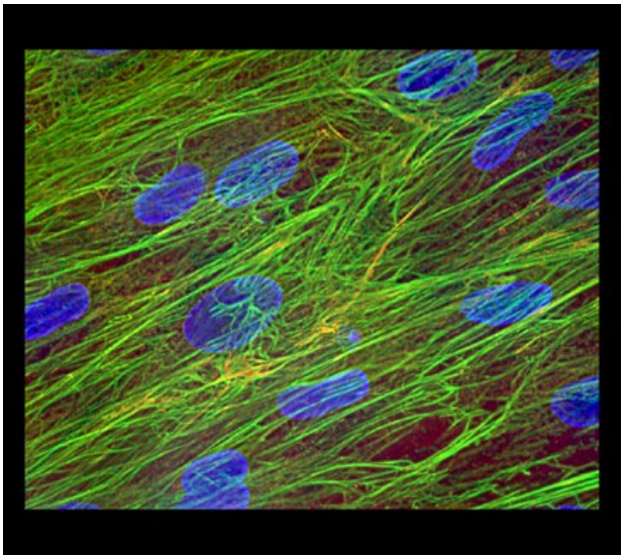
Icahn School of Medicine at Mount Sinai

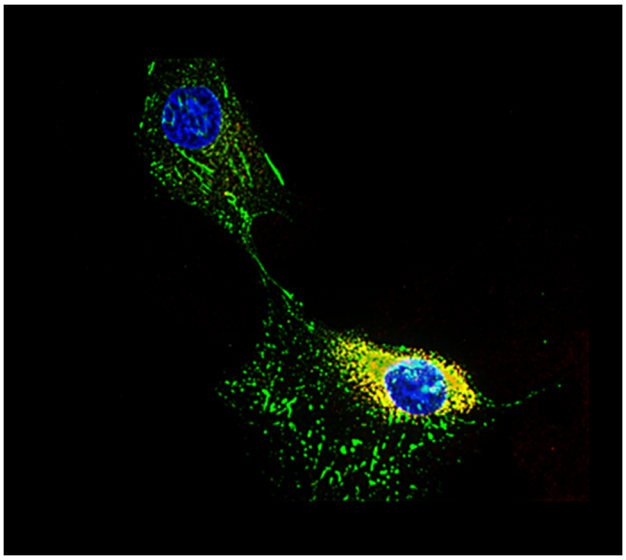
25th Annual Child Health Research Day

Sponsored by

The Jack and Lucy Clark Department of Pediatrics
The Mindich Child Health and Development Institute
The Department of Environmental Medicine and Public Health

Program





April 13, 2023
Hatch Auditorium & Guggenheim Pavilion Atrium

A Program of
The Jack and Lucy Clark Department of Pediatrics
The Mindich Child Health and Development Institute
The Department of Environmental Medicine and Public Health

Keynote Speaker:

Kathryn M. Edwards, MD
Professor of Pediatrics, Sarah H. Sell and Cornelius Vanderbilt Chair
Scientific Director, Vanderbilt Vaccine Research Program
Vanderbilt University, Nashville, TN

Child Health Research Day

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Icahn School of Medicine at Mount Sinai
25th Annual Child Health Research Day

Schedule of Events

April 13, 2023
In-Person and Live Stream

7:45-8:00 a.m.	**Coffee and Tea**
8:00-8:05 a.m.	**Welcome and Introductions** Bruce D. Gelb, MD Gogel Family Chair and Director, The Mindich Child Health and Development Institute Dean, Child Health Research at the Icahn School of Medicine at Mount Sinai Kecia Carroll, MD, MPH Division Chief, General Pediatrics, Department of Pediatrics Debra and Leon Black Professor, Pediatrics Professor, Environmental Medicine and Public Health
8:05-9:00 a.m.	**Grand Rounds: The Dr. Howard Rappaport Memorial Lecture** "Unraveling the Mystery of Periodic Fever in Children" Kathryn Edwards, MD Professor of Pediatrics Sarah H. Sell and Cornelius Vanderbilt Chair Scientific Director, Vanderbilt Vaccine Research Program
9:00-9:30 a.m.	**Breakfast**
9:30 a.m.	**Introduction of the Moderators and CHRD Oral Presentation Session** David Dunkin, MD, Chair, Child Health Research Day 2023 Organizing Committee Associate Professor, Pediatric Gastroenterology and Nutrition
9:30-10:30 a.m.	"**Long Talks**" **Moderators**: Bryan Li, MD, and Maria Rosa, DrPH
9:30-9:40 a.m.	**JAK/STAT Pathway Hyperactivity in Pediatric Focal Segmental Glomerulosclerosis** Carol Shen, Ashley Richardson, Louise Malle, Michael Espino, Sofija Buta, Marta Martin-Fernandez, Jeffrey Saland, Dusan Bogunovic
9:40-9:50 a.m.	**Sex-Specific Associations Between Co-Exposure to Multiple Metals and Externalizing Symptoms in Adolescence** Kristie Oluyemi, Elza Rechtman, Azzurra Invernizzi, Chris Gennings, Stefano Renzetti, Alessandra Patrono, Giuseppa Cagna, Abraham Reichenberg, Donald R. Smith, Roberto G. Lucchini, Robert O. Wright, Donatella Placidi, Megan K. Horton
9:50-10:00 a.m.	**Associations Between Neighborhood Childhood Opportunity, Race/Ethnicity, and Surgical Outcomes Among Children with Congenital Heart Disease** Sonny Q. Duong, Mahmud O. Elfituri, Isabella Zaniletti, Robert W. Ressler, Clemens Noelke, Bruce Gelb, Robert Pass, Carol Horowitz, Howard Seiden, Brett Anderson

10:00-10:10 a.m.	**Mannose Attenuates Hepatic Steatosis in the Mouse NASH Model and *In Vitro* Hepatocytes** John Hong, Joshaya Trotman, Yvette Carbajal, Peng Zhang, Liheng Wang, Charles DeRossi, Jaime Chu
10:10-10:20 a.m.	**Association Of Blood Pressure with Neurologic Outcome After Pediatric Cardiac Arrest Resuscitation** Adam Ushpol, Sangmo Je, Tanmay Majmudar, Matthew Kirschen, Jimena del Castillo, Corinne Buysse, Alexis Topjian, Vinay Nadkarni, Sandeep Gangadharan; for the pediRES-Q Investigators
10:20-10:30 a.m.	**Association of Ambient Temperature and Fine Particulate Matter (PM2.5) With Urinary Kidney Injury Biomarkers in Children** Maria Politis, Iván Gutiérrez-Avila, Allan Just, María Luisa Pizano-Zárate, Marcela Tamayo-Ortiz, Jason H Greenberg, Martha M. Téllez-Rojo, Robert O. Wright, Alison P. Sanders, Maria José Rosa
10:30-10:40 a.m.	**Break**
10:40-11:30 a.m.	**"Short Talks"** **Moderators**: Bryan Li, MD, and Maria Rosa, DrPH
10:40-10:44 a.m.	**Association of Hyperphagia Score with Race/Ethnicity in Children and Adolescents With Overweight/Obesity** Alison R. Forte, Marcus C. Rasmussen, Sarah K. Zafar, Clint E. Kinney, Joan C. Han
10:44-10:48 a.m.	**Reprograming of the Intestinal Immune Cell Compartment Defines the Response to Autologous Stem Cell Transplantation in Crohn's Disease** Daniela Guisado, Sayali Talware, Shishir Singh, Stephanie Gold, Moutasem Mansi, Elbek Fozilov, Aaron Etra, Judy Cho, Louis Cohen
10:48-10:52 a.m.	**Neuro-Environmental Interactions: A Time Sensitive Matter** Azzurra Invernizzi, Elza Rechtman, Stefano Renzetti, Claudia Ambrosi, Lorella Mascaro, Roberto Gasparotti, Cheuk Y. Tang, Donald R. Smith, Roberto G. Lucchini, Robert O. Wright, Donatella Placidi, Megan K. Horton, Paul Curtin
10:52-10:56 a.m.	**Prenatal Predictors of Postnatal Intervention in Prenatally Diagnosed Non-Critical Pulmonary Stenosis** Grace Kong, Jennifer Cohen, David Ezon, Erin Paul
10:56-11:00 a.m.	**Effects of Loxapine on Energy Balance in MC4R Deficient Mice** Clint E. Kinney, Sarah K. Zafar, Marcus C. Rasmussen, Liam McAllan, Tao Yang, Amanda S. Stayton, Erin J. Stephenson, Joseph F. Pierre, Michelle A. Puchowicz, Chino K. Eke, Sandra G. Yang, Frank M. Longo, Joan C. Han
11:00-11:04 a.m.	**A Quality Improvement Project to Reduce Antibiotic Use by Limiting Treatment for Culture-Negative Sepsis (CNS) in a Level IV NICU** Jessica Lewis, Laura N Hodo, Jennifer Duchon, Stefano Biguzzi-Velcich, Courtney Juliano

11:04-11:08 a.m.	**Application of Network-Based Heterogeneity Clustering for Investigation of Genotype-Phenotype Correlations in Biome Biobank** Meltem Ece Kars, Yiming Wu, Cigdem Sevim Bayrak, Bruce Gelb, Yuval Itan
11:08-11:12 a.m.	**Rapid Response EEG Decreases Time to Seizure Diagnosis in Pediatric ER and ICU Patients** Nevedha Rajan, Sandeep Gangadharan, Toni Kavanagh, Maite La Vega-Talbott
11:12-11:16 a.m.	**Baseline Epitope Profiles Are Predictive of Sustained High Threshold in the POISED Trial** Maria Suprun, Ashley Sang Eun. Lee, Robert Getts, Simon Peck, Sayantani B. Sindher, Kari C. Nadeau, R. Sharon Chinthrajah, Stephen J. Galli, Hugh Sampson
11:16-11:20 a.m.	**Clinically Relevant Clusters of Neonates Generated with Machine Learning** Emily Polidoro, Girish Nadkarni, Jessica Lewis, Jennifer Duchon, Justin Kauffman
11:20-11:24 a.m.	**Cardiac Specific Loss of RNA Binding Protein Ddx3x Reveals Sex and Cell Type Specific Roles During Development** Ivianis Nieves Carril, Bhavana Shewale, David Sachs, Tasneem Ebrahim, Xioting Zhou, Lauren Dierdorff, Nan Yang, Kristin Beaumont, Robert Sebra, Joseph Buxbaum, Silvia De Rubeis, Nicole Dubois
11:24-11:28 a.m.	**Associations Between Nitrogen Dioxide and Routine Vaccine Antibody Levels in Children** Mike Z. He, Maayan Yitshak-Sade, Itai Kloog, Allan C. Just, Corina Lesseur, Sally A. Quataert, Martha M. Téllez-Rojo, M. Cecilia Berin, Robert O. Wright, Todd A. Jusko, Elena Colicino
11:28-11:35 a.m.	**Oral Presentations Concluding Remarks** Lisa M. Satlin, MD Herbert H. Lehman Professor and System Chair, Jack and Lucy Clark Department of Pediatrics
11:45a.m.-12:45 p.m.	**Poster Session-Guggenheim Pavilion Atrium and To-Go Lunches**
12:45- 1:00 p.m.	**Poster Session Award Ceremony**

Dr. Howard Rappaport Memorial Lecture

Howard Rappaport was a member of the Department of Pediatrics from 1957 to 1994. His subspecialty was pediatric cardiology, but he chose to practice general pediatrics, an area in which he was loved by both patients and colleagues. His encouragement and caring for children and their parents were unique and became an inspiration for generations of younger doctors. Students and house staff were inspired by him. He was able to impart a unique clinical and teaching skill to them. In recognition of his medical contributions and his warm friendship, his friends, colleagues, patients, and their parents have provided the financial base for establishing an annual lectureship in his memory. It is the hope of the contributors that Howard's many fine qualities will serve as a role model to the pediatricians who succeed him.

Icahn School of Medicine at Mount Sinai

Annual Child Health Research Day

April 13, 2023

WELCOME

We welcome you to the 25th Annual Child Health Research Day at Mount Sinai! This event aims to highlight the outstanding research activities of students, housestaff, clinical and research post-doctoral fellows, research staff, social workers, nurses and junior faculty across the Icahn School of Medicine at Mount Sinai and Mount Sinai Health System whose work is broadly related to the health and welfare of infants, children, and adolescents. Today's plenary and poster sessions exemplify the commitment to scientific discovery and scholarship central to our academic mission. The event provides a unique opportunity for junior investigators in the Departments of Pediatrics and Environmental Medicine and Public Health as well as the Mindich Child Health and Development Institute to share the results of their research with colleagues, and thereby discover new applications for their work or identify potential future areas for collaboration. We thank you for attending and congratulate all the participants on their accomplishments!

Lisa M. Satlin, MD
Chair, The Jack and Lucy Clark Department of Pediatrics

Bruce D. Gelb, MD
Director, The Mindich Child Health and Development Institute

Robert O. Wright, MD, MPH
Chair, The Department of Environmental Medicine and Public Health

COVER IMAGE FIGURE LEGEND

Both images show costaining (yellow) of fibronectin (green channel) and fibrillin-1 (red channel) in the extracellular matrix of human dermal fibroblasts during late (left) and early (right) stages of extracellular matrix formation. (Images courtesy of Nandaraj Taye, PhD, Post Doc Fellow, Orthopaedics)

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ORAL "SHORT TALK" PRESENTATION INDEX

POSTER INDEX

ADDITIONAL ABSTRACT INDEX

ABSTRACT AFFILIATION INDEX

JAK/STAT Pathway Hyperactivity in Pediatric Focal Segmental Glomerulosclerosis

Author Name(s): Carol L. Shen, Ashley Richardson, Louise Malle, Michael Espino, Sofija Buta, Marta Martin-Fernandez, Jeffrey Saland, Dusan Bogunovic

Department: Pediatrics

Division: Nephrology and Hypertension

Institution Affiliation: Icahn School of Medicine at Mount Sinai

Institute Affiliation(s): Center of Inborn Errors of Immunity; Mindich Child Health and Development Institute

Introduction: Focal segmental glomerulosclerosis (FSGS) accounts for approximately 20% of cases of pediatric nephrotic syndrome and is the leading cause of end-stage renal disease among glomerular disorders in the US. Primary FSGS is thought to be caused by a permeability factor which targets podocytes, leading to podocyte, glomerular and endothelial injury, and presumably immune dysregulation. There is growing evidence that the JAK/STAT pathway is involved in various adult kidney diseases, however, its role in pediatric kidney diseases has not been thoroughly studied. We recently identified JAK1 gain-of-function mutation in a pediatric patient with nephrotic syndrome and multisystem immune dysregulation, which was successfully treated with a JAK inhibitor.

Hypothesis: We hypothesized that JAK/STAT pathway hyperactivity may play a role in the pathogenesis of FSGS.

Methods: We recruited eleven individuals age 2-18yr with FSGS and ten age- and sex-matched healthy controls. Mass cytometry (CyTOF) with antibodies against STAT members was performed on heparinized whole blood samples to characterize JAK pathway activity in immune cell subsets. Patients were clustered according to STAT phosphorylation using unsupervised learning algorithms, and clinical parameters were analyzed. Multiplex immunoassay was performed on plasma samples to quantify cytokine levels.

Results: Increased phosphorylated STAT3 (pSTAT3) activity is present in T cell subsets, and increased pSTAT1 and 5 in B cells in patients with FSGS compared to controls. STAT3 phosphorylation in T cell subsets correlates with lower kidney function, lower serum albumin, and increased proteinuria at 1 year. IL6, which stimulates STAT3 phosphorylation, is increased in the plasma of patients compared to controls.

Conclusions: JAK/STAT pathway overactivity is present in individuals with FSGS and correlates with severity of disease. Increased JAK/STAT activity by cytokine signaling may inform the use of targeted anti-IL6 therapy or JAK inhibitors in FSGS.

Sex-Specific Associations Between Co-Exposure to Multiple Metals and Externalizing Symptoms in Adolescence

Author Name(s): Kristie Oluyemi**,** Elza Rechtman, Azzurra Invernizzi, Chris Gennings, Stefano Renzetti, Alessandra Patrono, Giuseppa Cagna, Abraham Reichenberg, Donald R. Smith, Roberto G. Lucchini, Robert O. Wright, Donatella Placidi , Megan K. Horton

Department(s): Environmental Medicine and Public Health; Psychiatry; Neuroscience

Division: Environmental Epidemiology

Institution Affiliation(s): Icahn School of Medicine at Mount Sinai; University of Brescia; University of California, Santa Cruz; Florida International University

Introduction: Adolescent externalizing disorders increase risk for later-life psychopathology and are more commonly expressed among males. Although associations between adolescent metal exposure and externalizing symptoms are well established, little is known regarding modification of these associations by sex.

Hypothesis: We hypothesize that sex moderates the association between metal mixture exposure and externalizing symptoms during adolescence, with males being more vulnerable to increased externalizing symptoms following metal exposure.

Methods: Among 148 adolescents (13-25 years; 83 females), we measured five metals (manganese (Mn), lead (Pb), copper (Cu) and chromium (Cr), nickel (Ni)) in four biological matrices (blood, urine, hair, and saliva) using inductively coupled plasma mass spectrometry (ICP-MS). Externalizing symptoms were assessed using the Youth Self-Report (YSR) or Adult Self Report (ASR). We used weighted quantile sum (WQS) regression to examine the moderating effect of sex on associations between the metal mixture and externalizing symptoms, adjusting for age and socioeconomic status.

Results: Metal mixture exposure was differentially associated with externalizing problems and aggressive behavior in males compared to females (β = -0.66, 95% CI [-1.52, -0.067]; β = -0.064, 95% CI [-0.125, -0.085]. In males, exposure was associated with higher externalizing symptoms, driven by Pb, Cr, and Cu. In females, exposure was not significantly associated with any externalizing symptoms.

Conclusions: These findings suggest that the effect of metal exposure on externalizing symptoms differs in magnitude and direction between the sexes, with males being more vulnerable to increased externalizing symptoms following metal exposure.

Associations Between Neighborhood Childhood Opportunity, Race/Ethnicity, and Surgical Outcomes Among Children with Congenital Heart Disease

Author Name(s): Son Q. Duong, Mahmud O. Elfituri, Isabella Zaniletti, Robert W. Ressler, Clemens Noelke, Bruce Gelb, Robert Pass, Carol R. Horowitz, Howard Seiden, Brett Anderson

Department: Pediatrics

Division: Cardiology

Institution Affiliation(s): Icahn School of Medicine at Mount Sinai; NYC Health + Hospitals/Elmhurst; Children's Hospital Association; Heller School for Social Policy and Management; Brandeis University

Institute Affiliation(s): Mindich Child Health Development Institute; Institute for Health Equity Research

Introduction: Racial and ethnic disparities in outcomes for children with congenital heart disease (CHD) coexist with disparities in educational, environmental, and economic opportunity.

Hypothesis: We hypothesized that racial/ethnic differences in surgical outcome are mediated by local differences in neighborhood opportunity.

Methods: Pediatric Health Information System encounters aged <18 years from 2016-2022 with ICD10 codes for CHD and cardiac surgery were linked to ZIP code-level Childhood Opportunity Index (COI), a score of neighborhood educational, environmental, and socioeconomic conditions. Effects of race/ethnicity and COI on in-hospital surgical death were modeled with generalized estimating equations and formal mediation analysis. Neonatal survival post-discharge was modeled by Cox proportional hazards.

Results: Of 54,666 encounters at 47 centers, non-Hispanic Black (Black, OR 1.20;p=0.01), Asian (OR 1.75; p<0.001), and "Other" (OR 1.50;p<0.001) groups had increased adjusted mortality vs non-Hispanic White. The lowest COI quintile had increased in-hospital mortality in unadjusted and partially adjusted models (OR 1.29;p=0.004). COI partially mediated the effect of race/ethnicity on in-hospital mortality by up to 16.8% (p=0.029). In neonatal survival analysis (n=13,987; median follow-up 0.70 years), those in the lowest COI quintile had poorer survival (HR 1.21, p=0.04).

Conclusions: Children in the lowest COI quintile are at risk for poor outcome after CHD surgery. Black, Asian, and "Other" groups have disproportionally increased mortality which may be partially mediated by COI. Targeted investment in environmental, educational, and economic opportunity in low COI communities may improve outcomes. Identification of unmeasured factors to explain persistent risk attributed to race/ethnicity is an important area of future exploration.

Mannose Attenuates Hepatic Steatosis in the Mouse NASH Model and *In Vitro* Hepatocytes

Author Name(s): John G. Hong, Joshaya Trotman, Yvette Carbajal, Peng Zhang, Liheng Wang, Charles DeRossi, Jaime Chu

Department: Pediatrics

Division: Hepatology

Institution Affiliation: Icahn School of Medicine at Mount Sinai

Institute Affiliation(s): Recanati/Miller Transplantation Institute at Mount Sinai, the Mindich Child and Health Development Institute

Introduction: Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease worldwide, yet there are no approved therapies. We have previously shown mannose to mitigate liver fibrosis, but its role in NAFLD is unclear.

Hypothesis: Mannose protects from fat accumulation (steatosis) in NAFLD.

Methods: Mice were fed normal diet or FAT-NASH regimen (high fat, fructose, and cholesterol, and low dose CCl_4) for 12 weeks. Mannose was supplied in drinking water (5% or 20%) for either the full 12 weeks or after 6-week delay. We used an unbiased, AI-based approach to quantify steatosis phenotypes in liver histological sections (FibroNest^{TM}). Liver triglycerides were measured in all groups. To induce steatosis, human hepatocytes (THLE-5B) were treated with 1mM oleic + palmitic acid (2:1) and 100mM fructose for 72 hours. Hepatocytes were treated with 25mM mannose for 72 hours or after 48-hour. Oil red O (ORO) staining was used to assess steatosis. Liver bulk RNA-seq was performed (Novogene).

Results: AI-based histological assessment revealed mannose supplementation improved steatosis at 5% and 20% (-26% and -60%, $p<0.05$) with prophylactic and delayed treatment in NASH mice *in vivo*. Liver triglycerides were also decreased in mannose-treated groups. *In vitro*, 25 mM mannose treatment for 24- and 72-hour decreased steatosis based on ORO staining (-20% and -33% respectively, $p<0.05$). Mouse liver bulk RNA-seq revealed *PCK1* was decreased in mannose treated mice ($p=0.01$).

Conclusions: Our findings uncover a novel role for mannose in fatty liver disease. Ongoing studies will test the role of mannose and PCK1 in liver steatosis.

Association of Blood Pressure with Neurologic Outcome After Pediatric Cardiac Arrest Resuscitation

Author Name(s): Adam Ushpol, Sangmo Je, Tanmay Majmudar, Matthew Kirschen, Jimena del Castillo, Corinne Buysse, Alexis Topjian, Vinay Nadkarni, Sandeep Gangadharan; for the pediRES-Q investigators

Department: Medical Education, Pediatrics

Division: Critical Care

Institution Affiliation(s): Icahn School of Medicine at Mount Sinai; Children's Hospital of Philadelphia; Drexel School of Medicine; Gregorio Maranon University Hospital; Sophia Children's Hospital

Introduction: Post cardiac arrest blood pressure <5th percentile for age is associated with worse survival to discharge. There are limited data on the impact of mean arterial pressure (MAP) on favorable neurologic outcome. We hypothesized, in the first 6-hours post-return of spontaneous circulation (ROSC), that a minimum documented MAP >5th percentile is associated with better neurologic outcomes.

Methods: Prospective, multi-center, observational study using data from the Pediatric Resuscitation Quality Collaborative (pediRES-Q). Children (<18 years) who achieved ROSC (without ECMO) following index in-hospital or out-of-hospital cardiac arrest and survived ≥6 hours were included. Minimum documented MAP within the first 6 hours of ROSC was percentile adjusted for age based on normative data and categorized into 6 groups: Group I= <5th percentile; II= 5–24th; III= 25–49th; IV= 50–74th; V= 75–94th; and VI= ≥95th. Primary outcome was favorable neurologic status at hospital discharge, defined as PCPC score ≤2 or no change from pre-arrest baseline. Multivariable logistic regression was performed to estimate the association of favorable outcome with MAP group, controlling for illness category (surgical-cardiac vs. other), shockable rhythm, weekend/night arrest, age, CPR duration, and clustering by site.

Results: 787 patients were included: median [Q1,Q3] age 17.9 [4.8,90.6] months; male 58%; OHCA 21%; shockable rhythm 13%; CPR duration 7 [3,16] min; favorable neurologic outcome 54%. Median lowest documented MAP percentile for the favorable outcome group was 13 [3,43] versus 8 [1,37] for the unfavorable group. The distribution of blood pressures by MAP group was I: 37%, II: 28%, III: 13%, IV: 11%, V: 7%, and VI: 4%. Compared with patients in Group I (<5%ile), those in Groups II, III, and IV had significantly higher odds of favorable outcome (aOR, 1.84 [95% CI, 1.24, 2.73]; 2.20 [95% CI, 1.32, 3.68]; 1.90 [95% CI, 1.12, 3.25]). There was no statistically significant association between Groups V or VI and favorable outcome (aOR, 1.44 [95% CI, .75, 2.80]; 1.11 [95% CI, .47, 2.59]).

Conclusion: In the first 6-hours post-return of spontaneous circulation (ROSC) after pediatric cardiac arrest, a lowest documented MAP >5th percentile (specifically 5th to 74th percentile) is associated with better neurologic outcomes.

Association of Ambient Temperature and Fine Particulate Matter ($PM_{2.5}$) with Urinary Kidney Injury Biomarkers in Children

Author Name(s): Maria D. Politis, Iván Gutiérrez-Avila, Allan Just, María Luisa Pizano-Zárate, Marcela Tamayo-Ortiz, Jason H Greenberg, Martha M. Téllez-Rojo, Robert O. Wright, Alison P. Sanders, Maria José Rosa

Department(s): Environmental Medicine and Public Health; Pediatrics

Division: Environmental Epidemiology

Institution Affiliation(s): Icahn School of Medicine at Mount Sinai; Yale University School of Medicine; University of Pittsburgh

Institute Affiliation(s): National Institute of Perinatology; Mexican Social Security Institute (IMSS); National Institute of Public Health

Background: The association between exposure to ambient temperature and fine particulate matter ($PM_{2.5}$) with kidney function has not been extensively studied.

Hypothesis: Temperature and $PM_{2.5}$ exposure is associated with preadolescent estimated glomerular filtration rate (eGFR) and urinary kidney injury biomarkers.

Methods: Participants included 437 children enrolled in the Programming Research in Obesity, Growth, Environment and Social Stressors birth cohort based in Mexico City. eGFR and urinary kidney injury biomarkers were assessed at the 8-12 years study visit. Satellite-based temperature and $PM_{2.5}$ models were used to estimate mean daily temperature and $PM_{2.5}$ at participants' residences for the seven days prior to the study visit. We used distributed lag nonlinear models to examine associations between daily mean temperature and $PM_{2.5}$ exposure and kidney outcomes, adjusting for child's age, sex, body mass index and urine creatinine, socioeconomic status, indoor tobacco smoking report, and seasonality.

Results: Higher mean daily temperature exposure was associated with a cumulative decrease in urinary cystatin C of -0.56 ng/mL (95% confidence interval (CI): -1.08, -0.04) and in osteopontin of -0.09 ng/mL (95% CI: -0.16, -0.01). $PM_{2.5}$ exposure was associated with a cumulative increase in eGFR of 1.60 mL/min/1.73m^2 (95% CI: 0.36, 2.85) and urinary cystatin C of 0.14 ng/mL (95% CI: 0.03, 0.25).

Conclusions: Increased exposure to ambient temperature and $PM_{2.5}$ may impact preadolescent kidney health, through subclinical glomerular or tubular injury. Follow-up research throughout the life course is required to environmental exposures that may predict kidney disease risk.

