WINTER 2022

DELIVERING ON A PROMISE

Code Break:

New alliance provides hope for genetic neurological diseases

THE UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER

Le Bonheur Children's Hospital

ALL HEART

Heart Transplant Program celebrates five years, 50th transplant

17-year-old Ella Morrissey received the 50th heart transplant at Le Bonheur on Dec. 5, 2021.

Lyric Everhart was Le Bonheur's first heart transplant patient. Now 7 years old, she recently celebrated the fifth anniversary of receiving her new heart.

Le Bonheur Children's Heart Institute recently performed its 50th heart transplant and also celebrated the fifth anniversary of performing its first.

17-year-old Ella Morrissey from Overland Park, Kan., is recovering well after receiving the Heart Institute's 50th heart transplant on Dec. 5, 2021. Diagnosed with hypertrophic cardiomyopathy (HCM) at age 10, Ella managed her condition through medications and an implantable cardioverter defibrillator (ICD) to prevent cardiac arrest. After an intense bout of arrhythmia that required four shocks from her ICD, Le Bonheur cardiologists determined that Ella needed a heart transplant.

"We could not be more thrilled to be celebrating five years as a Heart Transplant Program here at Le Bonheur," said Le Bonheur President Michael Wiggins, DBA, FACHE. "Our team's dedication to children has allowed them to save 50 children with new hearts in the past five years. With the collaborative effort of our doctors, staff, donors and entire Le Bonheur family, we will be able to continue to provide a vital service to our region."

The first heart transplant at Le Bonheur was 20-month-old Lyric Everhart who received her new heart on Oct. 22, 2016. A team of surgeons who performed the transplant were led by Surgical Director of the Heart Transplant and Ventricular Assist Device Program Umar Boston, MD, Co-director of the Heart Institute Christopher Knott-Craig, MD, and Executive Co-director of the Heart Institute, Chief of Pediatric Cardiology and Medical Director of Cardiomyopathy, Heart Failure and Heart Transplant Services Jeffrey A, Towbin, MD.

Lyric was born with idiopathic dilated cardiomyopathy and after six weeks of waiting, she became the first patient to receive a heart transplant at Le Bonheur. Within two days of her surgery, Lyric was brushing her teeth, playing with dolls and blowing bubbles. Today, Lyric is a thriving 7 year old.

Le Bonheur Children's Hospital

Le Bonheur Children's Hospital in Memphis, Tenn., treats more than 250,000 children each year in regional clinics and a 255-bed hospital that features state-of-the-art technology and family-friendly resources. Our medical staff of more than 240 physicians provide care in 45 subspecialties.

LE BONHEUR LEADERSHIP

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Jon McCullers, MD – *Pediatrician-in-Chief*
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Code Break

New alliance provides hope for genetic neurological diseases

On Dec. 23, 2016, the U.S. Food and Drug Administration (FDA) approved the first successful genetic intervention for spinal muscular atrophy (SMA) — a genetic neurological condition that was then the No. 1 genetic killer of infants.

It was the first glimmer that scientists could "break the genetic code" and address underlying causes of disease, not just resign themselves to keeping babies comfortable in their short lives.

New discoveries seemed possible, but they would require a higher level of collaboration and partnership among physicians and scientists. Those at Le Bonheur, the University of Tennessee Health Science Center (UTHSC) and St. Jude Children's Research Hospital were ready to take advantage of the opportunity.

"We know there are new discoveries in basic sciences that are close to having a real impact for children with neurologic disorders," said Le Bonheur Neuroscience Institute Co-director James Wheless, MD. "The time is right for us to play a large role in translating these discoveries to treatments for patients as quickly as possible."

In a new collaborative effort, Le Bonheur's Neuroscience Institute and the St. Jude Pediatric Translational Neuroscience Initiative (PTNI) will partner to provide basic research, clinical trials and multispecialty care that will rapidly deliver new therapies to children living with genetic neurologic diseases. For many of these children, it is their first, best chance at a better quality of life — or even at surviving into adulthood.

Charleigh Jones was the first child at Le Bonheur to receive Zolgensma — the first gene therapy for children with spinal muscular atrophy (SMA) type 1 younger than 2 years. Now she's meeting basic childhood milestones that were previously unheard of for children with SMA type 1.

THE VISION

A neurologist by training, J. Paul Taylor, MD, PhD, director of the St. Jude Pediatric Translational Neuroscience Initiative, had experienced firsthand the pessimistic view that neurologic diseases were

untreatable. But he saw this starting to change.

"I could see that a revolution was coming with many therapies in the works for previously untreatable diseases," he said. "So, we designed the Pediatric Translational Neuroscience Initiative to leverage and build upon the experience and infrastructure of St. Jude. Our aim was to address catastrophic pediatric neurological disorders and speed up the time from basic research to therapeutics."

Genes for many pediatric neurological diseases were identified in the last 35 years, and the gene responsible for SMA was uncovered in 1995. Years of basic science discovery followed to determine what mutations occurred, the mechanisms of the disease and how to deliver gene-targeted therapies. But this plethora of basic research was not being translated quickly into treatments for children and adults, Taylor said.

To bridge the gap between basic research and treatments, Taylor knew he already had a partner with clinical care expertise in Memphis — Le Bonheur's Neuroscience Institute and its renowned epilepsy program.

In the past few years, Le Bonheur's Chief Neurologist Wheless, Taylor and Le Bonheur Pediatrician-in-Chief Jon McCullers, MD, who also serves as senior executive associate dean of Clinical Affairs at UTHSC, explored a new collaborative framework. By working together, they hope to leverage the strengths of each institution — translating basic research into treatments or even cures for children with devastating genetic neurologic diseases as quickly as possible.

"The St. Jude oncology model is unparalleled in its ability to conduct clinical trials for rare diseases that bring the latest treatments to children around the globe," said Wheless. "And we have the clinical care expertise and programs to support

Le Bonheur's Neuroscience Institute provides the clinical care expertise and programs to support children with neurological disease as a part of the research partnership with St. Jude. At right, Co-director of the Neuroscience Institute James Wheless, MD, sees a patient in neurology clinic.

children with neurological disease and conduct clinical trial protocols specific to those diseases."

The collaborative effort will initially focus on two major categories of neurological disease — neuromuscular conditions, including SMA and Duchenne muscular dystrophy (DMD), and genetic epilepsies such as Dravet syndrome. The existing infrastructure for clinical trials through the Children's Foundation Research Institute at Le Bonheur allows a unique focus on rare diseases with smaller patient populations.

"Our goal is fluid integration and doing the best by the patient," said Wheless. "We will focus on translating research into cures as quickly as possible through clinical trials and high-level clinical care."

J. Paul Taylor, MD, PhD, is director of St. Jude Children's Research Hospital's Pediatric Translational Neuroscience Initiative and has worked with Le Bonheur's Neuroscience Institute to create a new collaborative framework to bring treatments to children with neurologic diseases.

THE RESEARCH

The collaborative research effort will focus on moving discoveries across the continuum from basic science to clinical trial protocols conducted at both St. Jude and Le Bonheur.

Through PTNI, basic research will be led by Peter McKinnon, PhD, in the newly-formed St. Jude Center for Pediatric Neurological Disease Research. Clinical research will be led by Pediatric Neurologist Richard Finkel, MD, through the St. Jude Center for Experimental Neurotherapeutics. Finkel was recruited to St. Jude in 2020 to lead the clinical arm of the center. Finkel is an international expert in SMA and has more than 30 years in translational research into the biology and treatment of neurological disorders.

The goal: accelerate the translation of that research into therapies for kids.

The collaboration will also have a unique opportunity to develop, participate in and coordinate the earliest clinical trials for genetic therapies at Le Bonheur and St. Jude. The collaborators will work with external stakeholders, including pharma and biotech companies, to provide insights on the best ways these trials should be conducted.

"Important work is behind all clinical trials. That's not as flashy as being the first therapy for a disease," said Taylor. "Some of the trials will work to optimize how therapies are used or provide readiness for clinical trials by identifying biomarkers, registries and severity scales that are necessary for a trial to even take place."

Wheless has already initiated protocols for clinical trials at Le Bonheur for genetic epilepsies, through its well-established epilepsy program. One of the most imminent treatments that will be a focus of the collaboration is a gene-targeted treatment for Dravet syndrome.

