



Children'sSM
Healthcare of Atlanta



Looking Ahead to a Healthier Tomorrow

Children's Healthcare of Atlanta
and Emory University
2022 Research Report



EMORY
UNIVERSITY

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A Message from Dr. Lucky Jain



Dear Friends and Colleagues,

I am continually proud of our research and clinical teams, and for their unwavering commitment to do everything possible to make anything possible for kids. But their talent and determination really came to bear during the seemingly interminable battle with COVID-19.

It's been three years since our teams at Children's Healthcare of Atlanta and Emory University Department of Pediatrics started tackling the global pandemic, and I am delighted to say we have not only remained resilient but gone above and beyond during these challenging times. We continue to make new discoveries in research, with an increased focus on emerging infectious diseases, behavioral and mental health and diversity and inclusion, and thousands of children benefit from these efforts every day, across Georgia and throughout the world.

The Children's and Emory partnership is stronger than ever. We implemented our new physician leadership organization this year to become a more unified pediatric system. Our strategy, "One Children's," has aligned our leadership structure across all three missions – clinical, teaching and research – and has provided clearly defined physician leadership roles. We believe that combining our physician leadership in these areas is a step in the right direction.

The impact we've made through our dedicated and ambitious research efforts in 2022 was no small feat. We hired seven new researchers last year, funded through both our \$90 million gift from the Robert W. Woodruff Foundation and our \$1.3 billion academic quasi-endowment, to substantially grow our team of world class investigators over the next few years. Our new recruits are focusing their research on several areas important to pediatrics, including HIV persistence, cancer treatments, pulmonary sickle cell disease and complement biology, to name but a few. Our collaborative research team at Children's, Emory and Georgia Tech was chosen to lead the National Institutes of Health's (NIH) newly established National Institute of Biomedical Imaging and Bioengineering (NIBIB) Innovation Funnel Validation Center. In partnership with the Georgia Research Alliance, we also have launched a sickle cell disease initiative to dramatically improve the future of patients with the disease in Atlanta and beyond. This initiative aims to leverage Georgia's strengths in university research and healthcare, and break new ground in knowledge, treatment and cures.

Our dedication to training and career development has continued through the successful third renewal of the Atlanta Pediatric Scholars Program, funded by the NIH's Eunice Kennedy Shriver National Institute of Child Health and Human Development, allowing us to train physician-scientists for academic careers in fundamental pediatric research. We also were awarded a new Children's and Emory Pediatrics and Pathology Stimulating Access to Research in Residency (StARR) Program, funded by the NIH's National Heart, Lung and Blood Institute, designed to provide enhanced research training and mentorship to resident-investigators dedicated to researching heart, lung and blood health. Both programs are designed to offer in-depth training in research fundamentals, foster stellar research mentoring, and build a systematic approach for identifying and recruiting a diverse cohort of physician-scientists.

We look forward to expanding our behavioral and mental health services following the successful recruitment of Dr. John Constantino to become Chief, Behavioral and Mental Health at Children's and Professor in the Department of Psychiatry and Behavioral Sciences at Emory, and as well as through a generous donation from the Zalik Foundation of nearly 10 acres of land, including two office buildings, which will solely be dedicated to pediatric behavioral and mental health.

Children's continues to be ranked among the nation's top pediatric hospitals by U.S. News & World Report 2022-2023, with four specialties ranked in the top 10 and eight specialties in the top 20.

Two major construction projects have also made significant progress. Emory's Health Sciences Research Building II will open in early 2023 and we could not be more excited for the wellspring of research that will result in the years to come. Arthur M. Blank Hospital, the largest healthcare project in Georgia's history, also reached a major milestone this year, as construction reached its highest point this past May. We look forward to the projected opening of the hospital in fall 2024.

None of these accomplishments would be possible without numerous collaborations and outstanding teamwork. I am so grateful for Emory and Children's commitment to making kids better today and healthier tomorrow.

All the best,



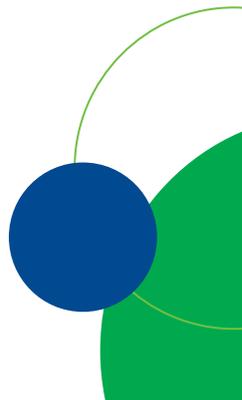
Lucky Jain, MD, MBA

Pediatrician-in-Chief,

Children's Healthcare of Atlanta

George W. Brumley Jr. Professor and Chair,

Emory University School of Medicine Department of Pediatrics



Better Together: Children's Healthcare of Atlanta and Emory University

Children's and Emory University work together to facilitate leading-edge pediatric research, training and innovation. This long-standing partnership between one of the country's largest freestanding pediatric healthcare systems and a leading research university is mutually beneficial. Emory University's expertise and oversight are invaluable during clinical trials, and Children's provides a training site for the Emory University Pediatric Residency and Fellowship Program. Discoveries in Emory University's research laboratories are deployed in real lifesaving situations at Children's. Together, our partnership advances research and facilitates evidence-based quality care for children.



In 1956, the board of trustees for both Emory University and the former Henrietta Egleston Hospital for Children signed an agreement to make Egleston a first-rate teaching hospital.

2022 Research by the Numbers

Ranked
No. 1
nationally in NIH funding for
pediatric departments*

\$77 million
in funding from NIH

\$111 million
in total
extramural funding

739
residents and fellows
in training



7
new
researchers
recruited in
fiscal year
2022



460
supplemental
awards



191
new grant and
contract awards
totaling

\$24.5 million

1,475 hours
of CME credits through

174
educational activities for

19,576
participants



59
new clinical trials
activated



2,281
publications
in **1,024** journals



2,281
visit hours in the
Children's Pediatric
Research Unit



2,089
Children's patients
enrolled in clinical
studies

Our research program has maintained a top five ranking for NIH funding since 2016.

*NIH funding period from Oct. 1, 2021 through Sept. 30, 2022.

Building the Future of Research

Emory University Builds Innovative Biomedical Research Facility

The new Health Sciences Research Building II (HSRB-II) at Emory University will be an eight-story facility with research space for imaging sciences, biomedical engineering, cardiovascular medicine, cancer, inflammation, immunity and immunotherapeutics, emerging infections and other innovative interdisciplinary research programs. It is funded in part by the Robert W. Woodruff Foundation and Children's with approximately two floors of laboratory space reserved for pediatric research. HSRB-II is scheduled to open in early 2023.

"HSRSB-II was designed with principles of connectivity, synergy, innovation, impact, efficiency and resourcefulness," said David Stephens, MD, Vice President for Research in the Robert W. Woodruff Health Sciences Center of Emory. "We believe the design of this space will encourage new thinking, collaborative conversations, and an environment that prioritizes wellbeing."

Each floor of HSRB-II will have collaboration spaces and a unique digital infrastructure for informal team meetings and to encourage connectivity. The building is designed to allow visibility and light flow through the space and to connect with the adjacent Lullwater Preserve.