Association of Hyperphagia Score with Race/Ethnicity in Children and Adolescents with Overweight/Obesity

Author Name(s): Alison R. Forte, Marcus C. Rasmussen, Sarah K. Zafar, Clint E. Kinney, Joan C. Han

Department: Pediatrics

Division: Endocrinology and Diabetes

Institution Affiliation: Icahn School of Medicine at Mount Sinai

Institute Affiliation(s): Mount Sinai Diabetes, Obesity, and Metabolism Institute and Mindich Child Health and Development Institute

Introduction: Hyperphagia is a condition of an abnormally excessive appetite, often paired with intense food cravings leading to overeating and weight gain. A caregiver-reported questionnaire was developed by Dykens et al. (2007) to assess severity of hyperphagia in persons with Prader-Willi syndrome, a genetic disorder associated with severe obesity. However, the population studied was predominantly non-Hispanic White (NHW).

Hypothesis: Patients with non-syndromic forms of obesity will also display hyperphagia and severity will vary by race/ethnicity and degree of overweight/obesity.

Methods: Parents or caregivers of children and adolescents referred to the Mount Sinai Healthy Lifestyle Clinic for weight management completed the Dykens hyperphagia questionnaire. ANCOVAs assessed differences in hyperphagia score among African American (AA), Hispanic White (HW), and NHW cohorts, adjusting for age, sex, and BMI-P95 (percent of 95^{th}%ile).

Results: Subjects had overweight (BMI 85-<95^{th}%ile; N=5) or obesity (BMI ≥95^{th}%ile; N=206) and were age (mean±SD) 13.6±3.8y (4.0-20.3y), 45% female, 29.4% AA, 51.2% HW, and 19.4% NHW, with BMI 37.6±9.8 kg/m^2 and BMI-P95 146±31%. NHW had a significantly higher mean hyperphagia score (26.6±8.8) compared to AA (22.4±8.5, $p<0.001$) and HW (20.7±8.3, $p=0.02$), and these differences remained significant after adjusting for age, sex, and BMI-P95. No significant correlation was observed between hyperphagia score and BMI-P95 ($p=0.47$).

Conclusions: Our findings suggest that specific thresholds for race/ethnicity may be needed when interpreting hyperphagia scores due to possible cultural differences in perceived norms for eating behavior. Furthermore, the lack of correlation between BMI-P95 and hyperphagia score suggests contribution of other factors besides only hunger in driving weight gain in children with overweight/obesity.

Reprograming of the Intestinal Immune Cell Compartment Defines the Response to Autologous Stem Cell Transplantation in Crohn's Disease

Author Name(s): Daniela Guisado, Sayali Talware, Shishir Singh, Stephanie Gold, Moutasem Mansi, Elbek Fozilov, Aaron Etra, Judy Cho, Louis Cohen

Department(s): Pediatrics; Internal Medicine

Division(s): Gastroenterology; Hematology Oncology

Institution Affiliation: Icahn School of Medicine at Mount Sinai

Introduction: For the treatment of refractory Crohn's disease (CD) autologous stem cell transplant (auto-SCT) is unparalleled in its ability to induce clinical and endoscopic remission. Auto-SCT is unique as a cellular therapy aimed to reset immune pathophysiology to a pre-disease state using hematopoietic stem cells. Here we report initial studies of high dimensional immune phenotyping of patients with CD during auto-SCT.

Hypothesis: There are distinct changes in the peripheral and intestinal immune cell compartments after auto-SCT and may provide insight into CD pathogenesis and treatment.

Methods: Patients with refractory CD were enrolled in a Phase IIa study of auto-SCT followed by vedolizumab (NCT03219359). 14 patients were transplanted (2018-2022). Paired blood and intestinal samples were taken prior to transplant and 6 months post-transplant and were analyzed by mass cytometry (CyTOF). Supervised clustering of immune cell populations using canonical markers was performed in parallel with unsupervised clustering by FlowSOM.

Results: 6 months post-transplant 12/13 patients had an endoscopic response and 10/13 patients' endoscopic remission. Supervised clustering of major immune cell subsets demonstrated distinct site-specific responses to transplant in myeloid and lymphoid cell populations. Naïve CD4+ and CD8+ T cells universally decrease in number 6 months post-transplant whereas all other B and T cell populations have discordant changes in the blood and intestine, especially naïve and transitional CD27- B cell populations which significantly increase in blood and decrease in the intestine. CD14+ populations are universally increased in number post-transplant with a specific increase in CD14+ CD206+ macrophages in the intestine. Unsupervised clustering of blood and intestinal immune cells resolve 100 cell clusters that correlate with canonical immune cell markers. Unsupervised analysis further highlights a significant increase in multiple intestinal CD14+ immune cell populations reflecting newly arrived/differentiating and mature monocyte derived macrophages. Principal component and hierarchical clustering analyses of immune cell clusters suggest a reprograming of the intestinal immune compartment post-transplant whereas changes in circulating immune cells populations fail to separate the pre- and post-transplant states.

Conclusions: We demonstrate the differences in the intestinal and peripheral immune response to auto-SCT. These studies highlight the changes in intestinal immune cell networks that define the transplant response perhaps through CD14+ cells.

Neuro-Environmental Interactions: A Time Sensitive Matter

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Introduction: Resting state (rs) neurophysiological dynamics are typically assessed through the control of sensory and perceptual environments during testing conditions. We investigated the effects of temporally-distal environmental inputs, specifically metal exposures, on rs functional dynamics.

Hypothesis: We tested if metal exposures experienced up to several months prior to testing impacted functional connectivity.

Methods: In 124 participants (53% females, ages: 13-25 years) enrolled in the Public Health Impact of Metals Exposure (PHIME) study, we measured concentrations of 7 metals in biological matrices and acquired resting-state functional magnetic resonance imaging scans. Using graph theory metrics, we computed global efficiency (GE) in 111 brain areas (Harvard Oxford Atlas). A predictive model based on ensemble gradient boosting was used to predict GE from exposure biomarkers. Models were adjusted for age and sex, and model performance was evaluated by comparing predicted versus measured rs functional dynamics. Finally, SHAP scores were used to evaluate feature importance.

Results: Observed rs dynamics were significantly correlated with rs dynamics predicted from our model utilizing chemical exposures as inputs ($P< 0.001$ $R = 0.36$). Feature importance metrics indicated that biomarkers of lead, chromium, and copper contributed most to prediction of GE metrics.

Conclusions: Our results indicate that a significant component of resting state dynamics, comprising approximately 13% of observed variability in GE, is driven by past and persistent metal exposures. These finding emphasize the need to estimate and control the influence of past and current chemical exposures in the assessment and analysis of rs functional connectivity.

Prenatal Predictors of Postnatal Intervention in Prenatally Diagnosed Non-Critical Pulmonary Stenosis

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Department: Pediatrics

Division: Cardiology

Institution Affiliation: Icahn School of Medicine at Mount Sinai

Introduction: Counseling patients with a prenatal diagnosis of non-critical pulmonary stenosis (PS) is challenging due to fetal hemodynamics, as well as the possibility of progression throughout gestation. Postnatal outcomes can range from a normal pulmonary valve (PV) to critical PS. We aim to identify echocardiographic findings that predict the need for neonatal intervention.

Hypothesis: We hypothesized that fetuses with non-critical pulmonary stenosis on initial fetal echocardiogram have echocardiographic markers that predict the need for neonatal intervention.

Methods: This is a single center retrospective cohort study of prenatally diagnosed non-critical, isolated PS from 2008 to 2022.

Results: Thirty-four subjects were included with a median gestational age of 22 weeks at diagnosis. Nine (26%) patients had a normal PV on postnatal echocardiogram. Thirty patients had follow-up beyond 2 months of age, and seven (23%) of these patients underwent balloon valvuloplasty of the PV prior to 2 months of age. The intervention group had a higher fetal peak systolic velocity (PSV), lower PV z-score, higher PV velocity time integral, and smaller effective PV orifice than the non-intervention group. A threshold of PSV >160 cm/s had a sensitivity of 100%, specificity of 90%, positive predictive value of 75%, and negative predictive value of 100% in predicting the need for postnatal intervention within 2 months of age.

Conclusions: Fetuses with an initial diagnosis of non-critical PS may require neonatal intervention, which can be predicted by the PV PSV. A threshold of 160 cm/s may guide counseling patients regarding the possibility of neonatal intervention.

Effects of Loxapine on Energy Balance in MC4R Deficient Mice

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Introduction: Although weight gain is an adverse effect of psychotropic medications, the antipsychotic loxapine frequently appears to reduce body weight in clinical practice and was associated with increased serum brain-derived neurotrophic factor (BDNF), a mediator of the weight-regulating leptin-proopiomelanocortin pathway, in a small cohort of patients with autism.

Hypothesis: We hypothesized that loxapine can have beneficial effects on energy homeostasis and has the potential to augment brain-derived neurotrophic factor (BDNF) signaling downstream of the leptin-proopiomelanocortin pathway as a targeted rescue of obesity in melanocortin 4 knockout mice (Mc4r-/-).

Methods: Mc4r-/- mice and wild-type littermates were randomized to drinking water with or without loxapine for 13 weeks. Weekly body weights and terminal body composition by MRI and hypothalamic TrkB phosphorylation were measured. In a separate short-term study, mice received once daily oral gavage with vehicle for 7 days, followed by loxapine for 5 days. Feeding, locomotor activity, and respiratory exchange were continuously monitored in metabolic cages.

Results: Long-term loxapine increased hypothalamic TrkB phosphorylation and blunted typical weight and fat gain in Mc4r-/-, with no significant effect in wildtype. Short-term loxapine suppressed feeding and stimulated lipid oxidation in both genotypes but to a greater degree in Mc4r-/-. Energy expenditure was reduced in both genotypes but to a lesser degree in Mc4r-/-.

Conclusions: Further studies to determine the potential of extending loxapine's clinical use for the treatment of obesity in patients with MC4R deficits are supported due to these findings of loxapine's genotype-specific adiposity ameliorating effects in Mc4r-/- mice.

A Quality Improvement Project to Reduce Antibiotic Use by Limiting Treatment for Culture-Negative Sepsis (CNS) in a Level IV NICU

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Division: Neonatal-Perinatal Medicine

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Introduction: Antibiotic use for suspected infection occurs frequently in neonatal intensive care units (NICUs). Prolonged antibiotic use has been associated with increased risk for late-onset sepsis and death and emergence of multi-drug resistant bacteria.

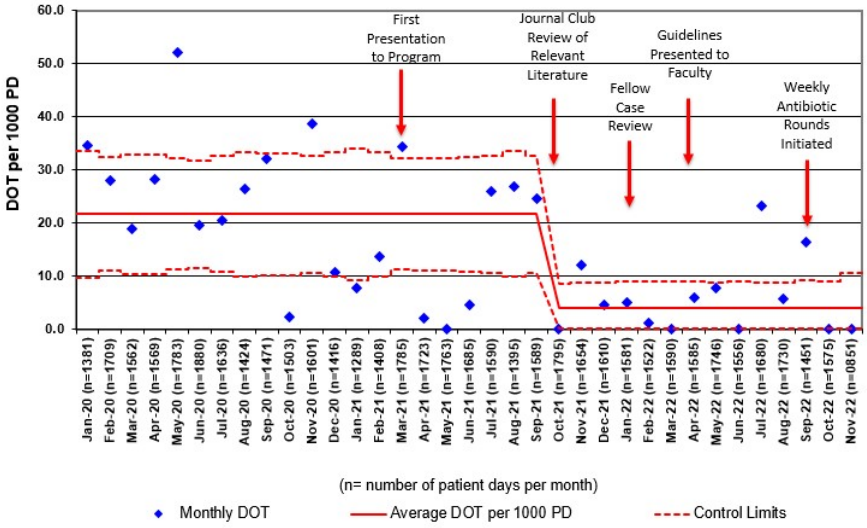
Hypothesis: We hypothesized we could reduce treatment of culture-negative sepsis (CNS) through interventions designed to 1) decrease the number of antibiotic courses and 2) decrease the length of treatment.

Methods: This quality improvement (QI) project was conducted using the Model for Improvement. Interventions included creation of antibiotic guidelines, review of relevant literature, case audits, antibiotic stewardship rounds, and review of CNS cases at staff meetings. The primary outcome measure was CNS antibiotic days of therapy (DOT) per thousand patient days (PD). We tracked number of antibiotic initiation events per month and re-initiation of antibiotics within 10 days of treatment for CNS as a balancing measure.

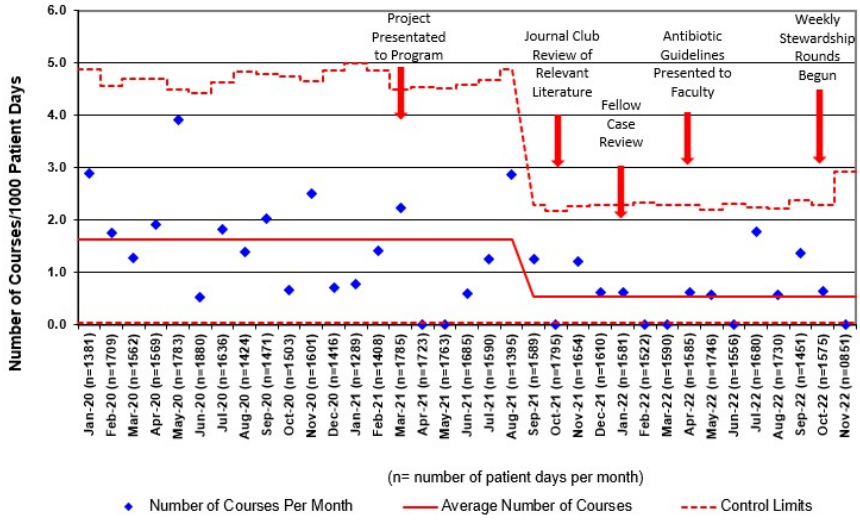
Results: Baseline data collection revealed an average of 21.7 DOT/1000 PD. Following initial interventions, there was a decrease in DOT for culture-negative sepsis by 81% to 4.1 DOT. This was driven by a decrease in EOS days of therapy with a reduction from 18.3 DOT/1000 PD to 3.5 DOT/1000 PD. Overall antibiotic DOT for the unit decreased from 240.4 DOT/1000 PD to 175.4 DOT/1000 PD. There was no change in antibiotic initiation events per month or re-initiation of antibiotics within 10 days of treatment for CNS.

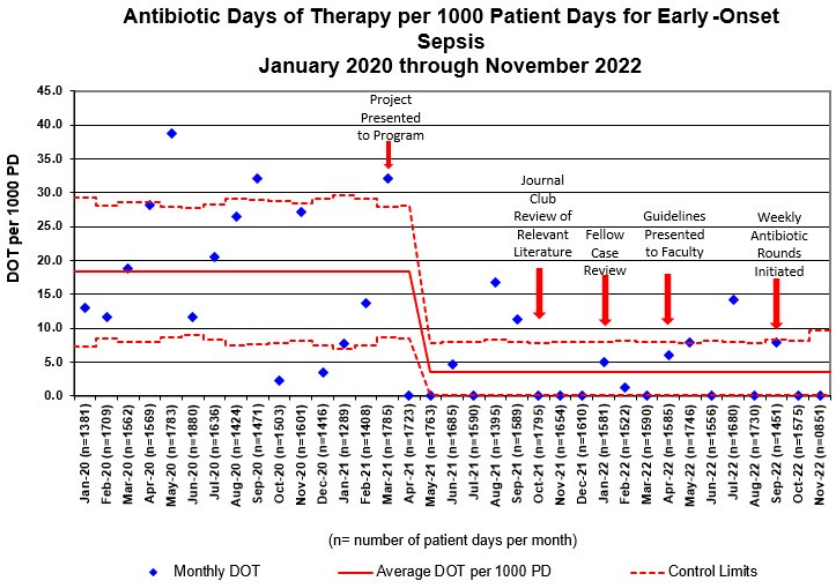
Conclusions: Implementing a QI initiative to reduce treatment of culture-negative sepsis decreased the days of therapy for culture-negative sepsis, particularly for early-onset CNS.

Antibiotic Days of Therapy per 1000 Patient Days for Culture -Negative Sepsis
January 2020 through November 2022



Number of Treatment Courses of Culture Negative Sepsis Per 1000 Patient Days
January 2020 through November 2022




Antibiotic Days of Therapy per 1000 Patient Days for Early-Onset Sepsis
January 2020 through November 2022
DOT per 1000 PD
45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
Project Presented to Program
Journal Club Review of Relevant Literature
Fellow Case Review
Guidelines Presented to Faculty
Weekly Antibiotic Rounds Initiated
Jan-20 (n=1381)
Feb-20 (n=1709)
Mar-20 (n=1562)
Apr-20 (n=1569)
May-20 (n=1783)
Jun-20 (n=1880)
Jul-20 (n=1636)
Aug-20 (n=1424)
Sep-20 (n=1471)
Oct-20 (n=1503)
Nov-20 (n=1601)
Dec-20 (n=1416)
Jan-21 (n=1289)
Feb-21 (n=1408)
Mar-21 (n=1785)
Apr-21 (n=1723)
May-21 (n=1763)
Jun-21 (n=1685)
Jul-21 (n=1590)
Aug-21 (n=1395)
Sep-21 (n=1589)
Oct-21 (n=1795)
Nov-21 (n=1654)
Dec-21 (n=1610)
Jan-22 (n=1581)
Feb-22 (n=1522)
Mar-22 (n=1590)
Apr-22 (n=1585)
May-22 (n=1746)
Jun-22 (n=1556)
Jul-22 (n=1680)
Aug-22 (n=1730)
Sep-22 (n=1451)
Oct-22 (n=1575)
Nov-22 (n=0851)
(n= number of patient days per month)
Monthly DOT
Average DOT per 1000 PD
Control Limits

Application of Network-Based Heterogeneity Clustering for Investigation of Genotype-Phenotype Correlations in Biome Biobank

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Institute Affiliation: The Charles Bronfman Institute for Personalized Medicine

Introduction: The genetic basis for many human diseases often exhibits heterogeneity, resulting in different genes in the same or related biological pathways being responsible for the same or similar phenotypes. Conventional gene burden methods, which are used to identify genetic signals in case-control studies, lack the power to detect these signals in the presence of genetic heterogeneity and small cohorts. To address this issue, we have previously developed a computational method called network-based heterogeneity clustering (NHC) that can detect physiological homogeneity within genetically heterogeneous cohorts with small sample sizes, and demonstrated that our method can effectively converge genes that are biologically related on a protein-protein interaction network and accurately identify gene clusters with potentially deleterious rare variants.

Hypothesis: We hypothesized that NHC facilitates the discovery of candidate disease genes in small population-specific cohorts.

Methods: Here, we utilized NHC to analyze three disease cohorts from the Mount Sinai BioMe BioBank, where previous gene burden approaches were ineffective in identifying candidate genes. The cohorts comprised 50 individuals with lactation disorders (agalactia or hypogalactia) and 500 controls, 71 patients with severe COVID-19 and 390 controls with mild-moderate disease, and 431 children with food allergy and 2,155 controls, which was also analyzed in a population-specific manner using data from individuals of Ashkenazi Jewish (AJ, n = 826) and non-AJ European (n = 1,760) ancestries.

Results: NHC analysis in the lactation disorders cohort identified gene clusters involved in intra-golgi vesicle transport, mammary stem cell differentiation and proliferation, and trans-differentiation of white adipocytes in the mammary gland during lactation. NHC also uncovered two gene clusters potentially related to increased risk for severe COVID-19, including genes that preserve endothelial barrier function and genes involved in snRNA processing, which have previously been implicated in susceptibility to HSV-1 infection. Furthermore, NHC facilitated the identification of candidate gene clusters in the food allergy cohort with population-specific signatures, including genes proposed to be associated with allergic asthma and food allergies, such as *DYNC1H1*, toll-like receptor encoding genes, genes involved in IL-17 signaling and cell adhesion, and genes encoding mitochondrial ribosomal proteins.

Conclusions: These findings indicate that NHC is a useful approach for uncovering candidate genes in disease groups with genetic heterogeneity, especially in smaller population-specific subgroups, outperforming traditional case-control studies for such cohorts.

Rapid Response EEG Decreases Time to Seizure Diagnosis in Pediatric ER and ICU Patients

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Division: Critical Care Medicine

Institution Affiliation: Icahn School of Medicine at Mount Sinai

Introduction: Establishing seizure activity on conventional EEG (cEEG) is essential but can delay treatment of subclinical seizures. cEEG requires technician expertise and equipment whose limited availability can further delay treatment. Rapid response EEG (rrEEG) device Ceribell can be used and interpreted rapidly by bedside providers with minimal training. This retrospective pilot study examines the impact of rrEEG introduction at a quaternary care children's hospital on time to definitive diagnosis.

Hypothesis: We hypothesized that rrEEG will decrease the time to determination of electrographic activity (TDEA) compared to cEEG.

Methods: This study analyzed data from patients 2-18 years old who presented to the PICU and pediatric ER with concern for SE who were placed on rrEEG and cEEG. For rrEEG patients, the bedside physician used the Brain Stethoscope at four discrete points.

Results: When compared to cEEG, rrEEG decreased TDEA (128 ± 59min vs 24 ± 9min, P = .00003) and had a shorter setup time (22 ± 4min vs 11 ± 7min, P = 0.001). Bedside physicians diagnosed electrographic activity using the Brain Stethoscope with 100% sensitivity (95% CI 54% to 100%) and 84% specificity (95% CI 65% to 95%). rrEEG ruled out SE in 7 patients and changed physician clinical decision-making in 3 patients.

Conclusions: rrEEG allowed for earlier diagnosis of brain electrographic activity in pediatric patients when compared to cEEG. rrEEG allowed for the bedside provider to initiate EEG monitoring, successfully diagnose patients using the Brain Stethoscope, and decrease delays associated with technician availability.

Baseline Epitope-Specific IgE Profiles Are Predictive of Sustained Unresponsiveness One-Year Post OIT in the POISED Trial

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Division(s): Allergy and Immunology; Pathology and Microbiology Immunology

Institution Affiliation(s): Icahn School of Medicine at Mount Sinai; Stanford School of Medicine

Introduction: Results from the POISED trial suggest that discontinuation of peanut desensitization can increase the risk of regaining clinical reactivity to peanut.

Hypothesis: We sought to determine whether those who achieved sustained unresponsiveness (SU) have different baseline sequential epitope-specific (ses-)IgE than those who achieved transient desensitization (TD). We hypothesized that those who achieved SU may have more favorable profiles than TD.

Methods: Subjects in the POISED trial (NCT02103270) were randomized to peanut (n=95) or placebo (oat flour, n=25) for 24 months. Then OIT-desensitized subjects were assigned to no peanut (PN-0, n=51) or 300mg (PN-300, n=30) for 12 months. SU was determined by passing 4000mg peanut oral challenge. Specific IgE and IgG4 levels to peanut, Ara h 1-3 proteins (ImmunoCap) and 64 allergenic epitopes (BBEA) were measured. We developed machine learning *glmnet* models with bootstrap simulations using baseline data to predict SU.

Results: Eighty (84%) subjects were desensitized to peanut during OIT. Of those, 13% (n=8) and 37% (n=13) achieved SU in PN-0 and PN-300. Decreases in epitope-and protein-specific IgE levels and increases in IgG4 levels were observed during 2 years of OIT. At baseline, only patients with SU in Peanut-0 but not Peanut-300 had lower ses-IgE and protein-sIgE levels compared to the TD group. A machine learning model with 15 baseline ses-IgEs could predict SU with an accuracy of 87%, 0.90 (sd=0.7) AUC 0.78 (sd=0.16), Sensitivity, and 0.9 (sd=0.21) Specificity.

Conclusions: Patients who achieved SU have different baseline protein- and epitope-specific IgE profiles than those with TD. These molecular markers may be helpful in identifying patients with an increased likelihood of achieving SU.

Clinically Relevant Clusters of Neonates Generated with Machine Learning

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Division: Neonatology

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Introduction: Neonatal pathology often presents with subtle and nonspecific findings. Automated processes that can aid clinicians in distinguishing disease states are desirable. Building machine learning (ML) models that make such predictions requires large, labeled data sets, a time intensive manual process. A ML methodology that clusters neonates into clinically relevant groups provides weak bayesian priors for use in assigning classification probabilities, which is a first step in building an automated labeling model.

Hypothesis: Clinically relevant clusters can be generated from unstructured EHR data by ML.

Methods: EHR data was retrospectively obtained. An antibiotic course is defined as a continuous course with less than 48 hrs between doses. EHR data was embedded with a combination of topographical analysis and factor analysis of mixed data (FAMD-PCA). Semantic groupings were recovered from the clinical embeddings by maximizing normalized mutual information (NMI) over the first two principal components.

Results: There were 6961 courses of antibiotics identified in 5829 neonates. Recurrent patterns were identified among demographic data, admission/discharges, and antibiotic administrations leading to cluster demonstration (Figure 1). Each of the machine derived groups reflects clinically relevant phenotypic information. The 9 clusters of antibiotic combinations are characterized by a distinguishing antibiotic with intragroup variability preserved (Figure 2). The 5 remaining clusters of demographic data reflect commonly observed clinical patterns (Figure 3).

Conclusions: Machine learning can be utilized to distinguish patients into clinically relevant clusters, a first step to gathering a machine generated labeled data set.

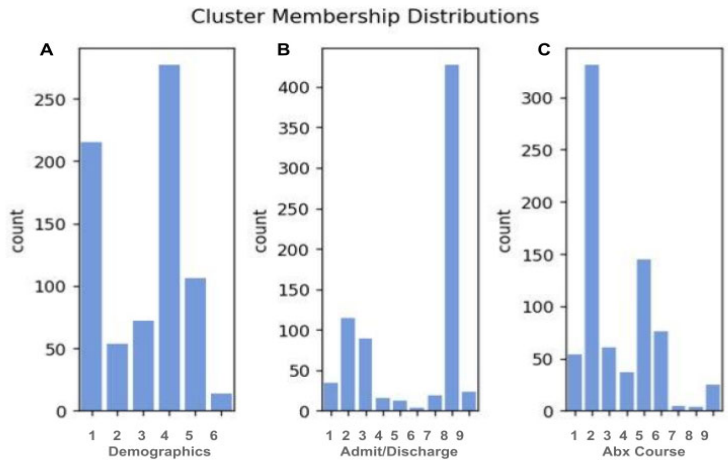

Figure 1. A-B) Numbers of patients sorted into 6 and 9 clusters with semantic recurrence of their characteristics across demographic and admission/discharge patterns, respectively. C) Numbers of antibiotic courses sorted into 9 clusters with semantic recurrence in their composition.

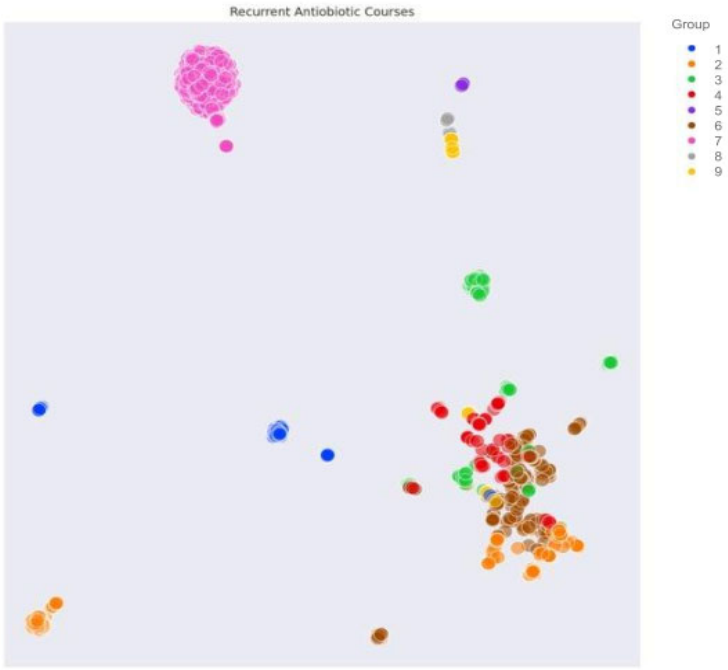

Figure 2. Resulting clusters of antibiotic course embeddings. Group membership is determined by a machine derived anchoring antibiotic exclusive to the group. Distance from group centers reflects presence of additional, potentially non-exclusive antibiotics.