"We're already participating in trials for novel

"Our ultimate goal is to combine what works best to push the envelope on moving treatments forward."

James Wheless, MD, Co-director of the Neuroscience Institute

genetic treatments for Dravet to determine if we can give patients an infusion to tweak and repair their genetic code," said Wheless.

Neuromuscular disease clinical trials will be conducted out of Le Bonheur's Muscular Dystrophy Association (MDA)/Neuromuscular Clinic. Led by Le Bonheur Neurologist Elena Caron, MD, the clinic will host clinical trials at Le Bonheur and provide expert clinical care in coordination with Finkel, who is recognized as a pioneer of many of the clinical trials leading to FDA approval of the first genetic therapy for SMA.

"Our ultimate goal is to combine what works best to push the envelope on moving treatments forward," said Wheless. "Some protocols will take place at St. Jude, and some will integrate at Le Bonheur. But no

Le Bonheur Neuroscience Co-director James Wheless, MD, sees 3-year-old McCall Wright in neurology clinic. McCall is one of many children with Dravet syndrome who relies on clinical trials held at Le Bonheur and is waiting for a gene-targeted treatment for the syndrome to become widely available.

A Beacon of Hope

Le Bonheur participates in clinical trial for Dravet syndrome

Dravet syndrome, a rare genetic epilepsy previously only managed by treating symptoms, causes seizures and developmental delays. Thanks to a new clinical trial, Le Bonheur is investigating a novel potential therapy to address the genetic root of Dravet syndrome. This is the first disease-modifying therapy to ever be in clinical trials for Dravet syndrome.

A defective SCN1A gene, which controls production of a specific protein needed for movement of sodium within brain cells that is critical to proper brain function, causes Dravet syndrome. Where most people have two functioning copies of this gene, children with Dravet have only one. The new, genetically-based therapy works by modifying the production of the functioning gene to produce up to twice as much protein in an effort to restore protein levels to a more functional degree.

The delivery system is called TANGO — targeted augmentation of nuclear gene output — and is delivered into the spinal fluid via lumbar puncture.

"Potential treatments like this are a paradigm shift — in the past we could only treat the symptoms," said Wheless. "Now we can target the underlying genetic issue."

matter what, we're all talking and collaborating to do what's best for this patient population."

THE CARE

Patients who come to Memphis to participate in clinical trials on either campus have a range of unique clinical care needs.

"Patients undergoing protocols for new therapies have clinical needs that Le Bonheur can partner with St. Jude to handle," said Wheless. "We have the multispecialty clinics already well established that can handle the plethora of needs these patients have."

For example, Finkel oversees St. Jude protocols at Le Bonheur's MDA/Neuromuscular Clinic for children who have clinical needs beyond the scope of the trial. Since this clinic is already set up with Le Bonheur providers from multiple specialties, patients can participate in a trial and have medical needs related to their condition coordinated in one visit.

Patients will also be screened for eligibility in the Le Bonheur clinics for any of the protocols underway in the collaboration. Whether the protocols take place through Le Bonheur or St. Jude, the children will be cared for according to what best meets their needs.

In addition to clinical care, Le Bonheur has the wide array of neuroimaging techniques needed to provide the best imaging possible for these conditions.

"We are pleased to be able to share our high-level technology resources," said Wheless. "With transcranial magnetic stimulation (TMS), high-density EEG (hdEEG) and the latest generation of magnetoencephalography (MEG), we can provide cutting-edge brain imaging and

Le Bonheur Neurologist Elena Caron, MD, (right) is director of the MDA/Neuromuscular Clinic. This clinic will host clinical trials for neuromuscular diseases and coordinate clinical care for children who are part of the trials.

MCCALL WRIGHT, 3
Dravet Syndrome
Loganville, Ga.

For many, a long wait in the doctor's office is a source of aggravation. But for McCall Wright, it led to a life-changing diagnosis.

Prior to a well-child visit, 4-month-old McCall and her mother, Nicole, spent more than an hour in their pediatrician's waiting room in Lexington, S.C., which was atypical for the organized office. When they were finally able to speak with the doctor, McCall started experiencing something unusual: her arm rhythmically bent and jumped on its own.

Her pediatrician quickly recognized this as a seizure and immediately called an ambulance to take McCall to the local children's hospital.

"I never would have thought it was a seizure, and if we hadn't waited so long in the doctor's office I might never have seen or recognized it," said Wright. "Right then the walls started closing in — my perfectly healthy, happy girl was on the way to the emergency room."

What followed were months of neurologist visits trying to capture the seizures that continuously eluded EEG testing. Unsatisfied with the diagnosis of general epilepsy, Nicole and her husband Justin kept advocating for their daughter to find out more.

After genetic testing and a referral to Le Bonheur Neuroscience Institute Co-director James Wheless, MD, McCall was diagnosed with Dravet syndrome, a lifelong genetic epilepsy characterized by seizures and a deterioration in development. She's one of many children who depend on the types of clinical trials conducted through the collaborative research effort underway among Le Bonheur, St. Jude Children's Research Hospital and the University of Tennessee Health Science Center in order to have better seizure control.

At 2 years old, McCall participated in the Fenfluramine trial at Le Bonheur, which proved successful in improving her seizure control and overall condition. After joining the trial, she went four months without a seizure, the longest seizure-free period in her life. In addition, her development increased by leaps and bounds since starting the medication.

"Our comprehensive Dravet program participates in all the clinical trials available, allowing McCall earlier access to new therapies," said Wheless. "Without clinical trials, access to this treatment could be delayed several years — a lifespan for someone her age."

Three-year-old McCall Wright was diagnosed with Dravet syndrome within her first year of life. Her parents hold on to the hope that one day this syndrome can be treated on a genetic level.

"At first we hoped [a genetic cure] would happen in her lifetime, but now we see that this treatment could be available for McCall in a matter of years."

Nicole Wright, McCall's mother

And now she is a part of the Envision study, an observational study of children with Dravet syndrome. The Wrights record their daughter's seizures and have regular appointments for evaluation. The hope is that this study will uncover more information about the disease, how it affects caregivers and avenues for potential therapies for the future.

Her family is holding out hope that a genetic cure is coming soon for McCall. When she was diagnosed, Dravet syndrome was a lifelong sentence. But rapid innovations show that advanced treatments are on the horizon.

"At her diagnosis, Dr. Wheless told us this is a lifelong genetic condition, so we prayed that a genetic cure would be found before she loses any quality of life," said Nicole. "At first, we hoped this would happen in her lifetime, but now we see that this treatment could be available for McCall in a matter of years."

Wheless is hopeful that forthcoming genetic therapies will treat the underlying genetic problem for McCall and children like her providing seizure control and improved development. Through the collaborative research partnership, this therapy would be able to take place at Le Bonheur Children's with her current care team.

Clinical trials and new medications have been instrumental to improving and preserving McCall's well-being and quality of life, said the Wrights. Plus they know that McCall's participation and input can help other children get adequate treatment in the future.

"Find a specialist you can trust and communicate with well," Nicole says to parents considering a clinical trial for their child. "We're confident we have found the very best in Dr. Wheless and his team to help us make decisions for McCall's benefit."

McCall Wright at a clinic appointment with Neuroscience Institute Co-director James Wheless, MD.

Genetic Neurological Diseases Under Research

The collaborative research partnership will focus on addressing the genetic root of neurological diseases. At present, the focus will be on the following diseases:

- **Dravet Syndrome**
- **Duchenne's Muscular Dystrophy (DMD)**
- **Spinal Muscular Atrophy (SMA)**
- **Charcot-Marie-Tooth (CMT) Inherited Neuropathies**
- **Friederich's Ataxia**

Bench to Bedside: *Bringing research developments directly to patients*

1 Basic researchers explore the mechanisms of genetic epilepsy at a cellular and genetic level through St. Jude's Center for Pediatric Neurological Disease Research.

2 Clinical trials are conducted through Le Bonheur and St. Jude clinics to bring basic research discoveries to children through new medications and therapies.

3 Children receive continuous follow-up care for their neurologic condition and related health needs through Le Bonheur's Neuroscience Institute.