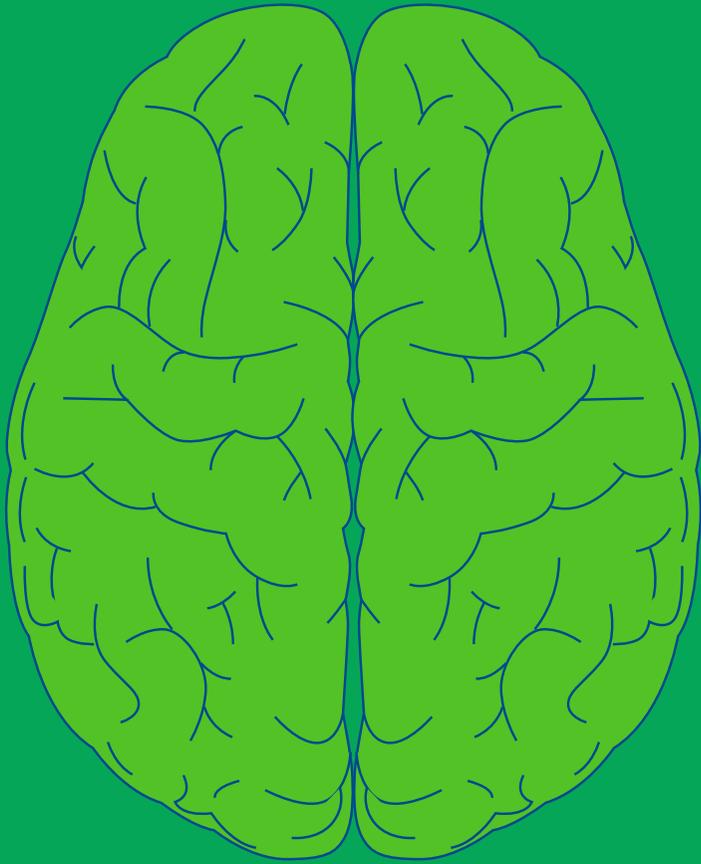


Children's Healthcare of Atlanta Arthur M. Blank Hospital Reaches Innovative Heights

Construction topped out at Arthur M. Blank Hospital, as the facility reached its final height of 19 stories during summer 2022 on the 78-acre North Druid Hills campus. Including one tower with two patient wings and a 16-story outpatient clinic, the hospital is the largest healthcare project ever in the state of Georgia. Once completed, it will be only dedicated Level 1 pediatric trauma center. Arthur M. Blank Hospital is scheduled to open in fall 2024 with three miles of walking trails and 20 acres of therapeutic green space and gardens, environmental enhancements that studies show improve healing.

In addition to overall patient care, the 1.5-million-square-foot facility will help enhance research by creating a dedicated space for discoveries, including The Marcus Center for Pediatric Advanced Cellular Therapy, and clinical research and trials across a variety of specialties that will help transform the future of pediatric healthcare.

"In 2008, we had more than half a million patient visits, and by 2021, that number more than doubled to more than 1 million patient visits," said Donna Hyland, Chief Executive Officer of Children's. "This trend shows no sign of stopping and that's why Arthur M. Blank Hospital is so critical to the kids of Georgia. To stay at the forefront of pediatric care, we need new facilities, resources and physicians to take care of all patients who need us. Arthur M. Blank Hospital will serve that increased demand for care."



Enhancing Brain Health

Research at the Forefront of Tackling a Behavioral and Mental Health Crisis

A nationally renowned researcher in pediatric behavioral and mental health, John N. Constantino, MD, joined Children's as Chief, Behavioral and Mental Health in August 2022. Dr. Constantino is tasked with tackling an enormous challenge: developing a comprehensive program to help stem a serious youth mental health crisis in Georgia and throughout the U.S., and research is at the forefront of his efforts.

"Mental health is a great unmet need in children," says Dr. Constantino, who also holds a joint appointment as faculty member in the Emory School of Medicine Department of Psychiatry and Behavioral Sciences. "It's been a serious problem for years, but the confluence of the effects of social media and the pandemic is a one-two punch that has made matters worse. America's health system doesn't provide adequate, evidence-based, outpatient recovery pathways for many children, and we're seeing a lot of kids in crisis."

Children's is committed to helping Georgia become a national leader in behavioral and mental health through an endowment greater than \$550 million, one of the largest investments in child mental health by a healthcare system in U.S. history. Established in 2019, the initiative is focused on expansive, integrated, clinical and research programs. Most recently, Children's announced the donation of 10 acres of land by the Zalik Foundation that will become Children's Healthcare of Atlanta Zalik Behavioral and Mental Health Center. Scheduled to open in 2023, this campus will be entirely dedicated to the efforts being led by Dr. Costantino with a focus on evidence-based intervention.

Research will play an integral role in the endeavor by systematically monitoring the impact of the delivery of timely, evidence-based mental health care to populations of children and families who would otherwise have only marginal access to such service under conditions of care as usual. Three initial areas of focus will be:

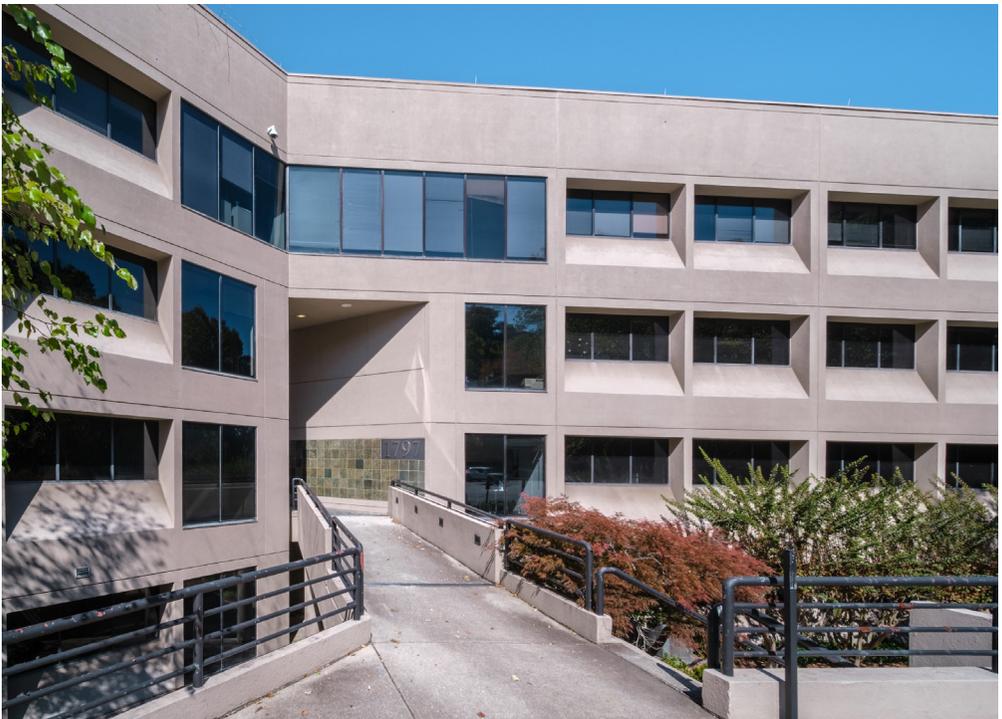


John Constantino, MD

- **Very young children and families.** This involves integrating a suite of interventions for fragile, young families whose children are at very high risk of mental health impairment. By stabilizing and supporting these families, from the early days of a child's life, practitioners may ward off mental health risks. "With a new baby, you have a brand new brain not yet affected by life's crises," says Dr. Constantino. He plans to establish a method to deliver evidence-based care to a cohort of infants and young children – within metro Atlanta and some rural environs – to assess and address these unmet risks from an early age.

