in these pathways along with cholesterol metabolism may be integral to the therapeutic actions of the ASBTi.

182. Participation in Pediatric MRI Research: A Focus Group Study Examining Parent Perspectives
Reineri, Carly; Sholar, Brittney; Shultz, Sarah

Background: Prospective longitudinal MRI studies of infant brain development have the potential to provide groundbreaking insight into the neural mechanisms that contribute to developmental disabilities. Unfortunately longitudinal MRI studies of infants can be challenging to complete. Although MRI is safe and non-invasive, the prospect of enrolling infants in clinically unnecessary scans may be daunting for parents, especially those unfamiliar with MRI. Additionally successful data acquisition often requires that infants be scanned during natural sleep. Finally, longitudinal research is a long-term commitment; adherence to study visits may be especially difficult for families with young children. Given the criticality of this research, efforts aimed at minimizing participant attrition and maximizing the likelihood of obtaining usable data are needed. The current study describes the results of focus group research designed to elicit parent feedback about their experience participating in infant MRI research.

Objective: The objective of this study is to elicit parent feedback about their experience participating in a longitudinal infant MRI study at Marcus Autism Center. This feedback will be
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used to design more family-friendly protocols for pediatric neuroimaging research to improve enrollment, data acquisition success rates and lower participant attrition rates.

Methods: Participants were recruited from a group of parents who recently completed a longitudinal MRI study of infants at high- and low-risk for Autism Spectrum Disorder (ASD). Overall, 13 caregivers of 12 children (aged 1-6 months at the time of the MRI study) participated in one of three focus groups. A semi-structured interview guide was used to elicit perceptions from parents about: (1) their experience participating in MRI research, (2) the acceptability of the infant MRI protocol; (3) suggestions for protocol improvements; and (4) their reasons for participating in research.

Results: Overall, caregivers recalled a positive experience in their participation and reported that if given the opportunity, they would participate again. Caregivers also gave constructive feedback that can be used to improve recruitment strategy, study materials, and study protocols. Notably, many parents reported feeling some anxiety during study visits, attributing this to whether or not their child would successfully complete the MRI protocol and provide usable data. The most common motivation for participation was to contribute to science.

Conclusions: Our findings provide important information about the experience of participating in infant MRI research. These parent perspectives can be used to improve participant experience (in pediatric neuroimaging and the broader field of infant research) and to advance research in this area.

183. HELLS as a downstream effector of Sonic Hedgehog signaling in cerebellar development and medulloblastoma
Robinson, M. Hope; Farooq, Hamza; Taylor, Michael D.; Kenney, Anna

Cancer is known to exploit developmental gene expression programs. One well known example of this is the Sonic hedgehog (Shh) pathway, which is critical both in early embryonic development and in postnatal cerebellar development. In medulloblastoma (MB), the most common malignant pediatric brain tumor, 30% of tumors are driven by aberrant Shh activity. Our efforts are focused on unraveling the downstream components of the Shh pathway to better understand medulloblastoma and better inform therapeutic treatment development and decisions.

Using well established in vitro and in vivo models, we identified Lymphoid specific helicase (Hells) as a gene whose expression is markedly induced by Shh. Additionally, Hells levels in the developing cerebellum of normal mice are much higher than in the cerebral cortex. Our preliminary analysis of a large cohort of MB patients also indicates overexpression of HELLS in human medulloblastoma. Hells is a unique member of the SNF2 family of chromatin remodelers with multiple epigenetic functions in DNA methylation, histone acetylation and methylation,
and chromatin remodeling. Additional roles in transcription activation and DNA repair have also been reported. Of interest, Hells was shown to delay senescence by inhibiting the expression of p16INK4a, a key tumor suppressor that acts as a brake in the cell cycle. Analysis of human MB tumor sample data revealed an inverse correlation between expression of HELLS and CDKN2A, the genetic locus of p16INK4a.

Our promoter analysis and experiments with Shh pathway inhibitors suggest regulation of Hells expression through members of the Shh proliferation program although it remains to be seen if this regulation is direct. We are continuing to investigate the mechanism of Hells regulation by Shh and determining whether Hells is required for medulloblastoma and cerebellar progenitor cell proliferation and survival. To ascertain Hells involvement in proliferation and survival we are examining the effects of Hells knockdown on these processes. In future studies, we will test the hypothesis that Hells may have oncogenic functions, by transduction of mouse medulloblastoma cells with Hells constructs and re-implanting into host pups, then assessing effects on tumor latency and growth.

184. Reassortant Reoviruses as Targeted Therapeutics Against Triple-Negative Breast Cancer
Rodriguez Stewart, Roxana M.; Berger, Angela; Guberman, Jaime; Mainou, Bernardo

Triple-negative breast cancer (TNBC) constitutes approximately 15% of all breast cancer, has a higher rate of relapse, and shorter overall survival after metastasis than other subtypes of breast cancer. There is a need for targeted therapeutics to treat this type of breast cancer as current therapies are largely limited to cytotoxic chemotherapy. Mammalian orthoreovirus (reovirus), a nonenveloped segmented dsRNA virus causes a mostly asymptomatic infection in humans. Reovirus has been shown to preferentially kill transformed cells and is currently in Phase I-III clinical trials to assess its efficacy as an oncolytic against a variety of cancers. To engineer reovirus with enhanced infective and cytopathic properties against triple-negative breast cancer cells, we coinfected a TNBC cell line (MDA-MB-231) with prototype reoviruses T1L, T2J, and T3D. Following serial passage we isolated two reassortant reoviruses, r1Reovirus and r2Reovirus. r1Reovirus and r2Reovirus contain gene segments predominately from T1L, with one (r2Reovirus) or three (r1Reovirus) gene segments from T3D and synonymous and nonsynonymous point mutations. Infection of two TNBC cell lines, MDA-MB-231 and HCC1937, showed that r1Reovirus and r2Reovirus infect both cell lines more efficiently than T1L and have enhanced capacity to induce cell death in MDA-MB-231 cells. Although r2Reovirus infected HCC1937 cells more efficiently, all reovirus serotypes tested impaired HCC1937 cell growth equally without promoting cell death. These data suggest that r1Reovirus and r2Reovirus encode genomic changes that enhance their ability to infect TNBC cells. The different inhibitory effects on cell growth by virus infection also suggests the genetic composition of the TNBC cells can affect the outcome of reovirus infection.
185. Neutropenia in Pediatric Heart Transplant Recipients
Rose-Felker, Kirsten; Mukhtar, Ayesha; Liverman, Rochelle; Kelleman, Michael; Mahle, William; Deshpande, Shriprasad

Purpose: Neutropenia has been reported in pediatric heart transplant recipients and may be related to infection, medications and posttransplant lymphoproliferative disease (PTLD). While associated with infectious morbidity and mortality in oncology patients, its impact on heart transplant recipients is unknown. No guidelines exist for management of neutropenia in this population. We sought to determine the prevalence of and impact of neutropenia on infection, survival and rejection.

