RESEARCH RETREAT 2021

VANDERBILT UNIVERSITY
MEDICAL CENTER

Department of Pediatrics

Keynote Address

"A Viral Trigger for Celiac Disease"

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Terence S. Dermody, MD is the Vira I. Heinz Distinguished Professor and Chair of Pediatrics at the University of Pittsburgh School of Medicine and Physician-in-Chief and Scientific Director at UPMC Children's Hospital of Pittsburgh. He completed an internal medicine residency at Presbyterian Hospital in New York and fellowships in infectious diseases and molecular virology at Brigham and Women's Hospital and Harvard Medical School. Prior to moving to Pittsburgh in 2016, Dr. Dermody was Dorothy Overall Wells Professor of Pediatrics and Director of the Medical Scientist Training Program and Division of Pediatric Infectious Diseases at Vanderbilt University School of Medicine.

Dr. Dermody is a virologist with interests in viral pathogenesis and vaccine development. Most of his research has focused on reovirus, an important experimental model for studies of viral encephalitis in the young, and chikungunya virus, an emerging mosquito-borne virus that causes epidemics of fever and arthritis. His research contributions have enhanced an understanding of how these viruses enter into host cells and cause organ-specific disease. He has published more than 250 articles, reviews, chapters, and editorials and has been recognized for his research accomplishments by the Vanderbilt Ernest W. Goodpasture Faculty Research Award, an NIH MERIT Award, and the American Society for Microbiology D. C. White Research and Mentoring Award.

Data Blitz Presentations

DBP – 1	Wubishet Belay
DBP – 2	Rachel Bernard
DBP – 3	Catherine Burger
DBP – 4	Meredith Campbell
DBP – 5	Conrad Cox
DBP – 6	Sara Duffus
DBP – 7	Benedicto Fernandes
DBP – 8	Thao-Phuong Hallett
DBP – 9	Kimberley Harper
DBP – 10	Jaycelyn Holland
DBP – 11	Jacob Kaslow
DBP – 12	Lindsey Knake
DBP – 13	William McEachern
DBP – 14	Michael Miller
DBP – 15	Aryaz Sheybani
DBP – 16	Shawn Sood
DBP – 17	Hillary Spencer
DBP – 18	Lindsay Sternad
DBP – 19	Daniel Tilden
DBP – 20	Duy Tran
DBP – 21	Shannon Walker
DBP – 22	Keadrea Wilson

SECONDARY PREVENTION OF RHEUMATIC HEART DISEASE (RHD) IN ETHIOPIA

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Background: The prevalence of rheumatic heart disease (RHD) continues to increase in low and middle-income countries like Ethiopia. Ethiopia has one of the highest prevalence of childhood RDH in the world. Despite this, the country has no national strategic guidelines for the prevention, treatment, and control of acute rheumatic fever (ARF) and RHD in children. There is no data on the status of secondary prophylaxis in exclusively children with RHD. Generating local data is essential to design an effective prevention and control strategy. This study aimed to describe the status of secondary prophylaxis of RHD in Ethiopian children with RHD.

Methods: A multi-center, cross-sectional study was conducted. Children aged 3-17 years with an echocardiogram-based diagnosis of RHD were included. Those with congenital heart disease and a recent diagnosis of RHD (<1 year) were excluded. Good adherence was defined as 80% completion of at least 80% of prophylaxis prescriptions within the previous year. The primary outcome measure was adherence to secondary prophylaxis of RHD, expressed as a proportion. Covariates include patient socio-demographics (e.g., age, sex, household size, household income, rural/urban residence), type and severity of RHD, history of recurrence of ARF. Students' chi-square test and t-test for difference in means were used to assess for differences among categorical and continuous variables respectively. A P value < 0.05 was considered statistically significant.

Results: A total of 264 patients were included. The mean age was 13±2.6 years. The majority were females (54%) and resided in rural areas (62%). Severe aortic/mitral disease was seen in 75% of the cases. Intramuscular benzathine penicillin (BPG) (76%) and oral Amoxicillin (24%) were the prophylaxis of choice. About 16% of patients met the criteria for self-reported low adherence. Patients on amoxicillin had lower adherence compared to those on BPG (24% vs13%, P=0.049). Those with low adherence were mostly males (P=0.046), older (13.7±2 vs 12.8±2.7, P=0.046), and has a longer mean duration of prophylaxis (59.2±34 vs 48.7±31, P=0.027). Recurrence of ARF was seen in 17% of patients. The amoxicillin group had a high rate of ARF recurrence (21% vs 15%, P<0.01). Running out of medication (38%) and the COVID-19 pandemic (26%) was the common reasons for low adherence.

Conclusion: Poor adherence is prevalent in Ethiopian children with RHD. Amoxicillin is suboptimal prophylaxis associated with a high rate of low adherence and recurrence. The majority of patients have severe valve disease signifying a higher rate of recurrent ARF.

Mentors: Muktar Aliyu, MD, MPH, DrPH and Jonathan Soslow, MD, MSCI

PEDIATRIC CYSTIC FIBROSIS AND THE RELATIONSHIP BETWEEN GASTROINTESTINAL MUCINS, THE MICROBOME, AND INFLAMMATION

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Objective: Cystic fibrosis (CF) is an inherited disease characterized by abnormal transport of chloride across secretory epithelia resulting in thickened, viscous mucus. Although often considered a pediatric pulmonary disease, patients with CF have significant gastrointestinal comorbidities including growth failure, vitamin malabsorption, meconium ileus, and constipation. It has been postulated that the same pathophysiologic triad of mucus obstruction, infection, and inflammation that causes disease in the airways also causes disease in the CF intestines. However, the link between CTFR dysfunction and the mucus phenotype, and its relationship with both the gastrointestinal microbiome and intestinal inflammation, are poorly understood. The objective of our study is to better define the role of intestinal mucus production in pediatric CF patients in relationship to the gastrointestinal microbiome and colonic inflammation.

Study Design: The study is a prospective observational study of pediatric patients actively being treated at Monroe Carell Jr. Children's Hospital at Vanderbilt for the diagnosis of CF. Patients were recruited during inpatient and outpatient visits and, after consent, provided a stool sample. Samples from healthy pediatric patient were obtained through a collaborative with the Centers for Disease Control and Prevention (CDC) and used as controls. Crude mucus was extracted from 0.1 grams of stool and dot blots were performed to assess adherent mucins MUC1, 3 and 4 and secreted mucin MUC2. Intestinal inflammation was evaluated through an enzyme immunoassay for calprotectin and the intestinal microbiome through 16S rRNA sequencing.

Results: Stool samples were collected from a total of 107 CF patients (53 females, 54 males) and 5 healthy controls. In controls and CF patients, MUC2 was found in the highest abundance, followed by MUC1>MUC4>MUC3. Compared to healthy controls, CF patients exhibited a trend towards decreased MUC1 and MUC2 and a trend towards increased MUC4. No changes were observed with MUC3. Calprotectin levels were significantly elevated in CF patients compared to HC patients. Controlling for antibiotic exposure, the relationship between samples from healthy controls and CF outpatients strengthened. Stool samples have been submitted for 16S rRNA sequencing and results are expected soon.

Conclusions: Transmembrane and secretory mucins are altered in the gastrointestinal tract of children with CF. CF patients have increased levels of MUC4 and this finding is associated with increased levels of intestinal neutrophilic inflammation. Elevated MUC4 has also been demonstrated in patients with inflammatory bowel disease, further supporting the link between the mucus layer and inflammation. Further studies are needed in to characterize the link between CTFR dysfunction, the mucus phenotype, and its relationship with the gastrointestinal microbiome.

Mentor: Maribeth Nicholson, MD, MPH

NEBULIZED ALBUTEROL DELIVERY IS ASSOCIATED WITH DECREASED SKELETAL MUSCLE STRENGTH IN COMPARISON WITH METERED-DOSE INHALER DELIVERY

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Objective: Acute asthma exacerbations are a frequent cause for pediatric ED visits in North America. Albuterol, a mainstay of treatment, leads to intracellular shift of potassium and temporary hypokalemia. Whole body hypokalemia causes skeletal muscle weakness; however, it is not known whether albuterol use is associated with skeletal muscle weakness. Albuterol delivered via metered-dose inhaler (MDI) or nebulizer results in comparable efficacy, however nebulized doses are higher. We sought to determine if treatment with nebulized albuterol is associated with decreased skeletal muscle strength when compared to treatment with MDI.

Study Design: We recruited children aged 5-17 years who presented to the ED with acute asthma exacerbation and received MDI (Ventolin®, 90 mcg/puff) or continuous nebulized (10 mg/hr) albuterol. Participants performed 3 strength measurements with a digital hand-dynamometer (Lafayette 5030D1) before and 1-hour after initiation of albuterol treatment. Asthma characteristics, Acute Asthma Severity Research Score (AAIRS), total dose and delivery method were recorded. We used the Wilcoxon rank sum method and multivariable linear regression to examine associations of delivery method with skeletal muscle strength change.

Results: A total of 50 participants received albuterol by MDI (n=40) or nebulizer (n=10) during the first hour of treatment, with median [IQR] MDI albuterol dose 8 [4, 8] puffs (720 mcg median total dose) and nebulized dose of 10 mg. In univariate analyses, change of skeletal muscle strength was 2.4 [-5, 13] % after MDI and -7.8 [-23.3, 5.1; range] % after nebulized albuterol ($p = 0.036$, Wilcoxon rank sum, Figure 1). In the multivariable linear regression model, nebulized albuterol was associated with a -12.9 [95% CI -27.6, -0.2, $p= 0.014$] % change of skeletal muscle strength in comparison with MDI albuterol, after adjusting for age and pre-treatment AAIRS severity.

Conclusions: Nebulized albuterol is associated with decreased skeletal muscle strength during asthma exacerbations, whereas albuterol administration via MDI is not. Additionally, there was notable variability of skeletal muscle strength change after nebulization (IQR -23.3, 5.1]. In children with greater decreases this may be clinically meaningful and treatment with MDI over nebulization may be beneficial when either route is deemed clinically appropriate.

Mentor: Donald Arnold, MD, MPH

CARDIOPULMONARY ALTERATIONS IN FORMER PRETERM INFANTS

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Objective: Prematurity complicates approximately 10% of U.S. births, with over 400,000 premature infants born each year. Among those born prematurely, extremely low gestational age neonates (ELGANs; born before 28 weeks gestation) are at risk for significant morbidities, including bronchopulmonary dysplasia, the most common lung disease of infancy. While the impact of bronchopulmonary dysplasia on pulmonary function in survivors of preterm birth throughout life is well described, the effect of prematurity on the pulmonary vasculature and cardiac function remains understudied. Recent data suggest that survivors of late prematurity are at high risk to develop persistent right ventricular hypertrophy and dysfunction as young adults, with a recent small study demonstrating that 45% of healthy adult survivors of prematurity met criteria for pulmonary hypertension. The risk of cardiopulmonary compromise may be amplified for individuals born at earlier gestational ages, and the ELGANs of the current era have not been studied beyond infancy.

Study Design: In a cohort study of former ELGANs using cardiac magnetic resonance imaging (CMR), we are testing the hypothesis that presumably healthy former ELGANs have detectable cardiopulmonary abnormalities in mid-childhood. Cases are defined as ELGANs between the ages of 9 and 17 years; controls are healthy subjects born at term in the same age range. Subjects are examined in the pediatric clinical research center, provide a urine sample, and undergo CMR. The primary endpoint is the ratio of right to left ventricular end diastolic volume (RVEDV:LVEDV), which is a surrogate marker for pulmonary vascular resistance by CMR. Secondary endpoints include 6-minute walk test, quality of life including the Peds QL Cardiac Questionnaire, markers of oxidant stress (urinary isoprostanes and isofuranes), and clinical metrics including height, weight, resting heart rate, and blood pressure.

Results: Since February 2020, 34 subjects have completed the study (12 cases and 22 controls). Of the remaining 26 study subjects needed for completion, 19 (11 cases and 8 controls) are scheduled for an upcoming study visit, leaving 7 additional subjects needed. CMR data analysis and investigator unblinding will be performed upon completion of study enrollment. In addition, urine samples will be sent for isoprostane and isofuran levels to VUMC Eicosanoid Core Laboratory.

Conclusion: Growing data in young adults born premature with no history of adult cardiopulmonary disease suggest a high prevalence of occult pulmonary vascular disease characterized by elevated pulmonary vascular pressure, stiffness, and RV dysfunction. Yet, key opportunities remain which this study will address, including: (a) identify the timing of these changes relevant to the pediatric life course; and (b) identify specific, potentially modifiable targets for therapeutic interventions in mid-childhood or even younger (e.g., infancy) to prevent or treat morphologic and functional cardiopulmonary impairments before adulthood.

Mentor: Eric Austin, MD (eric.austin@vumc.org)

THREE-DIMENSIONAL FUNCTIONAL ASSESSMENTS OF NEUTROPHILS IN SPECIAL PEDIATRIC POPULATIONS

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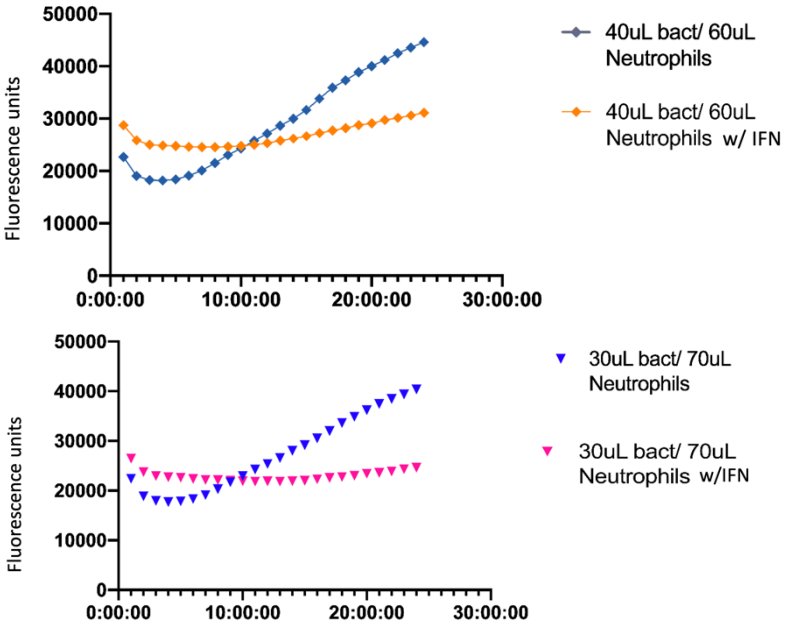
Mentor: Isaac Thomsen, MD, MSCI (isaac.thomsen@vumc.org)

Objectives: The overall objective of this study is to define the specific mechanisms by which neutrophils function in preterm are deficient, and to determine whether interferon-gamma (IFN-g) supplementation improves neutrophil function.

Study Design: Working within an IRB-approved protocol for each population, we are enrolling infants (both term and preterm, gestational age <34 weeks) and obtaining whole blood micro-samples for the isolation of unperturbed neutrophils using immunomagnetics. We are assessing and quantifying each step of neutrophil function using a novel assay involving the use of a fibrin matrix (a more physiologic and three-dimensional environment compared with standard in vitro or culture-based assays).

Results: We observed significant and reproducible differences in neutrophil-mediated killing of S. aureus in a 3D fibrin matrix with and without IFN. With a ratio of 40uL of fluorescent-labeled (GFP)-*Staphylococcus aureus* to 60uL neonatal neutrophils (1x10^6/mL), with and without IFN-g, we observed a mean difference of 3789.9 fluorescence units (95% CI 28.9, 7551), $p<0.05$, representing significantly enhanced phagocytosis after addition of interferon. Similarly, with a ratio of 30uL of GFP-Staphylococcus aureus to 70 uL neonatal neutrophils, the effect was similar, with a mean difference of 4699.5 fluorescence units (95% CI 1722.3, 7676.6), $p=0.003$ (Fig 2).

Conclusions: During an ongoing assessment of the mechanisms of neutrophil dysfunction in the neonatal (Term vs preterm) populations, we have so far observed significant differences in the migration and phagocytic ability of neonatal neutrophils, greatly enhanced by the addition of IFN-g in term infant neutrophils. Ongoing work will determine whether this remains true for preterm-infant neutrophils as well and will further delineate mechanisms of these differences. This may suggest an opportunity for interferon-based immunomodulation in certain situations for this population at high-risk for invasive bacterial infections.



BVES AND RSK1 IN THE INTESTINAL EPITHELIUM

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Background: Inflammatory bowel disease (IBD) affects 3 million adults and between 100 and 200 per 100 000 children in the United States.[1,2] The incidence of this heterogeneous disease is increasing, yet it is unclear why.[1] The pathological mechanisms underlying IBD are multifactorial, but it is agreed that epithelial barrier dysfunction is a key contributor to the development and chronicity of IBD.[3] Our lab has previously demonstrated how blood vessel epicardial substance (BVES), a three pass transmembrane tight junction-associated protein, plays an important role in the maintenance of the intestinal epithelial barrier.[4] Through yeast two-hybrid screening we discovered a protein interaction between BVES and RSK1, a serine/threonine protein kinase responsible for signal transduction in the MAPK/ERK pathway. This finding was significant because of RSK1's known role in cellular proliferation, survival, and motility; all of which are critical to epithelial barrier competency. RSK1 has previously implicated in human diseases affecting the cardiovascular and renal systems but has not yet been linked to disorders or important physiologic processes within the intestinal epithelium.[5]
Objective: The aim of this project was to determine whether BVES's role in intestinal epithelial barrier homeostasis is RSK1 dependent.
Methods and Results: After yeast two-hybrid screening, we confirmed an interaction of BVES with RSK1 through co-immunoprecipitation of endogenous RSK1 with cmyc-tagged mouse BVES in HEK293t. We then demonstrated an inverse relationship in BVES/RSK1 protein expression in HCT116 and CACO2 BBE where both si and sh BVES knockdown correlated with increased total expression and phosphorylation of RSK1. We also demonstrated this inverse relationship using immunohistochemistry to examine RSK1 cellular localization within the colon crypt of wild type (WT) and *BVES*$^{-/-}$ mice. WT colon crypts revealed RSK1 near the cell membrane and almost exclusively in terminally differentiated cells on the apical side of the colon, while *Bves*$^{-/-}$ crypts showed RSK1 in the cytoplasm throughout the entirety of the crypt including the crypt base. Next, to determine whether this inverse relationship existed in patients with Crohn's disease, we utilized RNA-scope to measure *BVES* transcript in samples from patients with colitis. We found that *BVES* was increased in human colitis ($M = 0.295$, $SD = 0.039$) as compared with adjacent normal colon epithelium ($M = 0.187$, $SD = 0.061$) ($p < .01$). We then demonstrated this same finding in a separate RNA-seq data set from patients with pediatric ulcerative colitis. There was a similar relationship between *BVES* and *RSK1* transcripts where more severe colitis was associated with increasing *BVES* transcripts and reduction in *RSK1* transcripts. In order to demonstrate the functional effect of this inverse relationship we disrupted RSK1 activity in CACO2 BBE and mouse colonoids using an ATP-competitive N-terminal kinase domain inhibitor, BI-D1870, and are currently investigating the effect this has on various surrogate markers of epithelial barrier function.[6]
Conclusion: BVES and RSK1 interact at the protein level and have an inverse relationship as demonstrated in *BVES*$^{-/-}$ mice and in patients with IBD. Ongoing studies are needed to determine its biological significance.

Mentor: Christopher S. Williams, MD, PhD (christopher.s.williams@vumc.org)

A Pragmatic Low Carbohydrate Diet Intervention Changes Neither Carbohydrate Consumption nor Glycemia Appreciably in Adolescents and Young Adults with Type 1 Diabetes

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Objective: Low carbohydrate diets (LCDs) have gained popularity as a purported tool to mitigate postprandial hyperglycemia among highly motivated patients with type 1 diabetes (T1DM). Despite this enthusiasm, no randomized, prospective study has quantified how much an LCD improves glycemic outcomes compared with a standard carbohydrate diet (SCD) in pediatric T1DM. Moreover, no study to date has addressed the feasibility of an LCD intervention in this population. We aimed to assess the feasibility and quantify the impact of an LCD intervention in adolescents and young adults with T1DM.

Study Design: We randomized 24 patients with T1DM aged 13-21 years who were using both an insulin pump and continuous glucose monitor (CGM) to one of three interventions. Participants received in-person instructions to consume an LCD (25-35% of daily caloric intake from carbohydrates, n=7) or an equicaloric SCD (45-65% carbohydrate, n=8) or underwent a general diabetes education program with no specific recommendations regarding diet (control, n=9). This study design allowed us to differentiate between the effect of each diet's composition (by comparing LCD vs. SCD) and the effect of receiving any prescriptive diet (by comparing the control intervention against each diet). The 12-week intervention included 3 education sessions via telephone that reiterated the nutrition or general diabetes education and reinforcing text messages 2-4 times per week. Glycemic outcomes included change in HbA1c and CGM parameters.