- **Adolescents at risk of suicide.** The U.S. has been lacking in systematically delivering mental health recovery pathways to young people at an intermediate risk for suicide, which is the second leading cause of death in adolescents. Explains Dr. Constantino, “Currently, in Georgia, if a child is discovered to be at imminent risk for suicide they are hospitalized. But those at intermediate risk, or who have left the hospital, often have no defined, evidence-based recovery pathway.” His plan is to develop an integrated pathway for these children, applying existing and upcoming research to the initiative so that fewer at-risk children will be making return visits to the emergency department.
- **Leveraging adjacent research programs.** In an extension of the efforts of leading experts from Emory and Children’s—pioneers in early childhood intervention, behavioral support for children with developmental disorders, school-based mental health, and the treatment of adolescent mood, anxiety, and substance use disorders—Dr. Constantino plans to incorporate cutting edge methods and technologies into the delivery of high-quality mental health care to the current generation of children in Georgia.

Research is key, Dr. Constantino says. “Basically, we need another kind of science to apply to the field. The way science has worked in pediatric mental health services has typically been through the analysis of singular types of intervention and their short-term impact and what we don’t know is the joint influence of multiple interventions and their long-term impact.”



Zalik Behavioral and Mental Health Center

Shown to Increase Confidence, Crisis Prevention Program Sees Global Application

As a leader in behavioral crisis prevention training, the Crisis Prevention Program at Marcus Autism Center, a subsidiary of Children's, is designed to fill the gaps of other commercialized programs by including training on trauma informed practices, whole-child care, staff resiliency and support, and adaptable de-escalation strategies.

But just how effective is that training? Program leaders sought to find out.

In collaboration with Seth Clark, MA, Program Manager of the Marcus Crisis Prevention Program, Nathan Call, PhD, Psychologist and Clinical Director of the Marcus Autism Center, led a study to evaluate the confidence of employees in safely managing behavioral crises in the healthcare setting after receiving training. Emergency department and non-emergency department employees answered survey questions before and after the training at three- and six-month follow-up times.

Results suggested that employees were more confident in managing and communicating during a behavioral crisis after the training. Before the training, only 39% of employees agreed they were confident in strategies to de-escalate behavioral crises; afterward, 90% agreed. The researchers published their findings in the Journal of American Psychiatric Nurses Association.

The Marcus Crisis Prevention Program training is now used in three countries, 24 states, including other pediatric healthcare systems in the U.S., in six major school systems in Georgia and across Children's in settings such as preschool and K-12 classrooms, residential care facilities, psychiatric care facilities, therapeutic and ABA clinics, emergency departments, inpatient and outpatient clinics, group homes, and crisis stabilization units.

"Outcomes demonstrate the program is adaptable to various settings and patients and is well-received by employees, suggesting that by teaching staff to focus on resiliency, whole-child care, and proactive strategies, their confidence and communication during behavioral crises can improve," said Clark.





Marcus Autism Center employee and mom sings to her infant

Singing to Infants Shown to Synchronize their Gaze

Synchronization is observed in physical and biological systems, such as synchronized sleep-wake cycles and the synchronization of heartrate and breathing.

A study from the Marcus Autism Center, which was designed to help researchers understand the most basic elements of social interaction, examined how infants react to the rhythm of music when caregivers sing to them. As part of a larger effort to discover how synchronization and social interaction may be disrupted in children with autism, the findings may help enhance future treatment approaches.

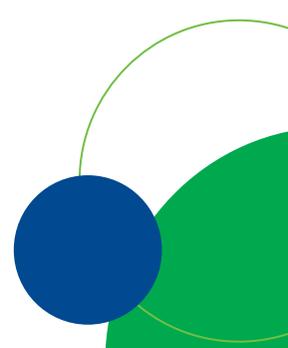
Results of the study, published in the *Proceedings of the National Academy of Sciences of the USA*, showed when caregivers sing to infants, babies instinctively synchronize their gaze by looking into their caregiver's eyes on the beat of the music. The caregivers also synchronized their facial expressions toward infants on each beat. Without conscious awareness, singing changed caregiver behavior to be more positive and engaging on each beat, and that change in behavior was synchronized with changes in how infants looked at their caregivers – more often on the beat.

"Synchronization shapes the social experience of infants, changing what they look at and what they see," says Warren Jones, PhD, study co-principal investigator, Director of Research at Marcus Autism Center, and Nien Distinguished Chair in Autism at Emory. "Infants and caregivers interact in an intricate dance. The study reveals the very basic steps of that dance and how those steps subtly but importantly change infant and caregiver behavior on a moment-by-moment basis."

Future work will test whether empirically validated behavioral treatment approaches in autism can be enhanced using music.

The study was funded by the Sound Health Initiative, a partnership of the NIH and the John F. Kennedy Center for the Performing Arts to foster research into the potential for music to promote health and well-being. Additional support was given by the GRAMMY Foundation, the National Institute of Mental Health, and the National Institute on Deafness and Other Communication Disorders.

Marcus Autism Center conducted the research with Emory and Vanderbilt University Medical Center.



Uncovering the Neuroscience of Social Behavior

Identifying the ‘Social Incentivization of Future Choice’

Does the company a person keeps impact the choices they make?

Shannon Gourley, PhD, wanted to find out whether social experiences impact decision making. Dr. Gourley, Associate Professor in the Emory Department of Pediatrics, and her team sought to better understand – at the biological level – how social experiences influence future choices. For instance, does a person wear a certain kind of clothing because their peers also wear it, or does a couple often return to a restaurant because it’s where they had their first date?

To delve into this topic, Dr. Gourley and team conducted an experiment offering limitless amounts of cookies, in chocolate and vanilla flavors, under two very different conditions. With the “chocolate” condition, a friend was also present; while in the “vanilla” condition, a novel toy was also present. Results showed a clear preference for the chocolate cookies, indicating that social experiences – in this case, the presence of a friend – impacted choice.