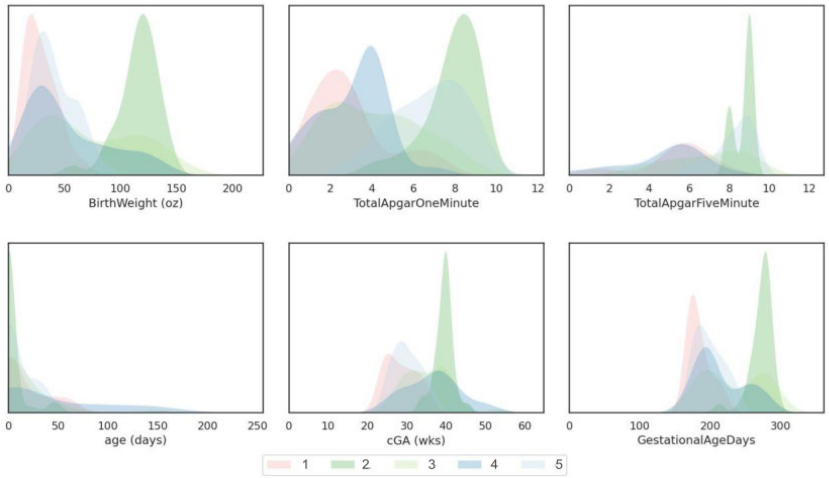

Figure 3. Demographic trends amongst 5 clusters of NICU patients showing recurrent patterns.

Cardiac Specific Loss of RNA Binding Protein Ddx3x Reveals Sex and Cell Type Specific Roles During Development

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Institute Affiliation: The Mindich Child Health and Health Development Institute

Introduction: Congenital heart defects (CHD) remain the most frequent birth defect in humans, affecting approximately one out of one hundred newborns. While CHDs arising from defects in gene regulatory mechanisms have been well-studied, the role of RNA regulators and RNA-binding proteins remains poorly understood. Mutations in the RNA-binding protein *DDX3X* are known to cause X-linked intellectual disability in humans, however they have recently been associated with a high prevalence of CHDs. In this patient population, CHD primarily presents as atrial and ventricular septal defects.

Hypothesis: We hypothesized that mouse with mutations in Ddx3x will express heart defects associated with those seen in our patient population.

Methods: We used previously established Ddx3x floxed mice and cardiac specific Cre mice to generate cardiac-specific conditional knockouts of *Ddx3x*.

Results: We find that a lateral plate mesoderm specific loss of *Ddx3x* results in sex-specific cardiac phenotype in mice, where the females are more severely affected than the male embryos. Both male and female embryos show signs of early cardiac specification, yet present with gross cardiac abnormalities. *Ddx3x* is expressed in other lateral plate mesoderm derived tissues including the endothelium.

Conclusion: We find that *Ddx3x* is not required for cardiac specification. Myocardial loss of *Ddx3x* results in late embryonic lethality with increased rates of proliferation in the trabecular and compact myocardium. Additionally, we observe a loss of organization within the compact myocardium. Similarly, the difference in embryonic lethality and cardiac phenotype indicate that *Ddx3x* has distinct cell-type specific roles in the cardiovascular system.

Associations Between Nitrogen Dioxide and Routine Vaccine Antibody Levels in Children

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Institutional Affiliation: Icahn School of Medicine at Mount Sinai

Institute Affiliation: The Institute for Exposomic Research

Introduction: The worldwide COVID-19 pandemic has magnified the public health importance of vaccine antibody response. Existing research suggests that vaccine antibody response is modified by environmental factors, although the association with nitrogen dioxide (NO_2) has not been assessed, despite evidence linking NO_2 with other immune-mediate outcomes.

Hypothesis: We hypothesized that NO_2 decreases routine vaccine antibody levels in children.

Methods: We assessed NO_2 at 1-km^2 spatial resolution via novel hybrid models, and serum antibody levels of diphtheria, tetanus, and pertussis measured postpartum in vaccinated children ages 4-6 years enrolled in the Programming Research in Obesity, Growth, Environment and Social Stressors (PROGRESS) cohort in Mexico. Using linear mixed-effects models, we examined the association between prenatal (trimester average) exposure and long-term postnatal (one-year average) exposure to NO_2 and log-transformed 4- and 6-year antibody levels to diphtheria, tetanus, and pertussis vaccinations

Results: Per 1 $\mu g/m^3$ increase in trimester average NO_2, diphtheria, tetanus, and pertussis antibody levels increased by 5.02% (95%CI: 2.43, 7.68%), 5.00% (95%CI: 2.33, 7.73%), and 5.00% (95%CI: 2.04, 8.05%) respectively. Per 1 $\mu g/m^3$ increase in one-year postnatal NO_2, diphtheria, tetanus, and pertussis antibody levels decreased by 3.86% (95%CI: -6.36, -1.29%), 3.71% (95%CI: -6.29, -1.07%), and 2.49% (95%CI: -5.39, 0.50%) respectively.

Conclusions: We found evidence of increased antibody levels to prenatal NO_2 exposure and decreased antibody levels to postnatal NO_2 exposure. Although exposure to environmental toxicants during and after pregnancy may impact children's immune systems, the positive associations observed in our study require further exploration.

Human Heterozygous *TBK1* Variations Lead to Autoinflammation

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Division(s): Allery & Immunology; Rheumatology

Institution Affiliation(s): Icahn School of Medicine at Mount Sinai; Columbia University Medical Center; Johns Hopkins University School of Medicine; Catholic University of Leuven

Institute Affiliation(s): Precision Immunology Institute, The Mindich Child and Health Development Institute

Introduction: TANK binding kinase 1 (TBK1) is a signaling intermediate that functions in the induction of both type I interferon (IFN-I) expression and nuclear factor-kB-mediated inflammatory cytokine production. Concomitantly, TBK1 is also shown to negatively regulate TNF-induced cell death through inactivation of RIPK1. Previous work from our laboratory has identified patients with biallelic loss-of-function mutations in *TBK1* that exhibit early-onset autoinflammatory syndrome. While the loss of TBK1 expression results in hypomorphic induction of IFN-I, there nevertheless remains sufficient antiviral response in these patients. Notably, the absence of TBK1 expression also releases the brake on RIPK1, thus favoring a RIPK1-mediated cell death that ultimately drives autoinflammation. Here we have discovered five patients, comprised of children and adults, with four novel heterozygous mutations in *TBK1*. All patients suffer from recurrent or chronic autoinflammation.

Methods: The impact of each *TBK1* variant on IFN-I response and induction of inflammatory cell death will be assessed using *TBK1* null cells lines that are transduced with wild-type or variant *TBK1* constructs.

Preliminary Results: Evaluation of a panel of interferon-stimulated genes (ISGs) in the blood of these patients revealed that some variations of *TBK1* can lead to increased expression of these genes.

Hypothesis: We hypothesize that novel heterozygous gain-of-function (GoF) *TBK1* variations could increase IFN-I signaling to drive putative interferonopathy-like symptoms.

Conclusions: Variations in *TBK1* contribute to a range of inflammatory conditions in children and adults. These *TBK1* variations can increase ISG expression in the blood of patients, an indicator of a possible TBK1 GoF. How these *TBK1* variations regulate inflammatory cell death modalities remains to be defined.

Prenatal Exposure to Phthalate Mixture and Childhood Respiratory Health Outcomes: A Study From the PROGRESS Cohort

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Department(s): Environmental Medicine and Public Health; Pediatrics

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Institution Affiliation(s): Icahn School of Medicine at Mount Sinai; Mexican Social Security Institute; National Institute of Perinatology; National Institute of Public Health

Institute Affiliation: Institute for Exposomic Research

Introduction: Prenatal phthalate exposure may impact lung development and lead to wheeze and asthma in childhood. There is limited epidemiologic data on these associations in Latin America.

Hypothesis: Prenatal phthalate exposure will be associated with asthma and wheeze.

Methods: We assessed 607 mother- child dyads enrolled in the Programming Research in Obesity, Growth, Environment, and Social Stressors birth cohort in Mexico City. We quantified 15 phthalate metabolites in 2nd trimester urine. Report of wheeze in the past 12 months (current wheeze) and asthma were obtained using a validated survey at 48 and 72 months. Mixture effects were assessed using Quantile G- Computation (g-comp) and Bayesian Weighted Quantile Sum (BWQS) regression, adjusted for covariates.

Results: We found similar joint mixture effects of higher 2nd trimester phthalate metabolites and higher odds of wheeze at 48 and 72 months using both methods. Phthalate mixtures were associated with higher odds of current wheeze at 48 months (g-comp, OR: 1.37, 95% CI: 0.96, 1.97) and (BWQS, OR: 1.21, 90% Cr: 0.91, 1.64) with mono-3-carboxypropyl as the largest contributor to the mixture. We saw similar results with higher odds of wheeze at 72 months (g-comp, OR: 1.92, 95% Cr: 1.06, 3.51) and (BWQS, OR: 1.95, 90% Cr: 1.25, 3.13) with mono-2-ethyl-5-carboxypentyl terephthalate the largest contributor to the mixture. Significant associations with asthma were not observed.

Conclusions: Increased prenatal exposure to phthalate mixture was associated with higher odds of wheeze in childhood. Future work investigating phthalate exposure and wheeze trajectories/lung function will be important for understanding how these may predict later disease.

PASS Study: Relationship of Food Insecurity and Parental Stress in Families Screened for SDH at a Pediatric Clinic in East Harlem, NYC

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Department(s): Medical Education; Pediatrics; Environmental Medicine and Public Health; Program in Public Health

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Introduction: Our Social Determinants of Health (SDH) screening program and on-site pantry provides families with food insecurity (FI) with an emergency food package and referrals to community resources such as New York Common Pantry (NYCP).

Hypothesis: We hypothesize that there is relationship between FI and parental stress (PS) from participation in the SDH program over 12-months.

Methods: Food insecure families were offered enrollment and completed baseline, 3-month and 12-month surveys that assessed FI with the 18-item USDA Household Food Security Survey and parental stress with Perceived Stress Scale-4 (PSS-4). A mixed-effects model adjusted for covariates was used to explore an association between FI and PS over time.

Results: 113 caregivers enrolled in the study (Table 1), 61 completed a 3-month follow-up, and 32 completed a 12-month follow-up. Average FI scores at baseline were 4.4 (SD 3.6), at 3-months 3.4 (3.4), and at 12-months 4.5 (4.5). The average PSS-4 scores at baseline, 3-months and 12-months were 6 (2.8), 6.6 (2.8) and 6.2 (2.8) (Table 2). A mixed-effects model that considered the interaction of FI by follow-up time along with race, housing assistance, insurance, caregiver education and employment showed that over time there was a decrease of PSS score with a decrease FI for the 32 families completing the 12-month survey ($p=0.05$).

Conclusions: Our analysis found that decreased FI was associated with decreased PS after 12 months of participation. Taking this into consideration, interventions that decrease FI could have an impact on PS and may inform parent-directed mental health interventions.

Analyzing Rasopathy Targets Using Drosophila CRIMIC Technology

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Introduction: RASopathies are autosomal dominant disorders typically caused by gain-of-function RAS/MAPK pathway variants. Drug testing with Drosophila models has relied on the classic UAS-Gal4 system, which results in non-physiological expression.

Hypothesis: We hypothesized that physiologic expression of RASopathy-associated alleles in Drosophila will provide novel insights into disease pathogenesis and drug efficacy.

Methods: We used the CRIMIC system, allowing Gal4 expression from endogenous promoters to drive UAS-transgenes. *CRIMIC-dMek*-Gal4 drove human *UAS-MEK1* variants in developing fly tissues. *Mek* resides on chromosome X. Thus, female adult flies are heterozygous for the mutant *Mek*, modeling gene dosage seen in patients. Embryos were raised on medium, either with drugs diluted in DMSO or DMSO only. Resulting pupae and adults were counted. Statistical testing was performed with Student's t tests using a significance threshold of $p < 0.05$.

Results: Preliminary data shows that *MEK-G128V* variant flies fed rigosertib show increased survival at the pupal stage compared to variant flies fed control food. Using our experimental strategy, 25% of embryos die as pupae due to absence of Mek (i.e., maximal 75% survival). In progeny of *MEK-G128V* variant flies, only 50% survived to pupal stages, indicating embryonic lethality from *MEK-G128V*. In the presence of rigosertib at 50 uM, pupal survival increases to 69%, but failed to achieve statistical significance. We are repeating these experiments to improve statistical power.

Conclusions: Overall, these data suggest that rigosertib may serve as a promising lead therapeutic to be further tested in *MEK-related* gain-of-function RASopathy models in vertebrates and ultimately in patients.

A Novel Case of FPIES After Pine Nut Food Challenge in an 18-Year-Old Female

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Introduction: Food Protein Induced Enterocolitis Syndrome (FPIES) is a non-IgE mediated reaction characterized by severe gastrointestinal distress occurring 1-10 hours of consuming a triggering food. It commonly occurs after ingestion of oat, cows' milk, and grains in the first year of life (1). FPIES secondary to tree nuts in adulthood is much rarer. Here, we present a unique case of an 18-year-old with FPIES in response to pine nut ingestion.

Case Presentation: An 18-year-old female with a history of atopic dermatitis and multiple food allergies presented for a pine nut oral food challenge after favorable skin and blood testing. She ate a total of 2 tablespoons of pine nuts in gradual increments over 35 minutes. Head to toe assessments performed every 15 minutes for 3 hours demonstrated no signs of an allergic reaction and the patient was considered to have passed the oral food challenge.

Results: Minutes after discharge, the patient developed nausea with several episodes of non-bloody emesis. She was given 8mg of ondansetron and monitored for 2-hours with resolution of her GI symptoms. As a result of the patient's delayed GI reaction to pine nuts, FPIES was confirmed.

Conclusions: Here, we present a case of FPIES in response to pine nut consumption in adulthood. To our knowledge, there are no prior cases of pine nuts as the causative agent of FPIES in an adult patient. Clinicians should be aware of non-IgE mediated responses to atypical foods in adulthood.

Characterization of CD14+ Monocyte Differentiation by Disease Status in Crohn's Disease

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Introduction: Circulating monocytes play an important role in innate immunity and continuously replenish intestinal resident macrophages in normal gut homeostasis. Dysregulated monocyte recruitment and differentiation in the gut lamina propria are key contributors in the pathogenesis of Crohn's disease. We believe bone marrow priming over time in Crohn's disease may result in altered phenotypes of circulating monocytes that retain plasticity and propagate pro-inflammatory and pro-fibrotic signaling pathways on infiltration to inflamed intestinal tissue.

Hypothesis: Patients with Crohn's disease have altered monocyte differentiation and phenotypes compared to healthy controls

Methods: We used a 14 day culture method to model CD14+ monocyte differentiation in the gut. CD14+ monocytes were isolated by negative selection from peripheral blood mononuclear cells (PBMCs) obtained from a human healthy control and a Crohn's disease patient in remission. CD14+ monocytes were differentiated *in vitro* with and without muramyl dipeptide (MDP) for 14 days. mRNA was extracted for quantitative PCR analysis of proinflammatory and profibrotic genes.

Results: No significant differences in gene expression were found in IL11, IL6, IL1B, and MFAP4 between CD14+ monocyte derived cells from the healthy control and Crohn's disease patient in remission. Stimulation with MDP in culture did not lead to significant changes in gene expression in either subject.

Conclusions: This Crohn's disease patient in remission may have phenotypically similar monocytes to a healthy control. Further experiments comparing gene expression and cytokine secretion in CD14+ derived cells from patients with active Crohn's disease to patients in remission and healthy controls are ongoing.

Clinical Utility of Repeat Fetal Echocardiography in Congenital Heart Disease

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Introduction: Fetal echocardiography (FE) is a highly accurate and can reduce morbidity and mortality in fetuses with major congenital heart disease (CHD). There is no consensus on how often serial FE should be performed for specific types of CHD. We aimed to investigate how often management or counseling changes occur based on a repeat FE.

Hypothesis: We hypothesized that fetuses with CHD lesions with potential for progression would have a higher incidence of management changes based on repeat FE.

Methods: We performed a retrospective review between 2012 to 2019 of patients who had repeat FE performed. We reviewed consult notes to determine whether management or counseling had changed based on findings at follow up visits. Fisher's exact test was used to assess the relationship between initial diagnosis and change in management.

Results: Among 267 patients the overall frequency of a management change based on a repeat FE was 41/267 (15.4%). A change in management was associated with the diagnosis made at the initial visit ($p<0.001$). The frequency of a counseling change based on a repeat FE was 108/267 (40.4%). Management and counseling changed most frequently for pulmonary valve abnormalities.

Conclusions: The clinical utility of follow-up FE is associated with the type of CHD diagnosed. Follow-up FE led to changes in management in several types of CHD, most commonly in right and left outflow obstructive lesions and AVC. In developing programmatic protocols for frequency of FE reassessments, the type of CHD should be a major determinant.

Short-Term Variable Immune Transcriptome Response to Ketamine Treatment in Children with ADNP Syndrome

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Introduction: Activity-dependent neuroprotective protein (ADNP) syndrome is a neurodevelopmental disorder caused by mutations in the *ADNP* gene, resulting in intellectual disability and behavioral disorders, including autism spectrum disorder (ASD). It is a leading cause of monogenic autism and individuals are often severely delayed across many neurodevelopmental domains. A single low-dose ketamine infusion was associated with behavioral improvements in an open-label clinical trial of patients with ADNP syndrome.

Hypothesis: We sought to explore the relationship between clinical findings and the blood transcriptome, particularly regarding the potential interaction between ketamine and the biology of ADNP syndrome.

Methods: Blood transcriptome data was generated from 10 cases of ADNP syndrome before treatment with intravenous ketamine (0.5mg/kg) and at 5 post-infusion timepoints (immediately, 1 day, 1-, 2-, and 4 weeks after). Computational analyses (including Weighted Gene Correlation Network Analysis, GO enrichment, and differential gene expression) were performed to identify gene networks undergoing expression changes after treatment.

Results: Blood transcriptional data confers clinical findings that ketamine is well-tolerated and safe, with most transcriptional changes returning to baseline levels after 4 weeks. Ketamine induces a general, low-grade immune response in the blood, some of which is uniquely associated with monocytes. We do not see biological evidence that ketamine specifically interacts with *ADNP* or its proximal targets.

Conclusions: We did not see a direct mechanism by which ketamine targets the unique biology of ADNP syndrome in blood data. Still, ketamine has clinical and biological potential as a safe and transient intervention to reduce behavioral difficulties associated with this syndrome.

Looking Towards 2030: Strengthening the Environmental Health in Childhood–Adolescent Cancer Survivor Programs

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Introduction: Childhood and adolescent cancer survivors (CACS) are a high-risk population for non-communicable diseases and secondary carcinogenesis. The Environmental and Community Health Program for Longitudinal Follow-up of CACS in the region of Murcia, Spain, is an ongoing pioneering program that constitutes a model for social innovation.

Hypothesis: We hypothesized that areas with poor outdoor air quality have lower survival rates.

Methods: This study aims to present the program tools and protocol as a whole, as well as a profile of the incidence, survival, and spatiotemporal distribution of childhood cancer in the region of Murcia, Spain, using 822 sample cases of cancer diagnosed in children under 15 years of age (1998–2020).

Results: While the crude incidence rate across that entire period was 149.6 per 1 million, there was an increase over that time in the incidence. The areas with a higher standardized incidence ratio have shifted from the northwest (1998-2003) to the southeast (2016–2020) region. Overall, the ten-year survival rate for all tumor types was 80.1% over the entire period, increasing the five-year survival rate from 76.1 (1998–2003) to 85.5 (2014–2018). CACS living in areas with very poor outdoor air quality had lower survival rates.

Conclusions: Integrating environmental health into clinical practice could improve knowledge of the etiology and prognosis, as well as the outcomes of CACS. Finally, monitoring individual carbon footprints and creating healthier lifestyles, alongside healthier environments for CACS, could promote well-being, environmental awareness, and empowerment in order to attain Sustainable Development Goals for non-communicable diseases in this population.

PIEZO1 Regulates Expression of BK and TRPV4 Channels in Mouse Cortical Collecting Duct (CCD)

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Introduction: Within the lumen of the CCD of the distal nephron, an acute increase in tubular fluid flow rate (TFFR) leads to an immediate high amplitude increase in intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$) due to release of internal Ca^{2+} stores coupled to extracellular Ca^{2+} entry at the basolateral membrane in both principal (PC) and intercalated (IC) cells comprising this segment (Liu et al., 2003, 2005, 2007). This is followed by a decay in $[Ca^{2+}]_i$ to a sustained plateau elevation due, at least in part, to luminal Ca^{2+} entry through TRPV4 channels (Berrout et al., 2012). This flow-induced increase in $[Ca^{2+}]_i$ is necessary for BK channel-mediated flow induced K^+ secretion (FIKS) in the microperfused CCD. We generated a mouse with IC-specific targeted deletion of gene encoding the mechanosensitive Ca^{2+} permeable channel, PIEZO1, which is expressed on the basolateral membranes of PCs and ICs in the mouse CCD (Dalghi et al., 2019). Microperfused CCDs isolated from these IC-PIEZO1-KO mice fed a high K^+ (HK, 5% K^+) diet and subject to an increase in TFFR did not exhibit either a peak or plateau elevation in $[Ca^{2+}]_i$ in response to flow, and FIKS was eliminated. The absence of FIKS and the plateau elevation in $[Ca^{2+}]$ during sustained flow in the CCDs of KO mice led us to examine whether BK and TRPV4 channel expression was impacted by deletion of *Piezo1*.

Hypothesis: BK and TRPV4 channel expression is altered in PIEZO1-deleted ICs.

Methods: Indirect immunofluorescence (IF) staining was performed to examine BKα and TRPV4 channel expression and localization in PCs and ICs of IC-PIEZO1-KO mice. Whole cell and apical + subapical fluorescence intensities in cryosections were analyzed using LAS X software in 3 male and 3 female control mice and 3 male and 3 female KO mice fed a HK diet x 10d.

Results: IF analysis showed reduced whole cell BKα expression in (i) ICs of both male ($p \leq .05$) and female ($p \leq .01$) IC-PIEZO1-KO mice and (ii) PCs from female but not male KOs vs. controls. However, the ratio of apical-to-whole cell expression of BKα was similar in PCs and ICs of KO and control mice. In addition, ICs and PCs in female but not male KO mice had reduced whole cell TRPV4 expression vs. controls ($p \leq .01$). Male, but not female, KO mice had modestly reduced apical TRPV4 expression in PCs vs. controls ($p \leq .01$).

Conclusions: PIEZO1 plays a role in the regulation of BK and TRPV4 channel expression in CCDs. In addition, sex differences exist in whole cell expression of these channels in response to IC-selective deletion of *Piezo1*.

Oral Mannose Supplementation Dampens Liver Fibrosis Through Glycolytic Regulation

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Background: There are currently no approved anti-fibrotic therapies for liver fibrosis despite its increasing worldwide prevalence. Extrapolating from congenital disorder of glycosylation in *mannose phosphate isomerase* (*MPI*; MPI-CDG), which results in disrupted mannose metabolism and presents with characteristic congenital hepatic fibrosis, we have reported that mannose metabolism has roles in broader liver diseases and found that mannose supplementation can reduce fibrogenic activation of hepatic stellate cells (HSCs), the drivers of liver fibrosis. Here, we aimed to investigate the mechanism and *in vivo* efficacy of mannose supplementation in liver fibrosis.

Methods: Using an established FAT-NASH mouse model to induce nonalcoholic steatohepatitis, mice were treated with 5 or 20% mannose in drinking water beginning at week 0 (preventative) or 6 (therapeutic). Liver tissue was collected for protein extraction and histopathological image analysis performed by FibroNest. Activated human hepatic stellate cells (LX-2) treated with and without mannose were used to perform glycolytic rate assays and metabolomics isotope-labeling.

Results: NASH-induced fibrosis decreased by >10% in Phenotypic Composite Fibrosis Score in high- and low- mannose treatments for both preventative and therapeutic groups. Investigating HSC activation and fibrogenesis, we found that mannose supplementation showed a dose-dependent reduction in glycolytic flux and decreased p-ERK protein expression, a known regulator of glucose utilization and cell proliferation.

Conclusions: Oral mannose supplementation at low- and high-concentrations suppresses liver fibrosis *in vivo*. Our findings suggest mannose dampens fibrogenesis through downregulation of glycolysis in HSCs, potentially mediated through ERK pathways. These data support mannose metabolism as a novel target in antifibrotic approaches.

Effect of Provider Education and Reminders on the Rate of Covid Vaccination in Children 6 Months Through 4 Years of Age

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Introduction: Vaccination against COVID-19 in children is effective at reducing disease severity and long-term complications such as MIS-C. Despite the CDC and The American Academy of Pediatrics recommendation to vaccinate children between 6 months and 4 years old, only a minority of patients in this age group were actually being vaccinated.

Hypothesis: We aimed to increase the COVID vaccination rate by 30% among eligible children 6 months through 4 years of age who were seen for well child visits in our Tuesday Primary Care Clinic.

Methods: After sending a survey to providers to assess their understanding and willingness to administer the COVID vaccine to this age group of patients, we attempted to increase vaccination rates by sending educational material (PDSA cycle 1) and then weekly reminders (PDSA cycle 2) to providers.

Results: The percentage of eligible patients 6 months through 4 years old who were vaccinated against COVID increased slightly from 10.8 % at baseline to 13.5 % and 16.4% during PDSA cycles 1 and 2, respectively. There was also a slight increase in the median, from 10% at baseline, to 15% during the intervention period.

Conclusions: Provider education and reminders regarding the importance of and recommendation to vaccinate this age group of children were not sufficient to effect statistically significant change in vaccination rates. Further identifying and addressing vaccination barriers are needed to improve the vaccination rate in this age group. We hope that providing multilingual vaccine educational material to parents may be a more successful intervention.

Irritable Bowel Syndrome is Mediated by Th2 and Th9 T Cells

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Introduction: Irritable Bowel Syndrome (IBS) presents recurrent abdominal pain and an increase in frequency/changes in the form of the stool. IBS is highly prevalent and has a large impact on the quality of life for patients suffering from it, yet the pathogenesis of IBS is not completely understood. It is thought to involve structural, neurological, and immune components in the intestine. The immune pathways involved have not been well characterized except that there is an increased frequency and density of mast cells around the nerve fibers in the intestines. Mast cells can enhance Th2 polarization and promote B cell maturation and class switching.

Hypothesis: IBS is driven by food antigens and mediated by mast cells interacting with Th2/Th9 cells and B cells class that have undergone class switching.

Methods: Cells were isolated from duodenum and colon biopsies from IBS and control subjects and cultured with PMA/ionomycin in the presence of brefeldin A to examine cytokine production after 6h and 17h respectively. Cells were stained with a panel of antibodies for deep phenotypic analysis of T and B cell subsets. qPCR was also performed to examine B cell class switching and Th2/Th9 related gene expression in colon tissue.