Results: Carbohydrate consumption decreased minimally in the LCD group (from 135 ± 65 to 126 ± 34 grams), remained nearly the same in the SCD group (from 145 ± 79 to 144 ± 66 grams), and increased in the control group (from 164 ± 91 to 184 ± 94 grams). HbA1c went from 7.9 ± 1.1% to 8.2 ± 1.2% in the LCD group, from 7.8 ± 0.7% to 8.2 ± 0.8% in the SCD group, and from 8.1 ± 0.5 to 8.0 ± 0.8% in the control group with no statistically significant differences between any group (p=0.53). Similarly, there were no discernable differences between groups in terms of CGM time in range (p = 0.44), glycemic variability (p=0.37), or total daily dose per unit body weight of insulin (p=0.86).

Conclusions: Despite ongoing nutritional instruction and education reinforcement that exceeded typical pediatric diabetes clinical care, carbohydrate intake did not appreciably change from baseline within any group. Likewise, all glycemic measures remained clinically unchanged. These findings suggest that nutrition education alone is insufficient to produce dietary change for adolescent patients with T1DM. While small, uncontrolled studies have suggested that an LCD can improve glycemia, it is possible that participants were highly motivated at baseline, not only to consistently restrict dietary carbohydrate consumption but in all aspects of diabetes self-care. This pragmatic study suggests that clinic-based LCD interventions are not acceptable for most adolescents and unlikely to improve glycemia in the general adolescent T1DM population.

Mentor: Justin Gregory, MD, MSCI

Galectin-3: A Novel Biomarker Predicting the Success of Staged Single Ventricle Palliation

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Objective: Patients with Hypoplastic Left Heart Syndrome (HLHS) are a vulnerable population requiring at least three surgeries to survive into adulthood with an average mortality rate of 12% between the first and second surgery. Utilizing biomarkers that predict which patients are at highest risk is needed. Three biomarkers – high sensitivity C-reactive protein (hsCRP), NT-pro-B-type Natriuretic protein (NT-proBNP) and Galectin-3 (Gal-3) have proven useful in predicting adverse outcomes in the adult population. Little is known about the combined predictive value in patients with HLHS. We sought to

1) Establish Medians and Standard Deviations (SD) for hsCRP, NT-proBNP and Gal-3 levels in patients with HLHS prior to their first palliative surgery.
2) Determine if pre-surgical baseline hsCRP, NT-proBNP and Gal-3 levels have predictive value in the long-term success of completion of Bidirectional Glenn (BDG).

Study Design: We conducted a retrospective cohort study using existing serum specimens to evaluate the utility of pre-surgical hsCRP, NT-pro-BNP and Gal-3 levels as predictors of post-surgical outcome. The primary outcome was successful completion of second palliative surgery. ROC curves of the biomarkers were generated individually and in combination for our outcome of interest.

Results: Serum samples from 77 neonates with single ventricle physiology between 2011 and 2018 were included. The median values for hsCRP, NT-proBNP and Gal-3 were 0.5 mg/L [0.5, 1.6], 13263 pg/ml [5804, 29,767] and 6.4 ng/mL [4.5, 9.6] respectively. Successful patients had a median Gal-3 level of 5.5 ng/mL [4.5, 8.0] compared to patients who failed to reach Stage II palliation had a median Gal-3 value of 8.0 ng/mL [5.6, 10.8], p=0.02. ROC curve of Gal-3 on success was 0.663; 95% CI (0.529 – 0.797).

Conclusions: We are the first to describe the mean baseline levels of hsCRP and Gal-3 in patients with HLHS prior to their first palliative surgery. Our findings support that baseline Gal-3 level may independently predict long term successful completion of second palliative surgery.
The Project Galectin-3: A Novel Biomarker Predicting the Success of Staged Single Ventricle Palliation was supported by VICTR Grants

Mentor: Dr. Mark Clay

Comparison of the Prevalence of Pediatric Poisonings Before, During and After COVID-19 Shelter-in-place

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Objective: The Governor of Tennessee signed an executive order for residents to shelter-in-place from April 2-30, 2020. This study evaluates associations between demographic and clinical characteristics of Tennessee children and the months of poison exposure surrounding the COVID-19 shelter-in-place order.

Study Design: This retrospective serial cross-sectional study used demographic and clinical data from calls to the Tennessee Poison Center about poison exposures in Tennessee children 0-17 years before (March 2020), during (April 2020), and after (May 2020) the declared shelter-in-place. We subtracted 2020 Census estimates of the resident population aged ≥18 years from the total resident population in Tennessee to calculate the total number of children aged <18 years. Aggregate call count and population data were used to derive the prevalence estimates of poisoning for each month. Month, acute care need (yes/no), gender (male/female), age group (≤5 years/6-12 years/13-17 years), and intentionality (unintentional/intentional) were examined using descriptive statistics and chi-square tests. Statistical significance was set at $p < 0.05$.

Results: Tennessee prevalence estimates of poison exposures among children was 0.147% in March 2020, 0.139% in April 2020, and 0.151% in May 2020. There was statistically significant evidence of association between reported poisoning exposure and month ($\chi 2 = 7.59$; $p = 0.023$). Among 6615 poison exposures, most were unintentional (93.1%), in children 0-5 years old (81.8%), in males (54.2%), and did not need acute care (86.4%). There was statistically significant evidence of an association between the need for acute care and month ($\chi^2 = 6.90$; $p = 0.032$).

Conclusion: The prevalence of reported pediatric poisoning was associated with timing of the COVID-19 shelter-in-place order between March and May 2020. The need for acute care was associated with the month of poison exposure surrounding the COVID-19 shelter-in-place order. Further epidemiological study into confounding variables and relations between demographic and clinical characteristics related to poison exposure across this period is needed.

Mentor: Rebecca E. Bruccoleri; rebecca.e.bruccoleri@vumc.org

OUTCOMES ASSOCIATED WITH A PEDIATRIC ICU SEDATION WEANING PROTOCOL

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Objective: Pediatric intensive care unit (PICU) patients are exposed to sedative infusions as a means of safety and analgesia. Adverse effects associated with the use of sedation have been well described, yet there is a paucity of data regarding the optimal method of weaning sedation in the PICU population. We sought to create a risk stratified sedation weaning protocol and compare patient outcomes before and after implementation.

Study Design: This observational cohort study compares outcomes pre- and post-implementation of a risk stratified sedation weaning protocol in a medical/surgical PICU. The protocol provides weaning guidance based on duration and dosage of sedation infusions and was implemented in September 2019. Patients requiring opioid, benzodiazepine and/or dexmedetomidine infusions were weaned per protocol, except patients receiving chronic sedation medications or end of life patients. Total duration of sedation wean, ICU length of stay, and withdrawal assessment tool (WAT) scores, were collected by chart review for a 12-month period pre- and post-protocol. In an interrupted time series analysis, we fit linear models for each outcome to evaluate the effect of the sedation weaning protocol. Both the main effect and interaction with time were evaluated.

Results: There were 49 patients pre and 47 patients post-protocol implementation. Mean opioid wean duration pre-protocol was 16.9 days (SD 20.9) and 12.1 days (SD 10.5) post-protocol (p= 0.18), with a change in slope (interaction with time) of -0.01 days per day. This slope value correlates to an average reduction of opioid wean duration by 0.01 days for each day during the protocol period. The pre-protocol mean benzodiazepine wean duration was 14.1 days (SD 14.5) vs. 11.0 days (SD 13.5) post-protocol (p=0.42), with a slope of -0.05 days per day. For dexmedetomidine/clonidine, pre-protocol mean wean duration was 15.9 days (SD 20.7) vs. 8.1 days (SD 9.2) post-protocol (p=0.04), with a slope of -0.03 days per day. Average WAT score was 2.1 (SD 0.95) pre vs. 1.8 (SD 0.95) post, with a slope of 0.003 points per day. ICU length of stay mean was 23.9 days (SD 21.8) pre vs. 25.6 days (SD 24.4) post, with a slope of -0.006 days per day.

Conclusion: Implementation of a risk stratified sedation weaning protocol in the PICU resulted in a decrease in average total duration of sedation wean for opioids, benzodiazepines and dexmedetomidine/clonidine. The association of protocol implementation with WAT scores and ICU length of stay requires further exploration.

Mentor: Kristina Betters, MD, FAAP (kristina.betters@vumc.org)

ASSESSMENT OF PERFORMANCE OF NON-TECHNICAL SKILLS BY MEDICAL STUDENTS IN SIMULATED SCENARIOS

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Objective: Caring for patients in an emergency requires non-technical skills such as teamwork, communication, and task management. However, medical training has traditionally focused on technical skills and discrete medical knowledge. Simulation has been used to train residents, fellows, and attendings in non-technical skills but not medical students. The Behaviorally Anchored Rating Scale (BARS) is a validated scoring system for non-technical skills that is simple and requires two hours of training. It has never been studied in the medical student population. Our objective was to determine the inter- and intra-rater reliability of the BARS when used in the medical student population to assess non-technical skills.

Study Design: We created a simulation curriculum for medical students during their core pediatric clerkship at a single medical school site. Students performed in teams caring for patients in simulated pediatric emergencies. The academic year is broken into five blocks. While we planned to complete the simulation curriculum in blocks 1, 3, and 5 to sample students throughout the academic year, block 5 was cancelled due to the coronavirus pandemic. Three content experts were trained to use the BARS. Experts reviewed video recordings of the student-performed simulations and assigned BARS scores for 4 performance components (Situational Awareness, Decision-Making, Communication, and Teamwork) for the team leader and for the team as a whole. Krippendorff's alpha with ordinal difference was calculated for the liability measurement of components of the BARS.

Results: 30 medical students participated and had recordings available for review. Inter- and intra-rater reliability for each performance score were, respectively: Individual Situational Awareness (0.488, 0.638), Individual Decision-Making (0.529, 0.691), Individual Communication (0.347, 0.473), Individual Teamwork (0.414, 0.466), Team Situational Awareness (0.450, 0.593), Team Decision-Making (0.423, 0.703), Team Communication (0.256, 0.517), and Team Teamwork (0.415, 0.490). None of the components met criteria for good inter- or intra-rater reliability.

Conclusion: This pilot study with a small number of subjects demonstrated limited reliability when assessing medical students during their core pediatric clerkship. Given the unique needs of this population, a modified or new objective scoring system for assessing non-technical skills may be needed for medical students.

Mentor: Dr. Daisy Ciener

Spirometry and functional muscle assessments in patients with Duchenne Muscular Dystrophy

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Objective: Duchenne Muscular Dystrophy (DMD), an X-linked recessive disorder caused by mutations in the dystrophin gene, is the most common neuromuscular disorder in childhood. Patients with DMD develop significant cardiopulmonary sequelae, with most of these sequelae occurring in non-ambulatory patients. Newer assessment tools such as accelerometry and quantitative muscle testing (QMT) can provide information on skeletal muscle capability, regardless of ambulatory status. At this time, the relationship between these evaluations and respiratory status is unknown. We sought to assess the correlation between spirometry measurements and functional muscle assessments such as accelerometry and QMT.

Study Design: Forty-nine patients with DMD were enrolled and underwent accelerometry and QMT at baseline, 1-year and 2-year clinic visits. Past medical history, current and previous medications, and ambulatory status were collected at each visit. Patients wore an Actigraph GT3X accelerometer on their dominant wrist and ankle for 7 days and 24 hours per day. The QMT assessment performed at each visit utilized a handheld myometer with arm, leg and total QMT scores being recorded and indexed to age. Temporally associated pulmonary function testing was obtained from the electronic medical record. Spearman correlation coefficient was used to assess the relationship between spirometry and functional muscle testing.

Results: At the initial clinic visit, forced vital capacity percent predicted (FVC%p) showed strong correlation with aspects of both ankle and wrist accelerometry. Awake ankle VM had the highest relationship with FVC%p (rho=0.8091, p = 0.0026), although all recordings showed either strong or moderate correlation. While FEV_1%p showed a similar pattern to FVC%p, the overall strength of the relationship between accelerometry and spirometry was not as strong with all ankle and wrist recordings demonstrating a moderate correlation with FEV_1%p. Maximal inspiratory pressure showed strong correlation with both wrist VM/min (rho=0.7697, p=0.009) and ankle VM/min (rho=0.7818, p=0.0075). There was variable correlation with MEP and accelerometry measures over the course of the study with no consistent findings. Arm and leg QMT exhibited moderate to strong correlation with all spirometry measurements. Total QMT count had strong correlation with both FVC%p (rho=0.7735, p=0.0001) and FEV_1%p (rho=0.7006, p=0.0008). Despite lower number of patients performing MIP and MEP, both had a strong relationship with total arm QMT counts (rho=0.7792, p =0.0079 and rho=0.8160, p=0.004, respectively). Longitudinal monitoring demonstrated a steady decline in accelerometry VM counts and QMT measurements.

Conclusions: Lung function, specifically FVC%p and FEV_1%p, has strong correlation with both upper and lower extremity skeletal muscle functional testing. This relationship was not affected by steroid use or ambulatory status. These data provide insight into the pathogenesis of pulmonary function decline and highlight the need for further exploration of the connection between skeletal muscle and respiratory disease progression.

Mentor: Jon Soslow, MD, MSCI (jonathan.h.soslow@vumc.org)

Developing and Testing of Clinical Decision Support for Neonatal Ventilator Management

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Objective: Mechanical ventilation (MV) in the Neonatal Intensive Care Unit (NICU) is a life-saving therapy but associated with multiple comorbidities. Compared to pressure-limited ventilation, volume-targeted ventilation (VTV) is associated with lower rates of bronchopulmonary dysplasia and intraventricular hemorrhage and fewer days of MV. Only 42% of neonatologists report use of VTV as the primary mode. The slow clinical adoption of VTV may be due to clinicians' lack of knowledge of appropriate tidal volumes (TV) for a patient's weight and disease. Clinical decision support (CDS) tools could be used to facilitate appropriate use of VTV. We hypothesize that incremental implementation of CDS will increase the usage of recommended initial tidal volume settings.

Study Design: We are conducting a prospective comparative interrupted time series study in two medical centers with the primary intervention being the implementation of a CDS tool designed to improve the use of evidence-based TV. The CDS was designed as a report targeted at the ordering clinicians in the ventilator order set to recommend the initial TV during the first MV course. The primary outcome is the use of an initial TV consistent with evidence-based guidelines stratified by birth weight: <700 grams (5.5 – 6 ml/kg), 700 – 1249 grams (4.5 – 5 ml/kg), and ≥1250 grams (4 – 4.5 ml/kg). Beginning in October 2018, we collected the initial TV/kg for ventilated patients in the Vanderbilt University and Jackson-Madison County General Hospital NICUs using data from the electronic health record and the mechanical ventilators. We included all infants who received conventional MV during the first two weeks of age and had ventilation data available. In both units, evidenced-based TV guidelines were introduced in July 2020. In September 2020, we implemented the CDS tool in the Vanderbilt University NICU with the Jackson NICU serving as the control NICU in our study. We plan to analyze the primary outcome using segmented regression. Sensitivity analysis will be performed to adjust for rounding errors in TV/kg by adjusting the recommended ranges by +/- 0.3 ml/kg.

Results: Since the beginning of data collection, 1,113 ventilated neonates were admitted to the Vanderbilt NICUs and 521/1,113 (47%) met study inclusion criteria. The pre-CDS cohort had 62/448 (14%) infants with TV within the recommended range, and the post-CDS cohort had 8/73 (11%) of the initial TV/kg within range. In sensitivity analyses, 114/448 (25%) infants in the pre-CDS cohort and 17/73 (23%) infants in the post-CDS cohort had TV within the target range.

Conclusions: In preliminary analyses, our CDS intervention has not improved evidenced-based use of initial TV. The CDS may be improved by implementing it in different places in the clinical workflow or targeting different clinical roles such as respiratory therapists. Work is ongoing to test deployment of decision support at different places in the MV workflow. The interrupted time series design will allow for analyses of additional interventions.

Primary Mentor**:** L. Dupree Hatch MD, MPH (leon.d.hatch@vumc.org)

Echocardiographic findings in adolescents presenting for activity clearance following COVID-19 infection

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Background: The incidence of abnormal cardiac function in adolescents seeking a return to physical activity following COVID-19 infection is not well known. We reviewed our center's experience with this cohort, including retrospective myocardial strain imaging using speckle-tracking echocardiography.

Methods: We reviewed outpatient transthoracic echocardiograms obtained between 11/01/2020 and 12/31/2020 for clearance for return to activity/sports of patients aged 12-18 with a history of mild or moderate COVID infection. Patients had at least one of the following: chest pain, shortness of breath, palpitations, syncope, or abnormal electrocardiogram. Two groups with similar complaints but without a known history of COVID referred during 1.) the same timeframe and 2.) the pre-COVID era were reviewed for comparison. Univariable analysis was performed using Spearman's rho and Wilcoxon rank-sum test. Multivariable analysis utilized linear and logistic regression following multiple imputation of minimal missing data.

Results: Our study groups are detailed in Table 1. In the prior COVID group, in addition to 1 patient with depressed left ventricular ejection fraction (LV EF), 6 others had abnormal LV global longitudinal strain (GLS) despite normal LV EF. In an intragroup analysis of the COVID cohort, controlling for age and gender, the presence of chest pain correlated with a decrease in global circumferential strain rate (GCSR) and trended in that direction for global circumferential strain (GCS). An abnormal electrocardiogram correlated with decreased right ventricular GLS and free wall strain. In intergroup univariable analysis, prior COVID was associated with lower LV GCS and GCSR and right ventricular GLS and free wall strain (Table 2). The association for LV GCS and GCSR was also observed when controlling for age, gender, and LV EF but disappeared upon adding presence of any symptoms and of an abnormal electrocardiogram as independent variables. No association between prior COVID and right ventricular strain metrics was seen in multivariable analysis.

Conclusions: In adolescents with prior mild or moderate COVID illness, ventricular function by conventional metrics is not categorically different from those without a COVID history. The presence of symptoms or an abnormal electrocardiogram may contribute to prediction of decreased myocardial strain; the clinical significance of abnormal strain with preserved EF is unclear. Future studies may further elucidate whether myocardial strain indices augment conventional metrics in evaluating cardiac risk in this cohort.

Table 1: Select Demographics of 3 Study Groups[1,2]

	Prior COVID+ (n = 38)	No COVID (n =54)	Pre-COVID (n = 36)	p-value COVID+ vs. All[3]	p-value COVID+ vs. Pre-
Age, years	15 (14.0 -16.0)	15 (14.3 – 15.7)	14.5 (12.9 – 16.1)	0.62	0.60
Male, %	57.9	44.4	36.1	0.29	0.07
Height, cm	168 (164.0 – 171.9)	167 (163.3 – 170.7)	164 (159.5 – 168.5)	0.44	0.10
Weight, kg	61.0 (56.5 – 65.5)	60.5 (56.7 – 64.3)	62.0 (55.5 – 68.5)	0.47	0.81
Systolic BP, mmHg	122 (118 – 126)	123 (119 – 126)	120 (116 – 123)	0.76	0.45
Diastolic BP, mmHg	65 (61 – 69)	67 (64 – 70)	64 (59 – 68)	0.75	0.68
Any symptoms, %	68.4	100	100	< **0.001**	< **0.001**
Borderline or abnormal ECG, %	23.7	33.3	27.8	0.52	0.79
Time since COVID-19 diagnosis, days	33.5 (22.0 – 45.0)	N/A	N/A	N/A	N/A

[1]Adapted from: Matsubara, et al. Echocardiographic findings in pediatrics multisystem inflammatory syndrome associated with COVID-19 in the United States. *JACC*. 2020;76(17):1947-61.
[2]For each of the 3 groups, the median values followed by bootstrapped 95% confidence intervals in parentheses are presented.
[3]Comparison of subjects with a prior history of COVID compared to all those without a history of COVID, whether from COVID era or prior.

The novel role of extracellular superoxide dismutase in the function of TNFα- and integrin-signaling in pulmonary endothelium

Michael R Miller, Hyehun Choi, Fred Lamb

BACKGROUND: Tumor necrosis factor-α (TNFα) signaling requires superoxide (O_2^-•) to be produced extracellularly by NADPH oxidase 1 (Nox1). It remains unclear how this redox signal is transduced into activation of intracellular signaling pathways. Due to the critical nature of TNFα and reactive oxygen signaling in the development of inflammatory pathologies like acute respiratory distress syndrome (ARDS), we sought to determine their role in endothelial cells, a crucial mediator of basement membrane integrity that is disrupted in ARDS. Mouse studies have shown that conditional knockout of the extracellular isoform of superoxide dismutase (SOD3), which metabolizes O_2^-• to hydrogen peroxide causes a rapid and lethal ARDS phenotype. We previously demonstrated that TNFα signaling is modulated by SOD3 as siRNA knockdown of SOD3 in vascular smooth muscle cells (VSMCs) decreased downstream Mitogen-Activated Protein Kinase (MAPK) phosphorylation and NF-κB activation by TNFα. In contrast, siSOD3 enhanced transactivation of integrin receptors as reflected by focal adhesion kinase (FAK) phosphorylation.