Methods: A retrospective analysis of pediatric heart transplant recipients from March 2005 - August 2015 was performed. Demographic variables were collected. Medications and dosages, viremia status, and rejection were collected for patients with neutropenia. Neutropenia was defined as an absolute neutrophil count (ANC) <1000 occurring >30 days after transplant and infection as clinical symptoms requiring hospital admission or intravenous antibiotic within 30 days of neutropenia. Continuous variables were compared using Wilcoxon rank-sum tests and categorical data were compared using Chi-square tests. Survival curves were generated and log-rank tests used. Competing risk factors methods were used to calculate the cumulative incidence of neutropenia accounting for death as a competing event over the duration of follow-up.

Results: 143 patients were included with a mean age of 3.9 y (0.6y – 13.1y) at the time of transplant. 77 patients (53.8%) developed neutropenia with a median time from transplant to onset of neutropenia of 4.7 months. Recurrent neutropenia was seen in 51 patients (66.2%). Anti-neutrophil antibody was detected in 6, however, only 14 patients were tested, most of whom had recurrent neutropenia. No significant differences in demographic variables in those who developed neutropenia and no increased risk of neutropenia with thymoglobulin induction. Neutropenia was not associated with anemia or thrombocytopenia. Fifteen patients with neutropenia developed infection, but there was no significant difference in survival, ANC, rate of rejection or PTLD in neutropenic patients with and without infection at the time of median follow-up (5.5 years). The dose of medications commonly associated with neutropenia (Valgancyclovir, mycophenolate or azathipropine) was lowered in 15 patients (19.5%) or discontinued in 42 (54.4%) patients with neutropenia.

Conclusions: Neutropenia is common in pediatric heart transplant recipients and is most likely to occur in the first 6 months after transplant. Neutropenia was not associated with thymoglobulin induction and had less than 20% risk of associated infection.

There was no difference in survival between patients with neutropenia with and without infection. Anti-neutrophil antibody was prevalent amongst those tested.
**186. Evaluation of Cell Delivery in a Novel Animal Model of Osteochondritis Dissecans**

Salazar-Noratto, Giuliana; Cobb, Destiny; Nations, Catriona; Hasain, Syed; Stevens, Hazel; Willimon, Clifton; Barry, Frank; Guldberg, Robert

Juvenile Osteochondritis Dissecans (OCD) of the knee is an increasingly common condition that predominantly affects adolescent and young adults, and progresses to early onset osteoarthritis. OCD initially involves the formation of an avascular lesion in the subchondral bone with secondary effects in the overlaying articular cartilage. During late stages of this disorder, the lesion becomes unstable and fragments. The etiology of OCD is not fully understood, and previous research has been primarily limited to retrospective clinical studies, thus hampering the creation of novel therapeutics. Furthermore, current pre-clinical animal models replicate only late stages of OCD, and their utility in the field is limited. It is the failure to treat OCD in its early stages that results in the progression of this disorder and the onset of osteoarthritis at an early age. Therefore, a new pre-clinical model is needed such that the disease progression mechanisms can be more fully investigated, with a view of developing and testing new therapeutic interventions.

The overall objective of this project is to develop a small pre-clinical animal model in order to better tailor diagnosis and treatment of this musculoskeletal disorder. The central hypothesis is that a pre-clinical animal model will prove advantageous in testing the efficacy and outcomes of current clinical procedures. We have developed a novel surgical procedure to induce osteonecrosis in the femoral condyle, which affects the overlaying articular cartilage. We continue to localize the lesion site region in order to better replicate the disease state. We expect that a localized necrotic lesion near the subchondral bone will extend and fragment over time.

Furthermore, we have created OCD- and control-patient-specific mesenchymal stem cells via induced pluripotent stem cell technology in order to evaluate the therapeutic benefit of cell delivery in the animal model. Patient-specific cell delivery is often coupled with marrow stimulation in current clinical practices; however, there is no literature about the efficacy of cell delivery in OCD, or whether OCD-specific stem cells differ that of non-OCD patients. Overall, this project seeks to introduce a novel, relevant OCD animal model, and to use as a platform to test a current clinical procedure.

**187. National Variability in the Utilization of Antireflux Surgery and Preoperative Testing in Infants**

Short, Heather L.; Braykov, Nikolay; Bost, James E.; Raval, Mehul

PURPOSE: Despite the availability of objective tests, diagnosis and management of reflux in infants remains controversial resulting in significant variation in care. Our purpose was to characterize national variation in diagnostic testing and surgical utilization for infants with gastroesophageal reflux disease (GERD).
METHODS: Using the Pediatric Health Information System (PHIS), we identified infants <1yo diagnosed with GERD between 1/2011 and 3/2015. Outcomes of interest included progression to antireflux surgery (ARS) and use of relevant diagnostic testing. Using a generalized linear mixed model we compared facility-level ARS utilization after adjusting for patient, hospital, and operative factors.

RESULTS: Of 5,299,943 infants, 149,190 had GERD (2.89%), and 4,518 (3%) of those patients underwent ARS. Although annual rates of GERD and ARS decreased, there was a wide range of GERD diagnosis (1.75%-6.16%) and utilization of ARS (0.2%-11.2%). Facilities varied in the use of laparoscopic versus open ARS (mean 66%, range 23%-97%). While 3.81% of patients underwent at least one diagnostic test, facility-level utilization varied from 0% to 13.8%. Variation in facility-level ARS rates persisted after adjustment. The proportion of surgeries done laparoscopically was independently associated with ARS utilization (OR 1.57, 95%CI 1.21-2.02). Facility-level utilization of diagnostics (P>0.1) and prevalence of GERD (P>0.1) were not associated with utilization of ARS.