Results: In IBS duodenum samples, the percentage of CCR4+ and IL-9+ cells within $CD4^+$ $CD45RA^-$ T cells were increased compared to control samples. There was also a significant increase in IL-4+, IL-9+, and IL-13+ cells within $CD4^+CD103^+CD69^+CD45RA^-$ T cells in IBS duodenum samples. In IBS colon samples, the percentage of IL-5+, IL-9+, and IL-13+ cells within $CD4^+CD45RA^-$ and $CD8^+CD45RA^-$ T cells tended to be higher than in control samples. Consistent with these results, we found increased expression of *IL4*, *IL9*, and *IL13* mRNA in the IBS colon samples compared to controls. *IGHG1* and *IGHG4* mRNA expression were also increased in IBS colon samples.

Conclusion: Our preliminary data show that there is an increase in both Th9 and Th2 cells and class switching to IgG1 and IgG4 isotypes in the mucosa of IBS patients. T and B cell responses to food antigens stimulation will be our next step. A better understanding of the immune dysregulation in IBS could lead to the development of novel immunotherapies.

Potentially Causal Associations Between Placental DNA Methylation and Schizophrenia and Other Neuropsychiatric Disorders

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Introduction: Increasing evidence supports the critical role of placenta in neurodevelopment and potentially, in the development of neuropsychiatric disorders. Recently, methylation quantitative trait loci (mQTLs) and interaction (iQTLs) maps have proven useful to the understanding of SNP-genome wide association study (GWAS) relationships, otherwise missed by conventional expression QTLs.

Hypothesis: We hypothesize that genetic predisposition to complex neuropsychiatric disorders acts partially through placental DNA methylation (DNAm).

Methods: We constructed the first public placental cis-mQTL database including nearly eight million mQTLs calculated in 368 fetal placenta DNA samples from the INMA cohort. We ran cell type- and gestational age-imQTL models and combined those data with the summary statistics of the largest GWAS on 10 neuropsychiatric disorders using Summary-based Mendelian Randomization (SMR) and colocalization. Finally, we evaluated the influence of the DNAm sites identified on gene expression in placenta in the RICHS cohort.

Results: We found that placental cis-mQTLs are useful to map the etiology of neuropsychiatric disorders to prenatal stages. Specifically, part of the genetic burden for schizophrenia, bipolar disorder and major depressive disorder could confer risk through placental DNAm. The potential causality of several of the observed associations is reinforced by secondary association signals identified in conditional analyses, regional pleiotropic methylation signals associated to the same disorder, and cell type-imQTLs, additionally associated to the expression levels of relevant immune genes in placenta.

Conclusion: The genetic risk of several neuropsychiatric disorders could operate, at least in part, through DNAm and associated gene expression in placenta.

Quantifying Pulmonary Regurgitation in Young Adults with Congenital Heart Disease: Comparison of Echocardiography and Cardiac Magnetic Resonance Imaging

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Introduction: Assessment of pulmonary regurgitation (PR) on echocardiography (echo) is important to guide testing and determine timing of intervention. Cardiac magnetic resonance imaging (CMR) is the gold standard to assess degree of PR. We compared echo measures of PR with pulmonary regurgitant fraction (PRF) by CMR.

Methods: We retrospectively collected echo and CMR measurements in patients with ≥mild PR by echo and a CMR within 3 months without intervening intervention. Echo measurements are described in Table 1. Patients were grouped into PR severity categories based on CMR PRF and accuracy of echo readers based on reported severity was calculated. Differences in median echo measurements were compared across PR categories and Spearman's rho correlation coefficient between echo measurement and CMR PRF were calculated. An ordinal logistic regression model including all echo features to predict PR classes of mild, moderate, and severe classes was trained with 10-fold cross validation.

Results: We included 145 subjects (46% male) with median age 22 (IQR 16-33) years, predominately repaired tetralogy of Fallot (50%) and valvar pulmonary stenosis (21%). Branch PA flow reversal was common in moderate and severe PR (94%) and less common in mild PR (18%). There were significant median differences across PR severity categories in all echo measures, with moderate correlations with PRF for: VC ratio, PR deceleration slope and PR duration index. Forward to reverse pulmonary velocity time integral ratio was weakly correlated (Table 1). Echo readers had 72% accuracy (expected agreement by chance is 34%) in classifying PR compared with CMR, with less accuracy in severe (63%) and moderate (67%) PR compared to mild (86%). The multivariable model had an average test set accuracy of 54% and area under receiver operating curve of 0.74.

Conclusions: In this largest cohort to date, several echo parameters were moderately correlated with PR severity but overlapped across severity categories, with the exception of PA flow reversal, which may discriminate mild vs. non-mild PR. A novel cross-validated PR severity classification model had some predictive ability, though less than human echo readers. Further research will focus on model selection, expansion of the feature set, and training/validation in a larger cohort.

Echocardiographic Measurement	Mild PR (MRI RF<20%) n=44	Moderate PR (MRI RF 20-40%) n=58	Severe PR (MRI RF >40%) n=43	P-value*	Spearman's rho (correlation coefficient)	Correlation p-value
MPA flow reversal	12/38 (31.6%)	51/54 (94.4%)	41/42 (97.6%)	<0.001		
Branch PA flow reversal	7/39 (17.9%)	46/52 (88.5%)	41/42 (97.6%)	<0.001		
Max Vena Contracta Ratio	0.35 (0.25-0.54)	0.66 (0.39-0.89)	0.85 (0.58-0.95)	<0.001	0.50	<0.001
PR deceleration slope (m/s^2)	3.0 (2.0-3.7)	5.2 (4.6-6.2)	6.0 (5.0-7.7)	<0.001	0.60	<0.001
PR duration index	0.92 (0.80-1)	0.82 (0.71-0.88)	0.74 (0.67-0.80)	<0.001	-0.44	<0.001
Forward to reverse pulmonary VTI ratio	0.78 (0.50-1.13)	1.19 (0.85-1.48)	1.16 (0.85-1.17)	0.02	0.25	0.02

Table 1: Echo measurements corresponding with mild, moderate or severe pulmonary regurgitation (PR) based on magnetic resonance imaging (MRI) regurgitant fraction (RF). Missing data is excluded and data presented as frequencies and percentages or median (interquartile range). *p-value obtained comparing mild, moderate and severe PR based on MRI using Fisher's Exact Test or Kruskal-Wallis. Maximum vena contracta (VC) ratio taken as maximum of vena contracta divided by pulmonary valve annulus in diastole (measured in both parasternal short and long axis views). PR time index is PR duration divided by diastolic time measured on continuous wave (CW) Doppler. PR slope measured in m/s^2 on CW Doppler. Forward to reverse pulmonary velocity time integral (VTI) ratio measured on parasternal long or short axis pulse-wave Doppler.

Diagnostic Performance of Saliva for Detection of Respiratory Pathogens in Children

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Introduction: Respiratory infections are the most common cause of childhood illness, and identification of culprit pathogens are vital to inform treatment and infection-prevention efforts. Nasopharyngeal (NP) specimens are the diagnostic gold-standard for molecular testing, but collection is invasive and anxiety-provoking for pediatric patients. However, saliva represents a non-invasive, safer alternative.

Hypothesis: As it is shaped by oro- and nasopharyngeal secretions, saliva can be utilized for detection of viral pathogens in patients with influenza-like illness (ILI).

Methods: We are conducting a cross-sectional study across pediatric patients at Mount Sinai Hospital with ILI, warranting respiratory pathogen panel testing (RPPCR). From December 2022-February 2023, subjects underwent collection of three saliva specimens (straight saliva (SS), Flocked-swab (FS), Polyester-swab (PS)) 0-2 days after NP collection/testing. Saliva specimens underwent RPPCR testing, and results were compared to NP results to assess diagnostic performance.

Results: Forty-three patients with detectable (N=31) or negative (N=12) RPPCR results were enrolled. Forty-four provided FS and PS, and 9 provided SS. Compared to NP specimens, SS demonstrated a moderate level of agreement (κ=0.550), 75.0% sensitivity (95% CI: 30.1-98.7%), and 80.0% specificity (95% CI: 37.6-99.0%). FS and PS showed fair (κ=0.298) and moderate (κ=0.418) levels of agreement, respectively. For both swabs, specificity was 100.0% but sensitivity was lower than SS (FS: 43.8%; PS: 54.8%).

Conclusions: Preliminary evaluation of saliva specimens demonstrates superior performance of SS over buccal swabs in comparison to conventional NP specimens. Continued studies are warranted to elucidate overall diagnostic performance and the performance of targets that correspond with viruses with distinct pathogeneses.

Family Perspectives on After Visit Summaries in a Multidisciplinary Pediatric Neuromuscular Clinic

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Introduction: Healthcare for children with medical complexity (CMC) remains fragmented, increasing burdens of caregivers. Multidisciplinary (multi-D) clinics are a growing approach to improve coordinated care. After Visit Summaries (AVS) are critical aspects of communication that can improve care coordination; however there are few published studies assessing families 'experiences with after visit communication.

Hypothesis: We hypothesized that there were areas of improvement for our current AVS.

Methods: A subset of the validated Family Experiences with Coordination of Care (FECC) survey was administered to 21 caregivers at our Pediatric Multi-D Neuromuscular Clinic, which includes up to 13 different specialty providers. Surveys were administered in English or Spanish and completed either online or over the phone. Answers were coded according to FECC standards. Additionally, four caregivers were interviewed using open-ended questions about their experiences with the AVS. Interviews were audio-recorded, transcribed, and coded for themes.

Results: The median age was 6 years (1-20), with 47.6% female and 52.4% Hispanic patients. 90.5% of caregivers indicated that a plan for follow-up care was always included. The lowest means were centered on shared care plans (mean = 72.73/100) and the inclusion of specialists 'names (mean=72.73/100). Recurrent themes in the qualitative interviews revolved around the organization, purpose, time of review, conciseness and comprehension of the AVS. Caregivers qualitatively mentioned that the AVS can be overwhelming when visually unappealing, superfluous, or with medical jargon.

Conclusion: This study suggests that structured AVS may enhance care coordination and decrease caregiver burden for families of CMC. Future improvement work is needed to optimize AVS content and readability.

Improvement of Extrauterine Growth Restriction Within a NICU: Quantitative Assessment Methods and Contributing Factors

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Introduction: Extrauterine growth restriction (EUGR) can have a significant impact on infants' later growth and developmental outcomes. Determining the rate of EUGR and contributing factors may lead to improved outcomes.

Hypothesis: We hypothesize that the incidence of EUGR within our NICU has improved compared to data from 2006 and that it's associated with common NICU comorbidities.

Methods: Included all infants <33 weeks gestation or <1500g at birth admitted to and discharged from Mount Sinai Hospital NICU between 1/2015-5/2019. We compared this to data with the same inclusion and exclusion criteria from 2006-2010. Incidence of EUGR (change in z-score <-1 from birth to discharge) compared to the historical cohort. Factors associated with EUGR were examined in the present cohort and analyzed with linear and logistic regression.

Results: Our sample included 604 neonates. The incidence of EUGR was 22%. Mean birthweight was comparable between both cohorts (1355 vs. 1360g respectively, p-value 0.8). There was a significant decrease in EUGR between the past and present cohort (22 vs 43.4% respectively, OR 0.396, $\chi 2$ p-value <0.001). Using a logistic regression model infants with EUGR were statistically more likely to be female sex, have longer TPN use, and low z-scores at birth.

Conclusion: EUGR continues to be a significant problem but has shown improvement over time when compared to historical data. This may be due to the implementation of nutritionists within our NICU. Neonates who are female, with longer TPN use, and lower z-scores at birth are statically more likely to have EUGR.

A Quality Improvement Initiative to Improve Discharge Communication for Children with Medical Complexity Through the Use of a Standardized Template

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Introduction: Children with Medical Complexity (CMC) have increased care coordination needs which places them at increased risk for poor discharge communication during care transitions. To evaluate this problem at our institution we conducted a needs assessment and spoke with our complex care outpatient providers from the Pediatric Visiting Doctors and Complex Care Program (PVD clinic) and parents of CMC. We found that the transfer of important information on discharge documentation was inconsistent and incomplete at times.

Hypothesis: Our SMART Aim was to increase the use of a novel Complex Care Discharge Summary (CCDS) template from 0% to 60% over 6 months.

Methods: We included patients enrolled in the PVD clinic who were discharged from the hospital medicine service at our institution. Our team worked together to build a novel CCDS template, create a process map, identify key drivers, and design Plan-Do-Study-Act (PDSA) cycles. Interventions included 1) piloting the template with end users to obtain feedback and make improvements, 2) resident and faculty education 3) weekly emails and daily Electronic Medical Record (EMR) chat reminders to the inpatient team and 4) template made into a EMR systems SmartPhrase. Data were entered into an annotated run chart to track the effectiveness of our interventions over time.

Results: The median percentage of CCDS template use in eligible patients increased from 0% to 100% over 5 months.

Conclusions: We successfully implemented and increased the percentage of use of a novel Complex Care Discharge Summary template for CMC discharged from the hospital medicine service.

Hepatocellular Carcinoma in Single Ventricle Patients: A Single Center Case Series

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Introduction: Single ventricle (SV) patients palliated with Fontan develop Fontan associated liver disease (FALD), which can lead to hepatocellular carcinoma (HCC).

Hypothesis: Discuss clinical findings and difficulties in diagnosing HCC in Fontan population

Methods: A single center retrospective review of patients with SV physiology, S/P Fontan, and diagnosed/suspected HCC. Patients included: ≥ 18 years, S/P Fontan palliation ad HCC on liver imaging, elevated alpha feto-protein (AFP) levels, or liver biopsy confirming HCC.

Results: Four patients with Fontan and HCC were identified. Mean age at diagnosis was 25y (range: 24-32y). Initial anatomy was pulmonary atresia with intact ventricular septum (PA/IVS) (n=2), tricuspid atresia (n=1), or double inlet left ventricle (DILV) (n=1). All had systemic left ventricular physiology. Three underwent extracardiac Fontan, while one had RA-PA Fontan. Each had at least one hepatic lesion concerning for HCC on imaging (size: 1.0 cm to 4.5 cm). On cardiac catheterization, mean Fontan pressure was 12 mmHg (range: 9-18 mmHg). A significantly elevated AFP level was only seen in n=1 (5785 ng/dL). MELD-XI score ranged from 8-11. All HCC cases were diagnosed via imaging (CL N=3; MRI N=1) after either routine surveillance scans or bloodwork.

Conclusions: Standard diagnostic modalities for HCC are not reliably predictive due to the heterogeneity of FALD, making diagnosis challenging in this population.

Peanut-Allergic Children Harbor Igg1 Memory B Cells that Recognize Ara H 2 with High Affinity

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Introduction: Peanut allergy (PA) is characterized by the development of high-affinity IgE antibodies against peanut antigens. Studies in murine models demonstrate the role of memory IgG1 B cells as precursors for high-affinity IgE-producing plasma cells through sequential class switching. In addition, evidence in humans suggests a similar differentiation model for human allergen specific IgE plasma cells.

Hypothesis: We hypothesized that peanut-allergic subjects harbor peanut-specific IgG1 cells that recognize Ara h2, the dominant peanut allergen.

Methods: Ara h 2 binding B cells were single cell sorted from PA patients using fluorescent Ara h2 multimers, and cDNAs synthesized from these populations were used for sequencing their B cell receptors (BCRs) and for gene expression analysis using real-time PCR. Ultimately, 15 unique sequences derived mostly from IgG1 memory B cells, were expressed as recombinant monoclonal antibodies (mAbs). Binding patterns of mAbs to peanut extract and to Ara 1/2/3 were determined by ELISA. Also, a bead-based epitope assay was carried out for epitope specificity of IgG1 mAbs and for plasma IgEs of PA subjects.

Results: Through the characterization of single allergen-binding B cells, we determined that highaffinity peanut-specific memory B cells belong to a CD23+IgG1+ population transcribing IGHE. Furthermore, the expression of FCER2/CD23, germline IGHE (GLT-IGHE), and total-IGHE were significantly higher in Ara h 2-binding cells than in DT-binding cells from PA or non-allergic subjects. Through the expression mAbs, we demonstrated that PA children have IgG1 cells that recognize Ara h2 with high affinity. Interestingly, reactivity analysis to peanut protein epitopes showed that most IgG1 mAbs and plasma IgE recognize similar regions of the Ara h 2 protein, especially in Ara h 2.008 and Ara h 2.019.

Conclusions: Peanut-allergic subjects harbor peanut-specific IgG1 memory B cells that recognize Ara h2 similarly to IgE antibodies in plasma from PA children.

Increasing Iron Supplementation in Breastfeeding Infants at the 4 Month Health Maintenance Visit

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Introduction: Full term infants require supplemental iron beginning at 4 months of age due to exhaustion of maternal iron stores. The American Academy of Pediatrics (AAP) recommends that all breast-fed infants receive iron supplementation of 1 mg/kg per day.

Aims/Objectives: Aim: To increase transition to iron containing vitamins in infants receiving any breastmilk by 30% from baseline over four months.

Methods: We conducted a quality improvement project using 3 PDSA cycles. We reviewed charts of all 4-month-old infants in the Pediatric Primary Care Clinic pre and post intervention to capture data for correct transition to iron containing vitamins. Exclusively formula fed infants were excluded. We performed 3 PDSA cycles - 1. Education on transitioning to iron containing vitamins 2. Email reminders for reinforcement. 3. Introduction of a hard stop phrase in EMR for all 4 months well child visit encounters.

Results: At baseline the iron containing vitamin prescription was at 55.2%. After PDSA cycle 1 overall prescription rates increased to 72.2%, after PDSA cycle 2 prescription rates increased to 79.3% and after PDSA cycle 3 prescription rates increased to 89.8%.

Conclusion: Education, email and EMR format changes helped improve effective transitioning to iron containing vitamins.

Screening for Elevated PHQ-9 Scores in an Adolescent Clinic Before and After COVID-19 Lockdown Measures

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Background: Little is known on the effects of COVID-19 and its changes on mental health in adolescents. The biannual Youth Risk Behavior Survey 2023, reported that 57% of teen girls had persistent sad or hopelessness in 2021, almost double the rate of boys and the highest levels reported this decade.

Hypothesis: To ascertain precise estimates of the elevated PHQ-9 scores in adolescents pre and post COVID-19 lockdown.

Methods: Data on patients seen in the adolescent clinic aged 12 to 22 that had a PHQ9 completed from January 2019 to February 2020 (pre-lockdown) and March 2020 to December 2021 (post lockdown) was obtained using a report dashboard in our EMR. SPSS 25 software was used to calculate the PHQ9 means, out of which two groups were obtained using paired sample t-tests. Chi-Square Test of Independence to determine an association between categorical variables and the outcome variable of positive PHQ-9. A logistic regression model was also used to determine factors associated with positive PHQ9 scores.

Results: 790 adolescents were seen during both time periods. PHQ scores (>/=5) increased from 8.8% to 14.2% from pre-lock down to post-lockdown($p<0.001$). For PHQ9 score >5, there was an average difference between pre and post lock down PHQ-9 score ($t_{102}=2.386$, $p=0.019$). In logistic regression model, none of the predictor variables were associated with changes in PHQ9 scores during both time periods.

Conclusion: COVID-19 has been found to be associated with mental health changes in adolescents emphasizing the importance of a holistic approach that focuses on mental health when managing COVID-19

PASS Study: Tackling Food Insecurity with a Clinic-Based Food Pantry and Referrals to Community-Based Food Pantry in New York City

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Introduction: As part of its socioeconomic determinants of health (SDH) screening program, the pediatric clinic at Mount Sinai provides families with FI an emergency food package, and referrals to community resources like the New York Common Pantry (NYCP).

Hypothesis: Changes in FI over a 3-month period among families with FI that were referred by a SDH program to an on-site clinic food pantry exist.

Methods: Families with FI were offered to participate in the study. We collected baseline sociodemographic data, and families completed the 18-item USDA Household Food Security Survey at enrollment and three months later. To explore changes in FI scores over time, we used a mixed-effects model.

Results: 113 families with FI enrolled in the study and 61 (54%) completed the 3-month follow-up USDA Survey. In a mixed-effects model, participation in SDH program was associated with a decrease in the mean FI score at 3 months [4.4 (SD=3.6) to 3.3 (SD=3.3)] ($p<0.05$). This remained significant after adjusting for covariates ($p<0.02$). All enrolled families accepted a food package, and 23 (20%) consented to information about SNAP and 10 (9%) accepted information about WIC. Forty-three (68.3%) families accepted a referral to NYCP, and 56% of them became clients.

Conclusions: Food insecure families who received food packages and referrals to community resources, experienced a decrease in FI score over a 3-month period. Future plans include assessing changes in FI over a 12-month period. Our program, which provides immediate food assistance while linking families to more long-term assistance may be a successful model for improving food insecurity.

Table 1. Baseline characteristics of families enrolled in the PASS Study (n=113), June 2021 – November 2022.

	Percentage (%) Median [IQR]
Child and Household Characteristics	
Child's sex assigned at birth	
Male	55%
Female	45%
Child Race	
Hispanic	63%
Non-Hispanic Black	27%
Non-Hispanic White	2%
Other and Multiracial	8%
Child Health Insurance	
Medicaid	91%
Private	9%
Caregiver's Level of Education	
College and/or Graduate School	21%
High School or Some College	59%
Less than High School	20%
Caregiver Employment Status	
Employed full-time	21%
Employed part-time	12%
Unemployed	61%
Other	6%
Housing	
Other	10%
Private	53%
Public	37%
# adults over 18 in household	2 [1, 3]
# children under 18 in household	2 [1, 3]
Food Security	
USDA Food Security Total Score	4 [1, 7]
USDA Food Security Level	
High food security (0)	14%
Marginal food security (1-2)	21%
Low food security (3-7)	44%
Very low food security (8-18)	21%
Family receiving public benefits	
WIC	62%
SNAP	60%
Cash Assistance	4%
Any benefit	83%
Financial Worry	
Worry Domain Questionnaire (WDQ) – Financial Domain[a]	15 [11, 20][b]

A Mixed Methods Approach to Understanding NYC Parental Attitudes on the COVID-19 Pediatric Vaccine

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Introduction: In late 2021, the FDA provided emergency use authorization for the COVID-19 vaccination in children ages 5+. While hesitancy was anticipated, we did not yet know what factors would strongly predict intentions to vaccinate amongst parents and caregivers.

Methods: From January to March of 2022, we conducted a mixed methods assessment of parents/caregivers' attitudes towards childhood COVID-19 vaccination in NYC. We surveyed 94 parents about their vaccination status, sources of trusted information, motivations to vaccinate themselves, and perceived safety/effectiveness of the vaccine against breakthrough infections and variants for themselves and children. We conducted bivariate analyses to identify factors significantly associated with pediatric vaccination intention.
In English and Spanish focus groups with 44 adults, we asked about their thoughts on the pediatric vaccine. We translated, transcribed, and uploaded transcripts to Dedoose for coding and analysis.

Results: Table 1 provides participant demographics. Factors significantly associated with parent/caregiver's report of child vaccination completion/intention include their own vaccination status, safety-oriented vaccine motivations, trust in doctors as a source of information, and a reported annual household income of $50,000+ (Table 2). In contrast to the quantitative data, qualitative analysis (Table 3) showed higher degrees of pediatric vaccine hesitancy regardless of personal vaccination status. Common concerns included children's inabilities to provide consent, short and long-term side effects, the sensitivity of children's bodies to the vaccine when compared to adults, children's relative low risk, and the lack of anecdotal evidence within their personal networks. Despite acknowledging fear and breakthrough infections, those who supported child vaccination cited increasing potential exposures, vaccine mandates, school-based access to vaccines, and offering children the same protection as adults.

Conclusion: Our survey results align with other recent studies examining parental attitudes towards the pediatric COVID-19 vaccine and predictors of uptake. However, results from our focus groups indicate that there is a depth of nuance in how adults, including parents, caregivers and grandparents, weigh the risks and benefits of the vaccine for children. As more information about COVID-19 and the vaccine becomes available, mixed-methods research may provide a more complete understanding of evolving perceptions.