METHODS: We studied MAPK and FAK signaling responses to TNFα in cultured human lung microvascular endothelial cells (HMVEC-L) and also characterized effects of TNFα on these cells in a model of lung endothelial barrier integrity.

RESULTS: SOD3 was expressed at lower levels in endothelial cells compared to VSMCs. However, similar to VSMCs, knockdown of SOD3 with siRNA decreased TNFα-induced phosphorylation of the JNK MAPK but increased FAK phosphorylation, consistent with impaired canonical TNFα receptor signaling but enhanced transactivation of integrin receptors. Overexpression of SOD3 with adenovirus produced the inverse result (increased JNK and decreased FAK phosphorylation). These data suggest a modulatory role for SOD3 both in canonical TNFα-receptor and in integrin-mediated signaling in endothelial cells. Finally, utilizing a transendothelial resistance (TEER) assay as an *in vitro* model of vascular permeability we found that SOD3 is required for formation of a fully tight monolayer while loss of SOD3 provides reduces TNFα-mediated endothelial injury.

CONCLUSIONS: These data demonstrate that SOD3 plays a critical role in endothelial cell function and modifies TNFα signaling in a complex manner. It may play a previously unrecognized role in preventing transactivation of integrins in the setting of inflammation. SOD3 may downregulate cytokine signaling during acute lung inflammation, thereby reducing capillary leak and preventing ARDS. This work therefore presents a novel connection of ecSOD and TNFα signaling that could likely play a key role in the pathological inflammation seen in ARDS.

UNCOVERING UNEXPECTED ACTIONS OF TOLERANCE-INDUCING ANTIBODY THERAPY

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Objective: Treatment with monoclonal antibody anti-CD45RB induces permanent, antigen-specific tolerance in mice and non-human primates. In this study, we establish a model using immune reconstitution of immunodeficient hosts to study its mechanism in a defined setting.

Study Design: Female NOD.Rag -/- mice were injected intraperitoneally with pooled B6 splenocytes adjusted to 5 x 10^6 T cells per recipient mouse. The mice were then enrolled into two separate arms. The first group received no further therapy. The second group was given 100 ug of monoclonal antibody to CD45RB on days 0, 1, 3, 5, and 7 after splenocyte transplantation. Mice were housed in sterile environments and monitored at regular intervals for signs of aGVHD. Mice were sacrificed at day 7 and spleens were harvested from the recipient mice for evaluation by flow cytometry at the Vanderbilt Flow Cytometry Core Facility.

Results: Unexpectedly, mice given the tolerogenic αCD45RB died before day 11 post-transplantation from exacerbated GVHD as opposed to mice given no treatment that all lived longer than 35 days. On gross examination, treated mice had noticeable splenomegaly as compared to the untreated population. Flow cytometry preformed at day 7 after splenocyte transplantation showed increased B6 CD4+ T cells and decreased B6 CD8+ T cells in the treated population.

Conclusion: These results suggest that the tolerogenic agent can also promote immune activation; using our controlled system we will be able to determine how this activation relates to specific cells of both the mouse soma and adaptive immune systems including roles of cell activation and secreted factors. Analysis of cell subsets and activation markers by flow cytometry as well as cytokine and chemokine concentration fluctuations throughout the course of therapy are ongoing to elucidate the mechanism of action. We are also investigating the contribution of the murine background to the outcome of immune therapy treatment (B6.Rag -/- mice receiving splenocytes from C3H donors) as well as a B6 x BALB/c F1 generation receiving splenocytes from B6 donors. These investigations will reveal new insights into the conditions required for immune therapies to favor regulation over activation of the immune system.

Mentor: Daniel Moore, MD, PhD, daniel.moore@vumc.org

THE USE OF ANTI-FACTOR XA ASSAYS IN A COMPREHENSIVE PEDIATRIC EXTRACORPOREAL MEMBRANE OXYGENATION ANTICOAGULATION PROTOCOL IS ASSOCIATED WITH INCREASED SURVIVAL AND SIGNIFICANT COST SAVINGS

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Objective: We augmented our standard extracorporeal membrane oxygenation laboratory protocol to include anti-factor Xa assays, thromboelastography, and antithrombin measurements. We sought to determine if we had fewer hemorrhagic complications, reduced blood product usage, and increased circuit life as well as quantify the cost savings realized for the potential decrease in blood product utilization.

Study Design: We performed a retrospective chart review to determine outcomes for patients placed on ECMO prior to and after the initiation of our anticoagulation laboratory protocol. A total of 663 consecutive ECMO runs were evaluated from January 1, 2007 to June 30, 2018. Of these patients, 252 were on ECMO prior to initiation of the anticoagulation laboratory protocol on September 1, 2011, and 411 patients were on ECMO after initiation of the protocol. There were no major changes to our extracorporeal membrane oxygenation circuit or changes to our transfusion threshold during this continuous study period.

Results: Transfusion utilization data revealed statistically significant decreases in almost all blood components and a savings in blood component inflation-adjusted acquisition costs of 31% bringing total blood product cost savings to $309,905 per year. In addition, there was an increase in survival to hospital discharge from 45% to 56% associated with the initiation of the protocol ($p = 0.004$).

Conclusions: Our data indicate that implementation of a standardized ECMO anticoagulation protocol, which titrates unfractionated heparin infusions based on anti-factor Xa assays, is associated with reduced blood product utilization, significant cost savings, and increased patient survival. Future prospective evaluation is needed to establish an anti-factor Xa assay-driven ECMO anticoagulation strategy as both clinically superior and cost-effective.

A QUALITATIVE ASSESSMENT OF NON-CLINICAL DRIVERS OF ANTIMICROBIAL PRESCRIBING FOR PEDIATRIC PATIENTS IN DIVERSE AMBULATORY SETTINGS

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Objective: Antimicrobial prescribing rates vary across ambulatory settings and clinician types. We sought to identify and compare non-clinical drivers of antimicrobial prescribing for children across diverse outpatient settings.

Study Design: We recruited physicians and advanced practice providers (APPs) working in primary care, urgent care (walk-in and pediatric after-hours clinics), and retail health clinics affiliated with Vanderbilt University Medical Center (VUMC). Interviews were conducted using a semi-structured guide focused on eliciting priorities and modifying factors when prescribing antibiotics in the outpatient setting. Analysis is ongoing using inductive methods. This study was approved with a waiver of consent by the VUMC IRB.

Results: Among the 55 clinicians interviewed, 28 (51%) were APPs. Forty-five (82%) interviews were conducted by telephone. In a closed-ended question, most clinicians (75%) identified "guideline recommended" as the primary factor informing their prescribing decisions. Clinicians perceived that providing guideline concordant care was determined by a complex interaction of patient-, clinician-, and environmental-level factors (**Figure**). Parental expectations were a primary factor influencing prescribing behavior and were frequently informed by previous experiences with antibiotics. Consistency in management practices among providers working in a specific clinic and across other outpatient clinics in the community was perceived to shape parental expectations for antibiotics. Shaping parental expectations in a way that aligns with guidelines is a process that happens over time ("a slow burn"), rather than being a one-time event.

Conclusions: Across diverse outpatient settings, both physicians and APPs describe guidelines as the most important factor influencing antibiotic prescribing. Outpatient antibiotic stewardship programs should focus on provision of and adherence to guidelines in order to standardize prescribing practices across settings which may, over time, shape parental expectations regarding antibiotics. Implications for public health policy include improving shared systems of patient care information and provision of guidelines across healthcare systems.

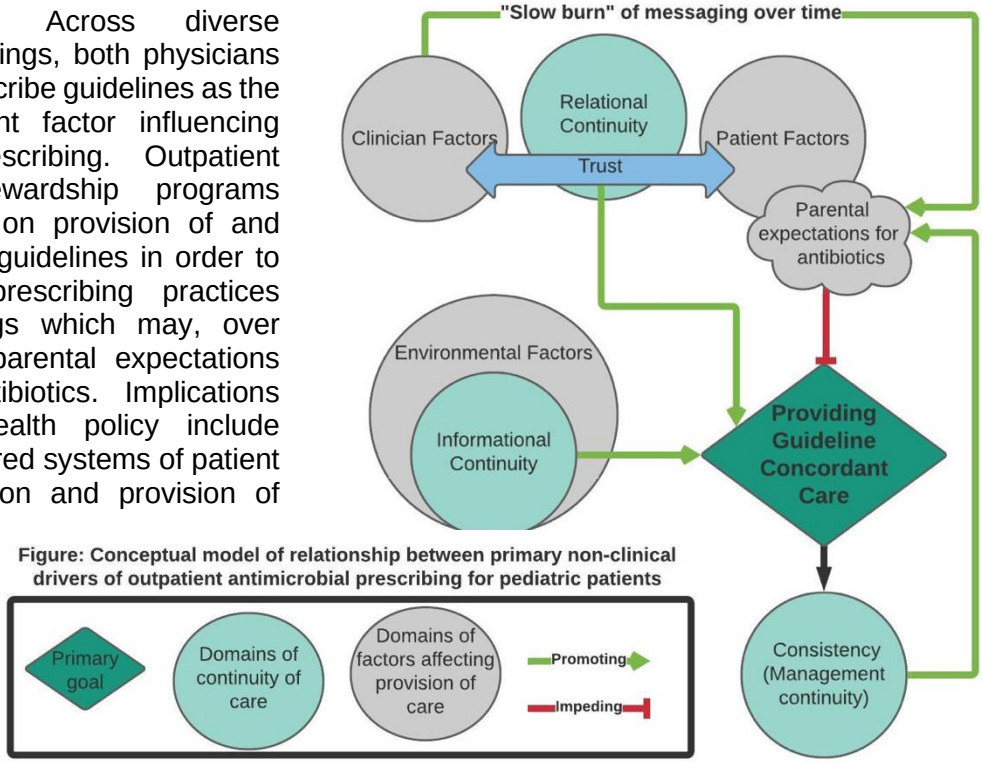

Figure: Conceptual model of relationship between primary non-clinical drivers of outpatient antimicrobial prescribing for pediatric patients

PARENTAL PRIMARY LANGUAGE, ACCESS TO CARE, AND DEVELOPMENTAL DELAYS IN NEONATES

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Objectives: Premature infants are at high risk for developmental delay, however, access to developmental services after hospital discharge may improve those outcomes. Previous research suggests families where English is not their first language, also known as non-English primary language (NEPL), face barriers in accessing medical care and have poorer clinical outcomes compared to English speakers. Despite the potential enhanced risk NEPL premature infants face for adverse outcomes, the literature evaluating this population is sparse. In a national sample, we sought to determine if premature infants of Spanish speaking caregivers had poorer reported access to medical care and higher prevalence of developmental delays when compared to infants of English-speaking caregivers.

Study Design: In this retrospective cross-sectional study we used data from the 2016-2018 National Survey of Children's Health (NSCH). Our outcomes were (1) caregiver report of access to care, including a comprehensive medical home and developmental therapies, and (2) caregiver reported prevalence of combined developmental delay, defined as: difficulty using hands or with coordination (if child < 5 years), difficulty walking/climbing stairs or dressing (6-17 years), speech delay, and/or general developmental delay. We also examined descriptive differences in infant characteristics (e.g., birth weight, sex), social determinates of health (e.g., maternal education, marital status, insurance status) and timing of parental immigration to the US. All analyses used survey weights to provide nationally representative estimates.

Results: Our weighted sample represented a total of 68.2 million children, 7.9 million of which were born preterm (prior to 37 weeks gestation). Children born to Spanish speakers were more likely to be uninsured ($p<0.001$), more likely to have public health insurance ($p<0.001$), and less likely to be born in the US ($p<0.001$). Spanish primary language caregivers were less likely to have a high school education ($p<0.001$) than English speaking caregivers and were more likely to be born outside the US ($p<0.001$). Children born to Spanish speakers were less likely to have a comprehensive medical home compared to English speakers (29.2% vs. 49.4%, $p<0.001$; see Table 1). Spanish speaking families were also less likely to report that their child received developmental therapies ($p=0.007$) or had a special education plan ($p<0.001$). Spanish speakers were more likely than English speaking caregivers to report their child having difficulty with coordination (29.6% vs 12.6%, $p=0.04$) and difficulty using hands (28.4% vs 10.5%, $p=0.02$). There were no statistically significant differences between Spanish speaking families and English-speaking families in regard to speech delays or general developmental delays.

Conclusions: In a national sample, children in Spanish speaking families were more likely to report that their child had specific developmental delays, and that they faced greater barriers to accessing healthcare, including a comprehensive medical home and developmental therapies. Our results suggest that children in these families may be at higher risk of experiencing certain early developmental delays without appropriate care. Addressing language-based barriers may be important to establishing equitable outcomes for vulnerable children.

Demographic Factors and Transition Timing Predict Successful Transition to Adult Care in Emerging Adults with Type 1 Diabetes.

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Objective: Adolescents and emerging adults (those 18-30 years-old) with type 1 diabetes mellitus (T1D) are a particularly vulnerable group among those with this chronic disease. Due to acute complications of diabetes such as hypoglycemia and ketoacidosis, 20–29-year-old males with T1D face a three-fold increase in mortality, and females in this age group have a six-fold increase compared to the general population. Even among patients who avoid acute complications, studies have repeatedly shown that the average hemoglobin A1c (HbA1c) among young adults is the highest among any age cohort of patients with T1D. This worsening of T1D control leads to accelerated micro- and macrovascular disease and hastens the onset of complications in patients even if they subsequently improve diabetes control. The current study used visit-level EHR data to analyze demographic and visit data to determine predictors of transition within our health care system.

Study Design: This is a retrospective cohort study of 4185 patients with T1D were included in this analysis if they had a clinic visit at any of the pediatric diabetes clinic locations at least once in three consecutive calendar years between 2004 and 2020. Provider assigned diagnosis was used to differentiate patients with T1D which previous work suggests is a highly specific predictor of diabetes diagnosis. Patient encounters in the pediatric endocrinology clinics, adult outpatient clinics as well as admissions at either the pediatric or adult hospital were included in the visit level analysis. The primary outcome of interest was completion of at least 1 adult endocrinology clinic visit for T1D care. Patients were then compared using descriptive statistics and logistic regression to analyze demographic factors and key disease metrics including HbA1c and hospital admission differing between the two groups. Secondary analyses were conducted to explore the timing, duration, and trajectories of HbA1c across transition.

Results: In our analysis, patients who completed transition to adult care within our health system, were about one fifth (aOR 0.22 95%CI: 0.15 – 0.32) as likely to have private insurance compared to patients in the pediatric clinic who did not transition. No other significant demographic differences were found between these two groups. Among those who did transition, the median time from last pediatric to the first adult visit was 190 days (IQR 100 – 542) and only 53.15% of patients completed transition within 6 months. Additionally, among those who completed transition, later age of transition was significantly associated with a higher likelihood of transitioning within 6 months (aOR 1.41 95%Ci:1.25 – 1.58). Other demographic or insurance factors were not significantly associated with completing transition within the recommended interval.

Conclusions: Our data suggest that insurance is the most significant barrier to transition from our pediatric to adult clinics for patients with T1D. Importantly, even among those who do ultimately receive care from our adult clinics, we identified significant gaps in care which may lead to an increased risk of both short and long-term complications for these patients. Improving our processes for transitions from pediatric to adult care may serve to close these gaps in care and ultimately improve care for emerging adults with T1D.

Differences in total body surface area assessments of burns between emergency medical service providers and burn physicians

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Objective: Burns are routinely assessed at the scene of the incident by Emergency Medical Services (EMS) providers. The initial management of burns is based on the calculation of the extent of the injury, reported as percent total body surface area (TBSA). While many methods have been developed to aid medical personnel in determining TBSA, to our knowledge none have been shown to be reliably accurate in the field. We sought to evaluate discrepancies that exist during the estimation of TBSA between pre-hospital providers and burn team physicians. We hypothesize that pre-hospital providers generally overestimate rates and degree of burns compared with burn surgeons.

Study Design: We performed a retrospective, cross-sectional study evaluating patients presenting over a 3 year period to an academic, university medical center serving as the regional burn center. Patients were included if they were brought directly from scene by the regional EMS to either the adult or pediatric emergency departments and were evaluated by a burn physician. We excluded patients who transferred from another facility, were brought in by another EMS or were not evaluated by a burn physician. We recorded patient age, gender, race, etiology of burn, percent TBSA, hospital length of stay, patient disposition, and patient's medical insurance. Continuous variables were reported using medians and interquartile ranges (IQR). Agreement in estimated TBSA between pre-hospital providers and burn physicians were compared using Bland-Altman plots.

Results: A total of 147 patients were included, with 95 (65%) male, 67 (45.6%) Caucasian, 62 (42.2%) without insurance, median age 35 (IQR 27) and 25 patients were under 12 years of age. The most common etiology of burns was due to hot liquid 39, (26.5%). Bland-Altman plots evaluating 2nd and 3rd degree burns separately and combined demonstrated that, as burns involved more TBSA, agreement decreased between EMD providers and burn physicians.

Conclusion: Agreement between pre-hospital providers and burn physicians decreased as total body surface areas of burns increased. This finding reaffirms the need for more standardized education and training for all medical personnel.

Mentor: Rebecca Kidd, MD (Rebecca.s.kidd@vumc.org)

DEVELOPMENT, VALIDATION, AND RANDOMIZED TRIAL OF A REAL-TIME RISK PREDICTION MODEL FOR PEDIATRIC VENOUS THROMBOEMBOLIC EVENTS

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Objective: Hospital-acquired venous thromboembolic events (HA-VTE) are increasing in pediatric populations. Given that risk prediction models can identify patients at risk for venous thromboembolism better than physician judgement alone, we developed and temporally validated a general pediatric risk prediction model from a large, single-center cohort. The goal was to create a model using only variables that are easily extracted from the electronic medical record (EMR), available at admission, and updated daily. To assess the utility of this model in identifying high-risk pediatric inpatients, we designed a randomized, pragmatic trial involving all pediatric admissions to Monroe Carrell Jr. Children's Hospital at Vanderbilt (MCJCHV).

Study Design: Data was extracted from the EMR on all admissions to MCJCHV from 1/1/2010 to 10/31/2017 for the derivation cohort (IRB#180116), and from 11/2/2017 to 1/31/2020 for the temporal validation cohort (IRB#200334). Cases were identified based on ICD-9/10 codes for acute thromboses; a subset of records were used to confirm the accuracy of diagnosis codes. Potential predictors were identified *a priori* from previous studies and known risk factors for VTE development. Final variables for the logistic regression model were based on data reduction methods including univariate analysis significance, availability in routine medical records, and assessment of collinearity between variables. A randomized, pragmatic trial was developed to include all pediatric patients admitted to MCJCHV (IRB#201629). Patients are randomized on admission via an automatic process built into the EMR. Risk scores are automatically calculated and displayed in descending order in an EMR Report. Patients in the intervention arm with elevated VTE risk scores receive an additional review by a hematology provider, and subsequent recommendations (including prophylactic anticoagulation) are discussed with admitting teams.

Results: A total of 111,352 admission encounters were analyzed in the derivation cohort, and 44,138 admission encounters in the temporal validation cohort. The variables with the highest adjusted odds ratio for developing VTE were a history of thrombosis (OR 8.7, 95%CI 6.6 – 11.3, $p<0.01$), presence of a central venous line (OR 4.9, 95%CI 4.0 – 5.8, $p<0.01$), and cardiology consultation (OR 4.0, 95%CI 3.3 – 4.8, $p<0.01$). Additional significant variables included whether a blood gas was performed, ID consultation, age, MCHC, RDW, lactate, cancer diagnosis, and whether surgery was performed. The final VTE model includes these eleven variables and yielded excellent discriminatory power (c-statistic = 0.908). The VTE model was applied to the validation data, without re-estimating the coefficients, and remained strong (c-statistic = 0.904). The pragmatic trial is ongoing, with data being collected in REDCap.

Conclusions: We have developed and validated a risk prediction model that can identify pediatric patients in real-time, starting at admission, who are at increased risk for VTE development. A randomized, pragmatic trial is currently in progress to assess the predictive efficacy of the VTE risk prediction model. We anticipate that identifying patients with elevated risk will increase the number of patients appropriately started on prophylactic anticoagulation and will decrease the overall incidence of pediatric VTE.

Mentors: Allison Wheeler (allison.p.wheeler@vumc.org) and Buddy Creech (buddy.creech@vumc.org)

THE ASSOCIATION OF DURATION OF BREASTFEEDING AND CHILDHOOD ASTHMA OUTCOMES

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Objective: Asthma is common in children and early postnatal exposures, such as infant diet, may influence subsequent asthma development. Therefore, in a large, racially diverse cohort of mother-child dyads, we investigated whether the duration of *any* and *exclusive* breastfeeding was associated with decreased asthma.