Dr. Gourley’s team named this process “social incentivization of future choice,” and published their findings in *Nature Communications*. Through their research observations, they were able to identify the neural circuits involved in this decision-making scenario. Their hope is that the findings will provide a way to study social processing impairment in autism spectrum disorder and other neurodevelopmental illnesses.

Flexible Actions Originate in a Flexible Brain

Most people drive the same familiar route to work every day.

But occasionally, life intervenes. Due to a variety of factors, one may need to alter the commuting routine to accommodate for an unexpected change, such as road construction or a major traffic jam on the route to work. During these circumstances, or interruptions of other familiar everyday routines, a person will ideally form new memories for these new strategies.



Shannon Gourley, MD

In a paper published in *Nature Neuroscience*, Dr. Gourley and her team revealed that they have discovered specific cell groups in the brain — called the “orbitofrontal cortex” — that form new memories for such flexible actions. They also found that early-life exposure to addictive drugs can impair the capacity of those cells to behave in a flexible manner or to undergo the anatomical changes that allow them to form functional networks.

According to Dr. Gourley, these discoveries are helping researchers understand how exposure to addictive drugs during childhood and adolescence can have long-term ramifications for memory and other brain functions. Ultimately, she and her team aim to apply these and other research revelations to develop treatments for the long-term cognitive ramifications of early-life drug exposure.

Achieving Consensus on Pediatric Feeding Disorder

For infants and children with pediatric feeding disorder, every bite may be painful, scary or simply not possible – which may hinder nutrition, development and growth.

To help improve outcomes for these children, William Sharp, PhD, Psychologist and Director of the Multidisciplinary Feeding Program at Marcus Autism Center, led a team of experts from seven U.S. pediatric healthcare systems in developing a pediatric feeding disorder multidisciplinary patient characterization form, which is a tool to guide research on assessment and treatment, and to promote best clinical practice.

The form involves evaluating an infant or child in four areas: medical, nutrition, feeding skill and psychosocial. It helps clinicians identify the primary attributes of a feeding disorder based on diagnostic criteria. (Pediatric feeding disorder may occur when a child has difficulty eating and swallowing food for their age, along with other medical, nutritional or psychological dysfunction.)

Developed by a 28-member multidisciplinary panel with equal representation from medicine, nutrition, feeding skill and psychology, the agreed-upon pediatric feeding disorder case report form was detailed in a report published in the *Journal of Pediatric Gastroenterology and Nutrition*.



William Sharp, PhD

“The form will be used by psychologists, physicians, dieticians, speech language pathologists and others to guide assessment and treatment of the disorder,” says Dr. Sharp, who is also an Associate Professor of Pediatrics at Emory. “It has the potential to improve patient screening and promote early detection, as well as spur new lines of research inquiry associated with atypical feeding and eating.”



Targeting Cancer and Blood Disorders

Cancer Precision Medicine Program Yields Impactful Results

When Edward Page's cancer returned, his family and doctors made the difficult decision to have his neuroblastoma tumor removed surgically. It's a decision that likely saved his life.

Once removed, the tumor was sent for genetic testing and DNA sequencing through the Precision Medicine Program of the Aflac Cancer and Blood Disorders Center of Children's, which operates through a clinical trial funded by CURE Childhood Cancer.

Using a new weighted scoring system developed during the study, analysis of the tumor revealed that Edward's had a specific genetic mutation, one that could be treated with a drug that targets that mutation. After undergoing treatment with that drug, 9-year-old Edward is now cancer-free.

Edward was one of 126 patients with high-risk, newly diagnosed, relapsed or refractory pediatric brain tumors, hematologic malignancies and extracranial solid tumors who participated in the study. An impactful genetic finding was revealed in 85% of the participants, and – like Edward – more than 15% were able to receive a targeted therapy to treat their specific form of cancer.

"To see an overall impact in 85% of patients and to know that genetic sequencing can have an impact beyond just the selection of a targeted therapy was really validating and gratifying," said Ryan Summers, MD, Pediatric Hematologist/Oncologist, who was first author of the study and a member of the Precision Medicine Program.

Added Kelly Goldsmith, MD, Pediatric Hematologist/Oncologist, Clinical Director of the Precision Medicine Program and principal investigator of the study: "This paves the way for future precision studies in pediatric and adolescent cancer patients, using more targeted and less toxic therapies that are agnostic to the tumor type."

The results from the first group of patients enrolled in the study were published in the *Journal of Clinical Oncology (JCO) Precision Oncology*.





Improving Outcomes for Kids with High-Risk Hodgkin Lymphoma

Children with advanced-stage Hodgkin lymphoma have a lower risk of relapse, thanks to a new targeted therapy tested in a clinical trial by pediatric oncologists at the Aflac Cancer and Blood Disorders Center and other leading pediatric cancer institutes.

By combining the targeted antibody-drug conjugate brentuximab vedotin with the standard chemotherapy regimen for Hodgkin lymphoma, children with the disease were 10% less likely to relapse according to study findings published in the *New England Journal of Medicine*.

The clinical trial was funded by the National Cancer Institute of the NIH and conducted at 153 sites affiliated with Children's Oncology Group (COG), the world's largest organization devoted exclusively to childhood and adolescent cancer research. Children's Healthcare of Atlanta is a member of COG.

According to the study's first author, Sharon Castellino, MD, MSc, Director of the Leukemia and Lymphoma Program at the Aflac Cancer and Blood Disorders Center, the trial results reflect a paradigm shift in treatment for advanced-stage Hodgkin lymphoma in children. In fact, the results paved the way for FDA approval of brentuximab vedotin for this population in late 2022.

"We were optimistic this trial would set the stage for FDA approval of this targeted antibody drug conjugate for children and adolescents," said Dr. Castellino, who is also Professor of Pediatrics at Emory and a research member at Winship Cancer Institute of Emory University. "The FDA approval is a win for children who now have access to a targeted therapy for Hodgkin lymphoma."

Hodgkin lymphoma is the most common cancer in patients 12-29 years old. Although it has a high five-year survival rate—97% of those under 19 are alive five years after diagnosis—about one-third of survivors are classified as high risk; of those, approximately 15-20% will relapse.

The study findings revealed that recipients of the standard pediatric chemotherapy regimen, combined with brentuximab vedotin, showed 92.1% event free survival about three and a half years after treatment. This was significantly higher than the 82.5% event free survival rate in the control group, with respect to risk reduction of relapse, death or a second malignant neoplasm.

Lucky Jain, MD, MBA, says, "A 10% reduction in relapse among children with high-risk Hodgkin lymphoma is a significant milestone for the field of pediatric cancer."



Sharon Castellino, MD



Hemophilia A Research Program Aims for More Effective Treatments

With a \$6.6 million grant from the National Heart, Lung and Blood Institute (NHLBI), a research team from the Aflac Cancer and Blood Disorders Center, the University of Washington and RTI International hopes to uncover the mystery that makes the bleeding disorder Hemophilia A even worse for one-third of patients.