Table 1. Participant demographics

		Surveys n = 94	**Focus Groups n = 44**
Race/Ethnicity:			
	Non-Hispanic Black	38%	51%
	Hispanic/Latino/a/x/e	12%	41%
	Non-Hispanic White	43%	7%
	Non-Hispanic Other/Multi-Racial	7%	5%
Gender:			
	Man	46%	39%
	Woman	51%	50%
	Transgender, Gender Non-Conforming, Non-Binary	2%	0%
	Other	1%	0%
Education:			
	≤Associates degree	48%	*Not available*
	≥Bachelor's degree	52%	*Not available*
Age		*mean (sd)*	*mean (sd)*
		32.2 (+/- 8.2)	32 (+/- 12.1)
Income			
	< $50,000	51%	*Not available*
	≥ $50,000	49%	*Not available*
Vaccination Status			
	Not vaccinated yet	13%	27%
	Vaccinated	87%	73%
	Mid-adopters	*Not available*	25%
	Early-adopters	*Not available*	48%

Table 2. Factors associated with parent/caregiver's report of child vaccination completion

	Vaccination Intent		
	No plan to vaccinate child (n=39)	Child is already vaccinated or Get them vaccinated right away (n=55)	
Self Vaccination Status			*Fisher's Exact test*
Yes, got one-dose vaccine	5 (13%)	15 (27%)	
Yes, got first dose of two-dose vaccine	5 (13%)	10 (18%)	
Yes, got both doses of two-dose vaccine	17 (44%)	30 (55%)	
No, have not gotten the vaccine	12 (31%)	0 (0%)	
			<.0001
Motivation for Self Vaccination			
I want to keep my family safe	18 (46%)	46 (84%)	0.0002
I want to keep my community safe	13 (33%)	33 (60%)	0.0128
I want to keep myself safe	19 (49%)	39 (71%)	0.0337
Trust the Federal government to ensure COVID-19 vaccine's pediatric safety			
Mostly / Fully	20 (51%)	39 (71%)	
Somewhat / Not At All	19 (49%)	16 (29)%	
			0.0825
Believe vaccine is safe / effective against breakthrough infections			
Yes	19 (51%)	47 (85%)	
No	11 (30%)	8 (15%)	
Don't know	7 (19%)	0 (0%)	
			0.0001
Believe vaccine is safe / effective against variants			
Yes	14 (37%)	40 (73%)	
No	18 (47%)	12 (22%)	
Don't know	6 (16%)	3 (5%)	
			0.002
Trust their doctor or healthcare provider for COVID-19 information			
No	4 (10%)	0 (0%)	
A little	9 (23%)	8 (15%)	
A great deal	26 (67%)	47 (85%)	
			0.0186
Income			
< $50,000	24 (65%)	22 (41%)	
≥ $50,000	13 (35%)	32 (59%)	
			0.0328

Table 3. Participant's perspectives and thoughts about the vaccinating children

Group	Exemplar
Early Adopter - English	FACILITATOR: [...] *why do you think people might feel differently about vaccinating adults than they do about vaccinating children, if you think that they do or, or don't they?* PARTICIPANT 1: *I think for me children are the most precious things. They're pure. I'm not trying to—I don't want to break that. I don't want to push nothing from this world into their little world. You know they're, they're pure, they have their own little world going on. I'm not about to inject them, I don't know but that sounds crazy. But I'm not going to do that to my child. Yeah, I'm just not going do that period.* PARTICIPANT 2: *Me too.*
Early Adopter - English	*I'm not sure. I haven't heard that much, but I can imagine that they don't feel it's as necessary to vaccinate kids as much as adults because we've been hearing so much that they don't get symptoms as badly as adults do. But since that's changing, more kids are getting infected people's opinions might change. But yes, I feel like it should be encouraged way more for kids to get vaccinated. I've still seen commercials for just adults, so yeah.*
Early Adopter - English	*To us, it was just, we was just we didn't have like other friends and family. He's the only young one in the family. He's only grandson for both grandparents. And you know there's not a lot of children around him only when he's at school, you know? All his little cousins live further away, they're all scattered. So we don't know who has been vaccinated. Like my nieces and nephews, like they have their young children and they're in the medical field and they have not vaccinated their children. So I wouldn't know. So if I had someone tell me like, hey, just, just go ahead, don't be reluctant, just give it to him. I think we would've been like sooner. You know, he would've received it sooner.*
Early Adopter - English	*[...] And also his, his school they do the, the vaccine, like the drives, where you could get them vaccinated at school too. So that's also like something that's good, you know that they provide that for the parents.*
Early Adopter - English	*I think it was like during the second time that they offered it, that, you know, my daughter asked me like, what do you think? And I said you should give him. I said the same way you got yourself vaccinated, you know, do it for him. You know, we're just upset that he tested positive today. His grandfather's really, really upset, you know. It's heartbreaking.*
Early Adopter - Spanish	*Now with this thing that, for example, I had like a conversation with my daughters, I say look. "If you don't vaccinate your kids you're going to have problems because it's a mandate already that they're doing. What do you have... you can't go out to eat. You can't go to the park. You can't go there because people are watching you. Then you have to get vaccinated." "No, something can happen to them." "You have to put fear aside". Because if we don't leave fear aside we will always have this mistrust. I know and I understand that it is very difficult and understandable for other people. But we shouldn't let ourselves fall either.*
Mixed Vaccination Group - English	*I'm going to be honest. I took the vaccine but I'm not sure if I want--I'm not sure if I want my grandbaby to take it. I don't know, I just have--I don't know.*
Mixed Vaccination Group - English	*Well, to me, I wouldn't do it. I mean, my kids that are of a conscious age to make a decision for themselves, in their teens. I have a son that's 13 about to be 14. I have a son that's 17 about to be 18. They made their decisions whether they were going to get it or not. Now, my 4-year old?* *No, I wouldn't do it, because like I said, I'm a staunch believer that there wasn't enough on it. I still feel like that, if I needed to be the sacrificial lamb, because nobody's going to tell us what's going to happen to us long-term. And how could they? Who have they practiced that vaccine on for 10, 20, 30 years to know what's going to happen down the line?*
Mixed Vaccination Group - English	*Like I said, my youngest son, I believe he's too innocent and he's not in school so he's not exposed. He doesn't go to daycare and stuff like that. I'm fortunate to have a family member that watches him when I'm at work, or sometimes things happen with family members and I'll bring him to work. - - my son - - that's my little helper. If I was Santa, that would be my helper.*
Mixed Vaccination Group - English	*My son is not vaccinated. He's 6. Yeah, just one of those decisions that, let me try it out first, you know? See what happens to me. But it's my job to protect him, and honestly, I don't know all the information about the vaccine, but circumstances present itself that I had to make a decision to get vaccinated. He's not in that position, so I'm - - [background noise] see what happens over time prior to my son being vaccinated, but I'm very against that for him at this current moment.*
Mid Adopter - English	*So firstly, like, these vaccines are not like completely tested, undergoing all their clinical trial basis. And they don't know if they are safe, like, like, we don't have a—we are not 100% sure that they are safe. So children vulnerable, it's not unlike others. They are—they are not like, they can't if there was some something bad happening after taking the vaccine, adults can tolerate but kids are like, very sensitive in that sense. So yeah, even if they are like—they're more vulnerable to get exposed to COVID and they get infected, because they are like, going to schools and like having all these like things going on. But I think—I personally don't feel like it's as safe for the kids to get vaccinated compared to adults.*
Mid Adopter - English	*Okay. For me, I think it's a more risk because [...] we have not noticed [...] the long time effect of the COVID-19, the vaccine. So I think it's a [...] bit too earlier for that and because the children are the future of tomorrow and they are leader of tomorrow. So I think we must, we must chill for about, let's say two to three years to see the effect and, yeah, it's, it's more earlier for that.*
Mid Adopter - English	*Okay. I think it's, it is not a good thing, and—because if adults are refusing it to take it and they have a say, what about those kids who doesn't have any say on what is being put in their body? Just because the kid, or you are the parents of, of, of these kids, you don't have like the right to like make that decision because it's their body, and they are not like in that age to like consent to like taking it. So I think they should like wait until the kids are of a legal age to consent to anything, may it be treatment, may it be vaccination, they should like wait. And also considering that the vaccination has just started, we are now like experiencing the short term effects. Those are the side effects, and we, we have not like even experienced the long-term effects. So we should like just put that on hold, and just wait and see how it, it unfolds.*
Mid Adopter - English	*Yeah, I would say maybe it's not yet the time to vaccinate kids under 18 years because, for instance, like let's say the side effects. If the side effect can get heavy on adults, what about a kids under 18 years? It may be so much worse, maybe. So I think it is not the time. The time has not come. Maybe the vaccines are not yet the fine, fine product of the vaccine that they say can cure the virus. So I think let's wait a little bit.*
Non-Vaccinated - Spanish	*Well, uhm I feel that uhm it- n- the percentage of kids that get COVID is very low. Uhm the percentage I think is lower than ten percent. I think that, if I'm not wrong, uhm and the kids uhm in the uhm the kids are generally not a group that are at a very at a very high risk of the vaccine. No, I mean, I'm sorry, I mean they are not at a high risk of getting COVID-19. I'm sorry. Uhm so I feel that the vaccine for kids is something that exists and it has to be an option. Uhm and for people who want it, for people who want to vaccinate kids. But it shouldn't be something obligatory. I don't know if uhm the city of New York obliges kids to be vaccinated to go to school or to uhm participate in uhm extra activities like being part of the school music band or in order to practice sports at school.*

Investigating the Therapeutic Role of Mannose in a Zebrafish Model of Biliary Atresia

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Introduction: Biliary Atresia (BA), a fibroinflammatory obliteration of the extrahepatic to intrahepatic bile duct system, is the most common indication for pediatric liver transplantation, yet its etiology is largely unknown. We have previously shown that disruption of mannose metabolism induces biliary fibrosis, and supplementing with mannose can dampen liver fibrosis. Here, we investigated whether mannose has a therapeutic effect in biliary atresia using a biliatresone, a plant isoflavonoid, that has been shown to induce BA-like phenotypes through increasing oxidative stress.

Hypothesis: Mannose supplementation will inhibit liver injury in a zebrafish model of biliary atresia by dampening oxidative stress.

Methods: We treated *Tg(Tp1:GFP)* zebrafish 5-8 days post-fertilization with 1.5mM and 3mM biliatresone. Widefield brightfield and fluorescent imaging was performed on the Leica Microsystems DMi8 microscope. Biliatresone-treated larvae were supplemented with zero, low (10mM), or high (50mM) dose mannose in egg water.

Results: Biliatresone-treated groups showed dose-dependent destruction of the gallbladder in zebrafish larvae. 50mM mannose supplementation improved survival of biliatresone-treated larvae and also improved bile duct structures (N=25 per group).

Conclusions: Biliatresone mimics BA in zebrafish. Our findings suggest a potential therapeutic role for mannose supplementation in BA. Studies are ongoing using CELLROX fluorogenic probe and qPCR targeting glutathione metabolism pathways to measure oxidative stress.

Quality Improvement of Admission Medical Reconciliation in a Children's Hospital

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Introduction: Incomplete admission medical reconciliations (AMRs) are common in pediatric hospitalizations and can lead to adverse patient outcomes. At the beginning of this study there was no formal process for completing an AMR at our institution, a 60-bed nested children's hospital. Similar quality improvement (QI) initiatives at other pediatric institutions have been shown to improve the rate of completed AMRs.

Hypothesis: Using a QI methodology, the percentage of completed and documented AMRs on our pediatric hospitalist teams could be improved to 90% or greater.

Methods: Our QI project was initiated in July 2021 by a team of resident physicians and one pediatric hospitalist. Our outcome measure was completed AMRs, defined as AMRs documented in the electronic medical record (EMR) or in the history & physical note, as well as relevant medications ordered within 12 hours of admission. Data from 345 AMRs over the course of the project were collected and analyzed via run charts to assess all interventions.

Results: Baseline data before interventions showed that a median of 70% of 40 AMRs were completed. Further collection of 305 AMRs completed over seven months has not changed the median significantly, though there have been weeks with 100% completion.

Conclusion: The measures showed non-significant improvement over the course of the study. A Hawthorne effect may have improved the baseline data because the project was well known to the residents completing AMRs. Ongoing interventions include an AMR process guide to be sent out monthly to all residents rotating on the hospitalist floor teams.

Characterizing Dendritic Cell Subpopulations for Cancer Immunotherapy

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I**ntroduction:** Dendritic cells (DCs) are a lineage of hematopoietic stem cells that originate from $CD34^+$ cells in the bone marrow and are effective antigen-presenting cells. Current principles for DC-based cancer immunotherapy include isolating DCs from blood, activation and antigen-loading, and reinfusion into patients for antigen-specific T-cell responses. Cancer is a leading cause of death among children, therefore, specific DC-based immunotherapy can play an important role in pediatric patients. Here, we highlight our efforts to characterize DC subpopulations using umbilical cord blood as a reliable source of DCs in their nascent state.

Hypothesis: We hypothesized that DCs can be enabled to be more effective at antigen presentation for cancer cells.

Methods: We used fluorescence-activated cell sorting to sort DCs from umbilical cord blood. We used bulk ATAC-Seq and scRNA-Seq for verification of sorted populations and differential expression analysis.

Results: We demonstrated that common DC precursors can differentiate into three lineage and unique transcriptional trajectories: plasmacytoid DCs, classical dendritic cells 1 (cDC1), and cDC2 that activate $CD8^+$ and $CD4^+$ T cells, respectively. We further demonstrated differential expression among these three branches that phenotype DC subpopulations, uniquely characterized by the TIM3 marker of T-cell exhaustion.

Conclusions: We identified specific DC subpopulations that carry the inhibitory TIM3 and markers that can enhance DC-mediated activation of antigen-specific T cells. These markers include inhibitory sialic acid-binding immunoglobulin-like lectin receptors, which are features of specific DCs from cancer patient samples. Our goal is to further delineate the complex character of these DC subpopulations using a multi-omics approach.

Assessing the Role of Peer Influence and Social Pressure on the Management of Food Allergies in Adolescents and Young Adults

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Division: Allergy and Immunology

Institution Affiliation: Icahn School of Medicine at Mount Sinai

Institute Affiliation: Elliot and Roslyn Jaffe Food Allergy Institute

Introduction: It is essential to understand behavioral factors related to food allergy management in adolescents and young adults (AYA) because this age group is at the greatest risk for food-induced anaphylaxis deaths related to risk taking behavior.

Hypothesis: We hypothesized that AYAs will modulate their behavior regarding their food allergies when with friends (peers).

Methods: We administered a questionnaire to AYAs aged 14-21 with an IgE-mediated food allergy. Data were analyzed by Chi Square with $p<0.05$ as significant.

Results: A total of 41 surveys were completed in this interim evaluation of the data (age range, 14-21 years, median 17 years, 57% female). AYAs were more comfortable speaking to restaurant staff about food allergies when with family (88% "comfortable" or "very comfortable") vs with friends (69% "comfortable" or "very comfortable"), $p<.05$. They were also more likely to accept food with unknown ingredients when coming from friends (91% "likely" or "very likely") vs. family members (71% "likely" or "very likely"), $p<0.05$. Regarding peer pressure, 12% responded that they "at least sometimes" felt peer pressure to: eat foods they would not otherwise eat, and to not carry their epinephrine injectors. Additionally, 12% indicated that they "at least sometimes" felt harassed, teased, or bullied by peers because of their food allergy.

Conclusions: The AYAs surveyed were more comfortable addressing their food allergies when with family members vs. with friends and admit to peer pressure that could relate to unsafe practices. This suggests that peer relations should be addressed in food allergy management.

Exercise Induced ECG Changes Predict Adverse Outcomes in Pulmonary Hypertension

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Division: Cardiology

Institution Affiliation(s): Icahn School of Medicine at Mount Sinai; Columbia University Irving Medical Center

Introduction: Cardiopulmonary exercise testing (CPET) is an important tool in assessing the functional status of patients with pulmonary hypertension (PH). During CPET, ECG is used as marker of exercise induced ischemia. We hypothesize that ECG changes with exercise may be an early indicator of clinical worsening in PH and could predict adverse outcomes.

Methods: Clinical, hemodynamic, and CPET data of 101 PH patients who underwent CPET between 2013 and 2019 were included. ECGs were analyzed for ST depressions and T wave inversions during the earliest CPET in this time frame, along with coincident hemodynamic data. These data were correlated to adverse outcomes, including shunt creation (atrial septostomy or POTTs shunt), lung transplantation, and death.

Results: Median age was 19 y (7-40 y, IQR 12-26), 68% were female, and median follow up time was 3 y (1-8 y, IQR 1-5). Sixteen patients had an adverse outcome (8 shunt creation, 4 lung transplant, 7 death). Twenty-two patients demonstrated significant ST/T wave changes with exercise, 18 ST depressions and 9 T wave inversions. Multivariate regression, including pulmonary arterial pressure, revealed exercise induced ST/T wave changes to be an independent predictor of procedure-free survival (without lung transplantation or shunt creation) (hazard ratio 11.10, p=.006). Only 21% with ST/T wave changes demonstrated procedure-free survival vs 85% without.

Conclusions: ST/T wave changes on exercise ECG are significantly associated with adverse outcomes in PH on a medium term follow up study. These ECG changes with exercise can be used as early indicators of clinical worsening in PH and predictors of adverse outcomes.

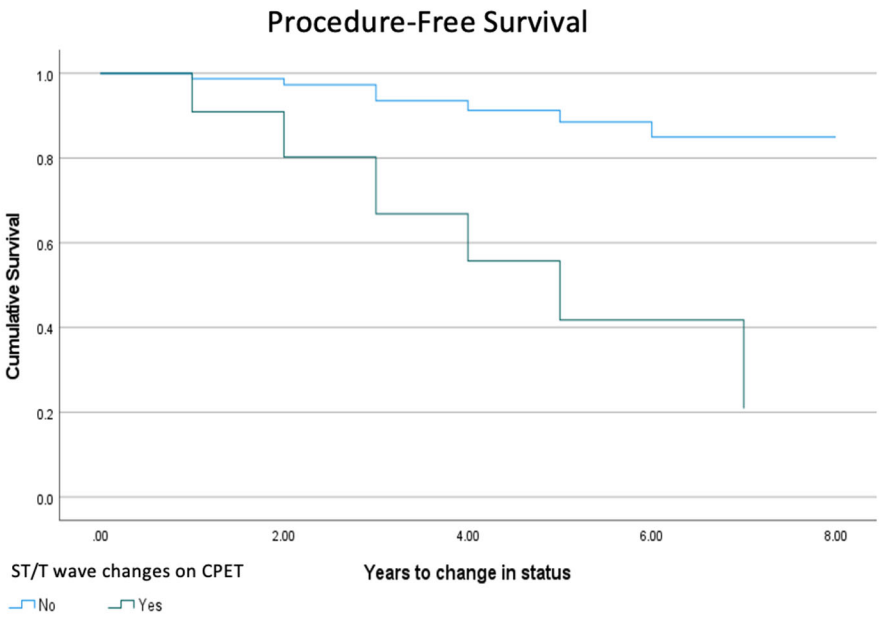
Table 1. Univariate and Multivariate Analysis

Variable	Hazard Ratio - Univariate Analysis (Confidence Interval)	P-value	Hazard Ratio - Multivariate Analysis (Confidence Interval)	P-value
ST/T change on exercise	.06 (.01 – .63)	.019	11.1 (1.96–62.82)	.006
Mean PAP*	1.03 (1.01– 1.07)	.006	1.00 (.97– 1.04)	.686
VO_2 (ml/kg/min)**	.88 (.80 - .97)	.012	.86 (.73 – .999)	.049
End Tidal CO_2**	.86 (.78 - .95)	.004	.93 (.69 – 1.23)	.594
V'E/V'CO_2**	1.09 (1.03 – 1.15)	.003	.97 (.82 – 1.15)	.747

*Measured on right heart catheterization within 6 months of CPET

**Measured at peak exercise

Figure 1. Kaplan Meier Survival Curve (N=101)



Years Post CPET	0	2	4	6	8
No ST/T changes, N (%)	79 (100%)	67 (97%)	40 (91%)	24 (85%)	24 (85%)
With ST/T changes, N (%)	22 (100%)	15 (80%)	5 (56%)	2 (41%)	1 (21%)

Endoscopic Removal of 16 Magnetic Balls in a Critically Ill 2-year-old

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Division: Gastroenterology

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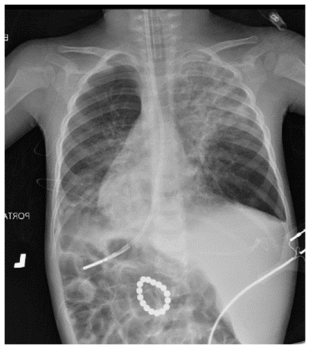
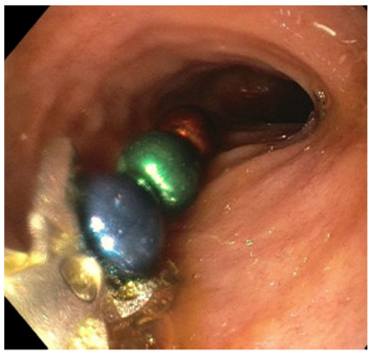
Introduction: When high-power magnets are embedded in the bowel wall (increasing concern for fistulation, perforation, and necrosis), there is not clear guidance for removal. Endoscopic and surgical techniques have been reported.
Here we present the case of incidentally identified magnetic balls (16 total) in a 2-year-old admitted for respiratory failure. The time of ingestion was not known and removal was delayed due to critical status of the patient.

Methods: During endoscopic evaluation multiple metallic balls were identified in a linear formation along the medial duodenal wall, one-fold proximal to the ampulla. The decision was made to proceed with an endoscopic approach given the retroperitoneal location that would be difficult to access surgically. The majority (14) were removed without difficulty, but the last 2 balls were incompletely visualized. The proximal ball was grasped with forceps and gentle traction was applied. The second more distal ball remained magnetically connected and both were successfully removed, revealing a small mucosal wall defect that was closed with an endoscopic clip.

Results: Following clip placement, fluoroscopy with contrast confirmed that all balls had been removed and there was no evidence of contrast extravasation.

Conclusions: If surgery can be avoided in a pediatric patient, especially in a severely ill child like our patient, it will decrease additional morbidity and mortality. This case demonstrates the ability to successfully remove multiple magnets endoscopically, even when magnets are embedded in the duodenal wall. Endoscopic removal should be considered in other patients if all resources (interventional endoscopy and pediatric surgery) are available to proceed safely.

1)  2)  3) 

Pubertal Status and Trends in Gender Affirming Treatment of Transgender and Gender Diverse Youth

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Introduction: Transgender and gender diverse (TGD) youth seek care to affirm their gender identities and improve quality of life and mental health. We sought to characterize the pubertal status of the TGD youth seeking gendering affirming care.

Hypothesis: TGD youth seek care in early to late puberty.

Methods: Retrospective analysis performed on 58 TGD youth patients. We labeled Tanner stage 1 as prepuberty; stages 2–3 as early puberty; and stages 4-5 as late puberty.

Results: 3.4% of the population presented in prepuberty (n=2), 27.6% in early puberty (n=16), and 69.0% in late puberty (n=40). Of the early puberty population 87.5% are transgender girls, 6.25% of are transgender boys, and 6.25% are non-binary. Of the late puberty population 62.5% are transgender boys, 27.5% are transgender girls, and 10.0% are non-binary.
Of the transgender girls (n=27), 7.4% were prepubertal, 51.9% were in early puberty, and 40.7% were in late puberty. Of the transgender boys (n=26), none were prepubertal, 3.6% were in early puberty, and 96.4% were in late puberty. Of the non-binary youth (n=5), 20% were in early puberty and 80% were in late puberty.

Conclusions: Trans feminine patients are evenly divided between early and late puberty. Trans masculine patients overwhelmingly present in late puberty. This present possible implications for fertility preservation strategies for transgender girls and suggest that the need for chest masculinization surgery cannot be entirely prevented for transgender boys.

Investigation of Cardiac Valve Disease Mechanisms in Noonan Syndrome with an iPSC Model

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I**nstitutional Affiliation:** Icahn School of Medicine at Mount Sinai

Institute Affiliation: The Mindich Child Health and Development Institute

Introduction: Noonan syndrome (NS) is primarily an autosomal dominant disorder that results from gain-of-function germline variants in the RAS/MAPK pathway. One of the main features of NS is congenital heart disease, with cardiac valve stenosis estimated to occur in over 50% of NS patients. To investigate this pathology, we have developed a novel human induced pluripotent stem cell (iPSC) differentiation strategy that allows us to recapitulate the steps of valvulogenesis *in vitro* and model valve disease in NS.

Hypothesis: NS-iPSCs can be differentiated into valvular interstitial cells (VICs) and allow for identification of novel molecular mechanisms that promote cardiac valve stenosis.

Methods: iPSCs were differentiated into endocardial cells that have the potential to undergo endothelial-to-mesenchymal transition (EndMT) to form VICs. CRISPR was used on otherwise isogenic iPSC lines to knock-in pathogenic NS variants and subsequently modeled with our differentiation protocol.

Results: iPSCs can be differentiated into endocardial cells that are transcriptionally and functionally distinct from vascular endothelial cells. These endocardial cells can undergo EndMT to become VICs and upregulate numerous mesenchymal genes. Applying this model to our NS-iPSCs, we find that NS-iPSCs have increased specification of mesoderm and endocardial cells. Interestingly, NS endocardial cells exhibit defective EndMT, specifically to VICs of the fibrosa layer, but not to those of the spongiosa layer. Lastly, we find NS VICs exhibit dysregulation of ERK signaling and aberrant production of TGFb2 protein.

Conclusions: Our iPSC model of NS cardiac valve disease reveals pathogenic mechanisms that may drive valve stenosis *in vivo.*

Milk-Responsive T Cells in Eoe Display Unique Disease-Associated Cytokine Profiles in Both Tissue and Peripheral Blood

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Institute Affiliation(s): The Mindich Child and Health Development Institute; Precision Immunology Institute

Introduction: Eosinophilic esophagitis (EoE) is an inflammatory disease of the esophagus driven by food antigens (with milk being the most common inciting antigen) and characterized by eosinophilia on esophageal biopsy along with symptoms consistent with esophageal dysfunction. Th2 cells and Tregs have also been identified in the esophagus of EoE by flow cytometry and single cell RNAseq, however functional characteristics of T cells in EoE remain poorly understood.

Methods: We examined T cell phenotype and response to milk in esophagus, duodenum and peripheral blood from patients with active EoE, resolved EoE and controls by spectral cytometry.

Results: Two distinct subsets of Type 2 cytokine-producing $CD4^+$ T cells with differential expression of CD8 were found in esophagus: a $CD4^+CD8^-CRTH2^+$ population that decreased in number with resolution of eosinophilia and a $CD4^+CD8^+CCR3^+$ population that was unchanged in number but had decreased cytokine production with resolution. Esophageal $CD4^+CD8^-$ cells were constitutively activated in active EoE, whereas resident $CD4^+CD8^+$cells responded to milk stimulation with an increase in IL-5 and IL-13 production, most notably in resolved EoE. These milk-responsive T cells were not found in the duodenum of active or resolved EoE, highlighting the esophageal localization of these cells. Responsiveness to milk in the peripheral blood was examined in controls and EoE and compared with IgE-mediated milk allergic subjects. Milk-responsive T cells could be found in the peripheral blood of active EoE and included populations of T follicular helper (Tfh) cells. Tfh cells from EoE were dominated by IL-10 production as compared to Tfh cells from IgE-mediated milk allergy which were dominated by IL-4/IL-13.

Conclusions: Two key $CD4^+$ T cell populations are prominent in EoE, a resident $CD4^+CD8^+$ T cell population responsive to milk even after resolution of inflammation, and a systemic Tfh cell population capable of driving IgG4 production.

The PACE (Pediatric Accessible Curriculum for Expecting Parents) Study

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Introduction: In-person prenatal parental education classes increase prenatal bonding, parental confidence at one month postpartum, exclusive breastfeeding rates at 6 months, and decrease postpartum depression at 3 months. Less is known about the efficacy of online prenatal parenting resources, specifically their ability to enhance maternal confidence and self-efficacy while decreasing anxiety. This study assesses the impact of a new online pediatric curriculum for parents.

Hypothesis: The prenatal pediatric curriculum will increase parental reported self-efficacy and confidence and decrease anxiety within 6 weeks postpartum.

Methods: A general pediatrician panel reviewed curriculum topics; selected topics were made into QR codes that link pediatric questions to answers in the form of endorsed resources. The QR codes will be distributed at the Obstetric clinic in the third trimester of pregnancy. A survey will be distributed at Mount Sinai Pediatric Associates Practice during well child checks within the first 6 weeks of life. Data will be analyzed to assess if prenatal access to the resources increased parental confidence and self-efficacy and decreased anxiety.

Results: Six topic areas addressing commonly asked pediatric questions were selected. Content is derived from pediatrician-recommended sources such as the AAP. Evaluation of curriculum usage is pending. This study will determine whether this resource impacts parental confidence, self-efficacy and anxiety.

Conclusions: If results are significant, this curriculum can increase parental access to much needed information and be customized by other cities for dissemination.

Encouraging Big Smiles: Improving Patients' Oral Health through Fluoride Varnish Application in Continuity Clinic

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Division(s): General Pediatrics; Hospital Medicine

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Introduction: Dental caries is the most common chronic disease of childhood in the United States, predominately affecting marginalized children. The AAP recommends fluoride varnish application in primary care settings for effective cavity prevention strategy. We implemented a new process to apply fluoride varnish during well child care (WCC) at a pediatric resident continuity clinic.

Hypothesis/AIM: To increase the percentage of eligible patients 12 months to 5 years old presenting for WCC receiving fluoride varnish from 0% to 50% by June 2023.

Methods: We utilized quality improvement methodology to create interventions to increase the rate of fluoride application. Outcome measure data of percentage of eligible patients with applied fluoride was generated from a weekly EMR report. Process measure data of available fluoride supply was recorded on weekly log. Balancing measure data of extra time needed per patient encounter was collected through resident feedback. Measures were tracked across PDSA cycles.

Results: Fluoride application varied between 0-18%. Data showed a significant shift above the median line at the end of our study period with a recalculation of our median from 8% to 12.5%. Fluoride supply documented as sufficient each week. Providers reported < 5 minutes of added time to visit.

Conclusions: Despite overall improvement throughout our study period, we did not achieve our aim of 50% of eligible patients receiving fluoride varnish. Our most impactful interventions were placing fluoride in a more convenient location, the EMR order set, and, most recently, rewarding top performers. Increase in provider time was minimal.

Partial USP18 Deficiency Leads to Early-Onset Childhood Inflammation

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Division: Pediatrics

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Institute Affiliation: The Mindich Child and Health Development Institute

Introduction: Type I interferonopathies are characterized by an overabundance of IFN-I, which cause a broad spectrum of clinical presentation. Ubiquitin Specific Peptidase 18 (USP18) plays an important role in regulating the interferon (IFN) response by dampening the IFN-I signaling pathway. Additionally, *USP18* removes *ISG15* from proteins, in a process termed de-ISGylation. Synergistically, *ISG15* prevents proteasomal degradation of *USP18.* Autosomal-recessive USP18 deficiency results in severe systemic inflammation and neurological anomalies, which is fatal in the perinatal period, unless treated with a JAK-STAT inhibitor. In our study, we identified three patients with genetic variations in *USP18,* who exhibited a spectrum of clinical features, including intracranial calcifications, lung opacities, hepatosplenomegaly, developmental delay, and high levels of circulating IFN-I. We sought to understand the pathophysiology of these *USP18* mutations and the mechanistic process by which they cause disease.

