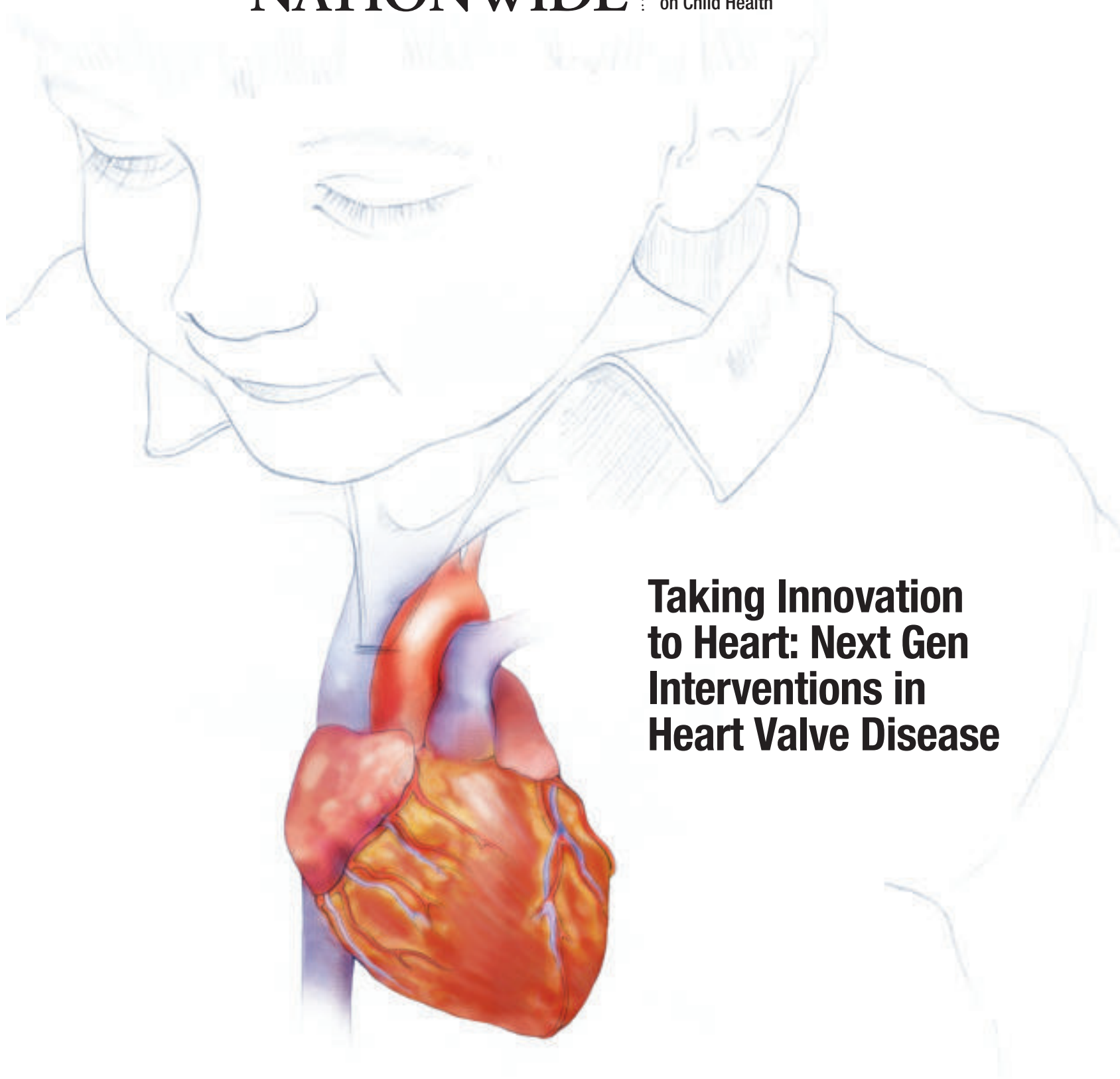


Fall/Winter 2017

Pediatrics

NATIONWIDE : Advancing the Conversation
on Child Health

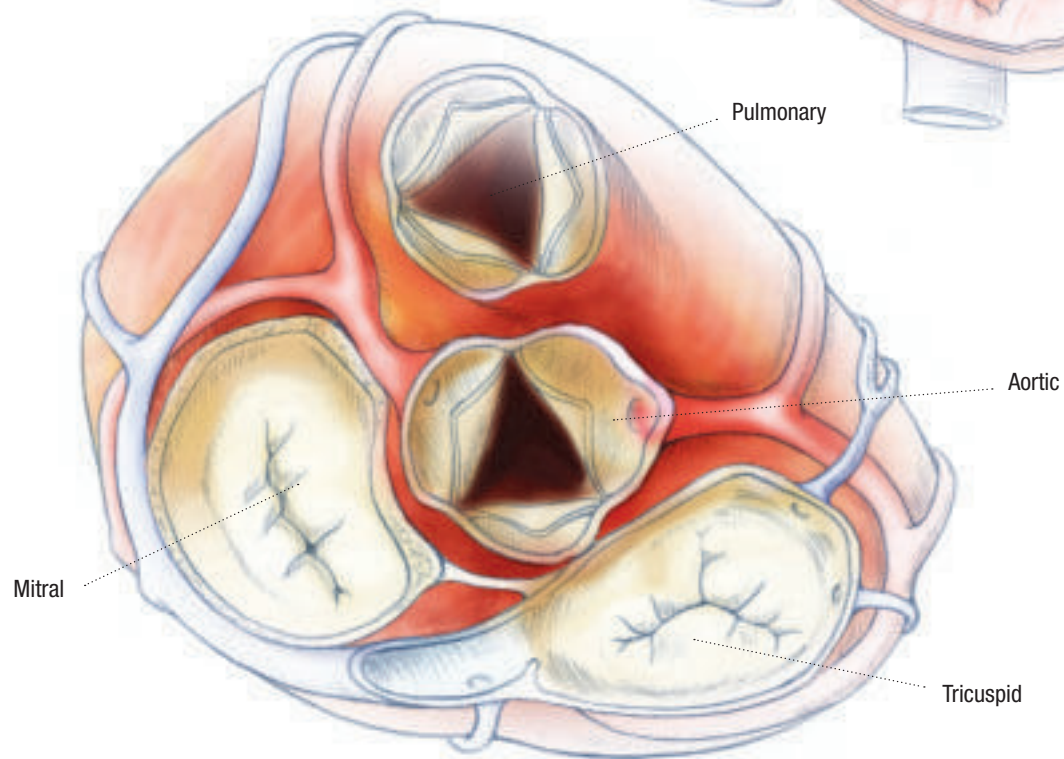
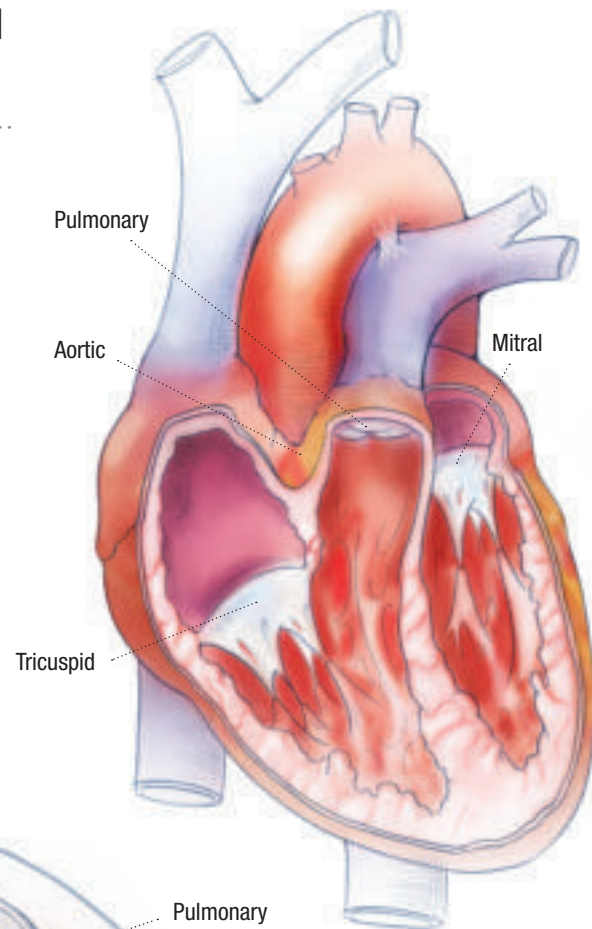


**Taking Innovation
to Heart: Next Gen
Interventions in
Heart Valve Disease**

18 TAKING INNOVATION TO HEART: NEXT GEN INTERVENTIONS IN HEART VALVE DISEASE

The heart's four valves ensure the unidirectional flow of blood through the heart. Pediatric valve dysfunction may involve any of these valves, but the right side is impacted more often than in adults.

Children with heart valve disease face multiple surgeries, procedures and morbidities over the course of their lives. Now, clinicians and scientists from across the spectrum of cardiovascular research are collaborating to improve and expand options for treatment of congenital heart valve disease.