Study Design: We conducted a longitudinal study of 2,105 dyads, enrolled in the ECHO PATHWAYS consortium that includes the CANDLE (births 2006-2011), TIDES (births 2010-2012) and GAPPS (births 2011-2015) prospective prenatal cohorts. The duration of *any* breastfeeding was characterized by maternal report at 4-6 year follow-up (none to <2, 2-4, 5-6 and >6 months). Duration of *exclusive* breastfeeding was characterized similarly among those who breastfed. Parent report of *ever asthma* and *current asthma* were ascertained at 4-6 years using the International Study of Asthma and Allergies in Childhood questionnaire. *Current asthma* was defined as having $\geq$2 of the following: wheeze in past 12 months, ever asthma, or asthma-specific medication use in past 12-24 months. We used multivariable logistic regression to determine associations of breastfeeding exposures and child asthma outcomes adjusting for factors, including maternal race, smoking, education, asthma history, and child sex, delivery route, and gestational age.

Results: Overall, 38% of women were Black and 57% had a college/technical degree or higher. The proportions of children breastfed at none to <2 months, 2-4 months, 5-6 months and > 6 months were 33%, 13%, 9% and 45%, respectively. The prevalence of *ever asthma* and *current asthma* were both 12%. Increased duration of *any breastfeeding* tended to be associated with decreased *ever asthma* for the 2-4 (aOR [95%CI] 0.78 [0.49, 1.24]), 5-6 (0.72 [0.42,1.25]) and >6 (0.65 [0.43,0.97]) month groups, when compared to the none to <2 month group. Associations for *any* breastfeeding and *current* asthma were not significant. The relative odds of both *ever* and *current asthma* decreased with increasing duration of *exclusive* breastfeeding. For example, for current asthma the aORs [95% CIs] were 0.64 [0.41, 1.02], 0.61 [0.38, 0.98], and 0.52 [0.31, 0.87] for children exclusively breastfed for 2-4 months, 5- 6 months, and >6 months, respectively, compared to the none to <2 month group.

Conclusion: Longer duration of *exclusive* breastfeeding was associated with decreased odds of asthma outcomes at ~age 4-6 years in this racially diverse cohort. Future work will investigate the association of breastfeeding and wheeze/asthma phenotypes and lung function in older children.

Mentor: Dr. Kecia Carroll, kecia.carroll@vumc.org

Poster Presentations

P – 1	Katherine Black
P – 2	Jonathan Boyd
P – 3	David Brooks
P – 4	Jordan Busing
P – 5	Alison Carroll
P – 6	Matthew Clark
P – 7	Katie Conover
P – 8	Amber Cooke
P – 9	Brittany Cowfer
P – 10	Emily Deaton
P – 11	Kimberly Ferguson
P – 12	Barron Frazier
P – 13	Kelsey Gastineau
P – 14	Alice Hackett
P – 15	Mary Grace Hash
P – 16	Kasey Jackson
P – 17	Caitlin Jacowski
P – 18	Shani Jones
P – 19	Elizabeth Keiner
P – 20	Rachel Klausner
P – 21	Lauren Klein
P – 22	Jennifer Laws
P – 23	Genesis Licona
P – 24	Kelsey Malloy
P – 25	Kathy Mendieta
P – 26	Nicholas Negretti
P – 27	Jenesis Negron
P – 28	Sourav Panja
P – 29	Kevin Patel
P – 30	Stephanie Rolsma
P – 31	Katelyn Rossow
P – 32	Bryce Schuler
P – 33	Natalia Sidhu
P – 34	Adam Skaff
P – 35	Hannah Smith
P – 36	Lauren Starnes
P – 37	Sudeep Sunthankar
P – 38	Isabel Vallecillo-Viejo
P – 39	Jennifer Walker
P – 40	Claci Walls
P – 41	Allison Weatherly
P – 42	Kaitlin Williamson
P – 43	Ryan Wolf

Risk Factors for Post-Operative Nausea and Vomiting after Tonsillectomy in the Pediatric Population

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Background: Ondansetron is an anti-nausea and anti-emetic medication which is used for post-operative nausea and vomiting (PONV) in the pediatric population. Tonsillectomy is a commonly performed procedure in the pediatric population that is highly emetogenic. Anti-emetics, such as ondansetron, are routinely given to prevent PONV though they are not always effective. Certain clinical characteristics such as age are known to increase risk of PONV. In addition, ondansetron may be rapidly metabolized by the enzyme CYP2D6, which may decrease the therapeutic effect. Identification of patients at high risk for ondansetron inefficacy may enable substitution of alternate agents such as granisetron or use of adjunctive therapies to better prevent PONV.

Objectives: Our primary objective is to evaluate clinical risk factors for PONV after receiving ondansetron and undergoing tonsillectomy in the pediatric population. Our secondary objective is to look at risk factors for worse outcomes after tonsillectomy as measured by increased emergency department visits and time spent in the post-anesthesia care unit (PACU).

Study Design: We performed a retrospective cohort study using BioVU, the VUMC DNA biorepository linked to de-identified electronic medical records. Individuals in BioVU who were less than 18 years old at the time of tonsillectomy and received ondansetron on the day of surgery were included. Exclusion criteria were a diagnosis of cyclical vomiting syndrome, or prior surgical procedures such as gastrectomy, gastrostomy, fundoplication, esophageal surgery, or bronchoscopy. Peri-operative data were used to determine the primary outcome of PONV defined as needing a dose of an anti-emetic or anti-nausea medication while in the PACU. Time spent in the PACU, emergency department (ED) visits within 7 days of surgery, and continued nausea and vomiting on follow-up phone calls after 24 hours were also recorded using a secure REDCap study database.

Results: 733 individuals were included in our study. PONV was seen in 126 (17.2%). The median age was significantly higher in those children that experienced PONV than those without at 7.6 years [interquartile range (IQR 4.0-9.6)] vs 6.3 years (IQR 5.5-11.2), respectively ($p = 0.005$). Females were more likely to experience PONV, (58.0% vs 45.1%; $p=0.009$). There were no differences in race or ethnicity between the two groups. The American Society of Anesthesiology (ASA) score, an objective way to evaluate pre-operative co-morbidities, did not differ between groups. The time spent under anesthesia was significantly shorter in subjects with PONV compared to subjects without PONV [45 (IQR 37-57) vs 55 min (IQR 41-64), $p<0.001$]. Those with PONV spent significantly less time in PACU phase 1 but longer in phase 2, where patients must tolerate oral intake prior to discharge. Total time spent in the PACU was longer in those with PONV compared to without PONV at 175 min vs 140 min ($p=0.003$). There were no differences in immediate PONV and ED visits within a week or continued nausea or vomiting on follow-up phone call between groups.

Conclusion: Increased age and female sex were associated with increased risk of PONV. Those with PONV spent less time under anesthesia and spent a longer time recovering in the PACU. Since ondansetron is metabolized by the polymorphic CYP2D6 enzyme, our next analyses will include CYP2D6 activity scores to determine the impact of genetic variation on ondansetron response.

Application of Kern's 6-Step Approach to the Pediatric Critical Care Resident Rotation

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Objective: To systematically revise the PCCM rotation curriculum applying Kern's Six Steps to increase resident comfort and knowledge of pediatric critical illness.[1]

Study Design: Curriculum assessment was through pre and post rotation Redcap surveys and board style questions in a prospective cohort.[2,3]

Methods: Literature review revealed no comprehensive pediatric critical care curricula. Rotation feedback from the prior 3 years was reviewed and demonstrated opportunities for improvement in the didactic curriculum, especially regarding lack of time and frequent interruptions. Faculty and residents were surveyed to identify which objectives required revision, barriers to education, and comfort with commonly encountered diagnoses; this data were used as a targeted needs assessment to update learning objectives in conjunction with ABP content specifications.

Resident orientation was also modified to include basics of mechanical ventilation. Other formal teaching opportunities during the rotation included 12 formal didactics and 4 high fidelity simulation scenarios. Residents completed pre and post rotation quizzes of board style questions.

Results: Seventy-five percent of eligible participants completed the surveys and rotation quizzes.

Pretest scores were equal before and after implementation (71%). Post test scores were 65% and 68%; this was not statistically different by t test. Residents scored as expected on PREP questions (74% expected, 70% by residents).

Residents reported improved comfort in PCCM topics post rotation. When comparing pre and post intervention groups, no difference was found in post rotation comfort attributable to the new curriculum. Residents cited frequent interruptions as a barrier to learning less often post intervention (from 81 to 67%).

Conclusions: A PCCM curriculum was revised but did not statistically improve resident comfort or knowledge compared to the prior curriculum. Future directions include review of simulations to assess learner's actions in clinical scenarios and implementation of case based didactics.

EVALUATION OF POINT-OF-CARE GLUCOSE ANALYSIS IN ILL NEONATES

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Objective: Accurate glucose monitoring is vitally important in neonatal intensive care units (NICUs) as neonates are at risk for hypoglycemia and hyperglycemia, which carry increased risk for morbidity and mortality. Clinicians in the NICU use point-of-care (POC) glucose meters, such as the ACCU-CHEK® Inform II, to measure glucose because these devices require very small volumes of blood (<1.0 µL) and quickly provide results. Although frequently used in neonates, POC glucose meters were developed for use in adults. Studies in adults have demonstrated several confounders may impact the accuracy of POC glucose meter results. Additionally, the studies examining neonatal POC glucose meters are limited to healthy, term infants. Therefore, extrapolating these data to preterm and/or ill neonates may be inappropriate. We will quantify the difference in plasma glucose measurements between aliquots taken from the same whole blood sample, one assayed by the ACCU-CHEK® Inform II versus one by laboratory analysis. Additionally, we will determine the difference between capillary glucose (measured by POC testing) and plasma glucose simultaneously drawn from the umbilical artery (measured by lab-based analysis).

Design: We will simultaneously collect blood samples from the capillary circulation via heel puncture and from the arterial circulation by intravascular catheter. Using the arterial sample, we will quantify the difference in glucose concentrations measured by the ACCU-CHEK® Inform II versus the lab-based YSI glucose analyzer. We will then determine the difference between capillary glucose (measured by the ACCU-CHEK® Inform II) and arterial plasma glucose (measured by the YSI analyzer). Using the YSI analyzer, we will measure plasma lactate as a surrogate for tissue perfusion. We will also quantify plasma triglyceride, albumin, and immunoglobulin G levels, as these large molecules have the potential to confound POC glucose results.

Results: We are planning a study with 60 participants. Prior neonatal data indicate that the variance in the difference in glucose concentrations obtained from capillary blood using the ACCU-CHEK® Inform II versus from whole blood obtained using laboratory analysis is normally distributed with standard deviation of 4.7 mg/dL. We will be able to detect a true mean difference between POC and reference glucose measurements of 2.0 mg/dL with probability (power) of 0.9. To assess the agreement between the ACCU-CHEK® Inform II and YSI Analyzer, statistical analysis will be performed using Bland-Altman analysis. We will also perform a series of multivariable linear regression analyses with mean bias as the dependent variable. A sample size of 60 patients allows for as many as 6 covariates to be studied in our multilinear regression model.

Conclusion: This study will provide valuable insight on the reliability of the ACCU-CHEK® Inform II glucose meter in preterm and ill neonates and potentially will impact how clinicians in the NICU use this device for glycemic monitoring.

VARIABLE COURSE OF RECOVERY AND ASSOCIATED GUT MICROBIAL CHANGES FOLLOWING FECAL MICROBIOTA TRANSPLANTATION FOR D-LACTIC ACIDOSIS IN CHILDREN

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Objective: D-lactic acidosis (D-LA) is a rare but severe condition that can occur in humans with short bowel syndrome (SBS). Patients present with metabolic acidosis and altered mental status due to increased production and absorption of D-lactate generated by colonic bacterial fermentation. Conventional treatments include aggressive rehydration, dietary carbohydrate restriction, and antibiotics. Bulik-Sullivan et al. recently described a 7-yearold patient at UNC-Chapel Hill (UNC) with gastroschisis and recurrent D-LA successfully treated with FMT. We present a 12-year-old with recurrent D-LA secondary to SBS due to a mesenteric lymphangioma, who failed conventional treatments and was treated with FMT at Vanderbilt Children's Hospital (VCH) and compare clinical course and composition/function of intestinal microbiota following FMT in the UNC and VCH patients.

Study Design: Patients were admitted to their respective pediatric gastroenterology services, PPPI therapy was initiated, and bowel lavage prep was completed. Donor FMT material was obtained from OpenBiome (FMT Upper Delivery Microbiota Preparation, FMP30) and administered via naso-enteric tube. Stool samples were obtained pre-FMT and approximately one week and one month post-FMT. Stool microbial DNA was extracted and analyzed using previously described metagenomic shotgun sequencing techniques. Kraken2 classification system was employed for microbial taxonomic analysis, and HUMAnN2 pipeline was used to profile the presence and abundance of metabolic pathways.

Results: Both patients ultimately had improved clinical outcomes; however, clinical courses differed. The UNC patient had no further recurrences of D-LA after FMT. The VCH patient had one recurrence 27 days post-FMT. Following FMT, there was shift in each patient's stool microbiota profile. FMT donor material exhibited a higher microbial taxonomic diversity than both recipients' stool samples, before and after FMT. *Lactobacillus* was the dominant genus in the UNC patient's stool samples both before and after FMT. Relative abundance of *Escherichia/Shigella* increased and *Veillonella* spp. decreased after FMT. *Lactobacillus* was dominant before and after FMT in the VCH patient. Relative abundance of *Veillonella* spp. in this patient's stool initially decreased after FMT, but later increased. Whole-genome metagenomic shotgun sequencing revealed the relative abundance of the relative abundance of adenosine ribonucleotides de novo biosynthesis (MetaCyc PWY-7219) decreased in the UNC recipient's

stool after FMT compared to that patient's pre-FMT stool. The opposite effect was observed in the VCH patient where relative abundance of this pathway increased.

Conclusions: FMT may be an efficacious and safe treatment option for children suffering from recurrent D- LA. Clinical course and microbial changes may vary considerably from patient to patient. It appears that FMT does alter the composition of the fecal microbiota in patients with D-LA, though not necessarily in a consistent manner. Importantly, microbial metabolic pathways are also impacted by FMT, which may be critical for achieving desired clinical outcomes.

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DECREASING PRE-PROCEDURAL FASTING TIMES IN HOSPITALIZED CHILDREN

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Objective: Prolonged pre-procedural fasting in children has been associated with increased distress, decreased patient and family satisfaction with care, and increased adverse effects on patient hemodynamic stability. Despite published practice guidelines which recommend a clear liquid fasting time of 2 hours, children at our hospital frequently experience fasting times exceeding recommendations**.** We sought to decrease clear liquid fasting time prior to anesthesia from an average of 10 hours 13 minutes to less than 5 hours for patients admitted to the hospital medicine service by September 2020.

Study Design: We included all children admitted to our hospital medicine service with an NPO (*nil per os*) order associated with a procedure requiring anesthesia from November 2, 2017 to the present. Children with fasting times <2 hours or >24 hours were excluded. The Model for Improvement was used to test interventions based on 5 key drivers aimed at reducing fasting times (Figure 1). Interventions included nursing and provider education on hospital NPO guidelines, use of standardized language (SmartPhrase) in the electronic health record (EHR) NPO order (Figure 2), and a change to the NPO order format hospital-wide (Figure 3). We used statistical process control charts to study all measures. The primary measure was the average time from documented clear liquid fasting end time to anesthesia start time. The process measure was the percent of NPO orders that included a documented clear liquid fasting end time. Balancing measures were aspiration events and case delays/cancellations due to pre-procedural fasting violations.

Results: Baseline data from November 2017 to September 2019 included 579 NPO/anesthesia events revealing an average NPO time of 10 hours 13 minutes. Shortly after implementation of a SmartPhrase in the EHR NPO order, there was special cause variation resulting in a centerline shift from a mean of 10 hours 13 minutes to 6 hours 36 minutes (Figure 4) as well as an increase in the process measure of percent of orders with a clear liquid fasting end time to 65.9% (Figure 5). There have been two NPO violations during the intervention period.

Conclusion: Creating and sharing a SmartPhrase was associated with a simultaneous improvement in our primary outcome and process measures reducing clear liquid fasting times. We hypothesize that a recent higher reliability intervention—a change to the hospital-wide EHR NPO order—will be associated with a further reduction in pre-procedural fasting time for all hospitalized children.

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IMPROVING PNEUMOCOCCAL VACCINATION IN PATIENTS WITH CHILDHOOD SYSTEMIC LUPUS ERYTHEMATOSUS

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Objective: The project seeks to increase the percentage of patients with childhood Systemic Lupus Erythematosus (cSLE) seen in the Pediatric Rheumatology clinic who are fully compliant with pneumococcal vaccination from 20% to 85% by July 1, 2021.

Study Design: This is a quality improvement project following the Model for Improvement methodology. A team was assembled including Rheumatology fellow and attendings, Rheumatology nurses, Pharmacist and administrative staff. A key driver diagram was developed through group consensus and baseline data was collected regarding the frequency and type of pneumococcal vaccine given, as well as causes for missed vaccination. Pareto analysis was performed on the causes of missed vaccination and multiple PDSA cycles have been conducted using this information. Balancing measures of flu vaccination and accidental over vaccination have been recorded. The primary process measure has been the percentage of patients seen in the DOT6 Pediatric Rheumatology clinic who receive a pneumococcal vaccine that they are a candidate for.

Results: Baseline rates of pneumococcal vaccination were 20% for full compliance, 41% for PPSV23 vaccine and 29% for PCV13. PDSA cycle using a nursing led intervention demonstrated a statistically significant shift in the proportion of patients receiving vaccine per week as seen by 8 consecutive data points above the mean. Current rates of pneumococcal vaccination are 44% for full compliance, 50% for PPSV23 and 63% for PCV13.

Conclusion: Pneumococcal vaccination in patients with cSLE can be improved using nursing led interventions. This project is ongoing.

Mentor: Dr. Lisa Buckley, MS – lisa.buckley@vumc.org

SAFETY AND EFFICACY OF FECAL MICROBIOTA TRANSPLANTATION FOR RECURRENT *CLOSTRIDIOIDES DIFFICILE* INFECTION IN IMMUNOCOMPROMISED PEDIATRIC PATIENTS

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Objective: Several studies have reported safety and efficacy of fecal microbiota transplantation (FMT) in adult immunocompromised (IC) patients. FMT is also performed in pediatric IC patients, but the literature for this population is limited. The need for more robust data became more pressing after a safety alert was released concerning invasive infections in two IC adults after FMT, one of whom died. This multicenter retrospective series aimed to describe safety and efficacy of FMT for recurrent Clostridioides difficile infection (rCDI) in pediatric IC patients.

Study Design: We identified IC patients in our national pediatric FMT registry, who were treated with FMT for rCDI with minimum 12-week follow-up. We collected data using a 76-item survey that was completed for 72 patients at 9 centers, of which 42 subjects met inclusion criteria. We report FMT efficacy and adverse events.

Results: Our 42 subjects ranged from 18 months to 18 years old. Etiologies for IC included: solid organ transplantation (18), malignancy (12), primary immunodeficiency (10), or other chronic conditions (2). Success rate was 79% after first FMT and 86% after second FMT. Five post-FMT hospitalizations were likely FMT related. There were no deaths or infectious complications related to FMT.

Conclusions: The success rate of FMT for rCDI in this pediatric IC cohort aligned with adult literature. Absence of death or infection from FMT provides reassurance, although severe complications, including aspiration pneumonitis and intestinal perforation, highlight the need for heightened vigilance. We recommend a careful assessment of risk versus benefit prior to considering FMT in pediatric IC patients.

Mentor: Maribeth Nicholson, MD, MPH

Clinicians' Perspectives on Integrating a Parenting Assessment Tool into the Well Child Visit

Amber Cooke MD (Child Neurology), Kate Carlson MD (General Pediatrics), Merrill Stoppelbein APRN (General Pediatrics), Seth Scholer MD (General Pediatrics)

Objective: To determine clinicians' perspectives on integrating the QPA (quick parenting assessment) into the well child visit.

Design/Methods: In our clinic serving low income families, we routinely administer the QPA as part of the 15 and 30 month visits. The QPA is a brief survey assessing parenting strategies. The QPA takes approximately 1 minute for parents to complete. Clinicians were trained to interpret and respond to the QPA with a 15 minute presentation. For parents who were given a QPA as part of the well child visit, clinicians were invited to complete a survey focused on their perspectives on integrating the QPA into the visit. Key measures were 1) time needed for the clinician to review the QPA, 2) whether the QPA increased clinicians' objectivity (i.e., make fewer assumptions) in determining the level of support needed for the caregivers, 3) whether the QPA affected communications with the caregiver about parenting, and 3) whether the QPA added value to the well child visit.

Results: 111 surveys were completed by resident physicians (42%), nurse practitioners (32%), and attending physicians (26%). For 90 surveys, the clinician reported that the QPA was reviewed with the parent. Most QPA reviews (71/90; 79%) took 1 minute or less; 14% took 1-2 minutes and 7% took 3-5 minutes. For most QPA reviews, the clinician reported that the QPA increased objectivity to determine the level of parenting support needed (62%), facilitated communication about parenting (70%), and added value to the visit (60%).