Pediatric Neurologist Richard S. Finkel, MD, (pictured below) director of St. Jude's Center for Experimental Neurotherapeutics, will conduct clinical trial protocols at Le Bonheur's MDA/Neuromuscular Clinic. Finkel is recognized as a pioneer of many of the clinical trials leading to FDA approval of the first genetic therapy for SMA.

analysis of brain connections for all children who are treated through this collaboration."

THE FUTURE

Taylor and Wheless say they hope the collaboration ultimately moves the needle for pediatric neurology therapies in Memphis, the country and the world. The partnership will bring more complex patients to Le Bonheur's campus, elevating research and clinical discoveries to improve the lives of children with devastating neurological disorders.

Le Bonheur will handle clinical care for children who are a part of clinical trials through the research partnership. In addition, Le Bonheur provides the neuroimaging needed for their care, including the latest generation of magnetoencephalography (MEG) technology – TRIUX™ Neo.

Furthermore, this collaborative effort also has implications for patients down the road as they begin to outlive their current life expectancies.

"With many of these diseases, children die young or have significant development issues," said McCullers. "If we're able to significantly treat these diseases, we have an entirely new set of issues to address if they live to adulthood that we haven't seen before."

The hope is that these forthcoming therapies will change thinking in the medical community that neurological diseases are untreatable.

"The collaboration has the potential to enhance care and research protocols on both sides of the street," said Wheless. "We're fortunate to partner with an organization where we can raise standards of care together and challenge each other to discover, test and deliver the most innovative care for the patients who depend on us."

"We're fortunate to partner with an organization where we can raise standards of care together and challenge each other to discover, test and deliver the most innovative care for the patients who depend on us."

James Wheless, MD, Co-director of the Neuroscience Institute, speaking about shared programs with St. Jude Children's Research Hospital

Le Bonheur Children's Hospital
PEDS POD

Genetic Epilepsy: Finding a Cure

Co-director of the Neuroscience Institute James Wheless, MD, explains the difference between genetic epilepsies and other epilepsies children might have, how parents can find out if their child has a genetic epilepsy and treatment options available. Listen at lebonheur.org/podcast or wherever you get your podcasts.

PERFECT HARMONY

Le Bonheur is first in region to perform pulmonary valve replacement for tetralogy of Fallot via catheterization using newly FDA-approved Harmony valve

Tony and Karyn Tanner of Bossier City, La., knew that this day was coming sooner rather than later for their 17-year-old daughter Madi.

Born with tetralogy of Fallot (TOF), a congenital heart defect that changes the flow of blood through the heart, she needed a pulmonary valve replacement, a necessary intervention for TOF patients as they reach their teens.

Until recently, open-heart surgery for valve replacement was the only option for Madi and children like her. But thanks to a new device — the Harmony Transcatheter Pulmonary Valve (TPV) system — Le Bonheur Medical Director of the Interventional Catheterization Laboratory Shyam Sathanandam, MD, FSCAI, can conduct pulmonary valve replacement for TOF patients through a minimally-invasive catheterization procedure. Le Bonheur is the first hospital in the region to offer this device and procedure.

Le Bonheur Medical Director of the Interventional Catheterization Laboratory Shyam Sathanandam, MD, FSCAI, prepares the Harmony pulmonary valve for 17-year-old patient Madi Tanner. Le Bonheur is the first hospital in the region to perform pulmonary valve replacement via catheterization using this devicve.

The TPV system is the first FDA-approved, minimally-invasive therapy for pulmonary valve replacement for children with TOF who had transannular patch repair as an infant. Previous expandable valves did not fit the anatomy of patients with TOF repair. The new device functions by reestablishing efficient blood flow from the right ventricle to the lungs.

"This valve is a game changer for patients who need a pulmonary valve replacement as it will prevent TOF patients from needing multiple open-heart surgeries throughout their lives," said Sathanandam.

Madi was diagnosed with TOF at 2 days old. She had her first open-heart surgery for TOF repair at 4 months and at 4 years old had a stent placed in her left pulmonary artery. Since then, she has been able to live a full, fun and active life. Still, she and her parents knew that once her heart was fully grown she'd need another open-heart surgery for pulmonary valve replacement.

At an annual MRI appointment, her cardiologist in Shreveport, La., decided it was time for the valve replacement to take place. But he had a new suggestion: undergo a minimally-invasive catheterization procedure for a valve replacement at Le Bonheur's Heart Institute. Having trained at Le Bonheur, the cardiologist knew he could be continually involved in conversations with Sathanandam throughout Madi's procedure and recovery.

"We asked our cardiologist, 'If this was your child where would you have this procedure?'" said Karyn. "He told us to go to Le Bonheur where he trusted all the cardiologists, knew them all and had worked with them all. That sealed the deal for us."

Throughout October, Madi and her family made several journeys to Le Bonheur to have cath procedures to remove her existing stent and prepare for the new valve.

Finally, on Oct. 25, Sathanandam conducted a cath procedure to put the new valve in place. During the procedure, blood flow was blocked to Madi's left lung, so he also placed a stent at the top of the valve — making Madi the only person in the world with a Harmony valve with a stent through it.

Madi Tanner (front right) with the nurses and staff who cared for her while at Le Bonheur for her cath procedure for pulmonary valve replacement. Born with tetralogy of Fallot, pulmonary valve replacement was a necessity. Thanks to a new device, Madi had the replacement via catheterization instead of open-heart surgery.

Less than a week later, Madi was at home in Louisiana celebrating Halloween with friends and family — something that would have been impossible with an open-heart procedure.

"This valve is a game changer for patients who need a pulmonary valve replacement as it will prevent TOF patients from needing multiple open-heart surgeries throughout their lives."

Shyam Sathanandam, MD, FSCAI, Le Bonheur Medical Director of the Interventional Catheterization Laboratory

"Currently, open-heart surgical valve implantation is the primary treatment option for kids like Madi, but this new valve and its minimally-invasive procedure covers many TOF patients who have the initial TOF repair operation," said Sathanandam. "Typically, these patients require multiple heart surgeries throughout their lives for valve replacements. Now, there is a good chance they won't need any more operations beyond the initial repair surgery as a child."

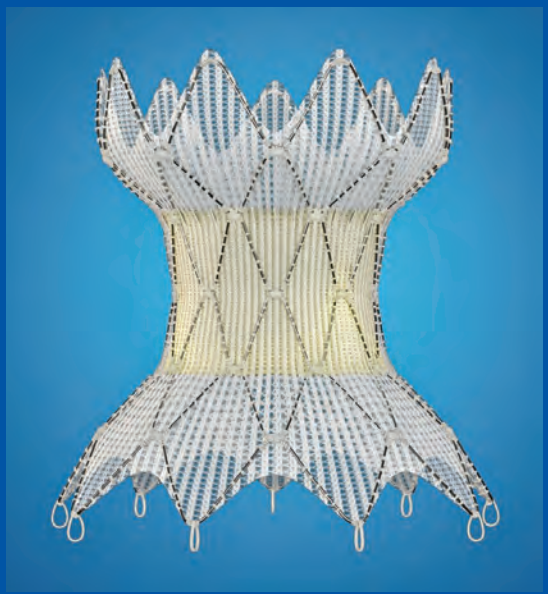
Since her valve replacement, Madi has had two ECHOs that showed excellent blood flow in her heart. And her parents felt lighter knowing that she didn't have to face the risks associated with open-heart surgery.

Madi will continue to have follow-up close to home with her own cardiologist, who is in communication with Sathanandam on Madi's progress. In the meantime, she can go back to enjoying her junior year of high school as an honor student with a talent for art and theater.

"Madi can take any heavy situation, even a valve replacement, and find the fun in it," said Karyn. "We felt like Le Bonheur took us in — from nurses putting Madi at ease by singing with her through needle sticks to staff offering to go shopping to get us necessities."

And Sathanandam is grateful to have another option to help this patient population who previously had to undergo risky open procedures for valve replacement. Because of these risks, valve replacement was put off as long as possible until the heart reached near failure.

"Now with this simple technique, we can replace the valve much earlier, before the heart fails," said Sathanandam. "This opens up a new frontier for future management of these patients: future percutaneous valves can be implanted within this valve."



At Le Bonheur's Heart Institute, the Harmony Transcatheter Pulmonary Valve (TPV) system pictured above is delivered via catheterization for tetralogy of Fallot patients in need of pulmonary valve replacement. This eliminates the need for open heart surgery for this patient population.