Hypothesis: Mutations in USP18 causes hypomorphism in their function and their role in inflammation is secondary to an inability to suppress interferon signaling.

Methods: HEK293T cells were transiently transfected with USP18 mutant variants, and expression of USP18 mRNA and protein were measured using qPCR and western blot, respectively. Cells were transiently transfected and stimulated with IFNa/B and expression of pSTAT1 and pSTAT2 were detected using western blot. Whole blood from patient sample and healthy control was stimulated with bacille Calmette-Guerin (BCG), IFNy, IL-12 and a combination and IL-12/IL-23p40 levels were assessed using ELISA.

Results: Expression of USP18 mRNA and protein was retained in all four of the patient's mutations. Additionally, in all four patient mutations, *USP18* maintained catalytic competency and was capable of de-ISGylation. *USP18* mutations also retained stabilization by *ISG15*. However, all four *USP18* variants demonstrated higher levels of phosphorylation of STAT1 and STAT2 as compared to WT *USP18*, indicating an inability to negatively regulate interferon signaling, an important function of USP18. Additionally, both patient-derived fibroblasts and fibroblasts transduced and stimulated with IFNα2b had persistence of interferon-stimulated genes as compared to WT fibroblasts after a 36-hour recovery period. In conclusion, partial USP18 deficiency leads to early-onset childhood inflammation through an inability to control IFN-I signaling.

Conclusions: Patients with distinct USP18 variants have normal expression of USP18 and retain catalytic competency and stabilization but are hypomorphic in their ability to prevent type I interferon signaling.

Readability Level of Articles on Websites About Dyslexia

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Introduction: Dyslexia, an impairment of fluent word recognition, decoding, or spelling, is a common learning disability that affects numerous people worldwide. The diagnostic process and treatment are complex, making accessibility to information about dyslexia important. We hypothesized that the information that is available online about dyslexia target those with reading disabilities and that they are easily readable. We analyzed the readability scores of dyslexia-related websites.

Methods: We performed a Google search for "What is dyslexia" and used a tool called WEB FX to calculate six readability scores for each website. These scores indicate the reading difficulty of the text, with higher scores indicating more complex language and lower scores indicating simpler language. We selected the first 50 English-language websites that appeared on Google search, extracted the texts, and analyzed their readability scores. The appropriate readability level for those with dyslexia is set at a 5th grade level or lower, corresponding to a score of 5.0 or lower.

Results: Analysis revealed that the mean readability score among the 50 websites was 11.59 on the SMOG Index, while the highest score was 15.39 on the Coleman Liau Index, which corresponds to a US grade level of at least 11th grade to comprehend the content.

Conclusion: Most dyslexia-related websites are challenging to understand, especially for those who have dyslexia. There is a need for improved accessibility to websites that provide information about dyslexia, especially if their target audience is those with reading disabilities.

Advancing Research Into Youth Diabetes Through a Novel, Comprehensive, Publicly Available Epidemiological Dataset

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Division(s): General Pediatrics

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Introduction: The prevalence of Type 2 diabetes (DM) and prediabetes (preDM) have been increasing rapidly among youth. One of the challenges limiting research and prevention efforts for youth preDM/DM has been the lack of comprehensive public data. We addressed this challenge by leveraging the rich information from the National Health and Nutrition Examination Survey (NHANES) to prepare such a dataset and disseminate it through a user-friendly web-portal.

Hypothesis: We could identify sociodemographic, health, and behavioral factors associated with youth preDM/DM risk in use cases of these data.

Methods: We processed NHANES data from 1999-2018. We built the *Prediabetes/diabetes in youth ONline Dashboard (POND)* to explore and share the data and its associated materials. We also provided use cases of the data by applying bivariate analysis and machine learning methods to identify correlates of preDM/DM risk.

Results: We extracted 95 variables potentially relevant to youth preDM/DM risk organized into 4 domains (sociodemographic, health status, diet, and other lifestyle behaviors). POND provides an interface to visualize the data (Fig. 1). The bivariate analyses identified 19 significant correlates of preDM/DM (Fig. 2). Complementarily, machine learning analyses identified several additional risk factors (Fig 3). Users can also access and download data from POND for further explorations.

Conclusions: Using NHANES data, we built the largest public epidemiological dataset for studying youth preDM/DM and identified potential risk factors using complementary analytical approaches. Further research through our data and user-friendly web-portal are expected to help address the important need of reducing the prevalence of youth preDM/DM.

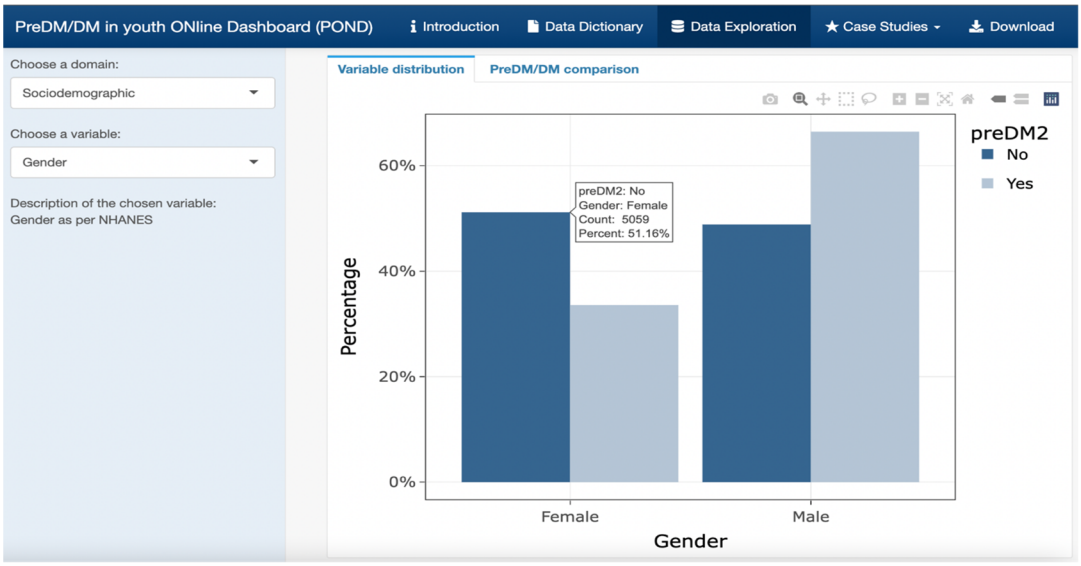

Figure 1. An example of "Data Exploration" in Prediabetes/diabetes in youth ONline Dashboard (POND).When users select a variable of interest in the left panel, POND will automatically display the distribution of the variable by the preDM/DM status (Yes/No) in a bar chart in the right panel.

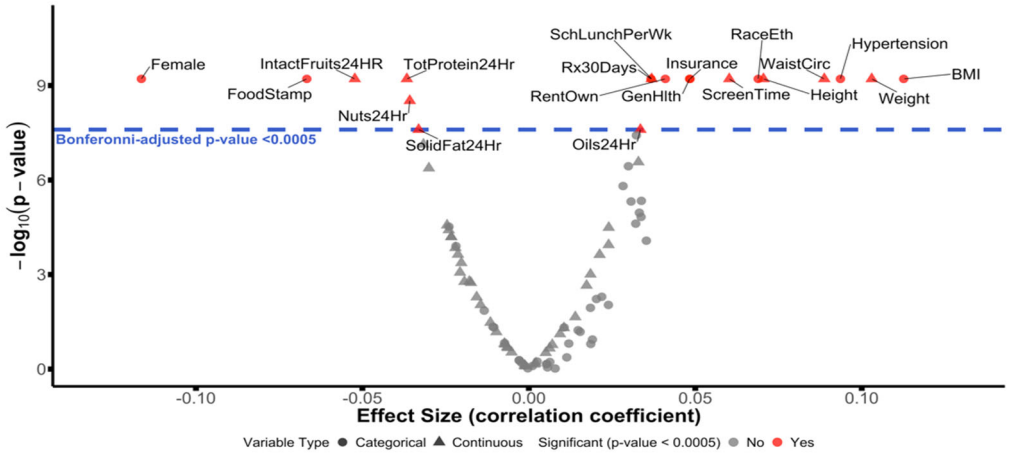

Figure 2. Results of the bivariate analysis showing 19 out of 95 variables were significantly (Bonferroni-adjusted p<0.0005) associated with youth preDM/DM. Chi-square and Wilcoxon rank-sum tests were used for testing the association of categorical and continuous variables respectively, and their corresponding correlation coefficients were used and shown on the X-axis as effect size measures. This plot and details of the significantly associated variables is shown as a user case and can be explored through POND.

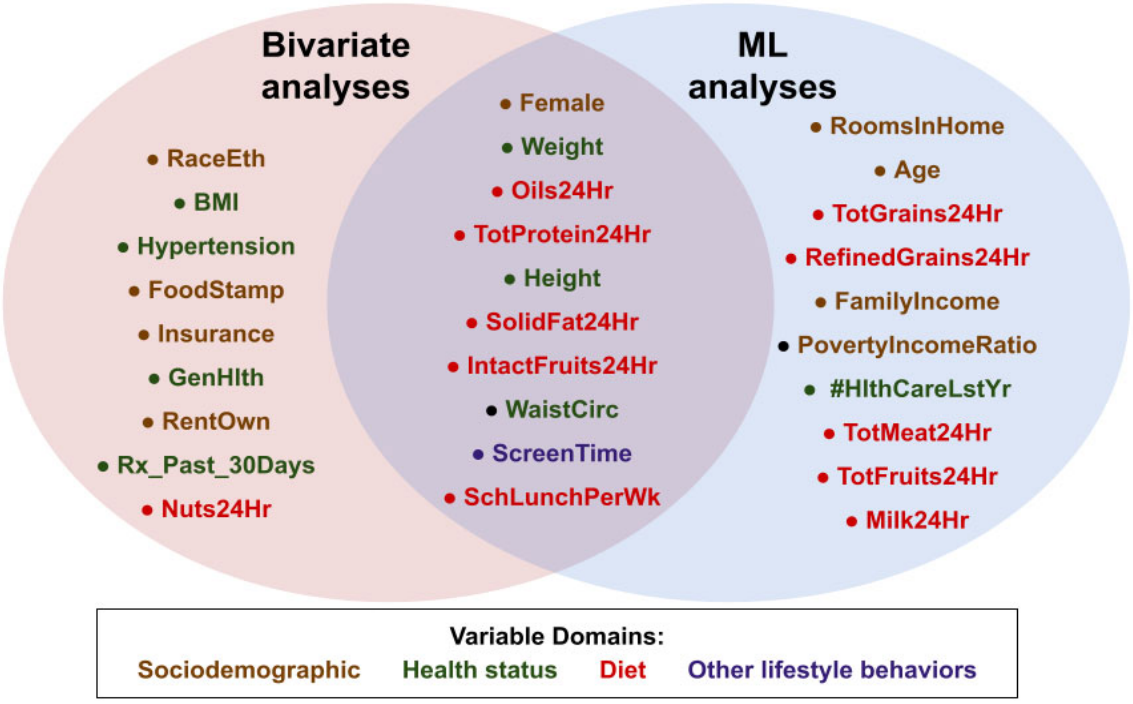

Figure 3. Venn diagram showing the overlap of important correlates of youth preDM/DM identified using bivariate (statistical) and machine learning (ML) analyses, as well as variables found exclusively by each approach. The variables are color-coded by their corresponding epidemiological domain (color code at the bottom of the figure). The results of both these analyses can be explored interactively through POND.

Comparison of Prevalence and Progression of Extrauterine Growth Restriction Using Intergrowth-21 and Fenton Growth Charts and Factors Associated With EUGR

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Division: Neonatology

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Introduction: There is currently no consensus for which growth assessment tool should be used to monitor postnatal growth of preterm infants with extrauterine growth restriction (EUGR).

Hypothesis: We hypothesized that the prevalence and progression of EUGR differs on the use of Fenton and Intergrowth-21 growth standards.

Methods: In this retrospective study, we reviewed weight, length and head circumferences at birth, 36 weeks corrected gestational age (CGA), 1st and 2nd outpatient follow-up visits for preterm infants who were seen in our NICU Follow-Up Clinic. We assessed the longitudinal progression of EUGR from inpatient to outpatient follow-up using Fenton and Intergrowth-21 growth standards. We evaluated factors associated with EUGR using a logistic regression model.

Results: Of the 647 infants seen in our follow up clinic since 2017, 369 were born between 24 and 32 weeks gestation. The prevalence of EUGR was 16% when using Intergrowth-21, and 61% when using Fenton growth standards. Although there was a significant decrease in z-score for weight from birth to 36 weeks CGA, there was no difference in the weight z-score from birth to the 2nd clinic visit ($p = 0.994$). EUGR was associated with lower GA at birth, a higher z-score for weight at birth, necrotizing enterocolitis (NEC), and need for CPAP at 36 weeks CGA.

Conclusions: Less infants were identified as EUGR when using Intergrowth-21 vs. Fenton growth charts. Growth failure during the NICU stay is common in preterm infants but catch up growth occurred as an outpatient with return to their birth weight z-score.

Implementation of an Eczema Action Plan in the Pediatric Primary Care Clinic

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Division: Primary Care

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Introduction: Eczema affects 12.5% of US children annually. Poorly controlled eczema can significantly affect a child's quality of life. Proper management of eczema is critical to ensure children with eczema are adequately treated.

Hypothesis: We hypothesized that the use of an Eczema Action Plan (EAP) would improve management of eczema based on severity.

Methods: We created an eczema management provider tool based on severity of eczema and an eczema action plan was created for the patient. We measured the appropriate management of eczema based on severity and the use of an EAP. The 1st PDSA cycle was a lecture, 2nd PDSA cycle was a dot phrase in the note and 3rd PDSA cycle was the use of a smart set for prescribing medications. Our process measure was percentage of patients with eczema and provider use of a dot phrase in the history and assessment area of note. Balancing measure was dermatology referrals.

Results: We appropriately treated eczema based on severity and provided an EAP to more than 50% of our patients.

Conclusion: Our QI project improved appropriate treatment of eczema based on severity and increased eczema educational materials provided to our patients. The use of a dot phrase in the note improved history gathering. Use of tools embedded in the electronic record were more useful than visual cues in the exam room. Future plans to sustain this project include expanding it to the entire Pediatric Clinic.

Validated Investigator Global Assessment scale for Atopic Dermatitis

vIGA-AD™

Instructions:

The IGA score is selected using the descriptors below that best describe the overall appearance of the lesions at a given time point. It is not necessary that all characteristics under Morphological Description be present.

	Score	Morphological Description
Code as Hx of Eczema Z87.2	**0 – Clear**	No inflammatory signs of atopic dermatitis (no erythema, no induration/papulation, no lichenification, no oozing/crusting). Post-inflammatory hyperpigmentation and/or hypopigmentation may be present.
Code as Hx of Eczema Z87.2	**1 – Almost clear**	Barely perceptible erythema, barely perceptible induration/papulation, and/or minimal lichenification. No oozing or crusting.
Code as Mild Eczema L30.9	**2 – Mild**	Slight but definite erythema (pink), slight but definite induration/papulation, and/or slight but definite lichenification. No oozing or crusting.
Code as Moderate Eczema L30.9	**3 – Moderate**	Clearly perceptible erythema (dull red), clearly perceptible induration/papulation, and/or clearly perceptible lichenification. Oozing and crusting may be present.
Code as Severe Eczema L30.9	**4 – Severe**	Marked erythema (deep or bright red), marked induration/papulation, and/or marked lichenification. Disease is widespread in extent. Oozing or crusting may be present.

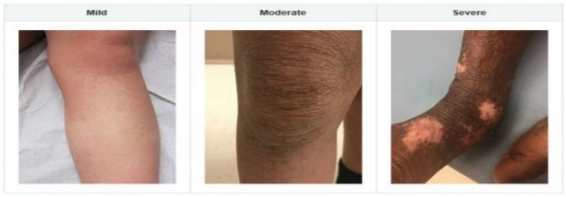
Notes:

1. In indeterminate cases, please use extent to differentiate between scores.

For example:

- *Patient with marked erythema (deep or bright red), marked papulation and/or marked lichenification that is limited in extent, will be considered "3 – Moderate".*

2. Excoriations should not be considered when assessing disease severity.



TREATMENT OF ECZEMA FLARE

Severity	Location	Infant	Child	Adolescent
Mild	Face/Genitals/Folds	Hydrocortisone 2.5% cream	Hydrocortisone 2.5% cream	Hydrocortisone 2.5% cream
Mild	Body	Hydrocortisone 2.5% cream	Hydrocortisone 2.5% cream	Hydrocortisone 2.5% cream
Moderate	Face/Genitals/Folds	Hydrocortisone 2.5% cream	Hydrocortisone 2.5% cream	Hydrocortisone 2.5% cream
Moderate	Body	Triamcinolone 0.025% oint or Fluticasone proprionate 0.05% cream or Fluocinolone oil 0.01% oil	Triamcinolone 0.025% oint or Fluticasone proprionate 0.05% cream or Fluocinolone 0.01% oil	Triamcinolone 0.1% oint
Severe	Face/Genitals/Folds	Triamcinolone 0.025% cream	Triamcinolone 0.025% cream	Triamcinolone 0.025% cream
Severe	Body	Mometasone 0.1% cream	Mometasone 0.1% oint	Mometasone 0.1% oint

-For night time itch consider hydroxyzine 2mg/kg/24 hr divided Q6 -8 hr prn, max single dose <6 yr 12.5 mg, 6 -12 yr : 25 mg, > 12 yr : 100 mg. Can give one dose prior to bedtime. (Contraindicated in prolonged QT). Or Benadryl 2-11 yr: 1 mg/kg/dose , max dose 50 mg/dose. >/= 12 yr : 50 mg. (Contraindicated w/ concurrent MAO inhibitor use, acute asthma attack, GI or urinary obstruction)

NONSTEROIDAL MAINTENANCE MEDICATIONS * may require prior authorization

Instructions: start 2 weeks after treatment for flare, if improving. Use twice a day for 1 to 3 months		
Medication	**Age Range**	**Considerations**
Crisaborole 2% (Eucrisa) Cream	> = 3 months	Side effect: burning sensation
Pimecrolimus (Elidel) Cream	> = 2 years	Side effect: stinging/burning
Tacrolimus (Protopic) Ointment	2-15 years: 0.03% ointment >= 16 years: 0.1% ointment	Side effect: stinging/burning Keep in the refrigerator to reduce the burning effect.

MAINTENANCE: IF FIDELIS MEDICAL INSURANCE OR ISSUES WITH GETTING PA :

Medication	Age Range	Considerations
Hydrocortisone 2.5% cream	All ages	Instructions: Use twice a day for 1 month then switch to once a day for 2 months. Side effects: thinning of skin, dyspigmentation, easy bruising, hypertrichosis

***PRIOR AUTHORIZATION (PA) STEPS (For HealthFirst or Metroplus)**

A PA lasts for 1 year; Note in EPIC note and EAP the expiration date.
- CVS Caremark 877-433-7643 or www.covermymeds.com
- To succeed in your request for PA, mention in your description: affected site (FACE/GROIN/SKIN FOLDS) with side effects (thinning of skin, dyspigmentation, easy bruising, hypertrichosis) or failure to improve with steroids.

Mitochondrial Haplogroups and Associations With Clinical Outcomes Among Probands With Congenital Heart Disease

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Introduction: Mitochondrial DNA (mtDNA) is maternally inherited and classified into region-specific haplogroups based on accumulated mtDNA variants during early migrations of populations. Current research has linked mtDNA haplogroups to specific diseases, including autism spectrum disorder, intellectual disability, and neurodevelopmental disabilities, but limited research has examined these associations in individuals with congenital heart disease (CHD).

Hypothesis: mtDNA haplogroup variation is associated with clinical outcomes (*i.e.,* neurodevelopment and neuropsychological outcomes, and cardiac function) among probands with CHD.

Methods: Mitochondrial haplogroups were determined for 846 probands with CHD who had genome sequencing in the Pediatric Cardiac Genomics Consortium study. We assessed associations between mtDNA haplogroups and (1) neurodevelopment outcomes and (2) cardiac function using logistic regression, and (3) neuropsychological outcomes using linear regression. Models were adjusted for proband sex, age at testing, and shared ancestry using principal component scores, estimated with principal component analysis from the nuclear genome.

Results: mtDNA haplogroup T (odds ratio = 4.50; 95% confidence interval: 1.19, 17.01) was associated with an increased risk of autism spectrum disorder compared to haplogroup H. Among European haplogroups, haplogroup U was associated with a higher depression ($\beta = 26.0$; p-value = 0.01) and anxiety ($\beta = 29.2$; p-value = 0.03) score. We observed null associations between mtDNA haplogroups and cardiac function.

Conclusions: mtDNA haplogroups may be associated with neurodevelopmental disabilities among probands with CHD. Mitochondrial mechanisms and pathways, especially related to oxidative stress, may contribute to increased risk for neurodevelopmental disabilities. Further research, with larger sample sizes, is needed to ascertain these findings.

Generation of Human Lymphatic Endothelial Cells (Lecs) From Ipscs in a Feeder-Free System

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Introduction: Lymphatic malformations are prevalent in RASopathies such as Noonan syndrome, however, are understudied due to a lack of cell or animal models with which to study them. Existing differentiation protocols for lymphatic endothelial cells (LECs) from human pluripotent stem cells have poor yield and require feeder cells. Here, we sought to develop a novel strategy to robustly differentiate human induced pluripotent stem cells (iPSCs) into LECs in feeder-free, serum-free conditions.

Hypothesis: Recapitulating lymphangiogenesis *in vitro* will allow for efficient differentiation of iPSCs into LECs.

Methods: We used a monolayer differentiation approach to push iPSCs to LEC fate in a 20 day protocol. The first eight days of the protocol utilized CHIR, bFGF, BMP4, VEGF-A and EGF in a sequential and dose-dependent manner to induce venous endothelial cell (VECs) fate, after which the VECs were trans-differentiated into LECs using HGF, ANG-1, VEGF-C and EGF. We characterized the differentiated cells using immunofluorescence (IF) imaging and qPCR for expression of lymphatic endothelial markers.

Results: Addition of HGF and ANG-1 to the LEC-condition media generated cells that robustly expressed LEC markers with almost 100% of the cells showing expression of LYVE-1, PROX1 and PDPN when analyzed with IF. HGF and ANG-1 functioned synergistically to promote lymphatic fate, with trans-differentiated cells expressing LEC markers around Day 14 and maintaining their LEC fate at least out to Day 20 of culture.

Conclusion: VECs cultured with HGF and ANG-1 transdifferentiate efficiently to LECs. Next, we will compare LEC characteristics using non-mutant and RASopathy iPSCs-derived LECs.

Socioeconomic and Clinical Factors Associated With Knowledge and Approach to Precautionary Allergen Labeling (PAL) in Food Allergy

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Introduction: There are limited data on knowledge and response to PAL labeling among those with different socioeconomic status (SES), education level, or time since diagnosis.

Hypothesis: Caregivers may take different approaches to heeding PAL for children with food allergy (FA).

Methods: 195 surveys were completed by legal guardians at their children's FA visits at a referral center in NYC. Surveys assessed demographics, FA history, purchasing habits in response to five sample PAL labels (always, sometimes, or never purchase) and three True-False questions about labeling laws. Public versus private health insurance was used as a surrogate for SES. Data were analyzed by Chi Square with $p<0.05$ as significant.

Results: Strictness of avoidance varied depending upon specific PAL wording. Those with public (n=29) versus private health insurance were stricter in avoidance for PAL verbiage including "Manufactured in a facility that also processes *allergen*" (66% vs. 25% "Never buy"), and "Packaged in a facility that also packages products containing *allergen"* (55% versus 24% "Never buy.") Education and time since diagnosis were not associated with PAL behaviors. Regarding labeling laws, scores were poor for knowing: (a) laws require labeling of major allergens (68% correct), (b) PAL is not mandated (21%), and (c) PAL is not based on protein amount (36%). Knowledge was better for question "a" among those with longer periods since diagnosis and for "c" for privately insured caregivers.

Conclusions: Knowledge about labeling laws is overall limited, particularly for those newly diagnosed or with lower SES. PAL verbiage has differential impacts on purchasing decisions across socioeconomic groups.

Associations of Adiposity and Visceral Fat Area With Race/Ethnicity and Variants of Energy Homeostasis Genes in Children With Overweight and Obesity

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Introduction: Body mass index (BMI) is currently used to define overweight/obesity, but racial/ethnic differences in body composition suggest a deficit in this weight-based approach. Furthermore, little is known about the role of variants in energy homeostasis genes in determining fat partitioning in children with obesity.

Hypothesis: Energy homeostasis genes contribute to racial/ethnic differences in percent body fat (PBF) and visceral fat area (VFA) among children even after adjusting for severity of BMI-defined obesity (percentage of 95th%ile, BMI-P95).

Methods: Children with overweight (BMI 85-<95th%ile; N=5) or obesity (BMI ≥95th%ile; N=167) referred to a hospital-based multidisciplinary weight management clinic underwent bioelectrical impedance analysis (InBody 770 Body Composition Analyzer) and buccal swab or blood draw for genomic DNA. Sequencing of 79 genes associated with leptin signaling, ciliopathies, and adipocyte function was commercially performed (Prevention Genetics). Chi-square assessed variant prevalence within African-American (AA), Hispanic White (HW), and non-Hispanic White (NHW). ANCOVAs (covariates: age, sex, BMI-P95) compared PBF and VFA by race/ethnicity and genetics.

Results: BMI-P95 differed by race/ethnicity (AA:166□34%, HW:145□27%, NHW:123□21%, p's<0.001); unadjusted PBF and VFA also differed with AA>HW>NHW. After adjusting for BMI-P95, AA had highest VFA (p's<0.002) despite having lowest PBF (p's<0.01). Genetic variants were more frequent in AA and HW compared to NWH (p=0.01) but were not correlated with body composition.

Conclusions: Our findings suggest that referral of AA and HW children for obesity treatment occurred at higher thresholds than NHW. Since VFA, a known predictor of metabolic health complications, was higher in AA despite their lower PBF, earlier referral for obesity treatment should be encouraged.

Understanding the Mechanistic Changes That Cause Hypertrophic Cardiomyopathy in Some Noonan Syndrome Mutations

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Introduction: RASopathies are a collection of genetic developmental disorders resulting from mutations to the RAS/MAPK pathway. Heterozygous variants of *RAF1* (S257L) and *PTPN11* (N308D) cause Noonan syndrome, the commonest RASopathy. Although alleles engender RAS gain of function, *RAF1* S257L is associated with hypertrophic cardiomyopathy (HCM) while *PTPN11* N308D is not.

Hypothesis: Cardiomyocytes (CMs) derived from *RAF1 S257L* iPSCs will exhibit cellular hypertrophy while CMs derived *PTPN11* N308D iPSCs will not.

Methods: Isogenic induced pluripotent stem cells (iPSCs) with CRISPR-based introduction of RASopathy alleles and the parent cell line were differentiated into cardiac embryoid bodies (EBs) using small molecules. EBs were dissociated and stained with troponin T to identify cardiomyocytes (CMs). Via microscopy, single-cell two-dimensional areas were imaged and measured as an assessment of cellular hypertrophy over three time points. Statistical comparisons were performed using Student's t test with a p-value threshold of 0.05.