Conclusion: A parenting assessment, when integrated into the 15 and 30 month well child visit, can be reviewed by clinicians with parents in less than three minutes for over 90% of encounters, can help clinicians offer higher precision parenting support, and can facilitate parent/clinician discussions about healthy discipline strategies. Our results have implications for mitigating ACEs and enhancing the pediatric primary care visit.

Mentor: Seth Scholer, seth.scholer@vumc.org

EFFECT OF TIME ON QUALITY OF PARENT-CHILD COMMUNICATION IN PEDIATRIC CANCER

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Objectives: High quality parent-child communication benefits children with advanced cancer, including reduction of child anxiety and distress and opportunities for active participation in treatment or end of life decision-making. Despite such benefits, many barriers exist. Little is known about the potential effect of time on the quality of parent-child communication throughout the illness trajectory. The objective of this study was to determine the effect of time since initial cancer diagnosis and relapse on quality of communication in children with advanced cancer and their parents.

Study Design: This secondary analysis utilized T1 data from a larger randomized controlled trial. Participants included children (7 to 17 years) with relapsed or refractory cancer and their parents, who spoke English, were not cognitively impaired, and had internet access. Children and parents completed the Parent-Adolescent Communication Scale (PACS), a 20-item measure of communication quality, with openness and problem subscales. Spearman's Rho coefficients assessed correlations between PACS scores and time since diagnosis/relapse.

Results: There was a statistically significant negative correlation between parent PACS scores and time since child's initial cancer diagnosis (Spearman's Rho = - .21, p = .02), indicating a tendency for overall worsening communication as time since diagnosis increased. There was a positive correlation between parent PACS problem scores and time since diagnosis (Spearman's Rho = + .22, p = .01), indicating more problematic communication as time since diagnosis increased. Correlations of time since relapse and PACS scores were small and not statistically significant.

Conclusions: Parent-child communication may worsen over time following a child's initial cancer diagnosis. Families may benefit from continued involvement of interdisciplinary teams, including psychologists, social workers, child life specialists, and palliative care providers, to support parent-child communication beyond the new-diagnosis period as the family encounters additional challenges of advanced childhood cancer.

Mentor: Terrah F. Akard, terrah.akard@vanderbilt.edu

ETHICAL DECISION-MAKING CLIMATE AND MORAL DISTRESS IN THE PEDIATRIC ICU

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Objective: Moral distress is an undermining source of anxiety and often burnout amongst medical providers. There is a paucity of data within the setting of the pediatric intensive care unit (PICU) and the pediatric cardiac intensive care unit (PCICU) in the multidisciplinary team members. The aim of this study is to understand the relationship of the ethical decision making climate and individual levels of moral distress. The hypothesis is that there will be a lower level of moral distress as measured by the Measure of Moral Distress in Healthcare providers (MMD-HP) in those with a higher perception of the ethical decision making environment as measured by the Ethical Decision Making Climate Questionnaire (EDMCQ) which includes topics such as end of life (EOL) care, physician leadership (PL), safety culture (SC) and job strain (JS). This study also evaluated whether or not demographic factors put an individual at increased risk for elevated moral distress.

Study Design: Single center, cross-sectional research study within the multidisciplinary team of the PICU and PCICU from February 1, 2020 to May 31, 2020. Each participant completed a demographic survey, ethics consult service survey, MMD-HP and EDMCQ.

Results: Results indicated a statistically significant inverse relationship between MMD-HP and the EOL factor with a probability of direction (PD) of 97.3% (> 97% probably existing relationship) and region of practical equivalence (ROPE) of 0.93% (<1% significant). No significant difference between role, age or religious beliefs.

Conclusions: Understanding the various factors that can be protective or put one at risk for moral distress is important to making a healthy work environment for all members of PICU and PCICU teams. Strategies to target improving patient end of life care and team member job strain may decrease moral distress, and thus potentially burnout, in all team members.

Mentor: Jessica Turnbull, MD, MA, jessica.m.turnbull@vumc.org

INTEGRIN α3β1 REGULATES AEC SURVIVAL AND DIFFERENTIATION DURING LUNG DEVELOPMENT

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Background: Cell-matrix interactions are essential for lung development. Alveolar epithelial cells (AECs) connect to the matrix through integrins, heterodimeric αβ proteins. We previously reported that β1 integrin is required for lung branching morphogenesis and alveolarization. Organogenesis of other branched organs requires Wnt signaling for epithelial cell function and ECM assembly. In the kidney, α3β1. one of the β1 containing integrins, regulates Wnt signaling, but the role of integrins in Wnt signaling in the lung remains undefined.

Objective: ***We hypothesize that α3β1 integrin is required for critical AEC functions during lung development through regulation of Wnt signaling***.

Study design: We deleted α3 in the lung epithelium at embryonic day 9.5 using Shh-Cre, (called $\alpha3^{Shh.Cre}$ mice) to specifically target to α3β1. Histological analysis and morphometry was quantified using ImageJ. Pulmonary function was assessed by FlexiVent. We performed Wnt arrays on EpCAM+ epithelial cells collected by FACS. We treated lung slices with XAV939, a Wnt inhibitor. We quantified AEC apoptosis by TUNEL assay, and AEC number and proliferation by pro-SP-C and Ki67 immunostain, respectively.

Results: P3 $\alpha3^{Shh.Cre}$ lungs exhibited thickened alveolar septa and decreased airspace number compared to $\alpha3^{f/f}$ control littermates, indicating impaired sacculation. P28 $\alpha3^{Shh.Cre}$ lungs exhibited increased mean linear intercept, increased AEC number/ hpf (64±5 $\alpha3^{Shh.Cre}$ AECs vs. 40±3 $\alpha3^{f/f}$ AECs, p <.05), and AEC differentiation defects indicated by co-expression of type 1/2 AEC markers, suggestive of AEC dysfunction. By pulmonary function assay, P28 $\alpha3^{Shh.Cre}$ mice exhibited increased resistance ($\alpha3^{Shh.Cre}$ 1.11 vs. $\alpha3^{f/f}$ 0.58 cmH2O/ml/s, p <.05) and decreased compliance ($\alpha3^{Shh.Cre}$ 0.02 vs. $\alpha3^{f/f}$ 0.04 ml/cmH_2O, p <.05). P3 $\alpha3^{Shh.Cre}$ AECs exhibited >2-fold increased expression of ligands *Wnt7a*, *Wnt7b,* and receptor *Fzd2* (p <.05). In contrast, *Wnt7a*/*7b* expression was decreased in P28 $\alpha3^{Shh.Cre}$ AECs, suggesting temporal regulation of Wnt pathway components. Treatment of $\alpha3^{Shh.Cre}$ lung slices with Wnt inhibitor markedly remodeled alveolar structure and increased apoptotic AECs.

Conclusion: Epithelial α3β1 is required for sacculation, AEC differentiation, and alveolarization. α3β1 integrin developmentally regulates Wnt component expression, critical for AEC function and maintenance of alveolar structure.

Mentor: Erin Plosa, MD; erin.plosa@vumc.org

Pediatric Emergency Medicine Neurosurgical Ventricular Shunt Evaluation Predictors and Impact of a Clinical Practice Guideline

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Objective: Children with neurosurgical ventricular shunts on rare occasions will have complications, such as malfunction or infection. In the pediatric emergency department (PED), it is common for a ventricular shunt to be evaluated using radiographic brain imaging and shunt series x-rays with many children undergoing multiple shunt evaluations annually. In May 2019, a clinical practice guideline (CPG) was published to help assist clinicians on the risk factors that increase the likelihood of a shunt infection or malfunction. Our study aimed to determine which findings are most reliable in indicating shunt malfunction or infection, the effect of a CPG on PED evaluation, and risk factors for repeat evaluation.

Study Design: Retrospective cohort study was performed from 01/2018-01/2020 for all encounters with neurosurgical shunt evaluation in the PED. Demographics, presenting symptoms, initial vital signs, exam findings, and outcomes were collected to determine predictors for shunt malfunction or infection. Diagnostic studies and time to completed diagnostic evaluation were collected to assess impact of the CPG. Risk factors for repeat evaluation include age, primary language, missed neurosurgical appointment in the last 3 months, and distance from the hospital. Pearson's chi-squared test and Wilcoxon's test were used for statistical analysis.

Results: 249 patients underwent 463 shunt evaluations during the study period. Headaches and nausea and/or vomiting were found to be predictors for shunt malfunction/infection ($p<0.001$) whereas shunt malfunction/infection were statistically less likely in patients with seizures and fever ($p=0.01$). Vital signs were not found to be predictive of shunt malfunction or infection. Exam findings found exposed tube shunting or overlying shunt rash as reliable predictors for shunt infection ($p<0.001$, <0.01). The CPG did not expedite diagnostic evaluation or reduce neurosurgical consultation. Risk factors for repeat evaluation were non-English primary language ($p=0.007$) and closer proximity to the hospital ($P<0.001$).

Conclusions: Predicting neurosurgical shunt evaluations can be difficult given vague symptom presentation. Headache and vomiting should be concerning for shunt malfunction. Shunt infection was rare, and fever or seizure alone, especially with history of seizure disorder, should not always lead to neurosurgical evaluation. Further investigation on recurrent visits is needed and whether primary language neurosurgical education or increased case management or outpatient visits reduce PED evaluations.

Mentor: Holly Hanson, Holly.R.Hanson@vumc.org

INCREASING PEDIATRIC FIREARM-RELATED HOSPITAL ENCOUNTERS DURING THE COVID-19 PANDEMIC

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Objective: Firearms are a leading cause of morbidity and mortality in US children with 9 children dying every day in 2019. In the setting of the COVID-19 pandemic, we hypothesized that social isolation requirements, social inequities and an unprecedented increase in firearm sales would elevate the risk for firearm-related injury and death in children leading to a higher than expected volume of pediatric firearm-related encounters. Our objective was to quantify pediatric firearm-related and total emergency department (ED) and hospital encounters during the initial COVID-19 pandemic compared to encounter volumes during the previous 3 years, matched to the same time period of March-August.

Study Design: We queried the Pediatric Hospital Information System (PHIS) administrative database to identify firearm-related and total encounters using ICD-10 discharge codes at 40 US children's hospitals from 2017-2020 during the months of March-August. We summarized and compared characteristics in firearm-related encounters comparing 2020 to the 3 years prior using Pearson's chi-squared test. Encounters were summarized by calendar week. Since firearm-related volumes were stable in 2017-2019, we used median weekly volumes for 2017-2019 as the referent. We calculated differences in volumes in 2020 for each calendar week from March-August and compared the mean weekly difference between 2020 and 2017-2019 in four-week periods using paired t-tests.

Results: There were 2,326 total pediatric firearm-related encounters during the entire study period, of which 746 occurred in March-August 2020. There were no significant changes in cohort demographics, rurality, or region comparing time periods. There was a decrease in 2020 total encounters overall by 42.3% (mean difference of -11,927 encounters/week; $p < .001$) and for each four-week block after March. Overall, firearm-related encounters increased by 39.2% in 2020 (mean difference of +8.4 encounters/week; $p < .001$). The range of differences across the four-week periods was 3 to 14.3 encounters/week.

Conclusions: Despite a national decrease in overall pediatric hospital encounters in 2020, compared to the three previous years, pediatric firearm-related encounters increased. This notable increase underscores the importance of a public health approach to firearm injuries, especially in the context of a global pandemic.

Mentor: Dr. Shari Barkin (shari.barkin@vumc.org)

APELINERGIC SIGNALING: A NEW TARGET FOR PULMONARY HYPERTENSION ASSOCIATED WITH BRONCHOPULMONARY DYSPLASIA

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OBJECTIVE: Bronchopulmonary dysplasia (BPD) is the leading morbidity in survivors of preterm birth. Preterm infants sustain injury from mechanical ventilation, hyperoxia, and inflammation during the vulnerable saccular stage of lung development, with resulting impaired alveolarization and fibrosis. Infants with severe BPD have associated vascular changes and pulmonary hypertension (PH), which may result in right ventricular dysfunction. The molecular mechanisms resulting in BPD and PH are poorly understood, and there are no curative therapies. Apelin is a peptide found throughout many biological tissues, including in endothelial cells of the heart and lung. The role of apelin in lung vascular development and injury response is poorly defined, although some preliminary studies have suggested it may be associated with endothelial repair. The goals of this study are to define the trajectory of apelin expression during normal lung development and characterize the effect of injury on apelinergic signaling.

STUDY DESIGN: To characterize expression of apelin and its receptor in lung development, we performed single cell RNA sequencing (scRNAseq) across 7 time points from embryonic day (E) 15 to postnatal (P) day 14. To study apelin expression during lung injury, we have developed a murine model combining hyperoxia (70% oxygen from postnatal day (P) 1-5) and inflammation with intratracheal administration of lipopolysaccharide on PN3 and 4. For validation, we examined human lung tissue from preterm infants with and without lung injury. Apelin and apelin receptor expression were localized in lung tissue using RNA in situ hybridization (ISH), with quantification using Halo software. To further characterize our lung injury model phenotype, we performed echocardiography on mice at 8 weeks of life both in control and hyperoxia groups.

RESULTS: By scRNAseq, apelin and its receptor are expressed by distinct subpopulations of endothelial cells in the lung, with apelin expression in a specialized population of alveolar endothelial cells. In normal development, Apelin expression increases before birth at embryonic day (E) 18 and is relatively constant across the lifespan. In acute lung injury, we found decreased expression of apelin by RNA ISH in endothelial cells when compared with normoxia-exposed controls at P5 ($p<0.001$). This decrease in apelin expression persisted during recovery at P14 ($p<0.01$) and P28 ($p<0.01$). There were no significant changes in apelin receptor expression with injury. Examination of human infant lungs in the saccular stage showed decreased apelin expression after 4 days of mechanical ventilation when compared with infants who were never mechanically ventilated ($p<0.001$). Preliminary results of echocardiography in injured mice aged to 2 months demonstrates a significant decrease in right ventricular stroke volume and increase in right ventricular wall thickness in injured mice relative to controls.

CONCLUSION: Apelinergic signaling is a conserved pathway that emerges in the saccular stage of lung development. During acute neonatal injury and recovery, there is a significant decrease in apelin expression. We have also preliminarily characterized the echocardiographic phenotype of our hyperoxia model. Future work to target the apelin pathway may identify novel therapies in infants with BPD and PH.

Mentor: Jennifer Sucre, jennifer.sucre@vumc.org

EFFICACY OF VIRTUAL AND ASYNCHRONOUS TEACHING OF COMPUTER-ASSISTED DIAGNOSIS OF GENETIC DISEASES SEEN IN CLINICS

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Objective: Diagnosing genetic diseases is an increasingly difficult problem because of the growing number and rarity of these diseases. Furthermore, detailed clinical and test information including candidate variants (CV) from next-generation sequencing (NGS) must be combined and analyzed to achieve success. Current software available to address these problems includes FindZebra, OMIM, and SimulConsult. All are web-based informatics tools that can be used to develop differential diagnoses (DDx) of genetic conditions. We selected the Diagnostic Decision Support System (DDSS) from SimulConsult because it is optimized to generate DDx and, unlike FindZebra and OMIM, accepts information on age of onset of findings, patient's age, gender and family history, regions of homozygosity (ROH) and provides CV prioritization. Here we evaluate the performance of the DDSS when used by a variety of medical care providers (MCP) to diagnose rare genetic diseases. We hypothesize that MCP can be virtually taught how to use the DDSS to generate DDx, ranked by probability based on phenotypic features, and the resulting outputs can be shared iteratively with laboratory specialists to help prioritize CV from NGS. Our aim was to determine the efficacy of virtual, asynchronous teaching methods for MCP to generate computer-assisted DDx of genetic disorders.

Study Design: On 7 November 2020, a cohort of 32 MCP were invited to participate in our IRB exempt quality improvement study. Our cohort included Clinicians (Clinical Geneticists, Neonatologists, Neurologists, Obstetricians, and Pediatric Surgeons) (40%), Molecular Geneticists/Cytogeneticists (16%), Nurse Practitioners (13%), and Genetic Counselors (31%). Three surveys were distributed to assess: 1) expectations about using the DDSS before instruction (*Baseline Survey*), 2) satisfaction of instruction on using the DDSS to solve case problems (*Training Survey*), and 3) the clinical impact of using the DDSS (*After >1 Month Use Survey*). Surveys were built in REDCap and placed on the Vanderbilt/Meharry ROCKET platform to maximize convenience for participant access. ROCKET also hosted links to teaching videos (total 15 minutes) and practice case problems (vignettes: 5 clinical, 2 with CV results from NGS, and 2 optional with microarray results with ROH).

Results: Thirty-one participants have completed the *Baseline Survey*. Most (68-84%) participants strongly agreed/agreed that the DDSS would likely be easy to use; be useful to their work and for clinical decision support and would help them in making a differential diagnosis and/or prioritize CVs. Of the participants, 15/31 (48%) have completed their *Training Survey* and all 15 achieved passing scores on the 7 required case problems (mean= 95, range= 80-100, with scores of 10, 9, 8 if they ranked the correct diagnosis as 1, 2, 3, etc. in order), 8/15 also successfully completed the optional cases with ROH (mean= 89, range= 70-100), and 0/13 requested additional training. Of these 15 participants, 75% reported that the DDSS was very easy/easy to use and 69% and 56% were completely satisfied with the video training non-video learning resources, respectively. Twelve participants also completed their *After >1 Month Use Survey*. Of these 12, 75% and 92% strongly agreed/agreed that the DDSS was useful to their clinical work and for clinical decision support, respectively.

Conclusions: Our early results show that a variety of MCP could successfully use the DDSS following asynchronous, virtual teaching to 1) generate computer-assisted, ranked DDx of rare

genetic disorders using DDSS to analyze phenotypic features that they extracted from case vignettes which required only 10-19 minutes/case and 2) produce formatted outputs of phenotypic features and DDx following loading of an annotated NGS variant table. This approach could facilitate iterative and synergistic interactions between clinicians and lab specialists in making such diagnoses and in prioritizing CVs.

APPLYING A RISK PREDICTION MODEL FOR FEBRILE NON-NEUTROPENIC FEVER PATIENTS IN A COHORT OF PEDIATRIC STEM CELL TRANSPLANT RECEIPENTS

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Objective: Blood stream infections are a significant source of morbidity and mortality in the stem cell transplant (SCT) population. This study sought to evaluate if previously published EsVan risk prediction models for pediatric cancer patients presenting with non-neutropenic fever could be applied effectively to predict bacterial blood stream infections (BSIs) in a retrospective cohort of pediatric SCT recipients.

Study Design: We reviewed the electronic medical records of all patients who received a SCT at Monroe Carell Jr. Children's Hospital at Vanderbilt from 2005-2019 and identified all episodes of post-SCT fever occurring in the setting of an absolute neutrophil count (ANC) >500/µl and with a central venous catheter (CVC) in place. We specifically collected the variables used in the EsVan2a model (type of CVC, hypotension, chills, history of SCT, upper respiratory symptoms (URIS), exposure to chemotherapy known to be associated with fever within 24 hours of administration (cytarabine and dinutuximab), age, highest reported or recorded temperature, ANC and absolute monocyte count (AMC)) and the EsVan3b model (which removes URIS, ANC, and AMC) to evaluate how the models performed on the dataset. We considered the performance of the models on the whole data set and separately among those who received an autologous SCT versus an allogeneic SCT. When the existing models were applied to the new dataset, a Harrells c-statistic was assessed, as well as a benchmark c-statistic which is the best possible c-statistic obtained using the same variables if a new model based on the new dataset was created.

Results: The final cohort included 505 post-SCT non-neutropenic fever episodes (233 allogeneic and 272 autologous). The overall BSI rate was 20.4% (103/505) with 59.2% of the BSIs being high-risk (gram negative bacilli or S. *aureus*). The BSI rate was higher in allogenic transplant recipients (24.9%), than in autologous transplant recipients (16.5%). When applied to the overall transplant dataset, the EsVan2a model performed well with a c-statistic of 0.805, close to the benchmark c-statistic of 0.814. The simplified EsVan3b also performed well with a c-statistic of 0.783 versus the benchmark c-statistic of 0.806. The models performed especially well on the auto transplant data (EsVan2a c-statistic 0.866 and EsVan3b c-statistic 0.872) but still reasonably well on the allogeneic transplant data (EsVan2a c-statistic 0.733 and EsVan3b c-statistic 0.693).

Conclusions: Both the EsVan2a and EsVan3b were effective in discriminating the risk of BSI in pediatric oncology transplant patients with c-statistics over 0.7. Both models worked especially well for those who received an autologous transplant, which indicates the models may be effective if used in clinical practice. The models also did a reasonable job discriminating allogeneic patients, but further study is needed to determine if adding transplant specific variables would significantly improve the predictions.