NICUSeq Study: Swift, Affordable Access to Whole-Genome Sequencing Could Enable Greater Diagnostic Equity

Photo credit: Mark Weber/The Daily Memphian

Le Bonheur Chief of Genetics Chester W. Brown, MD, PhD, recently co-authored a study about the impact of clinical whole-genome sequencing (cWGS) on diagnosis and care for critically-ill infants. Brown is now working with the state of Tennessee to make cWGS available to all critically-ill infants.

Le Bonheur was one of five children's hospitals in the nation to participate in a randomized clinical trial, coordinated by scientists from Illumina, Inc., to determine the effect of clinical whole-genome sequencing (cWGS) on clinical management of critically-ill newborns in the U.S. Le Bonheur Genetics Division Chief Chester W. Brown, MD, PhD, led the hospital's investigation efforts and has co-authored a study with Illumina and fellow Le Bonheur and University of Tennessee Health Science Center (UTHSC) investigators. Findings show that using cWGS outperforms the current standard of care twofold for critically-ill newborns suspected of having a genetic condition, both in terms of diagnostic efficacy and change of clinical management. Findings from the "NICUSeq Randomized Time-Delayed Trial" were recently published in *JAMA Pediatrics* and include data supporting the widespread adoption and implementation of cWGS for critically-ill newborns.

"The NICUSeq study has shown us the importance of large-scale genetic testing in newborns, leading to early diagnosis of genetic conditions and helping to inform decision making for physicians and families," said Brown, who also holds the St. Jude Chair of Excellence in Genetics at UTHSC.

A total patient population of 354 critically-ill newborns representing diverse ethnicities were enrolled in the study, which took place at four sites in addition to Le Bonheur — Children's Hospital of Philadelphia, Children's Hospital & Medical Center in Omaha/University of Nebraska Medical Center, Children's Hospital of Orange County/Rady Children's Institute for Genomic Medicine and St. Louis

Children's Hospital/Washington University. The newborns were randomized to receive cWGS results within either 15 or 60 days of evaluation for a suspected genetic condition, with a total observation period of 90 days. In both the early (15 days) and delayed (60 days) arms of the study, access to cWGS doubled the number of patients who received a precision diagnosis and corresponding change in clinical management.

> ***"The NICUSeq study has shown us the importance of large-scale genetic testing in newborns, leading to early diagnosis of genetic conditions and helping to inform decision making for physicians and families."***
>
> Le Bonheur Chief of Genetics Chester W. Brown, MD, PhD

Study findings complement a growing body of literature demonstrating that cWGS leads to more focused, and therefore improved, patient care and should be considered a primary tool when assessing critically-ill newborns with a suspected genetic condition. Results also suggest that swift, affordable access to cWGS may help reduce health care disparities by enabling greater diagnostic equity, as the study mirrored the real-world variables affecting patient care. The NICUSeq findings support the widespread adoption and implementation of cWGS as a first-line genetic test for critically-ill newborns, increasing the probability of greater diagnostic accuracy and potentially life-saving care changes.

The next step is to determine how to implement the findings from the NICUSeq study into clinical standards of care, which poses some challenges, says Brown. He is currently part of a state-wide initiative to make medical genetic services, including cWGS and other genetic testing, readily accessible to all Tennesseans with rare genetic disorders.

"Having this type of genetic information provides immediate and sustainable benefits that have lifelong value, providing a genetic 'report card' that can be used to help direct medical care throughout life," said Brown. "We are proud that Le Bonheur Children's Hospital and UTHSC were able to contribute to this important effort to help improve medical care for babies of the greater Memphis community."

In a recent study, clinical whole-genome sequencing (cWGS) for critically-ill newborns doubled the ratio of patients who received a precision diagnosis and corresponding change of clinical management.

COLLABORATION AND COMMUNITY

Centralized Pediatric Fellowship Office unites, advances fellowship programs

Former Le Bonheur Infectious Disease Specialist Joan Chesney, MD, CM, saw an opportunity to improve the infrastructure, curriculum and experience for fellowship programs at Le Bonheur Children's in the University of Tennessee Health Science Center (UTHSC) Department of Pediatrics. By uniting the programs in a centralized fellowship office, she could bridge gaps among programs and create a true community of fellows.

At the time, each pediatric fellowship program operated semi-autonomously, often working in silos. To mitigate this, Chesney worked with Le Bonheur Pediatrician-in-Chief Jon McCullers, MD, and previous Le Bonheur President and CEO Meri Armour in 2016 to create the Pediatric Fellowship Office — funded by Le Bonheur and the UTHSC Department of Pediatrics — with the intention of neutralizing imbalances among programs through a centralized administrative design.

"We wanted to standardize certain elements of the fellowships," said McCullers. "Some of the largest fellowships had more developed programming than smaller or newer fellowships. Developing an overarching office allowed sharing among programs and would address some imbalances so that all were able to operate at a high level."

Chesney retired in 2020 but left the legacy of the centralized fellowship office. Now led by Pediatric Cardiologist Michael Rebolledo, MD, MBA, MPH, director, and Jayme McGrail, administrative coordinator, the Pediatric Fellowship Office aims to create a centralized point of contact for pediatric fellows and help them navigate campus resources throughout their fellowship training.

> ***"Through our centralized office, we can focus on large-scale issues common to all pediatric fellowship programs and create a more uniform experience for fellows."***
>
> Michael Rebolledo, MD, MBA, MPH,
> Director of the Pediatric Fellowship Office

"Fellowships must meet uniform GME [Graduate Medical Education] requirements that can be difficult for smaller programs to accomplish," said Rebolledo. "Through our centralized office, we can focus on large-scale issues common to all pediatric fellowship programs and create a more uniform experience for fellows."

Michael Rebolledo, MD, MBA, MPH, educates first-year fellows on quality improvement and patient safety. Rebolledo is director of the Pediatric Fellowship Office.

Le Bonheur Hospital Medicine Fellow Mary Katherine Hood, MD, examines a patient. The centralized fellowship office allows fellows to connect outside of clinical time and better coordinate care within the hospital.

MUTUAL BENEFITS

The Pediatric Fellowship Office organizes all aspects of the fellowship experience outside of subspecialty medical training on behalf of the 20 programs that are part of the centralized administrative model. This includes everything from professional development to recruitment efforts to research training, which has proven to provide benefits for all entities involved in the fellowship experience — from program directors to the hospital to the fellows themselves.

In this centralized model, program directors from each fellowship can collaborate and synchronize recruitment, including interviewee feedback and marketing strategies. Regular meetings among all program directors allow discussion about fellowship issues in a collective manner with the intention to benefit from each other's ideas and efforts.

"Previously the program directors weren't getting in the same room," said McGrail. "Our monthly program director meetings allow them to ask the question 'How can I advance or better my program?'"

A centralized office positively impacts care in the hospital, too, as the community created among fellows allows for better coordination of care. Previously fellows may have shared patients and never known they were providing care alongside another fellow. Now they are able to connect with each other within the hospital.

And that community also positively impacts fellows' mental and emotional health. Since fellows spend several years in training, it's important for them to have community and friendship in order to focus clinically, and it's hard to do a good job if you're lonely, says McGrail.

Pediatric Fellowship Office Staff

Michael Rebolledo, MD, MBA, MPH
Director

Jayme McGrail
Administrative Coordinator

Joan Chesney, MD, CM
Founder and Director
Chesney retired from Le Bonheur in 2020.

Former Le Bonheur Allergy/Immunology Fellow Amy Ragsdale, DO, examines a patient in Le Bonheur's Allergy Clinic.

"The centralized office has successfully fomented a sense of connection between fellows from different programs that may not have occurred organically without the office," said McCullers.

In addition to making lifelong friends, the Pediatric Fellowship Office provides a centralized place to connect fellows with the right resource at the right time. Navigating resources can be challenging, especially for fellows who come from outside the UTHSC system, says Rebolledo. The office also provides opportunities for fellows to present their research. And the additional support from a central office fosters collaboration among fellows — whether in clinical care, research or socially.

"The centralized office could put me in contact with the right people and provide me with information about many more opportunities that are available to fellows," said former Le Bonheur Allergy/Immunology Fellow Amy Ragsdale, DO. "I was able to collaborate with other specialties in my research, too, and see what other fellows were doing for their projects."