CONCLUSIONS: There is notable variation in the overall utilization of ARS and in the surgical and diagnostic approach in infants with GERD. Fewer than 4% of infants with GERD undergo diagnostic testing. This variation in care merits development of consensus guidelines and further research.

188. The Challenge of Balancing Length of Stay and Readmissions in Children’s Surgery
Short, Heather L.; Parakati, Isaac; Heiss, Kurt F.; Wulkan, Mark L.; Sweeney, John F.; Raval, Mehul

PURPOSE: Surgeons balance competing interests of minimizing length of stay (LOS) with readmissions. Complications that occur early after discharge often result in readmissions. This study examines the relationship between LOS, timing of complications, and readmission risk.

METHODS: Cases from the 2012-2014 National Surgical Quality Improvement Project- Pediatric were organized into 30 procedural groups. Procedures where LOS approximated the median day of complication were identified. A theoretical model was applied to minimize readmissions by extending LOS.

RESULTS: From 30 procedures, 3 were identified where LOS approximated median day of compilations: complicated appendectomy (CA), antireflux surgery (ARS), and abdominal surgery without bowel resection (AS). The CA readmission rate drops from 12.2% to 8.2%, increasing LOS from 3 to 8 days at the cost of 16,428 additional hospital days among 4,740 patients (3.5 days/patient). Readmission optimization tapers after LOS of 8 days. Similar findings were observed for ARS and AS with readmission optimization at LOS of 5 days (2.6 days/patient) and 7 days (5.3 days/patient) respectively.
CONCLUSIONS: Our theoretical model aimed at balancing readmissions by extending LOS to capture early complications results in a substantial increase in hospital days illustrating the conflict between competing quality metrics and limited resources.

189. Comparing Outcomes Between Gastrostomy Alone and Gastrostomy with Nissen Fundoplication for Children with Severe Congenital Heart Defects
Short, Heather L.; Cutts, Richard P.; Clifton, Matthew S.; Travers, Curtis; Chanani, Nikhil K.; Oster, Matthew E.; Wulkan, Mark L.; Raval, Mehul

BACKGROUND/PURPOSE: Wide practice variation exists for infants with congenital heart defects (CHD) that require gastrostomy tube (GT) placement and/or Nissen fundoplication. Our objective was to compare outcomes among these patients undergoing GT alone vs. GT/Nissen.

METHODS: We retrospectively identified infants with complex CHD requiring 1 of 3 index cardiac operations between 2010 and 2015 at a single-quaternary pediatric hospital. Outcomes of interest included mortality, readmissions, gastrojejunostomy tube (GJT) conversion, and growth.

RESULTS: Among 104 patients identified, 83 (80%) were neonates at initial cardiac operation and 45 (43%) subsequently underwent a bidirectional Glenn. There were no significant differences in mortality between the GT/Nissen and the GT alone cohorts (20.2% vs. 33.3%, p=0.29). While 30-day readmissions were higher in patients who underwent GT/Nissen (40.5% vs. 13.3%, p=0.04), after controlling for age the difference was not detected. There were no significant differences in relative growth between groups. Readmissions, length of stay, and GJT conversion were reduced among patients who were older or weighed more at time of non-cardiac surgery.

CONCLUSIONS: Among infants with complex CHD, outcomes are similar between patients undergoing GT alone vs. GT/Nissen. For patients without severe reflux morbidity, delaying either GT or GT/Nissen may improve outcomes.

190. Hospital-Level Factors Associated with Non-Operative Management in Common Pediatric Surgical Procedures
Short, Heather L.; Fevrier, Helene; Raval, Mehul

INTRODUCTION: There are operative (OP) and nonoperative (NONOP) treatment options for many pediatric surgical conditions. The decision to operate is multifactorial and reflects patient and surgeon preferences but also the hospital-level comfort with NONOP surgical management. The purpose of this study was to examine hospital-level factors associated with use of NONOP management in common pediatric surgical diagnoses.

METHODS: A cross-sectional, retrospective review of the 2012 Kid’s Inpatient Database (KID) was performed to identify all patients age 0-20 years diagnosed with cholecystitis, bowel obstruction, perforated appendicitis, or spontaneous pneumothorax. Hospitals were
characterized as favoring OP or NONOP based on utilization of NONOP management for each diagnosis of interest after applying disease specific minimum case thresholds. Logistic regression models were used to determine the hospital-level characteristics associated with NONOP management.

RESULTS: In 2012, there were 36,026 admissions for the diagnoses of interest with nearly a quarter representing NONOP management (20.7%, n=7472). The highest incidence of NONOP management was seen with spontaneous pneumothorax (55.9%, n=394), while the lowest incidence was seen with perforated appendicitis (9.2%, n=1641). The utilization of OP management varied significantly between hospitals for all diagnoses ranging from a 10-fold difference for bowel obstruction and a 5-fold difference for all other diagnoses. Patients with a diagnosis of bowel obstruction (Odds Ratio (OR) 0.41; 95% Confidence Interval (CI) 0.30-0.56) and spontaneous pneumothorax (OR 0.28; 95% CI 0.14-0.56) had decreased odds of NONOP management when treated at an urban, teaching hospital when compared to a rural hospital. Patients with perforated appendicitis had increased odds of NONOP management when treated at an urban, teaching hospital (OR 2.42; 95% CI 1.78-3.30). Hospital-level factors associated with decreased odds of NONOP management included urban, nonteaching status (OR 0.54; 95% CI 0.31-0.91) and location in the South (OR 0.53; 95% CI 0.34-0.83) and West (OR 0.47, 95% CI 0.30-0.74). Hospital bed size was not associated with the use of NONOP management for any diagnosis.

CONCLUSIONS: Despite representing over 20% of surgical care for several conditions in children, NONOP is an understudied aspect of care with significant variation that warrants further research.