Mentor: Adam Esbenshade (adam.esbenshade@vumc.org)

PHYSICIAN ATTITUDES AND COUNSELING PRACTICES REGARDING INTERVENTION FOR CHILDREN WITH TRISOMY 18

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Objective: Trisomy 18 (T18) is a genetic condition, often identified prenatally, with a very heterogenous phenotype which often can include congenital heart disease or other surgical complications and is always associated with severe developmental disability. Due to the complications typically associated with T18, it has traditionally been regarded as a "lethal condition" and little to no medical intervention has been offered to children with this diagnosis. However, recently there has been a trend towards offering children with T18 more life prolonging interventions, sometimes including cardiac surgical repair. Several studies have shown that while the median survival has not changed for infants with T18, offering medical intervention can improve overall survival. It is also important when considering intervention for these infants to weigh the burden of some interventions given the low overall survivability of this condition. Many experts now recommend individual treatment courses based on each infant's phenotype, though it appears many physicians continue to counsel families and offer interventions based purely on the diagnosis of "T18". A family will undoubtably encounter several physicians of varying subspecialties when being told of the diagnosis and counselled on available interventions for their child. Several studies have looked at subspecialist attitudes regarding treatment of T18, but only a small few have attempted to directly compare attitudes of different subspecialists who would likely be involved in the care and counseling of these infants and their families. In addition, the majority of these studies were conducted prior to the shift seen in the literature to individualize the care of these children. This study aims to investigate the attitudes of obstetricians (OBs) /maternal-fetal-medicine (MFM) providers, neonatologists, and pediatric cardiologists/pediatric cardiac surgeons regarding intervention for infants with T18. We will compare attitudes between provider type while also investigate the counseling practices of these providers. We hypothesize differences in attitudes regarding intervention for T18 will exist between medical specialties and that counseling practices will reflect personal attitudes regarding intervention.

Study Design: This will be a cohort mixed-method study employing a quantitate survey with a qualitative interview follow-up. OBs, MFMs, neonatologists, pediatric cardiologists and cardiac surgeons will be sent a REDCap survey via email to complete. Each survey has free response text boxes to expand upon individual answers. Following the completion of the survey, a sample of responders will be contacted for a follow-up, qualitative interview to further elucidate themes surrounding attitudes and counseling practices.

Results: pending

Conclusion: The climate regarding treatment of children with T18 is changing with individualized treatment becoming more accepted. It is unknown if all medical providers guiding and counseling families through this difficult diagnosis agree with what options should be provided. More knowledge regarding this sensitive issue can lead to consistent information and counseling for these families to aid in decision making for their child.

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DIRECT-TO-PATIENT TELEHEALTH EQUITY: REACHING ENGLISH AND NON-ENGLISH-SPEAKING PEDIATRIC POPULATIONS IN PRIMARY CARE

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Objective: The 2019 coronavirus (SARS COV-2) prompted allowances for direct-to-patient telehealth visits with families in their home. Early data indicated lower telehealth use by adults among vulnerable populations, but pediatric data were lacking. Using quantitative and qualitative data, we examined telehealth video visit experience by Medicaid-insured pediatric populations who were English and non-English speaking during the early period of the pandemic.

Study Design: We conducted acute and well-child telehealth visits from April to May 2020 at an academic pediatric primary care clinic (80% Medicaid-insured, 40% non-English-speaking). Telehealth visits were scheduled using the clinic's patient-facing portal or other platforms (WhatsApp, FaceTime, Zoom) based on patient preference. Trained providers included pediatric residents and faculty members (70% faculty providers in April and 92% faculty in May). For quantitative data, providers completed an electronic survey describing platform and device used, interpreter use, ease of process, and video image quality. Group comparisons tested differences in telehealth visits by language spoken. For qualitative data, an iterative inductive/deductive approach informed coding categories extracted from free-text options on patient feedback and provider observations.

Results: Data from 258 telehealth visits (62% well-child and 38% acute visits) were analyzed. Most (80.6%) were in English, with the remaining in Spanish (14.7%), Arabic (3.5%), or other languages (1.2%). Most (77%) visits were conducted with patients using a mobile phone. English speakers (60.8%) were more likely than non-English speakers (26.5%) to use the clinic's patient portal ($p<0.001$). English-speaking patient encounters vs. Non-English experienced better process ease (85.6% vs. 63.3%; $p<0.001$) and video quality (81.8% vs. 49.0%; $p<0.001$). WCC visits were conducted in English significantly more often than acute visits were (91.3% of WCCs visits in English vs. 64.3% of acute visits in English; $p<0.001$). A qualitative framework emerged including family call environment, technology process and experience, value added, and barriers.

Conclusions: There were differences by language in telehealth use, communication platform, process ease, and video quality. Expanding direct-to-patient telehealth without worsening the health equity gap requires attention to the use of mobile phones as well as cultural and language preferences.

A PROSPECTIVE ANALYSIS OF COVID-19 VERSUS INFLUENZA SEVERITY IN TYPE 1 AND TYPE 2 DIABETES

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OBJECTIVE: Recent studies have identified that COVID-19 severity is increased in the diabetes community compared to patients without diabetes. We now aim to quantify the difference in illness severity between patients with diabetes infected with COVID-19 versus influenza.

STUDY DESIGN: We are conducting a prospective cohort study to identify patients with Type 1 or 2 diabetes with COVID-19 and influenza across an academic health care network of inpatient and outpatient locations. Using an electronic health record query and chart review, we are identifying clinical factors influencing illness severity. Disease outcome and severity of COVID-19 versus influenza will be compared among case subjects.

RESULTS: Record query and chart review of diabetes patients with COVID-19 or influenza identified between November 2020 through February 2021 is presently ongoing.

CONCLUSIONS: Illness severity of COVID-19 versus influenza in patients with diabetes is pending aforementioned analysis.

THE IMPACT OF DIGOXIN USE ON INTERSTAGE MORTALITY IN THE CURRENT ERA

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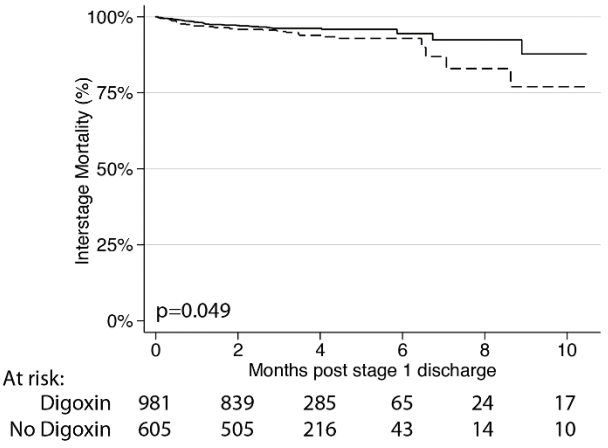
Objective: Digoxin was previously associated with an 8-fold reduction in interstage mortality (ISM) following stage 1 palliation (S1P) of single ventricle heart disease with a subsequent dramatic increase in use nationally. Despite this, there has been no further decline in ISM. We sought to determine the impact of digoxin on ISM and readmission in the current era.

Study Design: This study was a secondary analysis of the NPC-QIC database and included all patients who survived to hospital discharge following S1P. Patient demographics and digoxin use at S1P discharge were compared between eras (1: 2009–2014 vs. 2: 2015–2019). Patients with a NEONATE score (excluding digoxin) >8 were considered high-risk. A Cox proportional hazard model assessed the impact of digoxin on ISM and freedom from readmission in era 2 after adjusting for known risk factors.

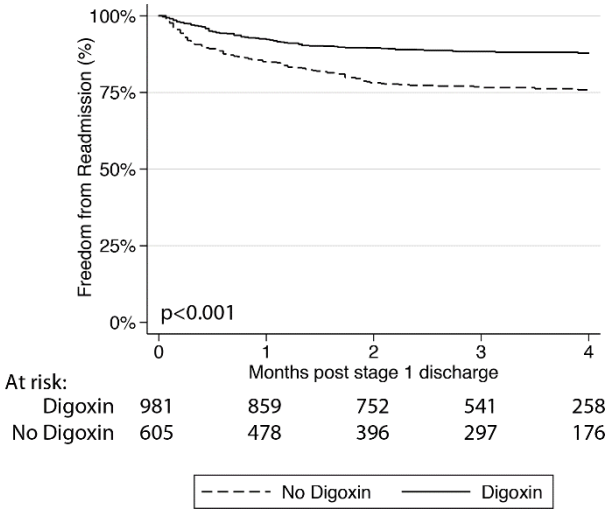
Results: Era 1 had 1400 (46.8%) patients and era 2 had 1589 (53.2%). Digoxin use increased across eras (22.4% vs. 61.7%, p<0.001). The proportion of high-risk patients was greater in era 2 vs. era 1 (20.3% vs. 9.1%, p<0.001), but there was no difference in risk between those who did vs. did not receive digoxin in era 2 (p=0.82). In era 2, Digoxin use was independently associated with reduced ISM (AHR 0.59, 95% CI 0.35-0.97, p=0.038, Fig. 1A) and greater freedom from readmission (AHR 0.41 95%CI 0.32 – 0.54, p<0.001, Fig. 1B).

Conclusions: Digoxin was independently associated with improved outcomes including a reduction in ISM and greater freedom from readmission in the current era. The lack of improvement in ISM in the current era may be secondary to an increase in the acceptance of high-risk patients.

A.



B.



EPIDEMIOLOGY OF PEDIATRIC FOREIGN BODY INGESTIONS AMIDST THE CORONAVIRUS DISEASE 2019 PANDEMIC AT A TERTIARY CARE CHILDREN'S HOSPITAL

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OBJECTIVE: The coronavirus disease 2019 (COVID) pandemic and resultant stay-at-home orders have altered caregivers' responsibilities and children's daily environments. We aimed to compare the epidemiology and morbidity of foreign body ingestions (FBIs) at our institution during the COVID pandemic with those from the prior year.

STUDY DESIGN: We performed a retrospective review of children cared for at our tertiary care children's hospital for FBI between March and July 2019 (pre-COVID) and between March and July 2020 (COVID). Cases were identified via a search of all diagnoses of foreign bodies (FBs) in the alimentary tract from emergency department visits, inpatient admissions, and outpatient endoscopies. All charts were reviewed to determine the types of FBs ingested and the patients' clinical courses.

RESULTS: A total of 72 encounters for FBIs were examined. Thirty ingestions occurred in the pre-COVID cohort, and 43 in the COVID cohort. One patient ingested two different FBs. There was a significantly higher rate of FBI per day in May 2020 (COVID) compared to May 2019 (non-COVID) (0.387 vs 0.161, p=0.046).The median age at presentation was similar between the two groups [pre-COVID: 63.8 months (28.6-128.5) and COVID: 62.6 months (46.2-105.4)]. Overall, boys more frequently ingested FBs (63%; p=0.025). Esophageal FBs were less frequent in COVID cohort (p<0.01). Fewer endoscopies were performed in the COVID cohort (53.5% vs 70%; OR: 0.49; 95%CI: 0.16-1.45).

CONCLUSIONS: The frequency of FBIs trended higher in the COVID cohort with significantly more ingestions in May 2020 when compared to the same month in the pre-COVID cohort. Patients in the COVID cohort more frequently had FBs located beyond the esophagus – indicative of later presentation and a lesser need for urgent endoscopic removal.

Project Mentor: Danielle Orsagh-Yentis, MD; danielle.k.orsagh-yentis@vumc.org

CREATING AND IMPLEMENTING A SUBSPECIALTY NIGHTTIME CURRICULUM

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OBJECTIVE: The transition from a 24-hour call to a night shift schedule at our institution led to a decrease in noontime conference attendance. These conferences often focus on high-yield pediatric subspecialty topics and are part of an 18-month board prep curriculum. A recent quality improvement study at our institution which provided pediatric hospital medicine education resources demonstrated improvement in nighttime teaching from 0 to 3 times per week sustained over 32 weeks. Feedback from this initial study cited time as a main barrier to nighttime education and suggested creating educational handouts to review. We aimed to identify high yield subspecialty topics and create a nighttime subspecialty curriculum to enhance our current nighttime teaching and board preparation.

STUDY DESIGN: Key topics were identified by subspecialty advisors as high yield general pediatric content. Pediatric residents created multimedia teaching modules focused on these topics, which were then reviewed by these content experts. High yield components from these modules were identified and used to create a summary handout which could be quickly referenced and used for teaching on nights with limited time for education. Each of these summary handouts were created using a standardized format and included etiology, signs and symptoms, key physical exam findings, differential diagnosis, workup, and basic treatment principles. Upper-level residents on the general hospital medicine service were encouraged to teach topics from the standardized subspeciality curriculum using either the longer, more detailed modules or high yield summary handouts depending on time available for teaching that night. Redcap surveys were provided following these nighttime education sessions in order to track the use of curriculum.

RESULTS: 23 education modules with associated high yield, standardized handouts over 10 subspecialties were created as part of the nighttime teaching curriculum to enhance resident education and board preparation.

CONCLUSIONS: We have created a standardized subspecialty nighttime teaching curriculum which has been utilized over the past six months. We aim to study the effectiveness of this curriculum in enhancing subspecialty knowledge by comparing pre- and post-questionnaires using paired t-tests. We are also evaluating if the use of this nighttime curriculum is sustainable over a 6- and 12-month period.

MULTI-DRUG RESISTANT INFECTIONS AMONG VERY LOW BIRTH WEIGHT INFANTS WITH LATE-ONSET SEPSIS IN SOUTH AFRICA

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Objective: The majority of neonatal deaths occur in the first week of life, with the highest risk of death on the first day of life. Neonatal mortality rates (NMR) vary throughout the world. Neonatal sepsis accounts for ~30% of neonatal mortality, with very low birth weight (VLBW) neonates (birth weight <1500 g) disproportionately affected. NMR in South Africa is 10.7 deaths per 1000 live births compared to 3.5 in the United States of America with an overall incidence of neonatal sepsis falling between 8.5-10%, with late-onset sepsis (LOS) accounting for most (83.7%) infections in South Africa. The mortality rate of LOS was found to vary between 19.7-22.5%, according to available South African data. Antibiotic use, either empiric, or targeted for proven infection, can lead to an increasing number of multi-drug resistant organisms (MDRO's) in neonatal intensive care units (NICUs) worldwide. MDRO type and prevalence vary across institutions. MDROs have proven to be a global public health emergency and threat to the vulnerable neonatal population globally. This study aims to characterize the prevalence and incidence of LOS caused by select MDROs and identify maternal and neonatal risk factors associated with increased mortality among a cohort of VLBW infants with LOS at an academic neonatal unit in South Africa. We hypothesize that the incidence of late-onset sepsis caused by MDROs in VLBW infants is increasing and that VLBW infants with late-onset sepsis caused by MDRO vs non-MDRO are at higher risk of mortality.

Study Design: This will be a retrospective cohort study of VLBW infants treated for LOS (defined as growth of a bacterial pathogen from a blood or cerebrospinal fluid (CSF) culture greater than 72 hours after birth) that were admitted to Charlotte Maxeke Academic Hospital between 2015 to 2020. Maternal and neonatal data collected in REDCap (UL1 TR000445 from NCATS/NIH) will be analyzed from an existing neonatal database using multivariable logistic regression to determine associations between demographics or exposures and LOS with MDROs (multi-drug resistant organism *MRSA*; carbapenem-resistant *Enterobacterales*; ESBL-producing *E. coli* or *Klebsiella* and any gram-negative with non-susceptibility to at least 1 drug in 3 or more antimicrobial classes).

Results: Pending.

Conclusion: Multi-drug resistant infections are a public health emergency worldwide. It is critical to monitor antimicrobial consumption and resistance patterns to optimize local antimicrobial usage.

TRANSPULMONARY ESTROGEN GRADIENT AND ESTROGEN RECEPTOR DENSITY IN PULMONARY ARTERIAL HYPERTENSION

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Objective: The strongest established risk factor for the progressively fatal disease pulmonary arterial hypertension (PAH) is female sex. Experimental data from our group and others support the concept that estrogen antagonism will be beneficial for humans with PAH. However, it is possible that not all subjects will benefit from estrogen antagonism, making a 'one size fits all' approach too narrow. We hypothesize that blood-based and radiologic markers of estrogen burden will support the determination of a phenotypic profile of subjects with PAH for whom estrogen antagonism will be an effective therapeutic approach. In a cohort of PAH patients, we will determine if transpulmonary (change pre- to post-pulmonary capillary bed) estradiol levels and/or lung ESR density associate with disease severity at cardiac catheterization, functional capacity, time to clinical worsening, and oxidant stress.

Study Design: This is an observational, natural follow-up study of group 1 PAH patients compared to group 2 pulmonary venous hypertension (PVH) patients. To test the hypothesis that among PAH patients, transpulmonary estradiol gradient associates with a more severe hemodynamic profile and worse 1-year outcomes, we screen and enroll patients at the time of diagnostic cardiac catheterization for initial pulmonary hypertension evaluation. Samples are obtained during cardiac catheterization from the pulmonary artery and pulmonary capillary wedge or left ventricle. To test the hypothesis that among PAH patients, higher lung estrogen receptor density associates with a more severe hemodynamic profile and worse 1-year outcomes, we obtain positron emission tomography (PET) with F-FES. F-FES is an estrogen receptor specific PET tracer to determine estrogen receptor density. Clinical information is obtained and documented over time.

Subjects are enrolled if they are at least 18 years of age and have group 1 (PAH) or group 2 (PVH) pulmonary hypertension. Subjects are excluded if they have type I diabetes mellitus, polycystic ovarian disease, breast/uterine/endometrial cancer, or use hormone-containing or hormone modifying therapy.

Results: Transpulmonary samples have been obtained for 21 PAH subjects, 8 PVH subjects, and 13 controls. Of the PAH subjects, 16 were on zero (n=2), 1 (n=8) or 2 (n=6) PH-specific medications at the time of diagnostic catheterization. Of the PAH subjects, 81% were female with ages ranging from 37 to 71 years at the time of catheterization. Two PAH subjects have undergone F-FES PET.

Conclusions: This study will lead to novel discoveries in the transpulmonary gradient of sex hormones, investigate a novel imaging approach in PAH, optimize our ability to precisely determine the correct patient for sex hormone modification, and potentially support the development of novel therapeutic targets in PAH.

WORKING IN THE PEDIATRIC CARDIAC INTENSIVE CARE UNIT: ARE YOU FEELING UNCOMFORTABLE AND DOES SIMULATION HELP?

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Objective: Gauge number of pediatric critical care (PCC) programs across the nation that have a cardiac simulation curriculum in place, as well as perceived benefit of said curriculum and comfort level in managing pediatric cardiac patients, including leading a code.

Study Design: A 14-question survey was distributed to fellows and advanced practice providers (APPs) in 64 PCC programs across the United States. Demographic data such as program size and presence of an existing cardiac simulation curriculum was obtained. Using a Likert scale, the comfort level of fellows and APPs was assessed in scenarios such as managing codes, pre- and postoperative management, arrhythmias, and the need for ECMO. A descriptive analysis was then conducted on the data obtained.

Results: A total of 25 institutions across the nation responded to the survey. Of those centers, 13 reported having a cardiac simulation curriculum in place. Of those centers, 13 stated having a simulation curriculum in place and 98% of total survey participants (n=102) stated having such a program was or would be beneficial. Most participants reported leading a code 3 or less times each year (83%), and 51% reported feeling "uncomfortable" leading codes. The majority of participants responded feeling "comfortable" in managing cardiac patients preoperatively (68%), postoperatively (65%), and on ECMO/mechanical support (56%), while up to 40% felt "uncomfortable" managing arrhythmias.

Conclusion: Simulation curriculums have proven to be an effective way for trainees to practice resuscitation skills. Our survey demonstrated that at least 20% of programs polled currently have a cardiac simulation curriculum in place, and at those institutions the majority of fellows and APPs found it be beneficial. However, many still feel uncomfortable when it comes to leading a code, thus implementation of a simulation curriculum that focuses on this may be beneficial.

Mentor: Dr. Isaura Diaz (Isaura.diaz@vumc.org)

A Single Cell Atlas of Late Lung Development Identifies Unexpected AT1 Expression Patterns and Mesenchymal Wnt Patterning

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Objective: A leading complication of preterm birth is bronchopulmonary dysplasia (BPD), an irreversible lung injury with no curative treatment and lifelong health impacts. BPD uniquely arises from lung injury during the saccular stage of lung development (23-32 weeks gestation in humans). While the environmental stimuli that increase the risk of BPD are well-described (e.g., hyperoxia, mechanical ventilation, and inflammation), the precise molecular mechanisms that result in BPD are not known. To further understand the factors that predispose the saccular stage lung to irreversible injury, we profiled the process of lung development in the mouse from the pseudoglandular to the alveolar stages of development using single cell RNA sequencing.
Study Design: Lungs from at least four wild-type mice were analyzed by single-cell RNA sequencing at embryonic (E) day 12, E15, E18, and postnatal (P) day 0, P3, P5, P7, and P14. Dissociated lung tissues were depleted of Ter119+ red blood cells and CD45+ immune cells prior to sequencing to facilitate detailed analysis of the structural lung tissue. Computational analysis determined cellular populations and inferred cellular trajectories by leveraging RNA velocity. Key findings were validated by localizing expression in lung tissues with RNA *in situ* hybridization, with image quantification by Halo software at single cell resolution.
Results: Analysis of 92,328 single-cell transcriptomes identified 22 distinct epithelial, endothelial, and mesenchymal cellular clusters. In this time series data, we observed that alveolar type I (AT1) and type II cells appeared as early as E15 and expanded through P0. While AT1 cells have primarily been characterized as facilitating alveolar gas exchange, we discovered a new role for AT1 cells in matrix assembly, with AT1 cells expressing *Fbln5*, a component of elastin assembly, and components of laminin-332. We also demonstrated a marked shift in the mesenchymal cell populations from E15 to P3. The lung mesenchyme at E15-E18 is predominately composed of *Wnt2*+ fibroblasts, a population that decreases after birth. This reduction in the *Wnt2*+ fibroblast population corresponds with an expansion of *Wnt5a*-expressing myofibroblasts from E18 to P3, with marked changes in the spatial relationships between the myofibroblasts and alveolar epithelial cells during the saccular stage.
Conclusions: The major cell types in the lung develop asynchronously, with the endothelium demonstrating early fate commitment in development, followed by the epithelial cells, with even later stabilization of the lung mesenchymal population. The finding that AT1 cells express components of matrix assembly suggests that AT1 cells may play an active role in the alveologenesis. Further, the dramatic redistribution and expansion of the *Wnt5a* expressing myofibroblasts may have important consequences during early lung injury, as aberrant *Wnt5a* expression has been shown to contribute to abnormal development and alveolar simplification in the setting of hyperoxia injury. In summary, this study provides context for gene expression in the lung by identifying the specific cellular contributions that facilitate lung organogenesis and provides a platform for understanding neonatal lung injury in future studies.