Results: *RAF1* S257L CMs exhibited no significant hypertrophy at the first two points (Day 20 and 25). On Day 30, *RAF1* S257L CMs exhibited a significant, ~30% cell size increase, ($p=0.034$). *PTPN11* N308D CMs showed no significant change in cell size at any points.

Conclusion: CMs derived from iPSCs with Noonan syndrome-related alleles faithfully recapitulated the expected cellular hypertrophy phenotypes. This provides the basis for our ongoing studies with transcriptomic analyses to understand why only certain RAS pathway gain-of-function alleles cause HCM.

Characterizing the Igg1 Memory B Cells That Are Precursors of Pathogenic Ige

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Introduction: IgE-mediated food allergy is a growing public health concern. Allergen-specific IgE is largely responsible for the clinical manifestations of allergic reactions, such as life-threatening anaphylaxis. The affinity of the IgE plays a major role in determining the outcome of a patient after exposure to food allergen. IgE that is of high affinity can trigger anaphylaxis, while IgE of low affinity poses little risk and may even be preventative. It is well understood that IgG memory B cells can differentiate into IgE producing plasma cells and in the context of type 2 regulated immunity, our lab has identified 3 transcriptionally, phenotypically, and functionally distinct subsets of IgG1+ MBC based on CD80 and CD73 expression. Cells within the CD80+ CD73+ double positive (DP) population are of great importance in the generation of pathogenic high affinity IgE plasma cells.

Hypothesis: the unique requirements for activation and sequential switching of an IgG+ memory B cell to IgE+ plasma cell involves 2 main mechanisms of B cell activation: i) cytokine stimulation ii) BCR signaling.

Methods: To test this, I have used a B cell culture system that mimics germinal center (GC) B-cell reaction. In this system, 40LB fibroblasts, that have been transfected to express CD40L and the pro-survival signal BAFF, are used to activate B cells. Sorted IgG1+ MBC from TBmc mice can be cultured using the Nojima culture with or without cytokine stimulation and/or B cell receptor (BCR) stimulation and analyzed by flow cytometry to quantify differentiation of MBC into plasma cells (PC; B220lo CD138+), MBC (B220+ CD138-), or GC-like cells (B220+CD138-GL7+).

Results: These experiments show that type 2 cytokines are important for some DP IgG1 MBC to switch to IgE plasma cells, but some DP IgG1 MBC can form IgE plasma cells without added type 2 cytokines. Additionally, we have found that BCR stimulation can augment class switching to IgE in DP IgG1 MBC stimulated with CD40L and BAFF.

Conclusions: BCR signaling, and type 2 cytokines can augment switching of DP IgG1 MBC to IgE PC in a culture system with CD40L and BAFF expressing fibroblasts. Understanding the mechanism by which these cells are reactivated to differentiate into IgE+ PC to develop strategies that target steps in this process.

Improving Plagiocephaly Anticipatory Guidance in the Pediatric Primary Care Clinic

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Introduction: Positional plagiocephaly is defined by the American Academy of Pediatrics (AAP) as the flattening of a baby's growing skull due to secondary mechanical factors. After the Back to Sleep campaign was started by the AAP in1992, a 2013 study showed a rise of positional plagiocephaly to 46.6% incidence among infants.

Hypothesis: We Hypothesized that appropriate education about the prevention of plagiocephaly early can help prevent the development and progression of positional plagiocephaly and avoid unnecessary referrals.

Methods: During the study period, charts were reviewed from September to December 2022. The outcome measure was the percent of infants presenting for the initial newborn visit through the 6 months Health Maintenance visit who were provided Plagiocephaly Anticipatory Guidance. The Process Measure was the use of a dot phrase for anticipatory guidance and the Balancing Measure was referral to specialists.

Results: After the completion of 3 PDSA cycles, a total of 69% (209) patients received complete anticipatory guidance on plagiocephaly. We did not refer any patients to specialists for evaluation. We also noted during the study period, 6 (2%) patients were diagnosed with plagiocephaly, showing a decreased incidence of positional plagiocephaly compared to baseline.

Conclusion: We were able to improve patient education to infants presenting for their initial newborn visit through the 6 months Health Maintenance visit. We also noted a decrease in the diagnosis of plagiocephaly and number of referrals to specialists. Providing detailed plagiocephaly anticipatory guidance should be emphasized early.

NICUnet: Genome Sequencing of Neonatal Fatalities

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Introduction: Each year, ~4000 infants die in neonatal intensive care units (NICUs) in the USA.

Hypothesis: Based on evolutionary theory and data from stillbirths and live infants with rare diseases, a large proportion of NICU deaths are likely caused by highly penetrant rare alleles.

Methods: We established a network of referral NICUs (NICUnet) under a central IRB. Enrollment criteria were gestational age at birth ≥28w0d, death and no genetic diagnosis. Neonatologists consented parents after the standard autopsy consent. We extracted trio DNA and performed infant genome sequencing. We developed a phenotype capture web app, a rare variant database and a web app for multidisciplinary genetics review, to identify pathogenic variants and discover novel etiologies.

Results: We consented 12 of 14 parents approached. Gestational ages ranged 28w0d–39w0d (median 33w5d) and deaths occurred between 0d and 27d old (median 2d). We found a genetic etiology in 1 of 8 sequenced cases thus far. The patient had clinical findings suggestive of autosomal recessive polycystic kidney disease with one paternal pathogenic allele in *PKHD1*, but no maternal pathogenic coding allele. We identified a maternal deep intronic variant in *PKHD1* with a SpliceAI score of 0.98, an extreme outlier with frequency ~1/100,000 in the general population. We are confirming this results in a non-canonical splice acceptor gain and premature stop in maternally derived renal epithelial cells.

Conclusions: We developed a collaborative network of NICUs, currently comprising 10% of level IV NICUs, to study genetic causes of neonatal death and other rare events.

Characteristics and Outcomes of a Large Cohort of Patients With FPIES to Peanut

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Introduction: Early introduction is a powerful tool to reduce IgE-mediated peanut allergy in high-risk infants. However, since early introduction guideline implementation, peanut food protein-induced enterocolitis syndrome (PN-FPIES) appears to be increasing.

Hypothesis: An increase in PN-FPIES will be observed.

Methods: Retrospective chart review was conducted to identify PN-FPIES patients seen at our pediatric allergy practice from January 2015-June 2022. Variables recorded included demographics, reactions, atopic comorbidities, testing, and oral food challenges (OFC).

Results: 28 patients with PN-FPIES were identified (61% male). Comorbidities included atopic dermatitis (54%), IgE-mediated food allergy (36%), and FPIES to other foods (21%). Median age of first peanut ingestion was 6 months, first PN-FPIES reaction was 6.5 months, and PN-FPIES diagnosis was 7 months. An earlier ingestion of peanut was tolerated in 61%, with 6/17 tolerating >3 prior ingestions. Reactions involved vomiting (100%), lethargy (75%), diarrhea (25%), and color change (14%). Skin testing was performed in 27; 81% were negative (median 0 mm). Serum IgE testing was performed for 17, with 47% negative (median 0.11 kU/L). 13 OFCs were performed. 5 were diagnostic, all of which elicited FPIES reactions (median age 11 months; median interval since latest reaction 0 months). 8 OFCs assessed for resolution; 5 (62%) passed (median age 24 months; median interval 14 months) and 3 (38%) failed (median age 48 months; median interval 42 months).

Conclusion: This is the largest case series of PN-FPIES, highlighting peanut as an emerging major FPIES trigger. Onset occurs in infancy, even after prior peanut tolerance. Like other triggers, reactivity may persist for years.

Communication Quality in Pediatric Rheumatology

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Introduction: Communication is an essential part of medical care, especially in Pediatric Rheumatology where children have varying complex chronic diseases. However, there is paucity of data about effective patient-provider communication.

Hypothesis: Children who endorse good communication quality will have lower disease activity and better health-related quality of life.

Methods: We consecutively recruited 41 patients with follow-up appointments between 10/27/2022 and 12/22/2022. Parent proxies completed surveys for children younger than 9 years. Participants completed a demographic survey, CAT, Patient-Reported Outcomes Measurement Information System Pediatric Global Health Measure 7 (PROMIS), and Connor Davidson Resilience Scale 2 (CD-RISC 2). Raw PROMIS scores were converted to T-scores using standard software. Spearman's correlations were performed with statistical significance set to $p<0.05$.

Results: The majority of our cohort was female (68%) and had Medicaid insurance (66%). The mean CAT score was 4.78 and median was 5, indicating overall high satisfaction with communication quality. Average PROMIS was 46.76 ± 8.89 and CD-RISC 2 was 5.24 ± 2.0, both consistent with reported means for the general population. CAT was only correlated with gender ($r = -0.34$, $p = 0.03$), with males endorsing lower scores.

Conclusion: The mean CAT score of 4.78 indicates overall high communication quality in our practice; however, the percentage of excellent scores (5) was 17.8% lower than the initial report, indicating that areas for improvement exist. Male patients endorsed worse communication quality; additional research is needed to determine the drivers of these lower scores. This study is limited by small sample size; next steps include validation of findings in a larger sample and multivariable analysis for further characterization.

Table 1. Demographic Data

Characteristic	N = 41
Age	
Mean years ± SD	12.98 ± 5.56
Median years (IQR)	15 (9,17)
<9 years	10 (24.4%)
≥ 9 years	31 (75.6%)
Gender	
Female	28 (68.3%)
Male	13 (31.7%)
Ethnicity	
Hispanic	21 (51.2%)
Not Hispanic	19 (46.3%)
Unknown / Not Reported	1 (2.4%)
Race	
Asian	4 (9.8%)
Black or African American	11 (26.8%)
White	12 (29.3%)
More Than One Race	8 (19.5%)
Unknown / Not Reported	3 (7.3%)
Other	3 (7.3%)
Insurance	
Private	14 (34.1%)
Medicaid	27 (65.9%)
Income	
Less than $20,000	12 (29.3%)
$20,000 - $60,000	13 (31.7%)
$60,000 - $100,000	4 (9.8%)
Greater than $100,000	5 (12.2%)
Not reported	7 (17.1%)

Clinic Day	
Tuesday	21 (51.2%)
Thursday	17 (41.5%)
Friday	3 (7.3%)
Diagnosis	
No Diagnosis	6 (14.6%)
Juvenile idiopathic arthritis	6 (14.6%)
Uveitis	4 (9.8%)
Systemic rheumatic disease	20 (48.8%)
Non-rheumatic other diagnoses	5 (12.2%)

Table 2. Spearman Correlation Coefficients

Characteristic	Sample Size	Communication Assessment Tool R Value	PROMIS PGH 7 R Value
Age	41	-0.11	**-0.65**
Gender	41	**-0.34**	-0.15
Diagnosis	41	0.13	-0.06
Clinic Day	41	-0.12	-0.03
Income	41	0.00	0.25
Insurance	41	-0.08	-0.11
Provider	41	-0.11	0.13
Parent vs. Patient	41	0.18	**0.32**
PROMIS PGH7	41	0.22	n/a
CDRISC 2	41	0.03	**0.31**

Depression Screening in Pediatric Endocrinology & Diabetes

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Division: Pediatric Endocrinology & Diabetes

Institution Affiliation: Icahn School of Medicine at Mount Sinai

Introduction: Depression in children with diabetes can negatively impact glycemic control. There is little research on improving depression screening in pediatric endocrinology practices. Our objective is to explore modalities of screening for depression in single practice and to quantify rates of depression in children.

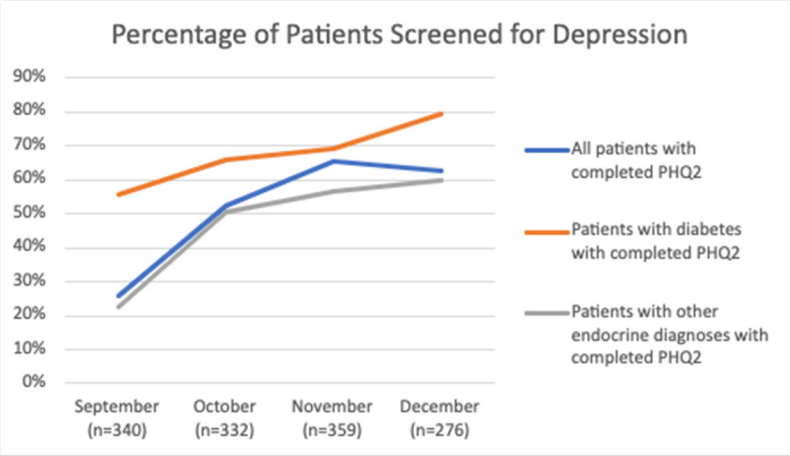
Hypothesis: Diabetic patients will have greater depression levels than those with other endocrine diagnoses.

Methods: A retrospective review of children over 12 years seen in Pediatric Endocrinology between 9/1/22 and 12/31/22 was conducted. Patient Health Questionnaire-2 (PHQ-2) were collected by medical assistants, initially via verbal questionnaire and later via paper questionnaire starting in October 2022. Positive PHQ2 was defined as score ≥ 3 and indicates need for further work up. Patients were stratified by the month of visit and primary visit diagnosis. Diabetes included patients with Type 1 and Type 2.

Results: Percent of patients with PHQ-2 completed increased from 25.9% to 62.68% for all patients. With the implementation of self-reported questionnaire, PHQ-2 screening increased 2-fold from 25.9% to 52.9%. There was an increase in positive screens of all patients each month from 1.14% to 6.94%. Diabetes patients consistently had higher rates of positive PHQ-2 scores across all months (5.0% to 16.13%) compared to other patients (0% to 4.9%).

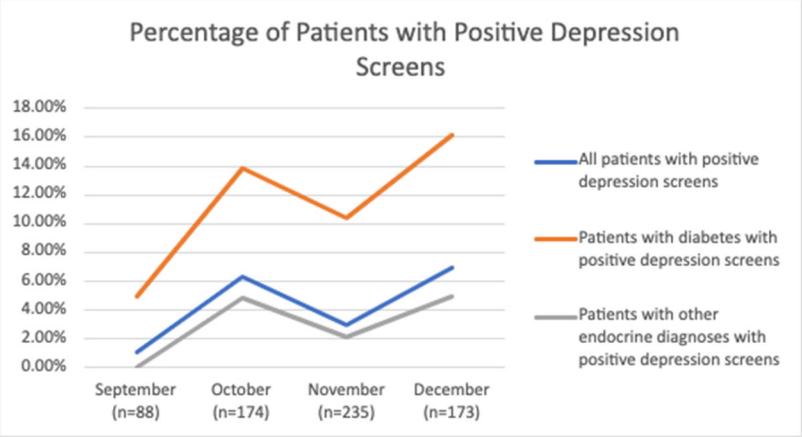
Conclusion: Consistent with published reports, children with diabetes had higher rates of positive PHQ-2 screens than other patients. A substantial increase in depression screening and positive screens was seen with the use of self-reported forms. Additional research is needed to continue to improve screening methodology.

Figure 1. Percentage of Patients Screened for Depression by Month



The percentage of patients screened for depression out of the total number of patients (n) with a clinic visit in Pediatric Endocrinology & Diabetes.

Figure 2. Percentage of Patients with Positive Depression Screens



The percentage of patients with positive depression screens (PHQ2 score ≥ 3) out of the number of patients screened for depression each month. N represents the number of all patients screened for depression.

Empowering Social Connection and Belonging in Youth Through Mascot Co-Creation

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Introduction: Youth living in group home settings may have increased trauma exposure and be at greater risk of low education, unemployment, incarceration, and emotional and behavioral problems. To facilitate heightened resilience and healthy emotional development, orphanages, foster care programs, and group homes need to be equipped with the guidance and framework for best practices.

Hypothesis: We hypothesize that after participating in a mascot co-creation workshop, youth in a group home setting will report an increase in sense of social connection and belonging.

Methods: A two-hour mascot co-creation workshop was developed as an intervention to increase sense of social connection and belonging. Community volunteers and staff were trained in the workshop delivery; group activities consisted of verbal warm-ups, mascot visualization, mascot stories, and long-term mascot implementation. Eligible participants included residents in state supported housing in Peru. Changes in sense of social connection and belonging were assessed through two separate validated measures of social connectedness and belonging administered prior to and immediately following the workshop.

Results: In this secondary analysis of existing data, 34 youth across two group home sites in Peru participated in a two-hour mascot co-creation activity. There was a significant increase in social connection from pre- to post-workshop in social connection across both sites ($p = .008$) but not in measures of belonging.

Conclusions: Mascot co-creation among youth in two group home settings supported a significant increase in sense of social connection. Further work will help develop programs that are culturally sensitive to build supportive attachments and resilience among children in this vulnerable population.

Role of Neuropilin-1 as a Novel Driver of Biliary Fibrosis

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Introduction: The unmet need for effective anti-fibrotic therapies for liver fibrosis highlights the demand for models to elucidate disease mechanisms. Mannose phosphate isomerase (MPI) is a key enzyme in mannose metabolism, and mutations in MPI result in a congenital disorder of glycosylation (MPI-CDG), characterized by early liver fibrosis. We have recently shown that Neuropilin 1 (NRP1), a co-receptor of VEGF, is increased in Mpi-depleted adult zebrafish liver in single-cell RNA sequencing and immunofluorescence. Here, we examine Nrp1 at earlier stages, using two larval in vivo zebrafish models of biliary fibrosis – *mpi* MT and chemical injury using methapyrilene (MP). Next, we test whether Nrp1 inhibition can mitigate fibrosis in human hepatic stellate cells (HSCs).

Hypothesis: Nrp1 is a driver of biliary fibrosis, and its inhibition can mitigate fibrogenesis.

Methods: Zebrafish larvae were treated with MP at 37.5uM from 5 to 7 days post-fertilization. quantitative PCR from the dissected livers was performed. Human HSCs were treated with bevacizumab (a VEGF inhibitor) and WB was performed to assess NRP1 and COL1A.

Results: qPCR analysis showed an induction of Nrp1 and collagen expression in both Mpi-depleted zebrafish liver and WT larvae treated with MP. Bevacizumab decreased NRP1 and COL1A expression in human HSCs.

Conclusions: Nrp1 is increased in larval and adult zebrafish models of biliary fibrosis. Inhibition of NRP1 in human HSCs decreases COL1A. These findings combined with the known role of NRP1 in promoting liver fibrosis positions NRP1 as an attractive target for future study and development of antifibrotic therapies.

Sesame Oral Desensitization Outcomes in a Pediatric Cohort

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Introduction: Limited data exists on sesame oral desensitization outcomes in the United States.

Hypothesis: We hypothesize that sesame-allergic patients can achieve sustained unresponsiveness to sesame through sesame oral immunotherapy.

Methods: A retrospective chart review of pediatric patients undergoing oral desensitization to sesame was conducted at a pediatric food allergy referral center.

Results: Eighty-six patients with allergist-diagnosed sesame allergy underwent oral desensitization to sesame. Oral desensitization involved initial low dose oral food challenge (OFC) to crushed sesame seeds or tahini with incremental dose escalation until patients reached a maintenance dose, usually 1 teaspoon of tahini (1000mg sesame protein). Fifty-one (59.3%) achieved maintenance. Twenty-six patients (30.2%) were still in the build-up phase. Nine patients (10.5%) discontinued desensitization due to reactions (n=3), uncontrolled asthma (n=1), difficulty with daily dosing (n=1), or unknown (n=4). Twenty-five patients (29.1%) experienced allergic reactions with daily dosing with only 1 reaction requiring epinephrine. Ten patients who reached maintenance dosing also completed a full dose OFC to 1 tablespoon of tahini (3000mg sesame protein); all had negative OFCs (100%). All ten patients then underwent a sustained unresponsiveness OFC to 1 tablespoon of tahini after discontinuing daily sesame dosing for 4-6 weeks. All 10 (100%) sustained unresponsiveness OFCs were negative.

Conclusions: Oral desensitization to sesame with crushed sesame seeds and tahini can be a safe and effective way to desensitize sesame-allergic pediatric patients.

Baseline Performance of Respiratory Quality Measures at Mount Sinai Beth Israel's Pediatric Short Stay: Phase 1 of the Multi-Center SIP Study

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Introduction: Asthma, pneumonia, and bronchiolitis are the top causes of childhood hospitalization in the US, leading to over 350,000 hospitalizations and ~$2 billion in costs annually[i]. MSBI's Pediatric SSU is a participant of the NIH-funded multi-center SIP Study[ii], to assess effectiveness and implementation of a QI intervention in community hospitals. We present our baseline quality performance for pediatric inpatient respiratory care.

Methods: we conducted a retrospective review of respiratory patients admitted to the MSBI SSU over the prior 2 respiratory viral seasons. Hospitalizations were reviewed for certain designated best practices. For asthma: adherence to PRAM scoring/asthma pathway use, inpatient adoption of albuterol MDI, and prescription of inhaled corticosteroids (ICS) at discharge for patients >5 years old. Patients with pneumonia were screened for narrow-spectrum antibiotic use and avoidance of macrolides without proof of *Mycoplasma* infection. Patients with bronchiolitis were screened for use of routine chest x-rays and albuterol.

Results: 33 patients with asthma, 8 with pneumonia, and 7 with bronchiolitis were included. 31 patients with asthma received ≥1 PRAM score (93.9%); 21.2% started an albuterol MDI in-house; 25% of patients received an ICS. 50% of pneumonia patients received narrow-spectrum antibiotics; none were given azithromycin unnecessarily. 42.8% of patients with bronchiolitis received albuterol, and 14.2% underwent chest x-ray.

Conclusions: the MSBI SSU is already demonstrating standard of care in two domains. However, there are several opportunities for improvement in quality of care for patients hospitalized with asthma, pneumonia, and bronchiolitis. The SIP study will address these gaps through a multi-pronged QI approach through 2026.

ASTHMA	***33 pts total***
Male sex	69.6% (23)
Age (mean)	7.2 years
PRAM score use	93.9% (31)
Average LOS (hrs)	23.4 hours
Early MDI use (switching at Q3 or Q4)	21.2%
Rx inhaled corticosteroid at discharge for age 5+	25% *(of the 20 pts >5 years)*
PNEUMONIA	***8 pts total***
Male sex	50% (4)
Age (mean)	8.8 years
Average LOS (hrs)	16.9 hours
Narrow spectrum antibiotics (ampicillin/amoxicillin >> ceftriaxone)	- 50% received narrow-spectrum - 25% received broad-spectrum but had a documented reason for it (PCN allergy, failed outpatient narrow spectrum etc.) - 25% received broad-spectrum unnecessarily
Avoidance of Azithromycin	100%
BRONCHIOLITIS	***7 pts total***
Male sex	28.6% (2)
Age (mean)	8.0 months
Received albuterol while inpatient	42.8%
CXR inpatient	14.2%
Inclusion criteria for eligible patients were primary diagnosis of asthma and aged 2-18 years; primary diagnosis of pneumonia and aged 2 months-18 years; primary diagnosis of bronchiolitis and aged <2 years. Exclusion criteria included: secondary diagnosis of SARS-CoV-2; patients transferred to PICU; those with certain pre-existing chronic conditions. *Respiratory seasons included: Nov 1st 2020–March 1st 2021; Nov 1st 2021–March 1st 2022*	

[1] Leyenaar JK, Ralston SL, Shieh MS, Pekow PS, Mangione-Smith R, Lindenauer PK. Epidemiology of pediatric hospitalizations at general hospitals and freestanding children's hospitals in the United States. *J Hosp Med*. 2016;11(11):743-749.

[1] Simultaneously Implementing Pathways for Improving Asthma, Pneumonia, and Bronchiolitis Care for Hospitalized Children. NIH R61HL157804. Principal Investigator: Dr. Sunitha V Kaiser MD, MD MSc, Associate Professor Pediatrics, UCSF Benioff Children's Hospital

Clinical Characteristics, Outcomes, and Interobserver Agreement of Point-of-Care Ultrasound Detected Mesenteric Adenitisin Non-Surgical Pediatric Abdominal Pain: A Retrospective Cohort Study

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Introduction: Point-of-Care Ultrasound (PoCUS) use in the Emergency Department (ED) may facilitate the bedside diagnosis of non-surgical sources of abdominal pain after surgical causes are excluded. Identifying mesenteric adenitis is a feasible PoCUS application due to its ease-of-use and speed. However, there is scant data regarding the diagnosis of mesenteric adenitis by PoCUS. The objective of this study was to describe the clinical characteristics, outcomes and interobserver agreement of mesenteric adenitis identified on PoCUS in pediatric patients with non-surgical abdominal pain.

Hypothesis: We hypothesize that mesenteric adenitis can be reliably identified by PoCUS by novice physician-sonologist.

Methods: This was a retrospective review at a single, tertiary-care, urban pediatric ED. All cases of mesenteric adenitis diagnosed on PoCUS from January 2018 to August 2022 were reviewed. Demographics and clinical data, including presentation and outcomes were recorded. All PoCUS videos with clinical information were reviewed by a senior sonologist-physician for determination of mesenteric adenitis in children 21 and younger with non-surgical abdominal pain. Interobserver agreement by Cohen's Kappa was calculated between experienced and novice physician sonologists blinded to diagnosis who reviewed 77 six second video clips for presence or absence of mesenteric adenitis.

Results: Thirty-three subjects were identified by PoCUS to have mesenteric adenitis in the setting of non-surgical abdominal pain presenting to our ED. Most common indications for POCUS were evaluation of suspected appendicitis, suspected intussusception or undifferentiated abdominal pain. Forty-eight percent of patients were male. The median age was 7 years old (IQR 4 to 14 years) for mesenteric adenitis. On 4-week clinical follow-up, no patients returned to our ED with a surgical abdomen. Cohen's kappa was 0.92 (95% CI 0.83, 1.0) between experienced physician-sonologists and 0.76 (95% CI 0.62, 0.91) between novice and experienced physician-sonologists.

Conclusions: Mesenteric adenitis, typically a diagnosis of exclusion, can be identified reliably by point-of-care ultrasound in pediatric patients with non-surgical abdominal pain, both by novice and experienced physician-sonologists. Use of PoCUS may help ED clinicians identify a common cause of non-surgical abdominal pain in children.

Patient-Specific *Adamtsl2* Knock-in Mouse as a Model for Geleophysic Dysplasia

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Introduction: Geleophysic dysplasia (GD) is a connective tissue disorder characterized by short stature, brachydactyly, joint stiffness, pseudomuscularity, and life-threatening heart valve anomalies and airway stenosis resulting in ~ 40% mortality during early childhood. GD is caused by mutations in the secreted extracellular matrix proteins ADAMTSL2, fibrillin-1, or LTBP3. ADAMTSL2 regulates TGF and Wnt signaling depending on the cellular context. Global *Adamtsl2* deletion resulted in neonatal lethality due to airway obstruction and a ventricular septal defect. Deletion of *Adamtsl2* in the limb resulted in bone shortening. While these models recapitulate aspects of GD, a patient-specific *Adamtsl2* knock-in mutation may more faithfully recapitulate GD pathogenesis and allow testing of candidate therapeutic strategies.

Hypothesis: Knocking-in the ADAMTSL2 D167N mutation, which causes severe GD, will recapitulate GD pathogenesis in mice.

Methods: Using genome editing, we generated *Adamtsl2* D167N knock-in mice (ADAMTSL2-KI) and characterized postnatal survival, bone growth, and tissue pathology. We also quantified consequences of the ADAMTSL2-D167N mutation on protein secretion.

Results: Homozygous ADAMTSL2-KI mice showed some embryonic lethality. However, most of the surviving KI mice died between 10-40 days after birth. Homozygous ADAMTSL2-KI mice were smaller with a 25-30% reduction in bone lengths and reduced weight. In addition, the vertebrae shape of ADAMTSL2-KIs was altered resembling ovoid vertebrae characteristic for GD. On a molecular level, ADAMTSL2-D167N secretion was reduced by 80%.