A UNIQUE DESIGN

Preparing fellows to become specialists requires more than just medical training. The Pediatric Fellowship Office organizes a Noon Conference series for personal and professional development, teaching skills that will transfer beyond the fellowship experience. Topics covered include professionalism, interviewing skills, personal finance, CV preparation, managed care and more.

"Attending Noon Conferences has helped me from an overall career perspective. They go beyond the scope of what we learn in fellowship medical training to actual career building," said Noel Joseph, MD, a current Critical Care Medicine fellow. "Fellowship training is a lot about the medicine, but the centralized office takes care of things that doctors might not think about when thrust into the real world."

Community and wellness are also important pieces of the Pediatric Fellowship Office's role. The centralized format provides an avenue to build friendships and have support outside of training. In addition, the office recently established a new wellness committee for all pediatric fellows, run by the fellows themselves with the purpose of providing regular opportunities to unwind and spend time with other fellows outside of the hospital. And a huge part of wellness is building connections and friendships during training, says McGrail.

"In fellowship training it's easy to stay in your own little world and be isolated in your specialty," said Ragsdale. "The centralized office provided that extra layer of support so that you don't work alone — you can meet people outside of your specialty and gain support from other fellows."

To execute a successful recruitment season, the Pediatric Fellowship Office develops a coordinated recruitment strategy among all programs.

For example, during the interview process McGrail meets with each prospective fellow to highlight the Pediatric Fellowship Office's resources and address specific questions. And the feedback is encouraging. Potential fellows are surprised by the centralized format and express that Le Bonheur is the only place they are interviewing with such an office, says McGrail.

Following interview season, McGrail and Rebolledo are able to collect and aggregate specific program feedback from applicants to implement during upcoming recruitment seasons. This past interview season the office hosted a virtual open house to provide potential fellowship candidates an opportunity to hear about Le Bonheur's culture and life in Memphis — as virtual visits are still required due to COVID-19 safety precautions.

"The Pediatric Fellowship Office allows us to more effectively recruit the very best candidates and then complement their training programs so they have a truly exceptional educational experience," said Le Bonheur President Michael Wiggins, DBA, FACHE.

A scholarly activity with a demonstrable work product is a key requirement of a fellowship. To assist with this training, the Pediatric Fellowship Office developed Research Week — a research "boot camp" free from clinical responsibilities for first-year fellows to learn core academic competencies for conducting research and to meet with mentors about their prospective research projects. The Fellows Grants Program is also administered through the Pediatric Fellowship Office and coordinated by McGrail. This merit-based internal grant award provides support for fellows who require funding for their research projects.

"Having the overarching office has allowed for development of added programming like Research Week that no single fellowship could have done on its own," said McCullers. "The baseline research education is a huge boon to all the fellowships as it provides basic knowledge and experience and connects fellows to the appropriate resources."

Research Week provides first-year fellows the opportunity to learn core academic competencies for conducting research and time to meet with their mentors about their projects. Above, fellows had the opportunity to hear from a panel of Le Bonheur researchers during 2021 Research Week.

SURVEYING THE FELLOWSHIP LANDSCAPE

To determine an overview of the landscape of fellowship offices across the country, McGrail and Rebolledo, with former Le Bonheur Scientific Editor Courtney Bricker-Anthony, PhD, recently published the article "Creating Value: Many Roles of a Centralized Pediatric Fellowship Office" in *Academic Pediatrics*. The intent of the article was to determine how frequently a centralized administrative model is used for fellowship programs and to better understand some of the barriers to implementation at other institutions.

"Not much has been published on fellowship office administrative models, and we wanted to build on the limited literature available," said Rebolledo. "Through this paper, we're also able to share the lessons we learned during the development of our own centralized fellowship office."

McGrail and Rebolledo conducted a survey of designated institutional officials from children's hospitals that ranked among the "Best Children's Hospitals" in *U.S. News & World Report* for 2019-20. The six-question survey asked which fellowship programs were offered at their institution and if they used a centralized pediatric fellowship office model.

Among survey respondents, 54% utilized a centralized fellowship office model. And of those who did not, 78% had considered developing a centralized fellowship office. The greatest barriers to achieving this model were satisfaction with the

current structure and difficulty achieving buy-in from stakeholders. The paper shared Le Bonheur and UTHSC's framework for a centralized office and the benefits they have seen from this model in just a few short years.

"Among our survey sample, a centralized pediatric fellowship administrative model is not only feasible but commonly utilized," said Rebolledo. "A centralized office can reduce overlap and streamline shared processes eliminating inefficiencies."

THE FUTURE OF LE BONHEUR FELLOWSHIPS

In just a short few years, the Pediatric Fellowship Office has been able to add multiple initiatives to the fellowship program

Former Le Bonheur Cardiology Fellow Karan Karki, MD, (left) reviews ECHOs with Le Bonheur Cardiologist Hugo Martinez, MD. After completing his fellowship, Karki joined Le Bonheur's Heart Institute as a cardiac critical care intensivist.

experience — a recruitment focus, coordination of marketing and post-interview surveys to name a few. The next goal: become more involved in and better support research for fellows.

"We've grown so much in just a short period of time," said Rebolledo. "We incorporate feedback to deliver high yield topics to our fellows in various formats including practical workshops."

Recently, the Pediatric Fellowship Office implemented Fellows Research Day — an opportunity for fellows to present their research and receive feedback from other fellows and UTHSC faculty — and additional opportunities to present research through the Children's Foundation Research Institute, Le Bonheur's research arm.

Ultimately, Rebolledo and McGrail aim to be a resource for fellows and program directors, provide a cohesive fellowship experience and build robust fellowship programs that emphasize collaboration and community. In the two to three years of pediatric fellowship, they make sure fellows' time is used efficiently and that fellows stay on track to meet their key milestones.

And former fellows can attest to the value of a centralized fellowship office.

"I continue to have the support of my fellowship and stay in contact with my attendings," said Ragsdale. "My experience as a fellow at Le Bonheur prepared me to be on my own but never made me feel like I was alone."

Creating Value: Many Roles of a Centralized Pediatric Fellowship Office

Academic Pediatrics

The survey was sent to 83 designated institutional officials (DIOs) among ranked children's hospitals in *U.S. News & World Report* 2019-20. Fifty DIOs completed the survey.

Outcomes:

- **54%** used a centralized fellowship office; **40%** did not use a centralized fellowship office; **6%** selected other
- Among those without a centralized fellowship office, **78%** had considered developing a centralized fellowship office, while **22%** had not.
- Among those with a centralized fellowship office, the governance structure was most commonly the Department of Pediatrics (66.7%) and Graduate Medical Education (GME) (51.9%) followed by hospital administration (11.1%) and other (8.4%)
- Funding source was most commonly the Department of Pediatrics (66.7%) and hospital administration (40.7%) followed by GME (33.3%) and other (11.1%)

PROFILE: PAUL KLIMO, JR., MD, MPH

Le Bonheur chief of Pediatric Neurosurgery named Neuroscience Institute co-director

In his decade-plus career as a boundary-breaking pediatric neurosurgeon, the success of Paul Klimo, Jr., MD, MPH, originates from two qualities: curiosity and the hunt for a challenge.

His exposure to the medical profession began early in his childhood when his father, a medical oncologist, took him on weekends to the hospital to make rounds. To satisfy his growing curiosity about all things medicine, Klimo would spend time looking through his father's old surgical textbooks. But it was during medical school at the Medical College of Wisconsin (MCW) where he developed his passion for neurosurgery.

Paul Klimo, Jr., MD, MPH

"My initial curiosity in neurosurgery was a result of two events. The first was exposure to the beauty of neuroanatomy," said Klimo. "The second was unrelated to the first. Nearly everyone who I talked to about neurosurgery as a career told me to steer clear — too long, too hard, terrible lifestyle, patients never get better, etc."

"For me, the most rewarding part of being a neurosurgeon at Le Bonheur has and will always be the honor of taking care of children and their families through difficult times. I want to be the person and the place that physicians and families turn to when they are told by others that 'Nothing more can be done.' or 'We don't have the experience.'"