As co-principal investigator, Shannon Meeks, MD, Pediatric Hematologist/Oncologist with the Aflac Cancer and Blood Disorders Center and Professor of Pediatrics at Emory, will use the funding from NHLBL, an arm of the National Institute of Health (NIH), to develop the Hemophilia A Analytical Cohort Research Program (HARP).

Hemophilia A, also known as factor VIII deficiency, is an inherited bleeding disorder that causes abnormal blood clotting, resulting in more bleeding than normal due to low levels of factor VIII, a protein needed to form blood clots. Many severe hemophilia A patients will develop even more bleeding due to the complication of inhibitors, which are antibodies generated by the patient's body against their factor VIII replacement treatment.

The program will include a longitudinal study to better understand severe hemophilia A in 50 pairs of genetic carrier mothers and their babies, following them from pregnancy through the first few years of life. The team will collect blood samples from the mothers as the babies grow and are treated for hemophilia A, while tracking which patients form inhibitors that cause the body to react to the factor VIII replacement treatment and which patients do not. The goal is to better understand why inhibitors develop in some people but not others and to identify more effective tests and interventions for patients.



Shannon Meeks, MD

The researchers also aim to lay the groundwork for a customized, precision-medicine approach based on each participant's profile by performing single-cell genetic sequencing to better understand underlying mechanisms. Dr. Meeks and team will build HARP as an NIH resource to advance research in maternal biology, perinatal biology, the newborn and immune system development in early life.

Developing a Culturally Relevant Chronic Sickle Cell Pain Intervention

Chronic pain is difficult to manage. Fear and anxiety about pain often cause patients to disengage from once-enjoyed daily activities, negatively impacting their quality of life.

And for chronic pain sufferers in marginalized groups, such as certain racial or ethnic groups, the problem can be even worse – non-pharmacological pain interventions may not be culturally acceptable and, therefore, these patients may not experience pain relief.

Soumitri Sil, PhD, Director of the Pediatric Psychology Clinic at the Aflac Cancer and Blood Disorders Center, received a \$6 million grant from Helping to End Addiction Long-term (HEAL) Initiative to address this issue. Dr. Sil and team are developing and testing a new pain management intervention for adolescents with chronic pain related to sickle cell disease, a disease that primarily affects Black and African Americans in the U.S.

With the funding, Dr. Sil will gather feedback from patients, families and community healthcare workers to form advisory boards on how best to modify an existing intervention for another chronic pain condition, juvenile fibromyalgia, to meet the unique needs of adolescents with chronic sickle cell pain. As a group-based, telehealth intervention made up of mind-body, cognitive-behavioral and neuromuscular movement treatment components, the existing tool will form the basis of a new multicomponent integrative intervention specifically tailored for sickle cell disease to reduce pain and increase engagement in daily activities.

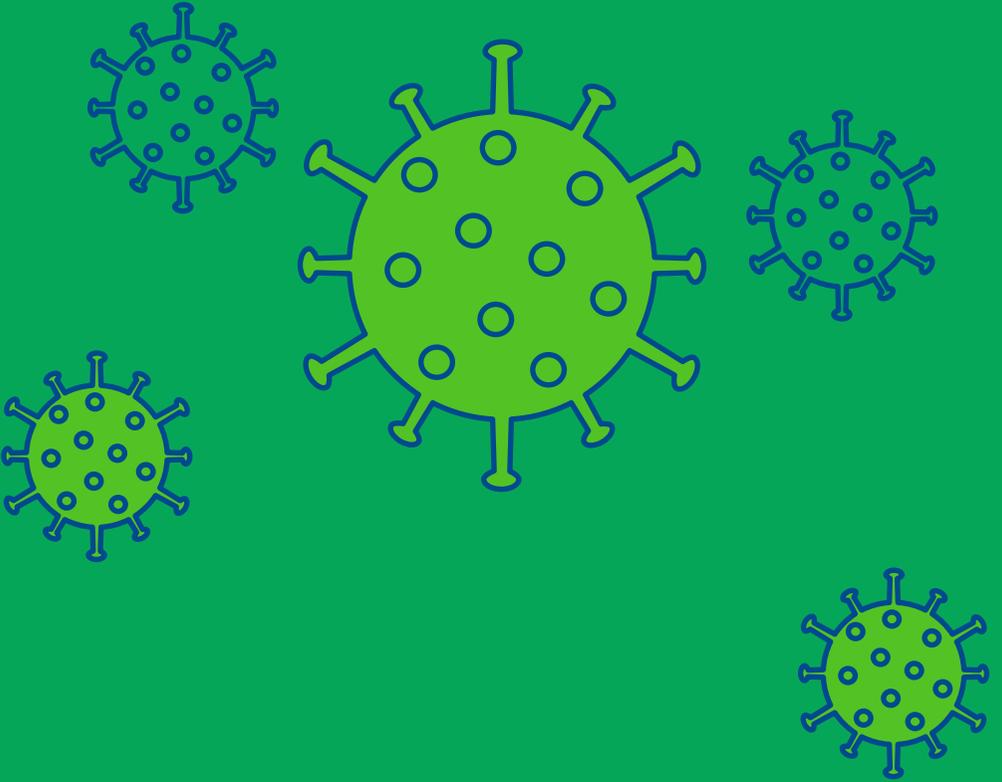


Soumitri Sil, MD

Next, Dr. Sil will lead a pilot test of the intervention to optimize its feasibility and acceptability based on multiple iterations of the group treatment. Once the final intervention is established, she will conduct a randomized trial of 150 adolescents across three sites to evaluate its effectiveness.

“Our work will fill a critical scientific gap – which is the availability of an evidence-based, multicomponent integrative intervention package for chronic sickle cell disease pain,” says Dr. Sil, who is also an Associate Professor of Pediatrics at Emory. “It is innovative because it is culturally tailored to individual family needs, targets psychological co-morbidities that are often excluded in clinical trials and utilizes telemedicine to enhance treatment access and delivery.”





Overcoming COVID-19

Clarifying the Relationship Between Myocarditis and COVID-19 Vaccination

Is the risk of myocarditis after COVID-19 vaccination greater than the vaccine's benefits?

Matthew Oster, MD, MPH, Pediatric Cardiologist at the Children's Heart Center and Associate Professor of Pediatrics at Emory, led a descriptive study to understand the risks and outcomes of myocarditis – which is inflammation of the heart from viral infection -- after mRNA-based COVID-19 vaccination with Moderna and Pfizer.

Dr. Oster examined data from the Vaccine Adverse Event Reporting System, a national early warning system to detect possible safety problems in vaccines licensed in the U.S., through the U.S. Centers for Disease Control and Prevention. This data was collected from more than 190 million individuals ages 12 and up in locations across the country from December 2020 to August 2021.