191. ThinkGenetic: Identification of educational gaps in patient and caregiver genetic knowledge in the age of the internet
Simmons, Morgan; Laney, Dawn

Purpose: To identify educational gaps for individuals and caregivers living with a genetic disorder. Methods: Patients and caregivers living with a confirmed genetic condition were invited to complete a survey containing demographic information, disease-specific knowledge questions, and allowing anonymous monitoring of their question/answer session on a patient-focused educational site called ThinkGenetic. A revolutionary educational website powered by IBM’s Watson™, ThinkGenetic was designed to provide increased access to accurate genetic information at a lay reading level to patients, caregivers, and healthcare professionals. Participant knowledge related to inheritance pattern, treatment, and clinical trials were determined from the survey. Results: A total of 53 participants completed the survey with an additional 90.6% of survey respondents (48 out of 53) continuing on to interact with the
educational website. The knowledge question responses indicate that 38% of participants could identify an inheritance pattern for their condition, 78% could identify whether there is an FDA approved treatment, and 53% could identify if there are ongoing clinical trials specific to their condition. Individuals living with a genetic condition were not significantly more likely to know how the genetic condition is inherited than those who are a family member of someone living with a genetic condition. Findings demonstrate an apparent gap in knowledge regarding inheritance patterns and clinical trials. In addition to specific knowledge gaps, users seemed particularly interested in practical information about living with genetic conditions and where they can find more information about the condition in question. Conclusion: The responses from the general knowledge questions asked suggest that providers need to focus on, provide additional resources for, or emphasize specific topics including: inheritance pattern, clinical trials and practical information about living with genetic conditions and where they can go for additional information and resources.

192. Autism Disparities: Assessing Quality of Care and Structural Barriers to Diagnosis and Services
Singh, Jennifer; Rubin, Leslie

Background: Autism spectrum disorder is the fastest growing developmental disorder in the U.S., affecting 1 in 68 children. Early diagnosis and interventions can improve the developmental trajectory and outcomes for people with autism. However, access to diagnosis and services are unequal, reducing future abilities and creating long-term financial burdens on families and support systems. Disparities to diagnosis and services are stratified by socioeconomic status (SES), race, and ethnicity, and are compounded by limited autism services.

The purpose of this study was to measure the quality of care at Children’s Healthcare of Atlanta Autism Clinic at Hughes Spalding, where 90% of patients rely on Medicaid or are uninsured. The study also identified structural barriers to autism diagnosis and services for low-income, minority and/or other underserved children and their families.

Methods: This study used a mixed method approach, consisting of an in-depth survey to assess quality of care offered by the Autism Clinic, followed by open-ended questions to identify barriers to autism diagnosis and services. Clinic encounters were also observed and in-depth interviews were conducted with clinic staff. Sixty surveys/open-ended questions were conducted with primary caregivers whose child receives services at the Autism Clinic.

Results: The strongest measure of quality of care was the family-centered care, including careful listening by the clinic staff, and ability of caregivers to ask questions or raise concerns. Overall, caregivers were very satisfied with the diagnostic processes, the diagnostic communication, the follow-up visits, and the range of services offered by the clinic. Respondents were less satisfied with the ability to access service referrals made by the clinic.
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and the time it took to get an initial appointment, which, on average, took 156 days. Social factors that shaped structural barriers included limited access to transportation, a single parent household, lack of flexible employment, and limited services available outside of metro Atlanta and/or through Medicaid.

Conclusions: This study identified structural inequalities that shape access to autism diagnosis and services. This knowledge will inform the development of new approaches to offer autism services to underserved populations, such as mobile therapeutic units that are available during the evenings and/or weekends. Caregiver feedback will be used to improve services. While the Autism Clinic provides outstanding family centered care, there is a need for more appointment availability, and updated referral resources, especially for families who rely on Medicaid insurance.

This study was supported by CHOA Center for Transforming Pediatric Healthcare Delivery.

193. The Pediatric Research Database, a Robust Data Mart and Cohort Discovery Tool to Strengthen Research Hypotheses, Increase the Efficiency of Study Workflows, and Facilitate Feasibility Assessment

Smith, Ebony; Ajayi, Oluwaseun; Mudunuri, Rahul; Vangteeravat, Teeradache; Huang, Eunice

Common challenges faced by clinical researchers include the level of difficulty involved in developing robust hypotheses that serve as the critical foundation for their research studies, obstacles associated with identifying reliable patient cohorts that support their hypotheses, and the arduous nature of performing rigorous feasibility assessments to ensure resources are well-invested to support promising, relevant studies that have high potential for successful completion.

The Pediatric Research Database (PRD) is a web-based, biomedical informatics cohort discovery tool delivering de-identified clinical data from the electronic medical record (EMR) at Le Bonheur Children’s Hospital. The application assists investigators in developing stronger, data-driven research hypotheses, facilitates preliminary cohort discovery, and provides information for evaluating the feasibility of conducting studies.

The PRD addresses limitations investigators face when attempting to utilize raw EMR data in its distributed native format by reorganizing and aggregating the data into an ancillary data mart that employs high-quality analysis techniques. The technical framework for PRD includes PHP, HTML, JavaScript, AJAX and MySQL databases. The backend database is designed in star schema format where the fact table is in long format, a format used for optimized query running time. Data migration via extraction, transform, and load (ETL) is performed using Pentaho data integration technology.

The PRD utilizes a robust exploratory data analysis (EDA) technique called multi-dimensional cross-filtering to make the process of data elaboration, information gathering, knowledge
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194. Differential Epigenome-wide DNA Methylation Patterns in Pediatric Crohn’s Disease
Somineni, Hari; Kilaru, Varun; Venkateswaran, Suresh; Chopra, Pankaj; Okou, David; Gibson, Greg; Conneely, Karen; Smith, Alicia; Kugathasan, Subra

Background: Crohn’s Disease (CD) is a life-long condition characterized by ulceration, pain, rectal bleeding, loss of quality of life and a need for bowel surgery. Recent evidences suggest the involvement of gene-environmental interactions in CD susceptibility. Epigenetic processes play an important role in mediating environmental influences. Therefore, we set out to examine CD-associated DNA methylation changes at a genome-wide level.