Paul Klimo, Jr., MD, MPH

Their words, ironically, were an instant challenge to Klimo. To further satisfy his interest, he shadowed Glenn Meyer, MD, a neurosurgeon at MCW, and was instantly hooked. He loved the complexity and intricacy of the operations, the often high-pressure and high-risk scenarios that it offered and most importantly, the ability to make lives of patients better.

Klimo completed his neurosurgery residency at the University of Utah in 2005, followed by a fellowship in pediatric neurosurgery at Boston Children's Hospital/ Harvard University.

"It's a little funny ... when I first rotated on the pediatrics service as a junior resident, I wasn't too interested. But when I did my senior rotation, something just clicked. I loved taking care of kids and interacting with families," said Klimo on why he chose pediatrics. "For some kids, I'll get to be their doctor for years and sometimes even into adulthood, which is truly a special privilege."

The breadth of diversity in pediatrics is unmatched compared to other areas of neurosurgery, says Klimo. He enjoys all aspects of pediatric neurosurgery, but has special interests in brain and spinal cord tumors, vascular disorders, cranio-synostosis, hydrocephalus/ neuroendoscopy and neurotrauma. He joined the faculty at Semmes Murphey/The University of Tennessee Health Science Center (UTHSC) Department of Neurosurgery in 2010.

But before coming to Memphis, Klimo's ambition led him toward a new challenge after he finished all his medical and neurosurgical training — as a neurosurgeon with the United States Air Force (USAF). Although he grew up in Vancouver, Canada, he was born in Madison, Wis., and always had a desire to return to the U.S. and serve his country. Klimo joined the USAF just prior to medical school and, after completion of all his medical training,

served on active duty for four years stationed at Wright-Patterson Air Force Base in Dayton, Ohio. As part of his active duty, he completed a six-month tour in Afghanistan in support of Operation Enduring Freedom. During his time in the military he received numerous awards and medals, receiving an honorable discharge in June 2010 at a rank of lieutenant colonel (select).

Now, after more than a decade of service at Le Bonheur, Klimo was recently named co-director for Le Bonheur Children's Neuroscience Institute. In this role, he will serve alongside Pediatric Neurologist James Wheless, MD, providing vision and leadership for the Neuroscience Institute, specifically in the area of pediatric neurosurgery. Klimo is also chief of the Division of Pediatric Neurosurgery, a professor at UTHSC and a chief of the pediatric neurosurgery division at St. Jude Children's Research Hospital.

Le Bonheur Neurosurgeon Paul Klimo, Jr., MD, MPH, was recently named co-director of the Neuroscience Institute. His vision for the Institute is to offer cutting-edge technology, bring in the best neurosurgeons and provide the most up-to-date and highest quality care.

He plans to continue expanding and strengthening the already robust programs in Le Bonheur's pediatric neurosurgery division.

"My vision for pediatric neurosurgery is to provide the best and most comprehensive care for children with neurosurgical diseases — offering cutting-edge technology, recruiting top-notch neurosurgeons and providing the most up-to-date and highest quality care," said Klimo.

Le Bonheur's pediatric brain tumor program, conducted in partnership with St. Jude Children's Research Hospital, will continue to be a major focus for Klimo. With close to 200 brain tumor surgeries yearly, it is already one of the highest volume programs in the country, but Klimo hopes to grow that number as much as possible. He wants to continue building upon existing well-established programs, such as epilepsy, and offer new multi-disciplinary services and technology such as spasticity/cerebral palsy, brain stimulation for dystonia and epilepsy and focused ultrasound techniques.

"In the last decade, the trend is to be less invasive in surgery as long as you can do things as well or better, and I think that quest will continue," said Klimo on the future of pediatric neurosurgery. "For neuro-oncology,, we will continue unlocking the molecular mysteries of various tumors that will better shape our surgical approach and treatment."

In addition to his new role in the Neuroscience Institute, Klimo will continue to conduct his award-winning research, train residents and fellows and mentor students. Klimo has approximately 200 peer-reviewed publications, including two consecutive Paper of the Year Awards from the Congress of Neurological Surgeons.

"For me, the most rewarding part of being a neurosurgeon at Le Bonheur has and will always be the honor of taking care of children and their families through difficult times," said Klimo. "I want to be the person and the place that physicians and families turn to when they are told by others that 'Nothing more can be done.' or 'We don't have the experience.' I cannot be more excited for the opportunity to lead pediatric neurosurgery forward here in Memphis, nationally and globally."

Paul Klimo, Jr., MD, MPH

Education and Training
Medical College of Wisconsin – Medical School
University of Utah – Internship in General Surgery and Residency in Neurosurgery
University of Utah – Masters of Public Health
Boston Children's Hospital – Pediatric Neurosurgery Fellowship

Board Certifications
American Board of Pediatric Neurosurgery
American Board of Neurological Surgery

Society Memberships
Diplomat, American Board of Pediatric Neurosurgery
Diplomat, American Board of Neurological Surgeons
Congress of Neurological Surgeons (CNS)
American Association of Neurological Surgeons (AANS)
AANS/CNS Pediatric Section
American Society of Pediatric Neurosurgery
Tennessee Neurosurgical Society

Awards and Honors
2019 Pediatric Paper of the Year Award, CNS Annual Meeting
2018 Pediatric Paper of the Year Award, CNS Annual Meeting
United States Air Force Surgical Excellence Award
United States Air Force Clinical Excellence Award – Field Grade Category

SURGICAL DIVIDE:

THE HUNT FOR HAEC

Le Bonheur fellow develops novel scoring system for HAEC diagnosis

In the largest study to date reviewing Hirschsprung-associated enterocolitis (HAEC) diagnostic scoring systems, Le Bonheur Pediatric Surgery Fellow Ruth A. Lewit, MD, MPH, published a novel scoring system for HAEC in the *Journal of Surgical Research*. This new scoring system may help reduce the rate of underdiagnosis of HAEC, allowing for earlier diagnosis and treatment of patients. Of the 369 episodes of HAEC reviewed in the study, 173 (46%) met the diagnostic cutoff for the new score but did not meet cutoffs for previous scoring systems used for HAEC.

Le Bonheur Pediatric Surgery Fellow Ruth A. Lewit, MD, MPH, developed a new diagnostic scoring system for Hirschpsrung-associated enterocolitis (HAEC) in an effort to reduce underdiagnosis of HAEC.

"Improved diagnosis of HAEC has the potential to reduce hospital admissions, limit morbidity and improve outcomes," said Lewit. "This novel scoring system for HAEC has several advantages over previous scoring systems, but most importantly may help reduce the rate of underdiagnosis of HAEC."

Two scoring systems exist for diagnosing HAEC: the Pastor score, published in 2008, and the Frykman score, published in 2018. The accuracy of these scores, however, is limited due to their restrictive nature, and neither has been widely adopted in clinical practice. Lewit and her team aimed to develop a new diagnostic tool that provided better utility and diagnostic accuracy in a clinical setting.

For the purpose of this study, an HAEC diagnosis was defined as treatment consisting of antibiotics, bowel rest and rectal irrigations. This study evaluated the existing HAEC systems and developed a new scoring system by evaluating 1,450 encounters with 200 patients and 369 HAEC episodes at four centers worldwide. The Pastor and Frykman scores were retrospectively calculated for each episode, and Lewit identified six variables to include in the new scoring system.

The variables that are significantly associated with diagnosis of HAEC — fever, bloody diarrhea, obstipation, distention, dilated loops of bowel on x-ray and leukocytosis — were used to create a new score. When reviewing HAEC episodes through the Pastor and Frykman scores, 46% did not meet their criteria but did meet the cutoff for the new score. This suggests that 46% of patients would have been underdiagnosed with HAEC using the previous scoring systems.

"The new scoring system offers several advantages," said Lewit. "The new score includes signs that are frequently seen in HAEC, maximizes sensitivity compared to previous scoring systems and is simple and designed specifically to be used in a clinical setting."

Further study is needed to externally validate the new score before implementing clinically on a wide scale.

> ***"Improved diagnosis of HAEC has the potential to reduce hospital admissions, limit morbidity and improve outcomes. This novel scoring system for HAEC has several advantages over previous scoring systems, but most importantly may help reduce the rate of underdiagnosis of HAEC."***
>
> Ruth A. Lewit, MD, MPH, Le Bonheur Pediatric Surgery Fellow

Le Bonheur researchers are working to improve diagnosis and treatment for children born with gastrointestinal congenital anomalies.