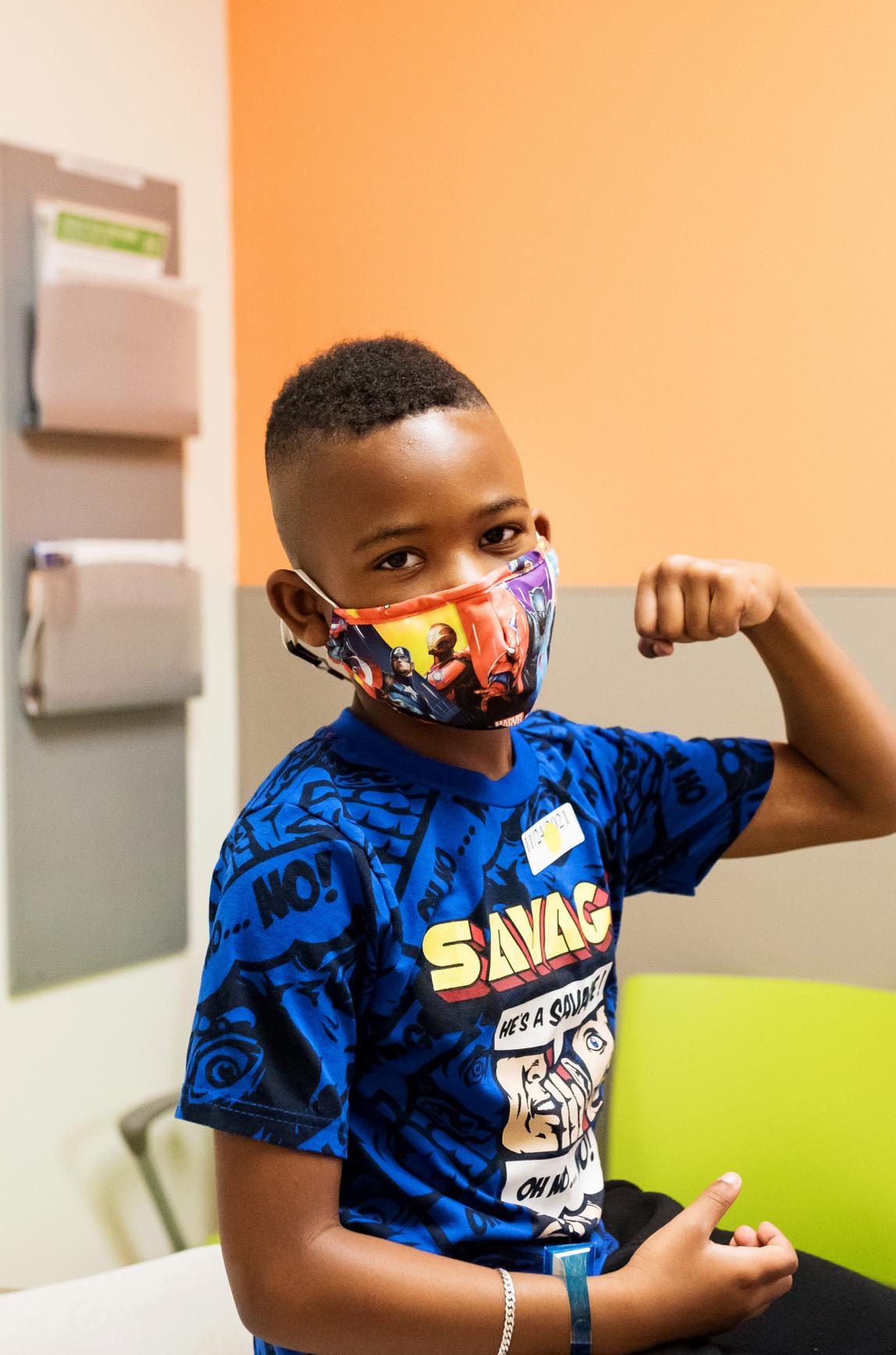
Results showed only 1,991 reports of myocarditis, which means less than 0.01% of those vaccinated met the case definition for the condition. Of those cases, rates of myocarditis were highest after the second vaccination dose in adolescent and young adult men, particularly those ages 16-17. The study was published in the *Journal of the American Medical Association*.



Matthew Oster, MD

"Myocarditis typically occurs after a viral illness," says Dr. Oster. "However, in rare instances, our analysis confirmed that the mRNA COVID vaccine can also be a trigger for myocarditis."

Because the occurrence of myocarditis after COVID-19 vaccination is so rare, Dr. Oster urges that "the benefits of COVID-19 vaccination continue to outweigh any potential risks, including myocarditis."



Testing a Pill to Treat Kids at High Risk for Severe COVID-19

The oral antiviral medication Paxlovid has been proven to be effective in treating individuals with mild-to-moderate COVID-19. But is it also a safe and useful treatment for children under 18 who are at high risk for progression to severe COVID-19 or who may have an underlying medical condition?

That's the question physicians at Children's are seeking to answer by serving as a testing site for a global clinical Phase 2 safety and efficacy trial of Paxlovid. Under the leadership of Pediatric Emergency Medicine Physicians Mark Griffiths, MD, and Claudia Morris, MD, Children's is one of 60 sites testing 140 patients for 18 months. Participants will receive a five-day course of Paxlovid within 72 hours of diagnosis and undergo a series of blood draws to determine the pharmacometrics of the drug in the blood.

"At Children's, we have nearly every demographic you could possibly want in one healthcare system to complete this study to determine if this COVID-19 therapy should be made widely available to children," said Dr. Griffiths, who is also the Medical Director of the Children's Healthcare of Atlanta Hughes Spalding Emergency Department and an Assistant Professor of Pediatrics at Emory. "We' have the people. We have the resources. We have the affiliations."

To be eligible for the trial, children under 18 must have a positive COVID-19 test result and be considered at high risk for progression to severe COVID-19, including hospitalization or death, as determined by their care providers. This may include patients with underlying medical conditions like asthma, obesity or diabetes, those receiving chemotherapy, and those taking immune-suppressant drugs.

While only 1.9% of patients hospitalized with COVID-19 are children, their symptoms are often different and can include more gastrointestinal issues or the development of MIS-C, as opposed to respiratory concerns that are more common in other COVID-19 patients. According to Dr. Griffiths, "The hope is that this will provide evidence for an effective treatment that can be taken as soon as parents know their child is positive to prevent worsening symptoms leading to hospitalization."

Dr. Morris is also a Professor of Pediatrics and Emergency Medicine at Emory.



Mark Griffiths, MD



Claudia Morris, MD

Becoming the Nation's Innovation Funnel Validation Center for Diagnostics

The NIH's National Institute of Biomedical Imaging and Bioengineering (NIBIB) selected Children's, Emory and Georgia Tech to lead the newly established NIBIB Innovation Funnel Validation Center. The Center seeks to accelerate healthcare diagnostic innovations for a variety of high-priority diseases over the next five years.