Methods: We utilized a subset of pediatric subjects recruited under the RISK - multicenter inception cohort study to elucidate the epigenetic basis of CD. We generated genome-wide DNA methylation data using Illumina HumanMethylation850 EPIC array in whole blood DNA samples of 76 controls and 167 newly diagnosed CD cases. β-values for each CpG site were modeled as a linear function of disease status (0 for control and 1 for CD patient) with age, gender, race, and blood cell-proportions as covariates to profile disease-related methylation changes. Holm significance method was used to correct for multiple test comparisons.

Results: A total of 220 differentially methylated positions (DMPs) exhibited significant association with CD. Of these, 143 DMPs were hypermethylated and 77 were hypomethylated in cases compared to controls. We noticed strong CD-associated signals peaking from chromosomes 17 and 19. A long non-coding RNA, LOC100996291 (chr 17) probed for the first time on 850k array, showed strongest association with CD. Four of the 7 probes on the array corresponding to LOC100996291 were hypomethylated and all 4 were enriched within top 20
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DMPs. In addition to detecting several novel DMPs, some of the previous 450k array findings from whole blood were replicated in our study. TMEM49/VMP1, SBNO2, RPS6KA2, ITGB2, and TXK genes showed significant differential methylation profiles between cases and controls. Furthermore, many of the significant DMPs exhibited strong correlation with disease-related plasma C-reactive protein, albumin, and hemoglobin levels.

Conclusion: Our findings suggest that dysregulated DNA methylation is associated with CD susceptibility and it may offer new pathophysiological insights and therapeutic targets to prevent the onset of CD and delay its progression.

195. Marine Organisms as a Source for Novel Antimalarial Compounds
Sweeney-Jones, Anne Marie; Gagaring, Kerstin; McNamara, Case; Kubanek, Julia

According to the 2016 World Malaria Report released by the World Health Organization, an estimated 212 million cases of malaria occurred in 2015 which resulted in about 429,000 deaths, including 303,000 children. While there are numerous pharmaceuticals available for the treatment of malaria, the persistent problem of drug resistance necessitates continued efforts toward identifying new compounds that can combat the disease-causing protozoa, Plasmodium. Living organisms have proven to be an invaluable source for compounds with antimalarial bioactivity. For example, one of the standard pharmaceuticals used for treatment of the strain Plasmodium falciparum, the endoperoxide sesquiterpene artemisinin, comes from the terrestrial plant Artemisia annua. A promising source for new antimalarial compounds are marine organisms, which have remained largely unexplored. Marine organisms produce a wide variety of secondary metabolites with unique features that are specific to the marine environment. Antimalarial bioactivity has been previously identified in our lab in natural products from the red alga Calliphycus serratus. Currently, a cyanobacteria Lyngbya sp. and the red alga Amphiroa tribulus show promising results that indicate the presence of new marine-derived antimalarial compounds. Our collaborators at the California Institute for Biomedical Research (CALIBR) worked with us to perform bioassay-guided fractionation to identify fractions that are active against the malarial parasite P. berghei. A vacuum liquid chromatography fraction from a crude extract of Lyngbya sp. had an EC50 of 0.18 µg/mL while a fraction obtained for A. tribulus had an EC50 of 0.44 µg/mL. Further fractionation has been done using reversed-phase solid phase extraction and high performance liquid chromatography. Efforts are currently ongoing to try to purify and identify the bioactive compounds. Preliminary mass spectral data collected for the bioactive fractions contained numerous brominated compounds while NMR data indicated the presence of aromatic compounds and fatty acids. Identifying new antimalarial compounds with novel backbones is of the utmost importance in the continued battle against drug-resistant Plasmodium strains.
196. Upregulated I2PP2A activates PI3K pathway and promotes tumor cell survival of Sonic Hedgehog medulloblastoma
Wei, Yun; Kenney, Anna

Medulloblastoma is the most common solid brain malignancy of childhood. Approximately 30% of human medulloblastomas show aberrant Sonic Hedgehog (Shh) pathway activity. Current treatment strategies comprise surgery, radiation and chemotherapy, which generate side effects that severely impact survivors’ quality of life, and tumor recurrence is typically fatal. The PI3 kinase pathway plays critical roles in medulloblastoma tumor-repopulating cell survival, as shown in recent patient sample research. This pathway can be inhibited by activity of the tumor suppressor protein phosphatase 2A (PP2A). Using NeuroD2-SmoA1 mouse model which faithfully recapitulates human Shh MB, I’ve confirmed that the protein levels of p-AKT, downstream effector of PI3 kinase pathway, along with p-ERK, downstream of MAPK pathway, increase 24 hours after irradiation on SmoA1 mice. This leads me to the question whether the negative regulator of p-ERK and p-AKT, PP2A, has been suppressed in Shh MB. Among three endogenous inhibitors of PP2A, designated as CIP2A (cancerous inhibitor of PP2A), I1PP2A and I2PP2A (inhibitor 1 and inhibitor 2 of PP2A, respectively), I found that protein level of I2PP2A but not the other two is markedly elevated in mouse medulloblastomas compared with neighboring normal cerebellum. However, the mRNA level of I2PP2A in SmoA1 mice or patient samples did not show significant difference in Shh MB compared to control group. In primary cultures of mouse SmaA1 medulloblastoma cells, lentiviral knockdown and a peptide inhibitor of I2PP2A reactivated PP2A C and decreased the PI3K and MAPK pathway activity, indicated by reduced downstream p-Akt and p-ERK in Shh medulloblastoma. Employing SmoA1 tumor allograft model, I’m also testing whether I2PP2A knockdown can inhibit SmoA1 tumor growth in vivo and prolong the host survival. I hope to extrapolate this research into a novel therapy design targeting I2PP2A:PI3K interactions in SHH or even other subtypes of medulloblastoma.

197. Oral and fecal microbiome characteristics in treatment naïve pediatric IBD patients over time; A prospective longitudinal study
Weitzner, Jordan; Ballengee, Cortney; Sauer, Cary; Venkateswaran, Suresh; Prince, Jarod; Dodd, Anne; Le, Kyoung; Chopra, Pankaj; Kugathasan, Subra

Introduction: Gut and oral microbiome dysbiosis has been demonstrated in subjects with newly diagnosed and chronic Inflammatory Bowel Disease (IBD). In this prospective study, we aim to characterize the treatment-naïve oral and gut Microbiome in pediatric patients and assess characteristics, which are associated with response to therapy or disease activity over time by repeated sampling.