Uncovering mortality and diagnosis inconsistencies in pediatric surgery

CLOSING THE GLOBAL MORTALITY GAP

Le Bonheur surgeon publishes research on improving global neonatal surgical outcomes

Children born with gastrointestinal congenital anomalies are eight times more likely to die in low-income countries and four times more likely to die in middle-income countries than children with the same conditions in high-income countries, says research published in the *Lancet* by the Global PaedSurg Research Collaboration. Le Bonheur Pediatric Surgeon and Director of Surgical Research at the University of Tennessee Health Science Center Ankush Gosain, MD, PhD, contributed to the study as a member of the collaboration.

Le Bonheur Pediatric Surgeon and Director of Surgical Research at the University of Tennessee Health Science Center Ankush Gosain, MD, PhD, contributed to a recent study that examined the gaps in neonatal care for children between low- and middle-income countries compared to high-income countries for children born with gastrointestinal congenital anomalies.

In order to reach the United Nations Sustainable Development Goal to end preventable deaths of children and neonates younger than 5 years by 2030, access to quality neonatal surgical care must improve in low- and middle-income countries (LMICs).

"In order to meet this goal, the study showed that dramatic improvements in access to care, guidelines and policies need to be made in LMICs to care for children with gastrointestinal congenital anomalies and allow them a chance at life," said Gosain.

The study focused on outcomes of the seven most common congenital anomalies — esophageal atresia, congenital diaphragmatic hernia, intestinal atresia, gastroschisis, exomphalos, anorectal malformation and Hirschprung's disease. The study examined 3,849 patients with 3,975 study conditions from 264 hospitals in 74 countries. Total mortality rates were 38.9% in low-income countries, 20.4% in middle-income countries and 5.6% in high-income countries. Country income status was associated with the highest risk of mortality. Several other barriers showed a wide discrepancy among high-, middle- and low-income countries including age at presentation, distance patients traveled from home to study hospital and access to parenteral nutrition.

Other results included:

- Chance of dying from a gastrointestinal congenital anomaly is two in five in a low-income country, one in five in a middle-income country and one in 20 in a high-income country.
- Leading causes of death were sepsis and respiratory failure.
- Higher mortality in LMICs was associated with sepsis at presentation, higher ASA (American Society of Anesthesiology) score at primary intervention and need for blood transfusion and ventilation.
- Many patients in LMICs do not have routine components of care including antenatal diagnosis, birth at a pediatric surgery center, effective resuscitation, timely ambulance transfer, use of surgical safety checklist, physician anesthetist at primary intervention and basic neonatal intensive care unit resources.

The results of the study shed light upon the stark differences in care for patients in LMICs further demonstrating that these patients do not receive the same neonatal surgical care that is essential and routine in high-income countries.

"Studying gastrointestinal congenital anomalies outcomes in these LMICs brings further attention to the wide disparities showing the neglect of surgery in the global health field. A focus on neonatal surgery has been almost non-existent and is needed to push the mortality rate down in LMICs," said Gosain.

Researchers hope the results of this study can provide the information necessary to create policies and guidelines to advocate for neonatal surgical care within national surgical obstetric plans developed in LMICs.

> ***"Studying gastrointestinal congenital anomalies outcomes in these LMICs brings further attention to the wide disparities showing the neglect of surgery in the global health field. A focus on neonatal surgery has been almost non-existent and is needed to push the mortality rate down in LMICs."***
>
> Ankush Gosain, MD, PhD, Le Bonheur Pediatric Surgeon and Director of Surgical Research at the University of Tennessee Health Science Center

A Better Map

Study: TMS is safe, effective in young children

Transcranial magnetic stimulation (TMS) is safe, reliable and effective to map motor, speech and language function in young children with refractory epilepsy or a brain tumor, according to research published in *Frontiers in Neurology* by Le Bonheur Neuroscientist and Director of the TMS Laboratory Shalini Narayana, MS, MBBS, PhD. In 47 TMS motor mapping sessions, motor cortices were successfully mapped in 90% of children younger than 3 years old, and in 13 TMS language mapping sessions, language areas were located in 92% of children ages 5 to 6 years old. This is the largest known study reporting TMS mapping of motor cortices in toddlers and language cortices in preschool children. TMS maps can be used for presurgical planning to preserve language and motor function and provide a baseline for post-surgical changes in these functions.

"Accurate presurgical mapping of motor, speech and language cortices, while crucial for neurosurgical planning and minimizing post-operative functional deficits, is challenging in young children with neurological disease," said Narayana. "Our data show that TMS can be a useful tool in mapping eloquent cortices in children with epilepsy or a brain tumor."

TMS provides several advantages for mapping the language and motor areas of the brain in young children. Mapping is still possible with TMS even when patients are unable to fully cooperate due to disease or developmental delay. TMS is non-invasive, never requires sedation, does not require the patient to remain still and can be guided by previous MRI scans. For all of these reasons, TMS is a promising method for brain mapping for a young child for whom other methods, such as magnetoencephalography (MEG) and functional MRI (fMRI), have been unsuccessful. Without a viable functional mapping method, surgical options that could greatly improve cognitive function and quality of life may be delayed.

This study was a retrospective review of TMS motor and language mapping studies at Le Bonheur. Forty-seven motor mapping sessions were performed with 36 children younger than 3 years old and were successful in locating the motor cortex in 90% of children. TMS was also used to assess the risks and benefits of surgery in 11 children with lesions near the motor cortex. TMS results were used in the surgical navigation system, and motor function was preserved or improved in nine of the 11 children who underwent surgery. Two children had mild, predicted weakness after surgery.

Le Bonheur Neuroscientist and Director of the TMS Laboratory Shalini Narayana, MS, MBBS, PhD, (left) conducts transcranial magnetic stimulation (TMS) with a 5-year-old patient. Her research shows TMS to be safe, reliable and effective in brain mapping this young age group.

A separate cohort of 13 children ages 5 and 6 underwent TMS language mapping, and language areas in the temporal lobes were localized in 92%. Seven of these children underwent surgery, and the TMS results provided a presurgical baseline and were used on the surgical navigation system. Post-operatively, none of the children were found to have speech or language deficits.

Overall, TMS was well-tolerated by most children and described as painless. About 20% of the children undergoing motor mapping experienced seizures during or immediately after TMS. All of the children who experienced seizures had a history of refractory epilepsy with frequent seizures, and seizures during or after TMS were consistent with their typical seizure pattern and deemed not to be directly caused by TMS.

"In our study, TMS was safely applied in young children with serious epilepsy syndromes," said Narayana. "All our data so far indicate that the use of TMS in children is safe and effective."

Le Bonheur Pediatric Cardiologist Jason Goldberg, MD, MS, (front left) consults with the cardio-oncology team members. Goldberg published research that could help physicians identify heart function problems in children who receive hematopoietic cell transplantation.

BEATING HEARTS, BEATING CANCER

Association of persistent tachycardia with early myocardial dysfunction in children undergoing allogenic hematopoietic cell transplantation

Children undergoing hematopoietic cell transplantation (HCT) have high rates of tachycardia, or fast heart rates, which were associated with the development of systolic and diastolic myocardial dysfunction, according to research published in *Bone Marrow Transplantation* by Le Bonheur Pediatric Cardiologist Jason Goldberg, MD, MS, and colleagues. University of Tennessee Health Science Center and Le Bonheur Heart Institute cardiologists care for children who receive

cancer therapy at St. Jude Children's Research Hospital. This research can help clinicians more closely evaluate and identify issues with heart function among children who receive HCT.

"We have to understand the early risk factors for development of cardiac dysfunction in pediatric HCT as we know that recipients of HCT during childhood are at increased risk of accelerated cardiovascular morbidity and mortality later in life," said Goldberg.

The study reviewed 80 pediatric patients who had allogenic (non-self) HCT between 2015 and 2019 at St. Jude Children's Research Hospital. All patients had echocardiograms at baseline (within 60 days prior to infusion), early post-HCT (between infusion and 90 days post-infusion) and at one year of follow-up (within 90 days of one year after infusion).

In the early post-HCT time period, 64% of patients had tachycardia, 25% had systolic (pumping) dysfunction and 48% had diastolic (relaxing) dysfunction. Patients with tachycardia were 13 times more likely to develop systolic dysfunction and four times more likely to develop diastolic dysfunction.