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“There is a constant systematic review of evidence that must occur for these trials and studies to take place at the highest level. It is a key element of success; we can be a great clinical program in part because we are also doing this research.”

— Nathalie Maitre, MD, PhD, neonatologist and director of NICU Follow-up Programs at Nationwide Children’s (page 12)

“This level of innovation at a pediatric institution is unique, but it shouldn’t be. This collaboration across divisions, departments and specialties should be the norm. Why can’t this happen everywhere? My thought is that it can. And it should.”

– Robert Strouse, MFA, User Experience designer, Research Information Solutions & Innovation at Nationwide Children’s (page 26)

Emergency Departments Can Help Prevent Suicide

Secondary screenings, safety plans and phone follow-ups are key to reducing death by suicide.

Suicide is the tenth leading cause of death in the United States and has increased in incidence 27 percent from 1999 to 2015. Interestingly, up to 40 percent of individuals who die by suicide visit an emergency department (ED) in the year before their death. In light of this touch point with at-risk patients, the Joint Commission issued a Sentinel Event alert in February 2016 asking that hospitals screen all medical patients for suicide risk, including patients presenting to EDs. However, the implementation of these screenings is often ill-supported given lacking resources to address mental health in most EDs in the United States.

A recent study published in *JAMA Psychiatry* found that a brief suicide prevention intervention initiated in the ED followed by a series of phone calls after ED discharge significantly reduced the overall number of patient suicide attempts during a 52-week follow-up.

“Many hospitals have initiated screening without the benefit of evidence-based tools and clinical pathways to guide them,” says Jeff Bridge, PhD, director of the Center for Suicide Prevention and Research at Nationwide Children’s Hospital and lead author of an invited editorial on the original research. “This study provides

evidence that targeted efforts to recognize and actively intervene with individuals at high risk for suicide can be life-saving – there was a 30 percent reduction in suicide attempts in the intervention phase compared to the control group.”

The study authors created an intervention based on the Coping Long Term with Active Suicide program. Following an initial positive screen, ED physicians performed a secondary standardized screening to evaluate suicide risk. Then, a self-administered safety plan was provided to patients by nursing staff. The end phase included a series of telephone calls to the participant.

While only 4 percent of participants received the secondary screening and 37 percent received the written safety plan, researchers looked to the number needed to treat (NNT) – an epidemiological measure used to communicate effectiveness. For the intervention in this study, the NNT was 22, which the authors note is comparable to other preventative interventions such as the influenza vaccine and statins for myocardial infarction.

“This study did not include children and adolescents younger than 18,” says Dr. Bridge, who is also a professor of Pediatrics, Psychiatry and Behavioral Health in The Ohio State University College of Medicine. “So, it will be important to study whether similar interventions delivered in pediatric populations will demonstrate similar effects. This population group is at even higher risk for suicide, and the implicit message to patients at risk of suicide in all age groups should be that they are as welcome in the ED as patients with broken bones and are equally deserving of standardized, algorithm-driven care.”

Bridge JA, Horowitz LM, Campo JV. ED-SAFE- can suicide risk screening and brief intervention initiated in the emergency department save lives? *JAMA Psychiatry*. 1 Jun 2017;74(6):555-556.

Miller IW, Camargo CA Jr., Arias SA, Sullivan AE, Allen MH, Goldstein AB, Manton AP, Espinola JA, Jones R, Hasegawa K, Boudreaux ED, ED-SAFE Investigators. Suicide prevention in an emergency department population: the ED-SAFE study. *JAMA Psychiatry*. 1 Jun 2017;74(6):563-570.

— Brianne Moore





Specialists Collaborate to Improve Ovary Preservation

A weekend case inspires an investigation into how pediatric surgeons and gynecologists treat the same patient differently.

When lesions persist on a patient's ovary, there are two options for treatment: oophorectomy, which removes the entire ovary, and ovarian-sparing surgery (OSS). Depending on referral patterns and access to specialists, either a pediatric surgeon or a pediatric and adolescent gynecologist will administer treatment. A recent retrospective study published in the *Journal of Pediatric Surgery* finds that whether a patient keeps her ovary or not depends largely on who is treating her.

“One of my fellows mentioned before a procedure that gynecology did it differently and recommended that I give our chief gynecologist a call,” says Katherine Deans, MD, a principal investigator in the Center for Innovation in Pediatric Practice and pediatric surgeon at Nationwide Children's Hospital as well as senior author of the study. “I told her I planned on doing an open operation to take the lesion and ovary out. She said, ‘I wouldn't take the ovary out.’ So she came in and we did the procedure together – that started this entire line of investigation.”