Methods: We performed a prospective cohort study of 14 treatment-naïve IBD subjects (9CD, 5UC), 13 established IBD subjects (9CD, 4UC), and 16 unrelated, healthy controls assessing the fecal and oral microbiome via repeated samplings. Associations between clinical characteristics and the microbiome were tested using generalized estimating equations. 16s rRNA sequencing
Abstracts of hypervariable regions was performed on extracted stool (n=88) and a subset of extracted oral samples from tongue, buccal surface, plaque, and saliva from CD and UC patients. Data processing and analysis was performed using Mothur software referencing the SILVA database. Oral samples from 135 individual subject encounters are currently being extracted.

Results: A total of 27 IBD patients were included in this pilot study, along with 16 healthy controls and were analyzed using principal coordinate analysis (PCoA). Results showed separation between oral samples and fecal samples (fig 1), clustering between CD and UC patients for all sample locations (fig 2), as well as individual subject clustering by oral sample location(fig 1). Serial stool collections show subject specific clustering on PCoA (fig 1). We found differences in specific microbiome genera between cases/controls including Fusobacterium (p=0.0138), Coprobacillus (p=0.028), Ruminococcus (p=0.015), Escherichia (p=0.0127). Previously reported bacteria approach statistical significance Enterobacteraceae (p=0.06), Veillonellaceae (0.08).

Conclusions: Oral Samples from CD and UC subject separate out on PCoA. Oral samples cluster by subject and not location on PCoA. Serial stool samples from individuals show stability on PCoA. Abundance of certain bacteria genera differentiates cases/controls as previously reported. Extension of the pilot data with 135 oral samplings at all four oral locations is currently under analysis.

198. Modeling Zika Virus Exposure And Screening Therapeutic Compounds With Human iPSC-Derived Neural Cells
Wen, Zhexing; Qian, Xuyu; Brennand, Kristen; Zhang, Wei; Jin, Peng; Tang, Hengli; Song, Hongjun; Ming, Guo-li

Zika virus (ZIKV), a mosquito-borne flavivirus, is currently reported to be circulating in approximately 60 countries and territories globally. While ZIKV infection has been linked to microcephaly in newborns and other brain abnormalities such as Guillain-Barré syndrome, how ZIKV impairs brain development and function is unknown. Here we show that three stains of ZIKV, Puerto Rican ZIKVPR, Asian ZIKVC and African ZIKVM, directly infects human induced pluripotent stem cell (hiPSC)-derived cortical neural progenitor cells (hNPCs) with high efficiency. Infected hNPCs further secrete infectious ZIKV particles. Importantly, ZIKV infection increases cell death and dysregulates cell cycle progression, resulting in attenuated hNPC growth. Gene expression analyses of infected hNPCs reveal transcriptional dysregulation, notably of cell cycle-related pathways. In addition, we performed a drug repurposing screen of ~6,000 compounds and identified leading compounds that either inhibit ZIKV infection or suppress infection-induced caspase-3 activity in hiPSC-derived neural cells. Our results thus fill a major gap in our knowledge about ZIKV biology and serve as an entry point to establish a mechanistic link between ZIKV and microcephaly. Our study also provides a tractable
experimental model system for investigating the impact and mechanism of ZIKV on human brain development. Of equal importance, our high-throughput screening platform with hiPSC-derived neural cells has led to the identification of therapeutic compounds that either suppress ZIKV infection or ameliorate its pathological effects during neural development, which may have an immediate effect on the development of anti-ZIKV therapeutics.

199. Analysis and Implications of Non-Invasive Knee Acoustical Emissions in Juvenile Idiopathic Arthritis: A Case Study
Whittingslow, Daniel; Semiz, Beren; Ponders, Lori; Wiens, Andrew; Prahalad, Sampath; Inan, Omer

Juvenile Idiopathic Arthritis (JIA) is the most common, chronic, childhood, rheumatic disease, and an important cause of disability. It is characterized by persistent inflammation of the joints, with onset prior to the age of 16 years. The diverse nature of the disease has resulted in variable epidemiologic estimates, between 16 to 400 per 100,000. Despite the long-term persistence of disease activity in most patients, a pronounced improvement in functional outcome has been documented in the past decade - largely due to advances in clinical diagnosis and treatment regimes. Despite these improvements, 10% of patients still have serious functional disability (eg. Steinbrocker functional classes III or IV) five years post diagnosis. Future outcome studies will be improved by advances in the standardization of clinical diagnostics and further refining of the treatment regimen.

One of the principal difficulties in standardizing the diagnosis of JIA is the lack of specific biomarkers for the disease and its concomitant progression. The advent of wearable technologies has beckoned a new era of possibilities for continuous health monitoring. Joint acoustic emission measurements via contact microphones (i.e., accelerometers) are one unobtrusive method of capturing information regarding the underlying physiologic processes of a joint that readily can be incorporated into a wearable platform. These emissions result from changes in the biomechanics of the joint: internal friction between the articulating structures in the knee give rise to various frequencies of vibrations that can be detected at the surface of the knee. The persistent inflammation in JIA provides the opportunity for utilizing a similar technology to diagnose and monitor the condition.

Proof of concept recordings were performed from two subjects with this device. The first subject was a 12 year old, male patient with systemic JIA; a healthy control was age and sex matched for comparison. The subjects’ knee sounds were recorded using a custom hardware setup consisting of LED motion tracking and accelerometers for vibration detection. They performed ten flexion/extension cycles with the recording apparatus in place. The angle of the leg in both appears as an oscillating function between 90 degrees and 180 degrees with no noticeable differences. The patient with JIA’s plot appears more chaotic with a periodicity to the sharp peaks corresponding to “clicking” of the joint. The JIA patient’s acoustic signal is an
order of magnitude larger than the healthy control. This finding encourages further work in the development of this technology.

200. Long-Term Outcomes After Surgery for Pulmonary Atresia with Intact Ventricular Septum: A Study From the Pediatric Cardiac Care Consortium
Wright, Lydia; Kochilas, Lazaros; Thomas, Amanda; Knight, Jessica

Background: Pulmonary atresia with intact ventricular septum (PA/IVS) is a rare congenital heart lesion. Because of the heterogeneity of the size and function of the right ventricle and the tricuspid valve, as well as extent of involvement of the coronary arteries, patients with this lesion may undergo a wide range of corrective surgeries. There is limited data on long-term outcomes in these patients, particularly data that focus on differences in survival based on surgical strategy.