Other risk factors for cardiac dysfunction included patients who received anthracyclines prior to HCT; those patients were seven times more likely to have early tachycardia. Systolic dysfunction was also more prevalent in the female gender and patients who received ace-inhibitor therapy pre-transplant.

Le Bonheur Pediatric Cardiologist Jason Goldberg, MD, MS, examines a patient during cardio-oncology clinic.

"Tachycardia likely exists as a marker of systemic inflammation," said Goldberg. "This, together with other acute post-HCT derangements and previous cardiovascular insults from known cardiotoxic agents, may result in cardiac dysfunction."

"We have to understand the early risk factors for development of cardiac dysfunction in pediatric HCT as we know that recipients of HCT during childhood are at increased risk of accelerated cardiovascular morbidity and mortality later in life."

Le Bonheur Pediatric Cardiologist Jason Goldberg, MD, MS

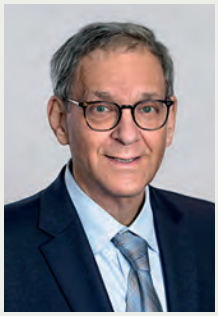
These findings can assist in creating a cardiovascular assessment protocol for post-HCT patients to help prevent and treat early myocardial dysfunction. In addition, this research can inform longer-term investigations to determine whether these early cardiovascular abnormalities are related to late cardiovascular morbidity.

MDA Care Center receives Care Center Grant Recertification Award

The Muscular Dystrophy Association (MDA) recently renewed Le Bonheur's MDA Care Center Grant for a three-year grant cycle. Programs designated as MDA Care Centers, such as Le Bonheur's, provide expert multidisciplinary care and medical research for children living with muscular dystrophy and other neuromuscular diseases.

Cohen receives Singleton-Taybi Award from Society for Pediatric Radiology

Le Bonheur Radiologist-in-Chief Harris L. Cohen, MD, FACR, has been named the 2021 Singleton-Taybi Award winner from The Society for Pediatric Radiology. This award recognizes his contributions to the understanding of genitourinary diseases in infants and children, devotion to education and service of representing pediatric radiology in other radiology organizations.



Harris L. Cohen, MD, FACR

Heart Institute launches Project ADAM chapter

Le Bonheur's Heart Institute recently became a Project ADAM (Automated Defibrillators in Adam's Memory) chapter. Le Bonheur's chapter is named "Lawson's Legacy" in honor of a young man who died suddenly from undiagnosed cardiomyopathy. Le Bonheur cardiologists will provide education to local schools working towards achieving a Heart Safe School designation. Project ADAM was founded in 1999 after the death of Adam Lemel, who collapsed and died while playing basketball at school. The mission of the organization is to provide education and resources to schools to help in the event that someone suffers a cardiac arrest.

Boop retires after two decades of service

Frederick A. Boop, MD, FACS, has retired from Le Bonheur Children's after 22 years of service where he was co-director of the Neuroscience Institute and medical director of the Neurosurgical ICU. He also served as chairman of the Department of Neurosurgery at the University of Tennessee Health Science Center and chief of the Division of Pediatric Neurosurgery at St. Jude Children's Research Hospital.

Frederick A. Boop, MD, FACS

Le Bonheur providers named *MBJ* Health Care Heroes

Cynthia Cross, MD, FAAP

Brandon Edgerson, MS, PharmD

Jamila Smith-Young, DNP, MPH, CPNP-AC

Le Bonheur Chief of Pediatric Hospital Medicine Cynthia Cross, MD, FAAP, Chief Operating Officer Brandon Edgerson, MS, PharmD, Pediatric Endocrinology Nurse Practitioner Jamila Smith-Young, DNP, MPH, CPNP-AC, and two Home Visitation Programs — Healthy Families America and Nurse Family Partnership — were named 2021 Health Care Heroes by the *Memphis Business Journal (MBJ)*. This annual recognition highlights the dedication and achievements of the local health care community.

State approves Le Bonheur and West Tennessee collaboration

The state of Tennessee approved the proposed collaboration with West Tennessee Healthcare to expand Le Bonheur's services and provide more specialized care in West Tennessee. This means that Le Bonheur Children's will move ahead with plans to establish a 21-bed pediatric unit inside Jackson-Madison County General Hospital. Le Bonheur plans to begin operating the unit as a satellite location in spring 2022.

Prajapati receives SIPR Pioneers Award

Le Bonheur Interventional Radiologist Hasmukh J. Prajapati, MD, FSIR, received the Pioneers Award during the annual meeting of the Society of Pediatric Interventional Radiology (SIPR). He received the award for his research on the safety and efficacy of the cryoablation of pulmonary and pleural metasteses in pediatric patients. This is the first time this type of study has been presented in pediatric patients. The Pioneers Award is presented each year to the scientific paper that best honors the pioneering innovators of pediatric interventional radiology.

Hasmukh J. Prajapati, MD, FSIR

Trauma center receives Level I Pediatric Trauma Center reaccreditation

Le Bonheur's trauma center was recently reaccredited by the American College of Surgeons as a Level I Pediatric Trauma Center. This news comes as the trauma division celebrates 10 years as a Level I Pediatric Trauma Center. As the only Level I Pediatric Trauma Center in a 150-mile radius, Le Bonheur provides exceptional critical care that children and families need.

AMERICAN COLLEGE OF SURGEONS
Verified Trauma Center

Wilroy named to UTHSC Outstanding Alumni

Former Le Bonheur Pediatrician Sid Wilroy, MD, was named to the 2021 Outstanding Alumni by the University of Tennessee Health Science Center (UTHSC) College of Medicine. This award was presented during UTHSC's recent Virtual Alumni Weekend. Wilroy was a pediatrician in Memphis for more than 50 years serving in many roles including chief of the Genetics Division at UTHSC.

Sid Wilroy, MD

Le Bonheur providers named to Top 40 Under 40: Urban Elite Professionals

Le Bonheur Neuropsychologist Billy D. Holcombe, PhD, Pediatric Urology Nurse Practitioner Chrisla Key, DNP, FNP, NP-C, and Pediatric Endocrinology Nurse Practitioner Jamila Smith-Young, DNP, MPH, CPNP-AC, were named to the Top 40 Under 40: Urban Elite Professionals. This award honors African-American rising Memphians who offer unique and innovative solutions to social problems, as well as those who shine in their respective professions.

Billy D. Holcombe, PhD

Chrisla Key, DNP, FNP, NP-C

Jamila Smith-Young, DNP, MPH, CPNP-AC

Le Bonheur Children's Hospital

848 Adams Avenue
Memphis, Tennessee 38103

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New construction will extend the west side of the hospital to the sidewalk of Dunlap Street between Poplar and Washington Avenues in Memphis and enlarge cardiovascular and neonatal floors, as well as the surgery recovery area and the main floor.

We're Growing Again!

Le Bonheur Children's breaks ground on major expansion for critical care, surgical areas

Le Bonheur Children's recently broke ground on the largest building expansion since the current hospital facility opened in 2010. The four-story, $95.4-million addition will allow Le Bonheur to continue on a sustainable, long-term growth trajectory. The expansion includes enlarging the cardiovascular and neonatal floors, in addition to the surgery recovery area and main floor.

"I am thrilled to announce this major Le Bonheur expansion. This addition will help us make a generational difference in the care provided to children across the country and beyond," said Le Bonheur President Michael Wiggins, DBA, FACHE. "This kind of momentum will allow Le Bonheur to continue attracting and retaining the best physicians and caregivers to achieve our mission of providing excellent health care for children, teaching the next generation of pediatric experts, pursuing scientific discovery and serving children in their communities. It will have an impact for decades to come."

The additional infrastructure will support an expansion of the Neonatal Intensive Care Unit (NICU) bringing 14 new beds to the existing 60-bed unit and will include eight additional surgery recovery bays. Le Bonheur will also convert 12 existing beds to critical care use immediately to ease capacity needs during construction.

The expansion will also bring additional beds to the Heart Institute to create a 31-bed dedicated Cardiovascular Unit by adding 10 additional Cardiovascular Intensive Care Unit beds to the existing 10-bed unit and creating room for an 11 bed step-down cardiac unit. A new MRI-guided catheterization lab will be added for a total of three catheterization labs.