To start, principal investigators Wilbur Lam, MD, PhD, Pediatric Hematologist/Oncologist at Aflac Cancer and Blood Disorders Center, and Greg Martin, MD, MSc, Pulmonologist, Intensivist and Professor of Medicine at Emory, received more than \$8 million in NIBIB grant funding to validate diagnostics focused on maternal health, monkeypox and hepatitis C. "These conditions affect a very large number of people, and by accelerating the validation and availability of new diagnostic and monitoring technologies related to them, there is the highest potential to improve the health of individuals and the public," said Dr. Martin. "By deploying our team to work first in these areas, we have the potential to help newborns, children, young adults and older adults for generations to come."



Wilbur Lam, MD, PhD

The Validation Center will provide technical and clinical validation services by verifying prototype technologies against key performance and design metrics. Working in collaboration with the NIBIB's Innovation Funnel Coordination Center and Commercialization Center, the Validation Center will aim to rapidly transform early, innovative technologies into widely accessible medical tests.

Together, the centers will function similarly to the NIH's Rapid Acceleration of Diagnostics (RADx) Tech program, which began shortly after the pandemic started. Heading the lead validation center, Drs. Lam and Martin worked to accelerate COVID-19 diagnostics, which resulted in the first Emergency Use Authorization for an over-the-counter test and to date has helped bring millions of COVID-19 tests to Americans.



Greg Martin, MD, MSc

"As the Validation Center for the NIH's new innovation funnel initiative, we'll be able to leverage all of our personnel, test validation processes and diagnostic know-how that we developed for RADx and apply them to other diseases and clinical conditions and diagnostic technologies," said Dr. Lam, who is also Professor of Pediatrics at Emory and Georgia Tech. "Because of our work since the beginning of the pandemic, we can take the 'best of' everything we developed for RADx and nimbly apply them to whatever diagnostic technologies the NIH needs us to validate."

Predicting Drug Resistance Mutations to HIV, Hepatitis B Virus and Coronavirus

Continuous exposure to drugs can render them ineffective. This phenomenon – called drug pressure – can create viral mutations that result in individuals experiencing drug resistance. It is a global problem hindering the long-term effectiveness of antiviral drugs to treat human immunodeficiency virus (HIV), hepatitis B virus and SARS-CoV-2 or coronavirus. To understand the mechanism of resistance and to suggest a promising treatment strategy to counter it, the ability to identify these mutations early on is essential.

To accomplish this, a team of drug discovery experts developed a computational workflow to predict drug resistance mutations for any viral proteins where the structure is known. Led by Raymond F. Schinazi, PhD, DSc, Frances Winship Walters Professor of Pediatrics at Emory, and Dharmeshkumar Patel, PhD, Instructor at Emory, the team used this methodology to predict resistance mutations in HIV and demonstrated accurate identification of the clinical mutations. They also predicted resistance mutations in hepatitis B virus and in SARS-CoV-2. Finally, they conducted mutagenesis experiments which corroborated the accuracy of the predictions.

Published in *Molecules*, their findings revealed that this approach could be used to develop drug treatment strategies for different antiviral agents quickly and more effectively.

“Until now, predicting mutations selected by antiviral agents in humans was not possible without first performing labor intensive cell-based assays which can take weeks to months to complete,” said Dr. Schinazi. “Using this novel approach provides results within days with surprising accuracy.”





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Homing in on Prevention, Treatment and Practice

A Very Low Sugar Diet May Benefit Teens with Nonalcoholic Fatty Liver Disease

Over the past several decades, nonalcoholic fatty liver disease (NAFLD) – a disease of fat metabolism in the body that results in excess storage of fat in the liver – has grown from being rare in children to the most common reason they are referred to specialty liver clinics.

With a team of supporting researchers, Miriam Vos, MD, MPH, Pediatric Hepatologist at Children's and Professor of Pediatrics at Emory, is studying the clinical needs of this condition, including better diagnostics, therapeutics and prevention. While it is well established in the scientific literature that diet plays a major role in NAFLD, which nutrients make the most difference and how fat is increased and decreased is not as well understood.

To shine a light on the key nutrients involved, Dr. Vos and her team conducted a study in collaboration with Jeffrey B. Schwimmer, MD, of the University of California at Berkeley, to determine if children who have NAFLD can reduce their liver fat if placed on a very low sugar diet.

With funding from the National Institute of Diabetes and Digestive and Kidney Diseases of the NIH, the investigators studied adolescent boys diagnosed with NAFLD and followed them for eight weeks. Half of participants were assigned a very low sugar diet and the other half remained on their usual diet. The researchers then measured how much new fat was being made within the liver, both before and after the very low sugar diet.

Results showed that synthesis in the liver of new triglycerides, a type of fat the body makes or obtains from food, decreases significantly when dietary sugars are reduced. Findings also demonstrated that a decrease in fat synthesis was most likely responsible for the decline in liver fat. Furthermore, insulin resistance and weight both improved in parallel with decreased fat synthesis. The study confirmed the pathological link between NAFLD and excessive sugar in the diets of children and was published in the *Journal of Clinical Investigation*.



NAFLD research team: Karla DeSantos RD, Julia Tisheh, Meera Shah, MD, Jean Welsh, RN, MPH, PhD, Miriam Vos, MD, MPH, Risha Nayee, MPH, Elizabeth Sinclair, RD and Irene Pyo.

Because of the high-impact results, Dr. Vos and co-investigator, Jean Welsh, PhD, RN, MPH, Research Director of Children’s Strong4Life and Associate Professor of Pediatrics at Emory, received a five-year \$2.5 million grant from the NIH’s National Institute of Nursing Research to conduct a new prevention-based study to test if reducing sugar earlier in childhood can diminish the onset of NAFLD, or reduce the severity of the disease in children who are highly susceptible due to genetics.

“As difficult as it is to for a child or teen to significantly limit their sugar consumption, these findings suggest that doing so may one day reduce the number patients we see with fatty liver disease,” says Dr. Vos. “After a decades-long rise in those patients, that would be a great day.”

Comparing Treatment Methods for Early Onset Scoliosis

Scoliosis is a curve in the spine, which appears like a “C” or “S” from the back and is the most common spinal abnormality in children. In early-onset scoliosis, the curve is greater than 10 degrees before a child reaches the age of 10.

Joshua Murphy, MD, Orthopedic Surgeon at Children’s, led a retrospective study looking at early onset scoliosis patients with growing rods. Working in collaboration with Nicholas Fletcher, MD, Orthopedic Surgeon at Children’s and Associate Professor of Orthopedic Surgery at Emory, and several spine surgeons, Dr. Murphy and team examined how the insertion of growing rods affects pelvic tilt and sagittal plane spinal-pelvic form. Historically, there are two ways to obtain control of early onset scoliosis using growing rods: fixation to the spine or fixation to the pelvis.