THE IMPACT OF SOCIAL DISTANCING ON CHILDREN WITH DOWN SYNDROME

Jenesis Negron, MD, Krissy Kalemaris, DPT, Mattie Goostree, BA, Angela Maxwell-Horn, MD

Objective: In early 2020 COVID-19 began to sweep across the United States. People were urged to "social distance"[1]. This entailed staying at least 6 feet apart from other people to help stop transmission of COVID-19. People with Down syndrome are generally considered to be very social. Their social skills are generally a strength of their cognitive profile[2]. This study sought to understand how social distancing affects the lives of children with Down syndrome.

Study Design: This survey-based study was approved by the Vanderbilt University Medical Center (VUMC) Institutional Review Board, with data collected between April and June of 2020. All data were collected via Research Electronic Data Capture (REDCap). The survey consisted of 13 questions asked to the caregivers of children with Down syndrome. The questions inquired about eating and sleeping habits, mood, and activities during the period of social distancing due to the COVID-19 pandemic. Survey data was collected from the family members of people who had attended the Down Syndrome Clinic at VUMC between March 2019 and March 2020. One hundred thirty-one families answered the survey about their child with Down syndrome.

Results: In response to the question, "Did your child socially distance themselves during the pandemic?" n=124 (94.7%) responded yes and n=7 (5.3%) responded no. Children with Down syndrome had been restricted from most of their routine activities during the pandemic, traditional school (n=122/93.1%), religious activities (n=63/48.1%), therapies (n=100/76.3%), playdates and social gatherings (n=89/67.9%), community outings (n=97/74.0%), team sports (n=20/15.3%) and other (n=7/5.3%)(Table 3). In response to the question, "In general, what is your child's overall mood at baseline (before social distancing or the pandemic)?," most families reported that their children were generally happy n=88 (67.2%). Most parents reported that their children were eating as they normally did at baseline (n=95/72.5%); n=36 (27.5%) reported that their child did have a change in their eating habits. Parents reported that their children had been engaged in a variety of activities since most routine group activities were cancelled.

Conclusions: Most families of children with Down syndrome were following the recommended guidelines and having their children stay socially distant during the COVID-19 pandemic. All the children who had previously attended school outside of the home had stopped going due to school closure. Most children (55.7%) did not have changes in their mood. Of those that did experience changes, 61.2% of them were reported to be more irritable/anxious. As noted earlier, children with Down syndrome are often noted for their happy and amiable dispositions[2]. Their social relatedness to others is often a strength. It can thus be postulated that the pandemic related social distancing has interfered with the social relationships and interactions that provided a source of happiness and fulfillment to children with Down syndrome. This combined with the disruption in normal routine has likely led to a more irritable and anxious mood in children with Down syndrome.

Characterization of normal and LPS-Induced Leukocyte Distribution at the Early Blastocyst Implantation Site of Mice

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Women who have infection are often at a higher risk for early pregnancy loss/defects despite progress in the management and treatment of infection. A hallmark of any infection-induced inflammatory response is that it elicits leukocyte migration and the release of many inflammatory mediators including cytokines from various cell-types. Though leukocytes and cytokines are implicated maintaining an optimized balance of immune and inflammatory dynamics at the BIS. However, excessive profusion of leukocytes and their hyperactivity at the BIS may induce an exaggerated inflammatory response that can either support pathogen elimination or cause incidental cell death or tissue damage at the BIS. With a better understanding of this infection-induced exaggerated inflammatory response at the BIS, development of a specific intervention strategy becomes a possibility.

In present studies, we have evaluated whether a low dose (1 µg/mice) of lipopolysaccharide (LPS) alters the profile of neutrophil and monocyte subsets of leukocytes at the BIS. The abundances of $CD45^+$ pan-leukocytes, $Gr1^+$, $Ly6G^+$ and MPO^+ neutrophils, $Ly6c^+$ monocytes, $F4/80^+$ and $CD206^+$ positive macrophages and $CD11c^+$ positive dendritic cells (DCs) were examined by immunofluorescence staining. On day 6 of pregnancy, BIS of mice injected (ip) with saline had an abundance of $CD45^+$ cells in the uterine muscle layer as well as in the non-proliferating stromal layer that locates above the circular muscle layer. A few $CD45^+$ cells were also evenly distributed throughout the decidua. An analysis of the relative abundance of monocytic and granulocytic myeloid cells within the $CD45^+$ myeloid population revealed the presence of largely monocytic myeloid ($CD11c^+$, $F4/80^+$ and $CD206^+$) cell populations at the BIS. However, when the day 6 BIS was evaluated following 24 hours after LPS injection (ip), we observed huge infiltration of neutrophils ($Gr1^+$, $Ly6G^+$ and MPO^+) were located within the uterine non-proliferating stromal region but not in the decidual area. Unexpectedly, injection of LPS compared with its vehicle did not have much of an impact on monocytic myeloid cell populations such as DCs ($CD11c^+$) and macrophages ($F4/80^+$ and $CD206^+$) at the BIS. These findings show that a hallmark of bacterial response at the BIS is the accumulation of neutrophil within the uterine non-proliferating stromal region. These infection-induced recruited neutrophils could either be involved in enhancing antimicrobial defense or be contributing to immune hyperreactivity leading to hostile inflammation and increased pathology at the BIS. Thus, pertinent future studies in deciphering the process of pathogen-induced neutrophil recruitment and the extend of inflammation that is harmful at the BIS may provide insights for the development of a plausible therapeutic strategy to enhance antimicrobial immune defense or alleviating harmful inflammation at the BIS.

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The Development and Validation of a Neonatal Intensive Care Unit Discharge Model for Preterm Infants

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Background: Patients admitted to the neonatal intensive care unit (NICU) can have complicated clinical courses, lengthy hospitalizations, and long-term sequelae. Discharge planning and coordination for these patients are resource-intensive, involving time for careful preparation and communication across multiple care teams. Families also need time to get ready discharge. Research shows 12% of families of late preterm babies felt unprepared for discharge through post-discharge surveys.[1] Identifying patients approaching discharge can afford families and providers time to improve discharge preparedness.

Objective: To develop and validate a Neonatal Discharge Model (NDM) that used clinical features within the Electronic Health Record (EHR) to identify patients nearing NICU discharge within 3-5 days.

Study Design: This study is a single-center cohort analysis on preterm neonates with gestational ages between 28-36 weeks admitted to a level 4 NICU. NDM development will occur on a retrospective cohort of infants discharged during the year 2020. During model development, we will observe how NDM variables change over the ten days prior to discharge and establish thresholds for each variable. Once the NDM variables and their thresholds are finalized, we will use a receiver operating characteristic (ROC) curve to evaluate NDM performance of forecasting discharge within 3-5 days with the area under the curve (AUC). NDM validation will occur on a prospective sample of 150 patients. Patients will be included upon meeting NDM criteria during NICU admission and will be excluded if they are transferred to another facility before discharge, transferred to a non-NICU unit before discharge, or if they require durable medical equipment (DME). During Model validation, we will use an eStar (Epic) workbench report to identify the date and time patients meet NDM criteria. These patients will be followed until discharge, with discharge date, time, and patient demographics and co-variates will be recorded. The NDM performance at forecasting discharge within 3-5 days will be evaluated with an ROC curve.

POPULATION PHARMACOKINETICS/PHARMACODYNAMICS OF BETA-LACTAM ANTIBIOTICS IN CRITICALLY ILL PATIENTS RECEIVING ECMO OR CRRT

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Objective: Patients receiving ECMO/CRRT have altered drug pharmacokinetics (PK) and pharmacodynamics (PD) through a variety of mechanisms, including increased volume of distribution, depletion of plasma proteins, changes in drug clearance, and the physiologic effects of the underlying cause of illness, such as sepsis. Since ECMO/CRRT patients are at higher risk of infection compared to other critically ill patients, personalized optimization of drug dosing and delivery is critically important for individual patient outcomes. This study employs a prospective observational popPK modeling approach to determine optimal beta-lactam antibiotic dosing strategies as a first step towards real-time therapeutic drug monitoring (TDM) in these patients.

Study Design: We will enroll approximately 100 patients in VUMC intensive care units receiving ECMO or CRRT who are also receiving cefepime, piperacillin-tazobactam or meropenem. We anticipate that patients will contribute an average of 5-10 plasma samples during the 14-day study period. Though the intent of the study is to use random sampling, there are specific high-priority timepoints that provide high value information about PK parameters for each drug. We will measure drug concentrations of cefepime, meropenem, and piperacillin-tazobactam in plasma samples using C18 HPLC with UV and fluorescence detection. After enrollment, patient information will be extracted from the EMR and recorded in a REDCap database. This will include demographic data (e.g., age, sex, race, and ethnicity, anthropomorphic measurements), relevant comorbidities (e.g., sepsis, acute kidney injury, hepatic dysfunction), and recent laboratory data. PK models for the pooled concentration data will be explored by non-linear mixed effects modeling. Covariate analysis will examine the potential correlation between model parameters and demographic/clinical factors.

Preliminary Results: We have enrolled and collected samples from 28 patients to date. This includes six pediatric patients on CRRT, one pediatric patient on ECMO, and 21 adult patients on ECMO. Most pediatric patients on CRRT received cefepime (4/6, with one each receiving meropenem or piperacillin-tazobactam). For adult patients, eight patients received cefepime, eight received meropenem, and five received piperacillin-tazobactam. A mean of three samples were collected per participant [range 3-9]. Infectious etiologies in participants were highly variable. Fifteen adult patients were diagnosed with SARS-CoV-2 during admission. Three pediatric CRRT patients were diagnosed with fungal infections within seven days of enrollment in the study. Five adult patients had positive blood and/or urine cultures within seven days of sample collection: two patients with *Staphylococcus epidermidis* (blood), one with *Candida guilliermondii* (blood), and three with *Candida* species (urine). Six adult patients also had positive cultures from endotracheal tube specimens, including three with MRSA, two with *Pseudomonas aeruginosa*, and one with *Escherichia coli*.

Conclusions: Our study will be among the first to derive popPK models of cefepime, meropenem and piperacillin-tazobactam exposure in children receiving ECMO or CRRT and adults receiving ECMO. Results from this study will lay the foundation for personalized TDM for three commonly used antimicrobial agents in these populations.

CUMULATIVE INCIDENCE OF AUTISM SPECTRUM DISORDERS IN TENNESSEE

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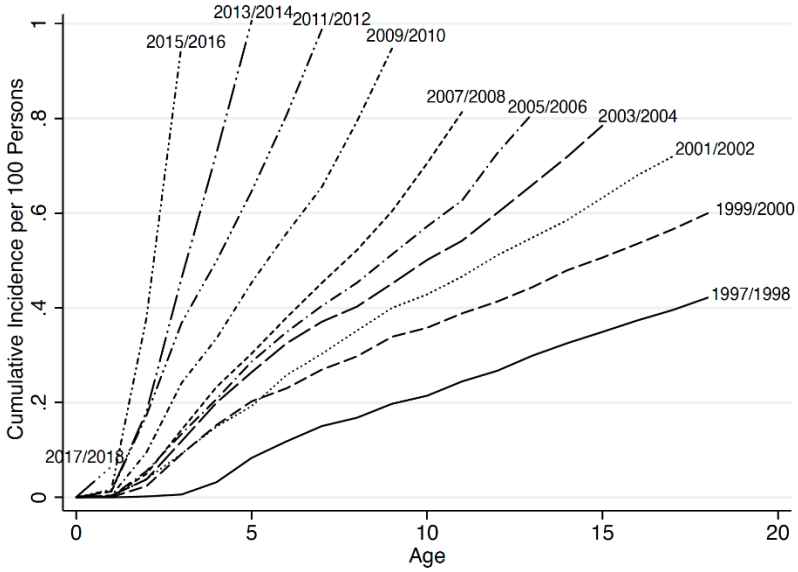
Objective: The prevalence of Autism Spectrum Disorder (ASD) has significantly increased over time, and the most recent prevalence estimate is 1.85% among 8 year old children. Currently, in the US the CDC reports the prevalence of ASD biannually based on the identification in 8-and 4-year-old children in 11 states using cross sectional methods. However, comprehensive longitudinal data identifying ASD diagnosis across time has not been available for the US with those purporting such estimates usually based on self-report methods. Standard ASD surveillance methods often require time and labor intensive strategies that result in a significant time delay when reporting statistics. Our objective was to utilize electronic health record (EHR) data for patients seen at Vanderbilt University Medical Center (VUMC) to estimate the cumulative incidence of ASD diagnosis over time in children in Tennessee born during 1997-2018.

Study Design: Our data source was Vanderbilt's Research Derivative clinical informatic platform which contains the electronic health record (EHR) data for all patients seen at VUMC including ICD codes used at each visit. Children were included as an ASD case if they were born between the years of 1997-2018; had at least one ICD code of ASD; last address in the EHR was listed in TN; and were not listed as deceased in the EHR. Incidence curves were calculated per birth cohort year dividing the number of cases of ASD per year by the total number of same aged-children living in Tennessee in the year of interest.

Results: A model for cumulative incidence curves for children living in Tennessee during birth cohort years 1997-2018 was successfully created using EHR data as shown in the figure. Final incidence estimates for ASD varied by birth cohorts with the lowest incidence of 0.42% in 18 year olds born in 1997/1998 with the highest of 1.01% in 3 and 4 year olds born in 2013/2014. Our methods yielded lower estimates than current CDC estimates. This figure shows an increase in autism incidence over time and across birth cohort years that has not yet flattened. Importantly, data for this study were extracted from the EHR over a 6 week period. Quantifying and creating the cumulative incidence curves took less than two weeks.

Cumulative Incidence of Autism Spectrum Disorder in Tennessee Children



Conclusion: Utilizing EHR based ASD identification might provide an efficient way to rapidly model ASD incidence. Future directions include linking these methods to statewide educational data and Medicaid data. This strategy could potentially provide a new method to model ASD incidence in real time in a cost effective manner.

AGE-DETERMINED EXPRESSION OF PRIMING PROTEASE *TMPRSS2* AND LOCALIZATION OF SARS-CoV-2 IN LUNG EPITHELIUM

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Objective: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) novel coronavirus 2019 (COVID-19) global pandemic has led to millions of cases and hundreds of thousands of deaths. While older adults appear at high risk for severe disease, hospitalizations and deaths due to SARS-CoV-2 among children have been relatively rare. We hypothesized that host factors governing SARS-CoV-2 infectivity and attachment in the lower respiratory epithelium may be developmentally regulated.

Study Design: We interrogated expression profiles of genes linked to SARS-CoV-2 infectivity by analyzing a single-cell RNA sequencing (scRNA-seq) dataset of mouse lung across five time points from embryonic day 18 (E18) to postnatal day 64 (P64). To spatially and temporally localize expression of candidate genes, we performed RNA in situ hybridization (RNA-ISH) (with automated quantification) and protein immunofluorescence. Developmental gene expression patterns in mice were compared to those at both the RNA and protein level in human lung samples in infants (0-2 years, n=7), children (3-17 years, n = 9), and adults (54–69 years, never smokers, n = 4). Lung autopsy specimens from patients who died of COVID-19 complications were analyzed for co-localization of SARS-CoV-2 viral particles and candidate genes.

Results: Expression of the cellular receptor for SARS-CoV-2, ACE2, did not significantly change over development whereas TMPRSS2, the canonical protease that mediates cellular entry for coronaviruses, showed increased expression with aging in mice and humans. Expression of TMPRSS2 was highest in ciliated cells and type I alveolar epithelial cells (AT1). Analysis of autopsy tissue from fatal COVID-19 cases detected SARS-CoV-2 RNA most frequently in ciliated and secretory cells in airway epithelium and AT1 cells in peripheral lung. SARS-CoV-2 RNA was highly colocalized with TMPRSS2.

Conclusions: Together, these data demonstrate the cellular spectrum infected by SARS-CoV-2 in lung epithelium and suggest that developmental regulation of TMPRSS2 may underlie the relative protection of infants and children from severe respiratory illness.

Funding: Supported by NIH grants R38-HL143619, K08HL143051 (to JMS), K08HL130595 (to JAK), R01HL145372 (to JAK/NEB), P01HL092470 (to TSB), K08HL127102 (to EJP), K08HL133484 (to JTB), R01AI077505 (to DWH), P30AI110527 (to SAM), R01AI142095 (to SAK/SAM), and TR002243.

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A MULTIMODAL BLACK HISTORY TOUR: INCREASING PHYSICIAN CONFIDENCE WITH CRITICAL RACE THEORY AND TRAUMA-INFORMED CARE

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Objective: With increased tension among communities of color nationally, there exists an ever-increasing recognition and responsibility for medical providers to have awareness of the social and historical roots of structural racism, or critical race theory, that impacts their patient population. Such understanding is critical in mitigating racial bias in medicine and allows for the provision of culturally competent and compassionate care. At present, although no formal curriculum for pediatrics trainees regarding implicit bias or race exists, we find it important that we first gain perspective on the historic and economic background that has led to the marginalization and disenfranchisement of Black residents in North Nashville.

We aimed to produce a multimodal Black history tour of North Nashville via exploration of pre-selected historically significant locations in North Nashville coupled with more in-depth investigation via selected readings, podcasts and documentaries to ultimately increase physician comfort in the critical race theory impacting patients from the area.

Study Design & Results: Although still in progress, we aim to perform a targeted cohort educational intervention with survey. Pediatrics residents will take a baseline knowledge test regarding concepts related to historical themes in North Nashville. Confidence scores via Likert scale will also be collected regarding critical race theory and provision of trauma-informed care. Following the multi-modal tour, the same knowledge assessment will be administered as well as a post-survey measuring self-reported confidence.

Statistical analysis of pre- and post-knowledge scores as well as confidence scores will be undertaken, and we anticipate preliminary results will be available for poster presentation.

Conclusion: Prior to this intervention, no such medical education curriculum exists. We aim to decrease knowledge and confidence gaps to provide a meaningful way for learners to understand the interplay between historical trauma and systemic racism to thus feel more empowered to address health disparities among our black patients and their families and to provide them with tailored community resources.

Mentor: Rosemary Hunter; rosemary.j.hunter@vumc.org

Utilization of echocardiography following repair of congenital heart disease in the current era

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Objective: Echocardiography is a key diagnostic tool for medical decision-making following congenital heart surgery. The overall utilization of echocardiography following cardiac surgery for specific congenital heart lesions has not previously been reported. This study aims to assess the utilization of echocardiograms following the surgical repair of congenital heart disease and to describe the variation in utilization across centers.

Study Design: All patients <18y undergoing surgical repair of congenital heart disease were identified from the Pediatric Health Information System (PHIS) using ICD-9 and ICD-10 procedure codes from 2010-2019. Surgical repairs included atrial septal defect, ventricular septal defect, tetralogy of Fallot, superior cavopulmonary anastomosis, total cavopulmonary anastomosis, coarctation, atrioventricular septal defect, transposition of the great arteries, total anomalous pulmonary venous return, truncus arteriosus, truncus arteriosus with interrupted aortic arch, and Norwood. Detailed billing data were used to assess the frequency of post-operative echocardiograms and phase of hospital care. All surgeries were grouped by their Risk Adjustment for Congenital Heart Surgery-1 (RACHS-1) scores. The mean and median number of post-operative echocardiograms performed for each RACHS-1 score and the lengths of stay were calculated. Data across all the PHIS hospitals were graphically compared using box plots with interquartile ranges for each RACHS-1 score.