Methods: This is a cohort study from the Pediatric Cardiac Care Consortium, a multi-institutional US-based registry of interventions for congenital heart diseases. We identified 626 patients with the diagnosis of pulmonary atresia with intact ventricular septum having adequate identifiers for linkage studies. Long-term outcome data are provided by linkage to the National Death Index (NDI) and the United Network for Organ Sharing (UNOS) up to the latest update of 12/31/2014.

Results: Patients with pulmonary atresia and intact ventricular septum underwent a variety of surgical procedures ultimately leading to one of several “definitive repairs”: one ventricle repair culminating in Fontan procedure, one and a half ventricle repair (two ventricle circulation with additional SVC to pulmonary artery anastamosis), or two ventricle repair without augmented pulmonary blood flow. Sixty-one patients underwent systemic to pulmonary artery shunt and did not undergo a second surgery within the PCCC. There were 163 in hospital deaths and 2 primary transplants. Among the remaining 461 patients, there were 63 deaths (two after heart transplant) with median follow-up of 17.4 years (IQR=13.7-21.6), as provided by linkage to the NDI and UNOS. Most deaths were in the first two years of life and were predominantly seen in those patients in the “inter-stage” period after initial systemic to pulmonary artery shunt and before definitive repair. The 15-year transplant-free survival rate was 86.3% for PA/IVS patients discharged alive irrespective of surgical strategy. Multivariate analysis demonstrated decreased long-term survival among patients in the one ventricle compared to two-ventricle pathway (adjusted hazard ratio 3.7, CI 1.01-13.56). Those who underwent one and a half ventricle repair had similar survival to two-ventricle patients.

Conclusions: Fifteen-year transplant-free survival for patients with pulmonary atresia and intact ventricular septum is 86.3%. For those patients who achieve definitive repair, either with one, one and a half, or two ventricle circulation, survival is even higher. There remains significant mortality in the neonatal period, both in-hospital and in the “inter-stage” period before definitive repair.
201. Spatiotemporal gait parameters in children with fragile X syndrome compared to children with and without Down syndrome: case studies
Wu, Jianhua; Henderson, Gena; Beerse, Matthew

Fragile X syndrome (FXS) is a common genetic condition which often causes intellectual, behavioral and learning challenges. However, compared to many locomotion studies conducted with children with Down syndrome (DS), another common genetic condition, few studies have been carried out to investigate gait patterns in children with FXS. This study aimed to examine spatiotemporal gait parameters from two children with FXS compared to groups of children with DS and typically developing (TD) children. Two children with FXS were recruited as a convenience sample. FXS01 was female, 8.0 years old, 1.28m, and 28.4kg. FXS02 was male, 7.7 years, 1.35m, and 39.6kg. Children with DS included 11M/2F, 9.0 years, 1.24m, and 30.6kg. TD children included 11M/2F, 9.1 years, 1.33m, and 29.6kg. All the subjects came to the Biomechanics lab at Georgia State University once for data collection. An 8-camera Vicon motion capture system and a modified full-body marker set were used to collect kinematic data. Subjects walked over the ground at three load conditions: no ankle load (no-load), and with external ankle load that was equal to 2% (low-load), and 4% (high-load) of the subject’s body mass on each side. Presentation of the load conditions were randomized across the subjects. Customized Matlab programs were used for calculate spatiotemporal gait parameters. Results showed that at each load condition, FXS01 walked at a slower speed and a shorter step length than the TD group, but at a faster speed and a longer step length than the DS group. FXS01 walked with a similar cadence compared to the DS and TD groups. However, FXS01 produced a greater step width than both the DS and TD groups. In contrast, FXS02 also walked at a slower speed and a shorter step length than the TD group, but a faster speed and a longer step length than the DS group at each load condition. However, FXS02 had a lower cadence than both the DS and TD groups. Most strikingly, FXS02 walked with a step width similar to that of the TD group, but narrower than that of the DS group. Our results suggested that the two FXS subjects are able to adapt to different load conditions, and walk faster and have a longer step length than the DS group. However, balance control differed between these two FXS subjects, with FXS02 demonstrating more TD-like step width.

202. Utilization of Inverse Propensity Treatment Weights (IPTW) as a Means of Balancing Baseline Confounding Effects in Non-Randomized, Longitudinal Research Studies
Gillespie, Scott; McCracken, Courtney; Leong, Traci; Travers, Curtis; Figueroa, Janet; Kelleman, Michael; Bryan, Leah; Camacho-Gonzalez, Andres

Introduction: Given the advancements in electronic data capture, many clinical researchers are turning to registries, data consortiums, and large public-use datasets, to estimate treatment effects in non-randomized clinical samples. Unlike randomized trials, where treated and control subjects are systematically similar in both measured and unmeasured baseline characteristics,
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non-randomized samples offer no such guarantees. Specifically, in non-randomized designs, the effect of treatment cannot be estimated by simply comparing outcomes between study groups, due to issues involving sample bias and confounding by indication. To counter this problem, propensity-based methods have been proposed with increased frequency. The propensity score is a balancing score where weighted treatment and control observations have analogous distributions of baseline covariates. In this work, we employ propensity methods to balance baseline confounders in a non-randomized, longitudinal trial for HIV+ participants at the Grady-Ponce Family and Youth Clinic in Atlanta, Georgia.

Methods: Ninety-eight participants were placed in either treatment or standard of care (SOC) arms for the HIV trial, with variables longitudinally collected over one-year. Primary outcomes were improvement in CD4 Counts and Viral Loads. Due to the non-randomized design, several variables differed between the two cohorts at baseline. A propensity score was estimated using binary logistic regression where treatment assignment (treatment versus SOC) was regressed on 12 baseline covariates (11 nominal and 1 continuous) involving demographics, drug use, sexual orientation and history. Average treatment effect (ATE) weights were calculated from the logistic model and further standardized/stabilized, to create the IPTW. Cohen’s d effect sizes (ES) were calculated for each of the baseline covariates, between treatment and SOC groups, both unweighted and weighted. Balance was confirmed if the weighted ES were <0.25.