Results, published in *Spine Deformity*, showed distal fixation to the pelvis treated with growth-friendly instruments, compared to spine-based fixation, was associated with an average decrease in pelvic incidence of 12.3 degrees over a two-year treatment duration. Although follow up studies are needed to determine the long-term implications of the findings on pelvic and spinal development, Dr. Murphy believes these results point to what may ultimately be a more optimal method of distal fixation in these patients.



Joshua Murphy, MD

Advancing Best Practices to Help Kids Who Need a Heart Transplant

Children in need of a heart transplant often require a mechanical circulatory support device, also known as a ventricular assist device, while awaiting their new heart. This device helps pump blood from the lower chambers of the heart to the rest of the body so that the heart produces enough blood flow.

Pediatric cardiologists around the nation differ on the amount of time a child should use a surgically implanted ventricular assist device prior to heart transplantation. To better understand what amount of time produces the best outcomes for kids, William T. Mahle, MD, Chief of Children's Heart Center and Professor of Pediatrics at Emory, and Arene Butto, MD, Pediatric Cardiologist at Children's and Assistant Professor of Pediatrics at Emory, conducted a retrospective analysis comparing children who were on the device for less than a month with those who were on it for a month or longer.

The cardiac researchers looked at length of hospital stay after transplantation and one-year survival in more than 1,000 patients over the course of eight years. They found that patients who were on the device for 30 days or more were more likely to survive for at least a year, and published their findings in the *Journal of Heart and Lung Transplantation*. Drs. Mahle and Butto indicate that follow-up studies using additional databases are needed to determine more exact recommended timing for transplantation after using a ventricular assist device.

"When children receive a ventricular assist device, they can be more active, participate in rehabilitation programs and improve their nutrition," says Dr. Mahle. "This may explain the benefit of giving children time to recover after their ventricular assist device implant before undertaking a heart transplant."



William T. Mahle, MD



A Research Enterprise Positioned for Growth

An open letter from Research Leaders at Children's Healthcare of Atlanta

While effectively meeting and overcoming the challenges presented by a global pandemic, the Children's and Emory pediatric research enterprise has also completed the first half of a bold five-year strategic growth plan, established in 2020, to recruit 30 new investigators and 45 medical residents and pediatric subspecialty fellows, and to accelerate research in seven critical areas. We are also now beginning a national recruitment effort to attract a new Chief Research Officer and are more dedicated than ever to addressing emerging infectious diseases, behavioral and mental health and diversity and inclusion. In addition to our research growth plan, we have also recruited a new chief of behavioral and mental health and received a donation of 10 acres of space and two office buildings specifically to address this crisis in pediatrics. Furthermore, Emory will open a new biomedical research facility with dedicated pediatric research space in early 2023, and Children's is on target to bring research from the bench to the bedside at Arthur M. Blank Hospital in fall 2024.

As our research portfolio and extramural funding continue to grow, we are well positioned to enhance our national reputation as one of the leading pediatric research partnerships in the country, especially in these seven critical areas:

- **Pediatric technologies** focuses on microsystems-engineered point-of-care technologies, nanomedicine for pediatric cancers and technology-enabled tissue engineering, such as 3D printing and bioprinting, often in collaboration with engineers at the Georgia Institute of Technology.
- **Health disparities research** includes outcomes and population-based research, growing our Sickle Cell Disease Program, and behavioral and mental health initiatives.
- **Sickle cell disease research** highlights stem cell biology, the basis for blood formation; cellular therapies, including stem cell transplant and gene-based therapy; and drug discovery and development, including small molecules and biologicals. We are recruiting "game changing" faculty to lead and support this effort.
- **Behavioral and mental health research** enhances behavioral and mental healthcare, improves access to community resources, pioneers prevention through innovative programs, and builds a strong foundation through leadership recruitment and partnerships.
- **Cell therapies research** involves rapid translation of "homegrown" discoveries into early phase clinical trials in our newly established Marcus Center for Pediatric Cellular Therapy.
- **Clinical informatics research** accelerates the development of evidence-based practices and their implementation into clinical care by partnering with frontline doctors and nurses, data analysts and electronic health record (EHR) developers.
- **Bioinformatics research** nurtures next-generation genome and large biological data driven discoveries for better treatment of complex and heterogeneous diseases.

We are proud to share with you these examples of some of the exciting work that reflects our progress. As we look to the future, we will continue to leverage our nationally leading clinical volumes and the unique Atlanta collaboration of Children's, Emory University and Georgia Tech to improve the health of children in Georgia, across the nation and around the world.



Clinton H. Joiner, MD, PhD
Chief Research Officer,
Children's Healthcare of Atlanta
Shary and Matt Price Chair for Pediatric Research,
Children's and Georgia Institute of Technology
Professor and Vice Chair for Research,
Emory University Department of Pediatrics



Melinda M. Downs, MPA, CRA
Vice President,
Research and Academics
Children's Healthcare of Atlanta

INFORMATION



Children's
Health



Notable National Awards and Distinctions

- **Wanda Barfield, MD, MPH (Neonatology):** AAP Virginia Apgar Award, American Academy of Pediatrics
- **Ann Chahroudi, MD, PhD (Infectious Diseases):** Elected Member, American Society for Clinical Investigation
- **Sofia Chaudhary, MD (Emergency Medicine):** Advocacy Award, American Academy of Pediatrics Section on Emergency Medicine
- **Joanna Goldberg, PhD (Pulmonology):** Elected At-Large Board of Directors, American Society for Microbiology
- **Saul Karpen, MD, PhD (Hepatology):** Elected Councilor, American Association for the Study of Liver Diseases
- **Gagan Kooner, MD (Emergency Medicine):** 2021 Mike Koran Scholar Award, Society of Pediatric Urgent Care
- **Wilbur Lam, MD, PhD (Hematology/Oncology):** Elected Member, American Institute for Medical and Biological Engineering College of Fellows
- **Rachel Linneman, MD (Pulmonology):** Screening Improvement Program Award, Cystic Fibrosis Foundation
- **David O'Banion, MD (Neurology):** Young Physician of the Year Award, American Academy of Pediatrics Georgia Chapter
- **Jeffrey Okonye, MD (Emergency Medicine):** Outstanding Research Presentation Award, Third Place, National Medical Association conference
- **Brenda Poindexter, MD (Neonatology):** Chair, Leadership Committee for the American Academy of Pediatrics Women in Neonatology Group, American Academy of Pediatrics
- **Saidie Rodriguez, MD (Cardiology):** 2022 National Compassionate Caregiver of the Year, Schwartz Center for Compassionate Healthcare
- **Ritu Sachdeva, MD (Cardiology):** Chair-Elect, Adult Congenital & Pediatric CV (ACPC) Section Leadership Council of the American College of Cardiology
- **Steve Simoneaux, MD (Radiology):** President, Society for Pediatric Radiology
- **Dan Wechsler, MD, PhD (Hematology/Oncology):** Chair, ABP Subboard of Hematology/Oncology, American Board of Pediatrics



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