Results: A total of 37,238 patients were identified for inclusion across 48 centers. The number of postoperative echocardiograms and length of stay increased with increasing RACHS-1 score (Table). When corrected for hospital length of stay, patients undergoing congenital heart disease repairs with higher RACHS-1 scores had lower echocardiogram utilization per day compared to patients with lower RACHS-1 scores (Figure 1). Within each RACHS-1 score there was significant variability in echocardiogram utilization across centers (Figure 2).

Conclusion: There has been little reported regarding the utilization of echocardiography following surgical repair for congenital heart defects. Our study found a positive correlation between the number of echocardiograms performed and post-operative length of stay with increasing surgical complexity as defined by the RACHS-1 scoring system. However, utilization of echocardiogram when adjusting for length of stay is lower in lesions with a higher RACHS-1 score. There is significant variation in the use of echocardiography across congenital heart surgery centers.

INCIDENCE OF SUICIDAL BEHAVIORS AND ASSOCIATIONS OF PATIENT CHARACTERISTICS IN CHILDREN BEFORE AND DURING THE SARS-COV-2 PANDEMIC

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Objective: Suicide is the second leading cause of death among children and young adults aged 10-24 in the United States. Between the years 2007 to 2018, suicide death rates in this age group increased by 57.4% with an additional rise in major depression, serious psychologic distress, suicidal ideation (SI) and suicidal attempts (SA). During the Covid-19 pandemic there has been a noted increase in pediatric ED (PED) chief complaints related to mental health concerns. Youth suicidal behavior is an established major public health concern; therefore, if we are to decrease the public health burden of suicide in children and young adults, we must understand the associations of Covid-19 with pediatric mental health. The primary objective of this study is to quantify the impact that Covid-19 has had on suicidal behavior in the population presenting to Vanderbilt's PED. A secondary objective of this study is to describe the population presenting with SI or SA.

Study Design: We screened and recorded relevant variables from the electronic medical records of patients requiring psychiatric consultation in the PED between March 2018 and March 2021. Patients were included for analyses if they had documented concern for SI or SA. Patient characteristics including age, gender, race, zip code, insurance, mode of arrival, results of Columbia-Suicide Severity Rating Scale, ED arrival date and time, ED length of stay, and disposition were collected from patient's electronic medical record. For patients admitted to the hospital, additional information was obtained including hospital length of stay, status of medical clearance on admission, avoidable hospital days and barriers to discharge. Descriptive statistics will be reported as means (SD), median [IQR], and proportions as appropriate. Multivariable logistic models will be used to examine associations between explanatory variables and outcomes of interest (SI, SA), with reduction of model covariates as needed to avoid overfitting. This study was approved by the Vanderbilt IRB (protocol # 161952).

Results: A total of 6,239 chart were reviewed (as of January 2021), and 2,185 had a presenting chief complaint of SI and SA and were included for analyses. An additional 4,054 charts were reviewed for SI or SA. Secondary review is still under way. Thus far 689 of these charts revealed suicidality on secondary review. Characteristics of patient population pending.

Conclusions: Pending.

Mentor: Marla Levine, MD (marla.levine@vumc.org)

FACTS BEHIND THE FAD: A DESCRIPTIVE SURVEY OF A CURRICULUM TO PROMOTE E-CIGARETTE EDUCATION IN HIGH SCHOOL STUDENTS

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Objective: To effectively convey the health risks associated with use of electronic cigarettes to high school students using a physician-lead, virtual curriculum. Teenagers are more likely to engage in risky behaviors than children of other ages and have been specifically targeted by tobacco makers through online marketing. E-cigarette products contain far more nicotine than traditional cigarettes in addition to other dangers such as thermal injury, carcinogen exposure, and e-cigarette or vaping use-associated lung injury (EVALI).

Study Design: Pediatric residents created a PowerPoint that they presented via Zoom to students at a local high school. Google form surveys were administered via QR code prior to the presentation ("pre-survey") and at the conclusion ("post-survey"). The pre-survey contained true/false questions to gauge baseline knowledge. The post-survey consisted of five-point Likert scale questions assessing whether participants would decrease their use of vape products or encourage their peers to do so. This scale ranged from completely disagree (1) to completely agree (5). Understanding of the side effects of vaping was assessed on both surveys using a similar Likert scale. A total of 36 students were involved in the study. Students were informed that survey participation was optional, anonymous, and would not impact their class grade.

Results: The response rate was 83.3% (n = 30) for the pre-survey. Of respondents, seventeen students (56.7%) reported that they have never tried vaping, eight students (26.7%) have tried vaping but will never do it again, four students (13.3%) occasionally vape, and one student (3.3%) vapes multiple times per week. Twelve students (40.0%) thought vaping is safer than smoking cigarettes. Six students (20.0%) thought that vaping is not addictive. Following curriculum implementation, the post-survey response rate was 55.6% (n = 20). Students marked an average of 4.78 (SD = 0.55) in response to the statement, "Following this presentation, I will decrease my use of vaping." Students marked an average of 4.11 (SD = 1.28) in response to the statement, "Following this presentation, I will discourage others to use vaping products." Students were also asked to respond to the statement, "I understand the side effects of vaping," on both surveys. A Wilcoxon rank sum test showed that the median for the pre-survey was 4.5 (IQR 4, 5), and the post group was 5 (IQR 5, 5) with p-value 0.0372.

Conclusions: Our pre-survey highlighted the need for adolescent education around the risks of vaping. Nearly half of the population surveyed have tried vaping or currently vape. Almost half believed vaping is safer than smoking cigarettes and many felt it has a low addiction risk. Post-survey responses demonstrated the program convinced students to decrease their use of vaping. Students reported on average that they would discourage others from the use of e-cigarettes. However, the standard deviation was wide, and several students disagreed with this. Future steps involve including information in the curriculum on the importance of discouraging their peers from vaping and advice on to have these conversations. Finally, comparisons of the pre- and post-surveys showed that the curriculum improved students' understanding of vaping side effects. Overall, results suggest that a physician-lead, virtual curriculum can effectively relay information about the risks of e-cigarette use in an adolescent population.

Mentor: McKenzie Vater, MD; mckenzie.vater@vumc.org

Propafenone Adverse Events in the Pediatric and Young Adult Population

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Introduction: Propafenone is a class IC sodium channel blocker used as a first line agent to treat supraventricular tachycardia (SVT) in children. Adverse events (AEs) of propafenone include EKG changes such as heart block, QRS and QTc prolongation, and systemic symptoms such as dysgeusia, increased secretions, and dizziness. Reported studies of propafenone AEs in children include a total of <100 individuals and indicate a wide range of AE incidence.

Objective: The aims of this study are to quantify propafenone AEs at our center and to identify possible AE risk factors.

Study Design: This was a single center retrospective chart review study. All patients less than 30 years old at the time of propafenone initiation, from 1994-2018, were identified through the electronic medical record. Manual chart review was performed to identify AEs within the first three years of propafenone use. Demographic, clinical, and AE data were collected using REDCap. Categorical variables were compared with Pearson's Chi square and continuous variables with Wilcoxon rank sum.

Results: 76 individuals (median age 0.31 years; range 0-23 years) were included. Of these, 31 (41%) had a documented propafenone AE, with 14 (18%) requiring propafenone discontinuation. The most common AEs were QRS (10) and QTc prolongation (6) with an average increase of 53ms and 103ms from baseline EKG respectively, first degree AV block (4), hypotension (5), and dysgeusia (4). The most common AEs requiring drug discontinuation were hypotension (4), dysgeusia (3), and 2nd degree heart block (2). Most AEs (23/31, 74%) occurred in the first 3 months of therapy. AEs were more common in those over one year of age at the time of propafenone initiation (17/29, 59%) compared to those less than one year old (14/47, 30%, p=0.013). These older individuals were also more likely to require propafenone discontinuation (10/29, 35% vs 4/47, 9%, p=0.005). Patient clinical factors such as presence of congenital heart disease or single ventricle lesions, history of cardiac surgery, or use of concomitant CYP2D6 medications were not associated with AEs. The maximum dose of propafenone (mg/m2/day) and the propafenone dose at the time of AE were also not associated with AEs.

Conclusion: AEs are common (41%) in young patients prescribed propafenone and were more common in patients older than one year at the time of initiation. No additional clinical factors were associated with development of AEs; pharmacogenomic variation may further explain and predict propafenone AEs.

Harnessing cell-penetrating peptides for non-viral gene editing

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Manipulating genetic information for correcting disease-causing mutations has recently evolved into a translationally-relevant therapeutic approach. The primary technology being developed is the CRISPR-Cas9 system, which has shown great promise for correction of single gene diseases. One major challenge for translating this technology from bench to bedside is impaired delivery, immunogenicity and production of off-targets. One way to circumvent this issue is via the fusion of cell penetrating peptides (CPPs) to Cas9 to establish carrier-free intracellular delivery of the active genome editing ribonucleoprotein (RNP). The main goal of this research is to systematically investigate the fusion of CPPs to Cas-proteins in order to establish non-viral genome editing via direct RNP delivery as a translatable therapeutic platform. As a first step, we generated and purified a library of twenty-four Cas9-CPP chimeric proteins using the Gibson Assembly Method and a cell-free protein synthesis technique. Proteins were designed to titrate the amount of cationic charge and hydrophobicity required to deliver the large, complex Cas9 RNP. Efficient synthesis of full-length recombinant proteins was corroborated by SDS-Page. Next steps are focused on testing protein stability, zeta potential and hydrodynamic radius by Nanosight, Proteostat reagent and DLS. Editing efficiency of the different recombinant proteins will also be corroborated both *in vitro* and *in vivo*. Once optimal CPP-Cas9 chimeras are determined as above, we will then proceed to investigate the efficiency of our system for targeting the dystrophin gene for the treatment of Duchenne Muscular Dystrophy using DMD mouse models.

IMPLEMENTATION OF SEDATION WEANING PROTOCOL IN A PEDIATRIC CARDIAC CRITICAL CARE UNIT

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Objective: Medications commonly used postoperatively for sedation and/or analgesia in critically ill congenital heart disease come with adverse events including withdrawal, bowel dysmotility, delirium and impairment neurodevelopmental outcomes. There is a paucity of literature regarding the optimal method of weaning continuous sedation with aims to mitigate and lessen these adverse effects, particularly in the cardiac population. By implementing a risk stratified weaning protocol, we aim to reduce the total time on wean, total dose exposure and number of patients discharged on a wean.

Study Design: A risk stratified weaning protocol was implemented in the Pediatric Cardiac Care Unit in September 2020 for all patients requiring continuous sedation. De-identified clinical outcomes and demographical data will be retrospectively collected for 1 year before and after protocol implementation. Patient data will be stratified by surgical STAT category. This data will includes wean duration, withdrawal scores, ICU length of stay, readmission related to withdrawal and need for discharge on sedative wean will be compared via statistical analyses to determine any difference in outcomes post-intervention correcting for demographics.

Results: Pending data collection, to be discussed.

Conclusions: While data collection is in process, anecdotally we have received positive feedback on the protocol and ability to wean in a quicker, more standardized fashion. Patients have been able to complete medication tapers while still in the ICU which was extremely uncommon prior to the protocol. Prior published literature has shown that having a weaning protocol will lead to decreased times on wean and we expect to see similar results. With decreased wean times leading to decrease in total dose exposure there is potential for downstream improvement in neurodevelopmental outcomes in a medically fragile group.

IMPROVING EDUCATION IN PEDIATRIC AIRWAY MANAGEMENT IN PEDIATRIC RESIDENTS

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Objectives: A critical component of the pediatrician's role is to triage and care for a patient in respiratory distress. The purpose of this study was to provide training on a pediatric airway toolkit and assess if this improved pediatric resident involvement, comfort, and knowledge of airway management.

Study Design: A pediatric airway toolkit curriculum was developed that highlighted airway management and procedural skills. Curriculum was taught to pediatric residents during their emergency medicine rotation. Participants completed a pre and post survey which detailed the frequency and comfort level on a 5 point Likert scale of performing the following procedures: Bag Valve Mask (BVM), Laryngeal Mask Placement (LMA), Oropharyngeal Airway Placement (OP), Nasopharyngeal Airway Placement (NP), Endotracheal Intubation (ETT), and overall comfort level with respiratory distress. Curriculum was taught in-person from November 2019 to March 2020 with simulation. Due to the COVID-19 pandemic, the curriculum was transitioned virtually from May 2020-present. In July of 2020 pre/post quizzes to assess knowledge were added. Data was collected via Redcap and statistical analysis was performed.

Results: There were 69 total pre survey responses and 46 post survey responses. As of July 2020, with the addition of a pre/post quiz, there are 32 pre survey responses and 21 post survey responses.

The data from Nov 2019 to June 2020 demonstrated that the mean frequency of all 5 procedures prior to the curriculum which ranged from 1.125 (SD= 0.49, OP) to 2.125(SD=0.91, BVM) was similar to the frequency after the curriculum 1.08(SD=0.28,OP) to 2.12 (SD=0.97, ETT). Overall resident comfort level averaged 2.6875 (SD=0.90) and 3.24(SD=0.78) before and after the curriculum respectively. A Wilcoxon rank sum test demonstrated that resident comfort with BVM placement was statistically significantly higher after the curriculum (p=0.02) and comfort level with the overall management of respiratory distress also increased (p=0.01).

From July 2020 to January 2021,14 participants completed both the pre/post survey. Statistical analysis via paired t-Test was performed. There was a statistically significant increase in the means for comfort level for NP placement (p=0.02), LMA placement (p=0.03), OP placement (p=0.04), ETT placement (p=0.04), and overall comfort level (p=0.03). The pretest mean was 60.2% and posttest mean was 67.3%, there was not a statistically significant difference between the pre/post test (p=0.15) or the frequency of procedures between the two groups.

Conclusions: The curriculum increased the overall pediatric resident comfort level with management of respiratory distress and different airway adjuncts. However, sample size was insufficient to demonstrate a difference in pre/post test scores. The frequency of resident participation in the management of airway procedures remained relatively similar before and after the intervention. However, opportunities for participation were impacted by COVID-19 safety protocols. This data further highlights the need for creative opportunities for pediatric resident education on airway management.

The Physical Abilities and Mobility Scale as a New Measurement of Functional Progress in the PICU

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Objective: Data on the effects of Early Mobility (EM) in the pediatric ICU (PICU) population are limited due to difficulty quantifying small functional gains with current validated tools. We assessed the utility of the Physical Abilities and Mobility Scale (PAMS), a validated pediatric rehabilitation scale, in the PICU population and compared it to the commonly used Functional Status Scale (FSS).

Study Design: Single center, retrospective chart review of patients ≥ 2 years of age admitted to the PICU or pediatric cardiac ICU at an academic tertiary care pediatric hospital from July 1, 2018-March 30, 2019. Patients who were not on the EM protocol (i.e., patients with ICU length of stay (LOS) <72 hours or patients who met EM exclusion criteria) and those who had <2 PAMS scores were excluded from analysis. Spearman's correlation coefficients were used to assess the association between the FSS and PAMS. Comparisons of scores in relation to disposition used a Mann-Whitney U-test.

Results: 130 patients met inclusion criteria. Median age 9.4 years, median ICU LOS 9 days, and median hospital LOS 16 days. Primary diagnoses included respiratory failure or insufficiency (20%), cardiac disease (15%), and status post elective surgery (15%). Patients had a median of 7 physical and/or occupational therapy visits while in the ICU. The association between the PAMS and FSS was strong (rho = -0.85), but non-linear. As the FSS ranged from 26 to 13, the PAMS ranged from 20 to 40. However, for an FSS between 7 and 13, the PAMS ranged between 40 and 95, suggesting much greater sensitivity to small changes in function. In comparing patients discharged to an inpatient rehabilitation facility (n=17) to those discharged home (n=105), the median FSS score at discharge was 9 vs 13, while the median PAMS at discharge was 66 vs 40. The difference in magnitude of the differences (4 vs 26) further suggests PAMS exhibits greater sensitivity to small changes in functional status.

Conclusions: The PAMS is a useful tool to assess and track functional progress in critically ill children and may be helpful in prognosticating final disposition needs. Next steps include investigating its use in quantifying patient progression during hospitalization and for informing disposition decisions.

DEVELOPING A PEDIATRIC CARDIAC SURGERY POSTOPERATIVE INFECTION COHORT

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Objective: Every year in the United States, approximately 40,000 children undergo cardiovascular surgery, and about one-third develop post-operative infections. Rapid, prospective identification of patients at high risk of infection could improve patient safety and outcomes. Predictive modeling has successfully forecasted risk of infection in other settings and requires a high quality, curated data set. The objective of this study was to develop a high-quality single center cohort of pediatric cardiac surgery patients, including infectious outcome labels and relevant predictors to enable future development of predictive models for post-operative infection.

Study Design: We obtained clinical data from the Vanderbilt Research derivative (RD). The RD contains structured and unstructured data elements obtained from the Vanderbilt University Medical Center's electronic health record, including laboratory values, vital signs, diagnostic codes, procedure codes, provider notes, and demographic information. We identified patient record for inclusion by querying for CPT codes corresponding to pediatric cardiac surgeries. Patients 18 years of age or younger who underwent cardiac surgery on or after January 1, 2015, were included in our cohort. We identified possible predictors from literature review and expert opinion. Predictors included demographics, vital signs, laboratory values, drug exposures (including vasopressors, antibiotics, and steroids), comorbid medical conditions, and infectious disease history. Outcomes included bacteremia, clinical sepsis, urinary tract infection (UTI), surgical site infection (SSI), pneumonia, and necrotizing enterocolitis (NEC). Patients were assigned to an outcome group if they received a new diagnosis from a corresponding SNOMED code set within 30 days of their procedure. We validated the data collection via manual review of a subset of approximately 1% of patient charts.

Results: We identified 1681 patients, undergoing 6217 distinct procedures of interest during 2022 distinct operative encounters. Of the 2022 surgical encounters, 1070 (52.9%) were performed on males; 952 (47.0%) were performed on females. The mean age at surgery was 4.41 years, with a range of 0.00 to 18.00 years. In our data set, 343 (16.9%) of the 2022 operative encounters were followed by an infection of interest. The distribution of infectious complications was as follows: Bacteremia in 108 (5.2%), pneumonia in 88 (4.3%), surgical site infection in 85 (4.2%), sepsis in 70 (3.5%), UTI in 57 (2.1%), and NEC in 37 (1.8%).

Conclusions: We queried a single center data repository to obtain a cohort of pediatric cardiac surgery patients, including post-operative infection labels and possible predictors of infection. Our cohort is significantly larger than others reported in the literature for this population. We plan to use this cohort to train and validate predictive models for post-operative infection, using logistic regression and machine learning methods.

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HAND-ON: A PROSPECTIVE COHORT STUDY OF DIRECT OBSERVATION OF I-PASS HANDOFFS IN PEDIATRIC INTERNS

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Objective: I-PASS (Illness severity, Patient summary, Action list, Situational awareness, Synthesis) is a handoff tool shown to improve communication and patient safety. Direct observation by faculty has been used for documenting adherence to I-PASS previously. We aim to determine the effects of direct observations by chief residents on sustained adherence to I-PASS handoffs in pediatric interns.

Study Design: We led I-PASS training during intern orientation. This included handoffs modeled by senior residents and scenarios role-played by interns. Three chief residents observed intern handovers from day to night shifts on the wards for six months. Observations were scored with the standardized evaluation form (Figure 1). We determined the mean score for each I-PASS component, engagement, prioritization of concerns, miscommunications, omissions, and tangential conversations. We observed interns at multiple points over time and compared mean values between the two three-month blocks of observation using a two-tailed t-test (Table 1).

Results: We completed 52 observations, 27 in Phase 1 and 25 in Phase 2. In Phase 2, we found interns more often included Illness severity and Patient summary but less frequently included Action list, Situational awareness, and Synthesis. Only the decrease in Synthesis was statistically significant (mean 3.63 v. 2.84, P = 0.02). Interns showed improvement in engagement, prioritization, miscommunications, and omissions, but an increase in tangential conversations. However, none of these were statistically significant (P < 0.05).

Conclusions: Direct observation alone may not have an impact on sustained adherence to I-PASS handoffs. Additional interventions such as training refreshers may be needed.

Table 1. Comparison of direct observation I-PASS form items between Phase 1 and Phase 2

Direct Observation Form Item	Phase 1 (n=27) Mean	Phase 2 (n=25) Mean	P value
1. Illness Severity	2.67	3.04	0.29
2. Patient Summary	3.48	3.68	0.37
3. Action List	3.85	3.84	0.91
4. Situational Awareness	3.70	3.48	0.21
5. Synthesis of Receiver	3.63	2.84	0.03
6. Engagement of Receiver	3.30	3.48	0.30
7. Prioritization of Key Information	3.26	3.44	0.33
8. Miscommunications of important information	0.61	0.45	0.76
9. Omissions of important information	0.77	0.70	0.76
10. Tangential conversation	0.96	0.76	0.28

*For items 1-7 the mean was calculated by assigning numerical values to a Likert scale of: never (0), rarely (1), sometimes (2), usually (3), and always (4)

*For items 8-10 the mean was calculated by assigning numerical values to a Likert scale of: very often (0), fairly often (1), occasionally (2), rarely (3), and never (4)