Conclusions: We generated a disease model recapitulating several aspects of severe GD. This model will now be used to test candidate therapeutic approaches including inhibition of TGF signaling or ER stress reduction.

Blunting of Sympathetic Activation of Pancreas as a Cause for Hypoglycemic Unawareness in Hypoglycemia Associated Autonomic Failure

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Introduction: Hypoglycemia activates the autonomic nervous system to suppress pancreatic insulin and release glucagon to normalize blood glucose. These effects occur partly via sympathetic innervation of pancreatic islets. Recurrent hypoglycemia leads to a blunted autonomic response known as Hypoglycemia Associated Autonomic Failure (HAAF), which further exacerbates hypoglycemia. The mechanisms underlying HAAF are not well-understood, but changes in pancreatic innervation may contribute.

Hypothesis: Decreased activity and remodeling of sympathetic innervation to the pancreas contribute to autonomic dysfunction with repeated hypoglycemia.

Methods: To examine pancreatic sympathetic innervation with repeated hypoglycemia, 26 C57Bl6 mice were treated with 0, 1, or 5 (0, 1x, or 5x) doses of insulin to induce hypoglycemia. Pancreata, sympathetic celiac ganglia, and brains were harvested. Pancreatic tissue was immunostained for insulin, glucagon, and tyrosine hydroxylase (TH), a marker for sympathetic innervation. Samples were then cleared using iDISCO+, imaged, and analyzed using Imaris to examine the 3D distribution of innervation and islets.

Results: 3D image analyses suggest acute hypoglycemia (1x) upregulates islet glucagon staining intensity. By comparison, recurrent hypoglycemia (5x) decreases pancreatic TH+ innervation and may blunt hypoglycemia-induced increases in islet glucagon staining intensity.

Conclusions: Our data suggest repeated episodes of hypoglycemia may remodel the structure and function of peripheral pancreatic sympathetic innervation as compared to one episode of hypoglycemia. Further evaluation of sympathetic innervation of harvested brains and celiac ganglia may help elucidate changes in activation along the sympathetic chain.

Fertility Preservation Rates Among Transgender Girls in a Multidisciplinary Transgender Program

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Introduction: Fertility preservation (FP) should be an important step in health care prior to initiating gender affirming hormonal therapy (GAHT) or puberty blockade in transgender and gender diverse (TGD) people. However, FP is often not integrated into comprehensive gender affirming care. Prior studies show low rates of FP in transgender youth.

Hypothesis: We hypothesized that integration of a pediatric urology team into our Center for Transgender Medicine and Surgery program would support high levels of fertility preservation amongst TGD youth with testes

Methods: To assess the success of fertility preservation, we performed a retrospective review of a database of all TGD patients who were 18 years or younger with testes, and sought GAHT. Patients were evaluated and followed in our Center for Transgender Medicine and Surgery from 5/2022 through 10/2022. Demographics, age, hormonal treatment, Tanner stages, and FP use were recorded from the medical record. Successful sperm banking was defined as freezing >1 vial of sperm.

Results: Twenty-seven patients ranging from ages 10-17 years old were referred to pediatric urology for FP. Of patients referred to the clinic, 20 (74.1%) were interested in pursuing/are in the process of sperm banking. Of the patients who didn't pursue FP, 1 (3.7%) of the patients were prepubertal (Tanner I), 4 (14.8 %) patients declined to attempt FP because they wanted to avoid masturbation, and 2 (7.4%) patients declined referral altogether. Twelve patients began the process of FP with sperm banking - ten of whom successfully froze sperm within WHO reference ranges of semen parameters and 2 children were azoospermic. Upon review, these 2 patients with azoospermia were found to already have started hormonal suppression.

Conclusion: Our data suggest that a large percentage of patients may be interested in fertility preservation. The integration of a pediatric urology team can help to support access to this service. Importantly, that the children who already started pubertal suppression were azoospermic highlights the importance of the integration of pediatric urology and FP into the health care process prior to pubertal suppression therapy. In our program, counseling on GAHT and puberty blockers' impact on fertility is introduced early and pediatric urology consultation is offered concurrently or even prior to endocrinology consultation.

SOCS1 Haploinsufficiency Presenting as Severe, Early-onset Dermatitis and Arthritis

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Case Presentation: A 27-year-old man presented to the Mount Sinai Immunology clinic with a ~15-year history of erythematous/pustular rash, recurrent MRSA folliculitis, enthesitis, and arthritis. The patient reported intermittent joint pain and swelling since infancy which acutely worsened at age 12 resulting in outside hospital admission for inability to ambulate. At that time, he had severe, diffuse joint pain and swelling of the hips, knees, ankles, elbows, and finger joints, which on exam were edematous, warm, and erythematous. Infectious history was notable for two episodes of pneumonia and multiple sinus infections.
His labs at that time showed elevated lymphocytes (60%), normal CMP, and negative rheumatologic/infectious workup (including ANA, ANCA, RF, Parvovirus IgM/IgG, Ehrlichia, RPR, Chlamydia, and Gonorrhea). CT Chest was notable for diffuse lymphadenopathy throughout the abdomen, axillary, and R hilar regions, suggestive of inflammatory/infectious process. Following a course of steroids, he was trialed on multiple medications from age 12-26 including etanercept, infliximab, methotrexate, canaknumab, and colchicine with minimal improvement in joint pain and stiffness. He developed frequent respiratory infections in this time period, as well as recurrent MRSA folliculitis and new onset rash around age 15 (Figure 1), with skin biopsy showing focal lymphocytic and neutrophilic dermatitis with arrector pili muscle involvement. He was being treated with cosentyx at presentation.

Result: Immunodeficiency workup at Sinai was notable for normal immunoglobulins (IgG 1368, IgA 54, IgM 43), normal CD3, CD4, CD8, and CD19 counts, and variable vaccine responses (9/23 pneumococcal Ab, positive vaccine responses to rubeola, diphtheria, Hib, and tetanus, and low vaccine titers to mumps, rubella, and varicella). Whole exome sequencing revealed a mutation in the SOCS1 gene (suppressor of cytokine signaling 1; c.202_203delAC p.Thr68fs). Western blot confirmed constitutive activation of STAT pathway as well as excessive IL-4 production in this patient. Given this, treatment was continued with cosentyx, with addition of dupixent for IL-4 suppression and doxycycline. Patient experienced significant clinical improvement on this regimen as depicted below and continues in remission.

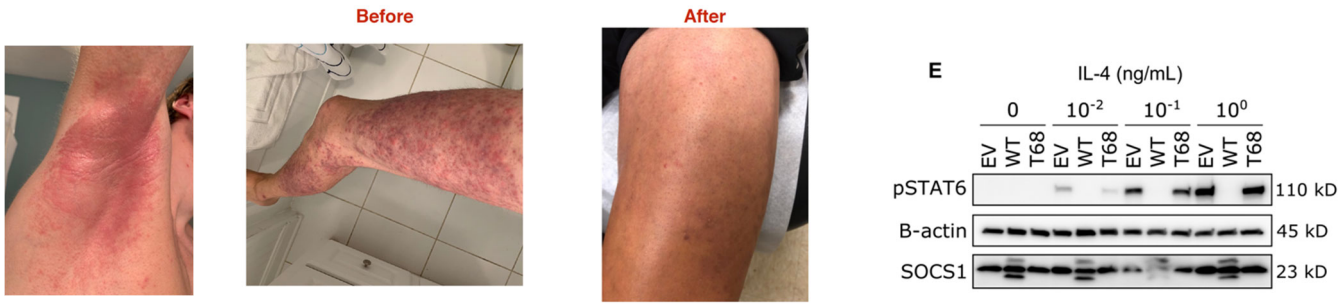

Figure 1. i) Pre-treatment: diffuse pustular rash with erythematous and violaceous patches on arms, legs, and torso with regions of lichenified and excoriated plaques. Erythematous patches on the axillae. ii) Post-treatment: resolution of rash. iii) Western blot demonstrating inability of T68fs SOCS1 to inhibit IL-4 signaling.

Conclusion: SOCS1 directly inhibits JAK kinase activity through its KIR domain, downregulating signaling by proinflammatory cytokines. SOCS1 haploinsufficiency has previously been associated with uncontrolled STAT pathway activation and early-onset autoimmunity. In this case, IL-4 blockade through the use of dupilumab is thought to have contributed to significant clinical improvement.

Congenital Dyserythropoietic Anemia Type 1 Presenting as Neonatal Acute Liver Failure

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Introduction: Congenital dyserythropoietic anemia type 1 (CDA1) is a disorder caused by a mutation in the CDN1 gene that leads to ineffective erythropoiesis and chronic hemolytic anemia, ultimately leading to hemochromatosis. It typically presents with jaundice, anemia, hepatosplenomegaly, and rarely as neonatal acute liver failure (NALF). Here we present a case of CDA1 presenting as NALF, masquerading as gestational alloimmune liver disease (GALD).

Case Report: We present a four-month-old, full-term male who presented with NALF, a patient who exhibited severe hepatic dysfunction with marked cholestasis. The patient also had persistent pulmonary hypertension and chronic macrocytic hemolytic anemia necessitating multiple transfusions. Further workup for NALF led to GALD diagnosis based on MRI and salivary gland biopsy results that showed siderosis. The patient received IVIG with minor improvements. Two months later, in the setting of a viral illness, the patient developed decompensated cirrhosis with large ascites and was evaluated for a liver transplant. Due to suspicions that the patient's presentation was inconsistent with GALD, a liver biopsy was performed, with findings favoring inborn errors of metabolism. An ultra-rapid whole genome sequencing was done, supporting the diagnosis of CDA1. Liver function improved significantly with treatment for CDA1, and the patient is thriving with his native liver.

Discussion: Our case highlights the importance of outside-of-the-box thinking for timely and appropriate diagnosis- in this case, by utilizing rapid genetic testing when the clinical presentation does not fit the expected course. For this patient, CDA1 presented as NALF at the time of diagnosis, which is extremely rare, and the mechanism of hepatic injury is still unclear.

Examining a Subpopulation of Cortical Glutamatergic Neurons in a Mouse Model of DDX3X Syndrome

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Background: DDX3X syndrome is a rare neurodevelopmental disorder primarily manifesting in females. This syndrome is caused by mutations in the X-linked gene *DDX3X*, yet its neurobiological mechanisms remain not fully understood. *Ddx3x* heterozygous female mice ($Ddx3x^{+/-}$) show developmental and behavioral deficits, accompanied by cortical malformation. Specifically, there is an increase in a glutamatergic neuronal subpopulation that coexpresses two contradictory molecular markers (CTIP2+BRN1+). We examined the significance of this neuronal subpopulation at postnatal timepoints and analyzed its disruptions in $Ddx3x^{+/-}$ mice.

Methods: We assessed by immunohistochemistry the presence of CTIP2+BRN1+ neurons at postnatal intervals. Birthdating studies were conducted by injecting pregnant females with bromodeoxyuridine (BrdU) at different time points of neurogenesis. The cerebral and subcerebral projection targets were found by performing stereotaxic injections of a retrograde pAAV-CAG-GFP virus into cortical and subcortical targets.

Results: Approximately 30% of CTIP2+BRN1+ neurons are generated during early neurogenesis (embryonic day 13.5). This population remains present in the cortex of $Ddx3x^{+/-}$ and control mice at different postnatal ages, and continues to be disrupted at 4 months of age in $Ddx3x^{+/-}$ mice, aligning with our previous results. Tracing experiments indicate that this subpopulation projects to subcerebral targets (striatum and superior colliculus), but does not display corticothalamic or callosal projection identities.

Conclusions: We believe that differences in this subpopulation may underlie the developmental and behavioral impairments caused by DDX3X syndrome. Studying the genesis and function of these neurons and how they are disrupted in $Ddx3x^{+/-}$ mice will advance our understanding of DDX3X syndrome.

Gene Expression Profiling of Ige Secreting Plasma Cells

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Introduction: Allergy persistence relies on the production of allergen specific IgE antibodies by plasma cells (PCs). High-affinity IgE PCs differentiate in a unique way by the sequential switching of affinity-matured IgG1 memory B cells. IgE PCs were found mostly in lymphoid organs and were described to be short-lived. However, chronic allergen exposure can lead to the accumulation of long-lived IgE-producing PCs in the bone marrow (BM).

Hypothesis: We aimed to characterize the features of IgE PCs associated with anatomical localization and life span.

Methods: Using a mouse model of Type 2 responses, we performed functional analysis of secondary lymphoid IgE-secreting PC and single-cell transcriptomic and BCR analysis from PCs from secondary lymphoid organs and BM.

Results: Functional analysis from secondary lymphoid organs. suggests reduced glucose uptake and Ig secretion by IgE PCs compared to other isotypes. This was associated with abnormal ER morphology. The single cell transcriptomic analysis confirmed a scarcity of IgE PCs in the BM and enrichment in lymphoid organs. IgE PCs in the lymphoid organs were defined by the upregulation of Mzb1, MHCII, unfolded protein response (UPR), and cellular stress responses. We identified a rare subpopulation of IgE PCs in the BM characterized by the upregulation of genes associated with prolonged life span, such as BCMA, Mcl1, Il6r, Cd44, and Itgb7. In addition, IgE PCs had more nucleotide mutations but fewer affinity-increasing mutations than IgG1 PC.

Conclusion: Our findings suggest that IgE PCs have a distinct metabolic adaptation and an especial secretory program, which may contribute to their short lifespan. These results provide insights into the pathogenesis IgE responses.

Characterization of Follicle Stimulating Hormone in Down Syndrome Mouse Model Ts65Dn

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Introduction: Down Syndrome (DS) is a congenital condition caused by trisomy 21, which can lead to developmental delays. Previous research has shown that patients with DS show a high prevalence of obesity, osteoporosis, and early-onset Alzheimer's disease. These diseases have been linked to high levels of follicle-stimulating hormone (FSH), a peptide hormone secreted by the pituitary gland. Elevated FSH has also been observed in children and adolescents with DS. Hence, we sought to characterize FSH in the DS mouse model, Ts65Dn, and validate previous findings.

Hypothesis: We hypothesize that Ts65Dn transgenic mice have higher fat composition, lower bone mass, and elevated serum levels of FSH compared to their wild type (WT) littermates.

Methods: We used enzyme-linked immunosorbent assay (ELISA) to measure circulating FSH levels in serum samples obtained from both female and male WT and Ts65Dn mice. We weighed the mice daily from birth until 21 days to observe growth differences. We measured fat and lean mass in WT and DS mice with quantitative magnetic resonance imaging (qMRI) and bone mineral density with Dual-energy X-ray absorptiometry (DEXA).

Results: We found that DS mice have significantly higher levels of FSH, less lean mass, and lower bone mineral density compared to WT mice. There is also a growth difference between DS and WT mice starting from when they are 7 days old.

Conclusions: Our findings suggest a strong correlation between high levels of FSH, osteoporosis and lean mass and creates an opportunity for a therapy targeting FSH to help with these conditions in DS patients.

Assessing False Positive Rates of Congenital Hypothyroidism on Newborn Screening During the COVID-19 Pandemic

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Introduction: With the COVID-19 pandemic, hospital stays shortened for infants causing newborn screens (NBS) to be obtained earlier. Timing of NBS is essential for diagnosing congenital hypothyroidism (CH). We aimed to determine overall and false positive rates of CH prior to the COVID-19 pandemic compared to during the COVID-19 pandemic.

Hypothesis: Infants born during the COVID-19 pandemic have earlier discharges and higher false positive CH rates.

Methods: We performed a retrospective chart review of infants with abnormal NBS result for CH. Infants born between 3/1/2019-3/1/2020 was the pre-COVID group and 3/2/2020-2/1/2022 was the COVID group.

Results: There were 61 infants in the pre-COVID group and 332 in the COVID group. The COVID group had higher birth weights, earlier NBS obtainments, and earlier discharge (Table 1). Among all infants, 9.2% had a confirmed diagnosis of CH with a false positive rate of 90.8%. The false positive rate was higher in the COVID group compared to the pre-COVID group (92% vs. 84%, $p=0.03$). The COVID group was 5.85 times more likely to have an early discharge (95% CI:2.70-12.66, $p<0.01$); however, there was no association between early discharge and the likelihood of a false positive result ($p=0.56$).

Conclusions: Infants born during the COVID-19 pandemic had earlier NBS obtainment, earlier discharges, and higher false positive CH rates, but earlier discharge was not associated with higher false positive rates. Continuous consideration needs to be given to timing of NBS obtainment.

(Please see next page for Table 1)

Table 1. Characteristics of infants with abnormal newborn screen results for congenital hypothyroidism.

Characteristic	All infants (n=393)	Pre-COVID group (n=61)	COVID group (n=332)	*P*-value
Sex – no. (%)				0.07
Male	197 (50.1)	37 (60.7)	160 (48.2)	
Female	196 (49.9)	24 (39.3)	172 (51.8)	
Race/Ethnicity*– no. (%)				0.06
Non-Hispanic White	239 (64.9)	41 (69.5)	198 (64.1)	
Hispanic White	13 (3.5)	3 (5.1)	10 (3.2)	
Hispanic Black	6 (1.6)	3 (5.1)	3 (1.0)	
Non-Hispanic Black	33 (9.0)	3 (5.1)	30 (9.7)	
Non-Hispanic Asian	31 (8.4)	6 (10.2)	25 (8.1)	
Other	46 (12.5)	3 (5.1)	43 (13.9)	
Singleton vs Multiple – no. (%)				0.10
Single	381 (96.9)	57 (93.4)	324 (97.6)	
Multiple	12 (3.1)	4 (6.6)	8 (2.4)	
Delivery Method – no. (%)				0.39
Vaginal	232 (59.0)	33 (54.1)	199 (59.9)	
Cesarean section	161 (41.0)	28 (45.9)	133 (40.1)	
Gestational age at birth, weeks – median (IQR)	39.1 (38.1-40.1)	39.1 (37.6-40.0)	39.2 (38.3- 40.1)	0.21
Prematurity (gestational age < 37 weeks) – no. (%)	34 (8.7)	10 (16.4)	24 (7.2)	**0.02**
Birth weight, grams – median (IQR)	3210 (2890-3540)	3010 (2700-3430)	3232.5 (2907.5-3560)	**<0.01**
Age at hospital discharge, hours – median (IQR)	47.8 (33.1-65.7)	67.0 (48.5-82.1)	46.5 (29.9- 61.9)	**<0.01**
Age at newborn screen collection, hours – median (IQR)	24.0 (24.0-27.0)	27.0 (24.0-43.0)	24.0 (24.0- 26.0)	**<0.01**
NICU admission – no. (%)	62 (15.8)	20 (32.8)	42 (12.7)	**<0.01**
Oxygen requirement – no. (%)	30 (7.6)	9 (14.8)	21 (6.3)	**0.03**
Perinatal iodine exposure – no. (%)	13 (3.3)	5 (8.2)	8 (2.4)	**0.04**
* 6% of the data were missing.				

Disparities in Child Abuse Reporting: Predictors of Making a Referral to Child Protective Services Prior to Expert Consultation

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Introduction: Suspicion for child abuse is influenced by implicit biases. Evaluation by a Child Abuse Pediatrician (CAP) may reduce avoidable child protective services (CPS) referrals.

Hypothesis: There is an association of patient demographic, social and clinical characteristics with CPS referral before consultation by a CAP (pre-consultation referral).

Methods: Children under 5 years-old undergoing in-person CAP consultation for suspected physical abuse from February 2021 through April 2022 were identified in CAPNET, a multicenter child abuse research network. Marginal standardization implemented with logistic regression analysis examined hospital-level variation and identified demographic, social, and clinical factors associated with pre-consultation referral adjusting for CAP's final assessment of the likelihood of abuse.

Results: Among the 61% (1005/1657) of cases with pre-consultation referral, the CAP consultant had low concern for abuse in 38% (384/1005). The adjusted percentage of children referred prior to consultation ranged from 27% to 78% across 10 hospitals ($P<0.001$). In multivariable analyses, pre-consultation referral was associated with public insurance, caregiver history of CPS involvement, history of intimate partner violence, higher CAP level of concern for abuse, hospital transfer, and near-fatality (all $P<0.05$). The difference in pre-consultation referral prevalence for children with public versus private insurance was significant for children with low CAP concern for abuse (52% vs 38%) but not those with higher concern for abuse (73% vs 73%), ($P=0.023$). There were no differences in pre-consultation referral based on race or ethnicity.

Conclusions: Biases based on socioeconomic status and social factors may impact decisions to refer to CPS before CAP consultation.

Knowledge of Epinephrine Auto-Injector Use Among Caretakers of Pediatric Food Allergy Patients

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Introduction: Epinephrine auto-injectors (EAIs) are life-saving interventions for food-allergic patients experiencing anaphylaxis. With three new types of EAIs recently approved, identifying if caretakers can correctly use their prescribed EAI and the factors associated with proper use is important.

Hypothesis: We hypothesized that the rates of correct EAI use will be associated with type of EAI, socioeconomic status, and prior education on EAI use.

Methods: The caretakers of pediatric patients with positive skin prick and/or serum IgE tests for food allergens and an EAI prescription were surveyed and assessed on demonstration of correct EAI use.

Results: Of 136 participants, 63% were able to correctly demonstrate how to use their child's prescribed EAI, but rates of correct use were significantly different depending on EAI type (89% Auvi-Q, 42% Mylan, 43% Teva, 27% Adrenaclick; $p<0.01$). Correct EAI usage significantly differed in groups according to several demographic and other factors ($p<0.05$), with worse outcomes exhibited in the following groups: Hispanic/Latinx ethnicity, lower education attainment, lower family income, use of public insurance, fewer number of food allergies, history of fewer allergic reactions, shorter time since prescribed EAI, and not being taught with a demo using a trainer.

Conclusions: Knowledge of EAI use is relatively low among surveyed families, although correct Auvi-Q use was significantly higher than other types. Factors associated with appropriate use such as socioeconomic status, EAI type, and allergic history may guide providers in their prescription choices, and in teaching patients of diverse experiences how to properly use their EAI.

Assessing Factors That Impact Parental Willingness to Vaccinate Their Children Against COVID-19 in a Primarily Immigrant Patient Population in Elmhurst, Queens

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Introduction: Parental concerns surrounding COVID-19 vaccination of their children often include fear of side effects and perceived lack of information. Specifically, immigrant parents may face additional barriers in this decision, such as language barriers or low health literacy. As COVID-19 has disproportionately affected vulnerable populations, this study focused on a largely immigrant cohort in Elmhurst, Queens to gauge factors that influence parents' decisions to vaccinate their children against COVID-19, specifically maternal COVID-19 illness history, a variable that has been scarcely studied.

Hypothesis: The primary goal of this study is to assess the relationship between history of maternal COVID-19 illness, defined as having tested positive for COVID-19 at least once, and the willingness of a mother to vaccinate their child for COVID-19. Our hypothesis is that mothers who had tested positive for COVID-19 may be more likely to be comfortable vaccinating their child due to existing research that shows that past familial experience with COVID-19 may be a factor in vaccine decisions.

Methods: A cross-sectional survey was conducted with women who had a pregnancy encounter at Elmhurst Hospital between March 1, 2020 and September 1, 2021 and whose children were between 6 months and 2 years at the time of survey completion. The survey contained questions about demographics, COVID-19 vaccination/illness history, and child development.

Results: In preliminary analysis with data from 24 mothers, all of the survey respondents self-reported their race as Non-white, with 79.2% of respondents identifying as Hispanic. 66.7% reported not being born in the U.S. 70.9% of respondents' highest level of schooling was a high school diploma or less. 50% of the respondents had tested positive for COVID-19 at some point. The rate of willingness to vaccinate their children was 59.1% overall, 80% within those with a COVID-19 history, and 42% within those who had no experience with COVID-19. There was no significant association found between maternal COVID-19 illness status and mothers' willingness to vaccinate their children (Fisher's exact = 0.099).

Conclusions: While the results of this study show no significant association between maternal COVID-19 illness and willingness to vaccinate their children, the understudied factor of maternal COVID-19 illness history merits further study in a larger sample. Future plans for this ongoing study include increasing sample size and examining the relationship between maternal COVID-19 illness and child development.

Meeting People Where They're At: The Association Between Utilization of Community Based Organizations and Mothers' Willingness to Vaccinate Child Against COVID-19

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Introduction: The CDC reports that over 4 million deaths worldwide are prevented by childhood vaccination. In recent years the United States has seen a historic drop in childhood vaccination, attributed to parental vaccine hesitancy, surrounding safety and side effects, and the COVID-19 pandemic. While public health entities have tried effortlessly to increase vaccine confidence amongst communities, literature suggests it may be more effective to increase efforts in partnership with trusted community-facing and community-based organizations (CBO).

Hypothesis: The primary goal of this proposal is to determine the association between maternal utilization of community-facing (e.g, WIC and Planned Parenthood) and community-based services (e.g., church and cultural organizations) and maternal willingness to vaccinate their child against COVID-19. We hypothesize that those who have had more contact with such organizations would be more willing to vaccinate their child against COVID-19.

Methods: Our team conducted a cross-sectional survey of mothers with children between the ages of 6 months and 2 years, who had one pregnancy encounter at Elmhurst Hospital between March 1st, 2020 and September 1, 2021. Our preliminary analysis included responses from 22 mothers.

Results: The majority (64%) of our participants identified as Hispanic non-White, while no participant identified as White non-Hispanic. While all of the mothers in our study were vaccinated; around 41% of the respondents demonstrated an unwillingness to vaccinate their child against COVID-19. With many citing vaccine hesitancy attributed to safety and efficacy as their primary concern. About half of our participants reported utilization of services provided by CBOs. Of those who did utilize a service, 62% were willing to vaccinate their child, in comparison to 38% in the group who reported no utilization of CBO services. Our preliminary findings show no statistically significant association between maternal willingness to vaccinate children and utilization of services provided by CBOs.

Conclusions: Our findings demonstrate a marked maternal COVID-19 vaccine hesitancy that is linked to concerns about vaccine safety. Those who did utilize services had a higher percentage of willingness to vaccinate their child. While our preliminary finding was not statistically significant, the trends suggest further partnership with CBOs on vaccine education may have the potential to impact vaccine confidence amongst community members.

Reflections on the Formation of an Interdisciplinary Pediatric Health Equity Journal Club: Turning Team-Based Education into Clinical Action

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Introduction: Following the 2020 murders of Ahmaud Arbery, Breonna Taylor, and George, academic medical centers across the country recognized the need to develop new curricula to teach about racism, health inequity, and social justice within their respective institutions. Successful anti-racist medical education and clinical practice must include successful collaboration among an interdisciplinary team of front-line providers in both learning and clinical environments.

Hypothesis: The Pediatric Health Equity Journal Club (PHEJC), a monthly interdisciplinary journal club that highlights publications discussing health inequities faced by the pediatric population, provides a shared space to engage in discussions around racism and other causes of health inequity and establish partnerships across disciplines to address racism in the units.

Methods: On a monthly basis, co-facilitators recruited from Pediatrics Residency, Social Work and Child Life presented a relevant article from an academic journal with accompanying case studies for facilitated discussion among the target audience (members of Pediatrics Residency, Social Work and Child Life divisions) in an in-person and virtual "lunch and learn" format.

Results: The creation of a didactic space to discuss racism, bias and other factors of health inequity allowed for an exchange of ideas and brainstorming while in a low-pressure, low-stakes environment, and created the opportunity for interdisciplinary collaboration on health equity efforts which can then be implemented on subsequent clinical interactions.

Conclusions: A health equity journal club such as the PHEJC may provide an opportunity for collaboration with other healthcare professions, promote anti-racist teaching through acknowledgment of racist elements of the medical model, and lay the groundwork for a culture of accountability in the clinical space.