Results: The distribution of stabilized IPTW had mean 0.98 and standard deviation 1.1, with minimum and maximums of 0.48 and 9.36, respectively. The largest weighted ES for baseline nominal characteristics between treatment and SOC arms were for race (0.230) and condom usage (0.249), with the remaining ES under 0.20. The single continuous covariate (participant age) was considered linearly, as well as with squared and cubic terms (i.e. Age2; Age3). In each case, weighted ES met our balance criteria.

Conclusions: In this clinically disparate sample of treatment and control patients, we successfully employed propensity methods to balance baseline covariate differences in a non-randomized, longitudinal study. Researchers working with both small and large data structures should consider the benefits of propensity methods when making inferential conclusions between dissimilar study groups.

McCracken, Courtney; Travers, Curtis; Figueroa, Janet; Kelleman, Michael; Gillespie, Scott; Bryan, Leah; Garica-Roig, Michael

Introduction: Survey data collection has moved from paper and pencil to almost entirely electronic-based data capturing (EDC). While EDC has improved efficiency, it has not solved the problem of quickly identifying survey respondents and capturing data. Crowdsourcing has become a popular technique to recruit participants for surveys. Amazon’s Mechanical Turk
(MTurk), an online labor market, is an attractive solution for researchers who want to obtain large volume survey responses in a relatively short timeframe for pennies on the dollar. MTurk is frequently used for scientific inquiry and has shown to be a valid and reliable method for collecting survey responses; however, the generalizability of the survey respondents may not be representative of one’s target population. Methods: We utilized MTurk as a crowdsourcing platform to survey people about attitudes regarding surgical scar location preference and attitudes about factors affecting surgical choice for adults and children. In addition, we collected demographic data including: sex, age, US residency, US region, race, education, occupation, and marital status. To determine if MTurk users are representative of the general US population, we compared the demographic make of our survey respondents to summary data from the 2010 US census.

Results: We were able to collect 1079 survey responses within 7 days for $216. Seventy-nine (7.3%) were incomplete. Forty-six responses (4.6%) had discordant information and were considered invalid. Among the 954 responses, participants were primarily female (54.8%), 25-34 years-old (41.9%) and Caucasian (67.1%). Eighty-one percent (n=811) were US residents and lived in the Southeast (26.5%) or Midwest (23.4%). Over 70% had an Associate degree or higher and were employed. Only 47% of respondents had children. Compared to the 2010 census, our sample had a higher percentage of females (55% vs. 51%), Asians (22.3% vs. 4.8%). There were only a small percentage of African American respondents compared to the general population (6.2% vs. 12.6%). Our geographical representation was similar to the US census data. Educational attainment was strikingly different with over 70% of the sample having at least an Associate degree compared to only 42% of the general population.

Conclusion: MTurk is a fast, reliable way to collect survey responses in a timely, low-cost, and efficient manner. While the survey responses have been validated in multiple studies when compared to in-person data collection, the generalizability of these respondents do not seem to mirror the general US population based on demographics. Researchers should be careful when using these results to make generalizations about their research population.

204. RStudio on Amazon Web Services for Dummies: From a Dummy
Travers, Curtis; Gillespie, Scott; Raval, Mehul; McCracken, Courtney

As the use of technology in clinical research has grown, so has the ease of collecting and compiling information into large datasets. Cloud computing resources are now often necessary to analyze these datasets as traditional computing power is insufficient. With little- to no prior experience in cloud computing, we utilized online tutorials to create an Amazon Web Services (AWS) instance with sufficient computing power to analyze a dataset containing over 13,000,000 observations.

The first step to utilizing cloud computing on AWS is to create an account, which requires some basic user information and a credit card. There are several pricing structures available. Specifically, the “Free-Tier” provides access to basic resources for 12 months and provides 750 hours per month of 1 CPU, 1 GB computing. An Elastic Compute Cloud (EC2) instance is a virtual
computing environment on AWS, providing scalable computing power ranging up to 128 CPUs and 1952 GB RAM, with increasing costs for more power. Using a security group with specified IP addresses and a downloadable key pair file, users can create secure connections for accessing their EC2 instance. Virtual servers containing RStudio for statistical analyses are available at no additional charge. Other servers are available with more sophisticated programming such as Python, Perl, and Java. The virtual server is accessed via a URL through an internet browser enabling a complete version of RStudio to be used with all the computing power specified for the instance. Any additional required statistical packages for RStudio can be installed onto the virtual server. In the specific server used for this project, a DropBox package is included which allows synchronization of data between DropBox accounts and the instance.

A statistical process that crashed the first author’s laptop, due to lack of memory, was easily performed using RStudio on AWS in minimal time. The costs are relatively affordable; a 16 CPU, 64 GB RAM instance is only charged 86 cents per hour, and we were able to complete this project for under four dollars. Users are no longer bound by the computing power of their own PCs, and by utilizing AWS, can affordably analyze large datasets with lessons learned through trials and tutorials.

Service Core Posters

See descriptions in conference program

205. Pediatric Biostatistics Core
206. Animal Physiology Core
207. Cardiovascular Imaging Core
208. Center for Systems Imaging-Biomedical Imaging Technology Center
209. Pediatric Imaging Research Core
210. Experimental Models Support Core
211. Integrated Cellular Imaging
212. Laboratory and Pathology Clinical Research Core
213. Ian’s Friends Foundation Brain Tumor Biorepository
214. Molecular Clinical Trials Laboratory and Biorepository
215. Molecular Evolution
216. Georgia Tech Optical Microscopy Core
217. Pediatric Biomarkers Core
218. Pediatric Heart Diseases Data Registry Core
219. Systems Mass Spectrometry Center
220. Emory Integrated Genomics Core
221. Emory Integrated Computational Core

Research IT Services Posters

See descriptions in conference program

222. LabKey
223. Emory Research Laboratory Information Management System
224. Tableau
225. REDCap
227. Children’s Healthcare of Atlanta Data Assessment & Extraction
228. Children’s Healthcare of Atlanta Research, Big Data & Warehousing Services
229. eCREST

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