The study showed that patients managed by gynecologists were more likely to be given OSS, while patients admitted through the emergency department and those managed by pediatric surgeons were more likely to receive an oophorectomy. Variation in treatment across institutions was almost 30 percent, with variation in performance of OSS nearly 60 percent.

“As I was consulting the literature, I found that there wasn't much at all, and nothing had been done on a large

scale,” says Dani Gonzalez, MD, lead author of the study. “We were shocked that one child could get a completely different operation depending on what hospital they presented to and the specialty of the doctor. This led to a change in our institution and our current work toward a multi-institutional intervention.”

The team is working on an algorithm that performs preoperative risk stratification to more objectively determine whether a patient requires an oophorectomy, building in additional testing and discussion about a patient's options in hopes that the only ovaries removed are the ones that need to be.

“I can't overemphasize the importance of collaboration, open-mindedness and intellectual curiosity,” says Geri Hewitt, MD, section chief of Pediatric and Adolescent Gynecology and Obstetrics at Nationwide Children's and a contributing author of the study. “This study would not have been possible without working with open-minded clinician-scientists who are willing to consider a different perspective and use research to innovate practice on a larger national scale.”

“We're not saying that oophorectomy isn't necessary, because sometimes it is,” adds Dr. Deans. “But taking out an ovary decreases a girl's reproductive life span. It increases risk of heart disease, stroke and dementia. We want to save every ovary that we can.”

Gonzalez DO, Cooper JN, Aldrink JH, Hewitt GD, Fallat ME, Minneci PC, Deans KJ. Variability in surgical management of benign ovarian neoplasms in children. *Journal of Pediatric Surgery*. 2017 Jun ;52(6):944-950. [Epub ahead of print]

— *Brianne Moore*

Combining Quality Measures to Improve Surgical Outcomes

Use a refined morbidity and mortality conference with a national database, a new study suggests.



A pediatric surgery morbidity and mortality (M&M) conference that applies quality improvement practices borrowed from industry can be a significantly more effective tool for learning from mistakes and making corrections, researchers from Nationwide Children's Hospital show in a new study.

In parallel, the National Surgical Quality Program-Pediatrics (NSQP-P) identifies nearly twice the number of complications, the study found.

To give a hospital the best opportunity to make improvements, use both, the researchers say. "Each has their advantages," says Gail Besner, MD, chief of Pediatric Surgery and principal investigator in the Center for Perinatal Research at Nationwide Children's. "If your hospital utilizes both systems in combination, then you can really improve the quality of health care you deliver."

Dr. Besner, who was appointed surgery chief five years ago, noticed that the same type of complications were being presented in the M&M conference month after month. She and colleagues borrowed from the airline and manufacturing industries' methods for analyzing failure and tailored the process to determine whether patient complications were due to an individual's mistake or to system errors.

M&M conferences are held weekly to discuss complications reported in any patient – a portion

of whom don't qualify for NSQP-P reporting. Surgeons and other health care workers collaborate to analyze the issues, determine the cause of the complication and initiate corrective measures to be expeditiously completed.

Over time, the number of repeat complications has decreased, processes found to be problematic have been eliminated and medication formularies and equipment carts have been modified – all to decrease preventable patient harm in the future.

Dr. Besner, who is also a professor of Surgery and Pediatrics at The Ohio State University College of Medicine, and colleagues compared the refined QI-directed M&M conference and NSQP-P in a recent issue of the *Journal of the American College of Surgeons*.

NSQP-P is a national database that prospectively collects outcome data and allows comparisons with other hospitals. Over the course of the five-year study period, NSQP-P identified 194 events per 1,000 patients whereas the M&M conference identified 100 per 1,000. The researchers found no differences in reporting for wound, neurologic and renal complications, but NSQP-P identified higher rates for respiratory, cardiovascular and other infectious complications, as well as readmissions.

As the number of samples grows over time, they reflect the hospital's experience with patients as a whole, the researchers say. The database is ideal for comparing variables between large cohorts of patients to identify and track areas of improvement.

"The more cases we review in M&M, the more action initiatives directed at improving the system we can put in place," says Brian Kenney, MD, MPH, surgical director for Quality Improvement, member of the pediatric surgical team at Nationwide Children's, associate professor of Pediatrics at OSUCOM and study co-author. "The two systems are complimentary."

Cromeens BP, Lisclandro RE, Brilll RJ, Askegard-Giesmann JR, Kenney BD, Besner GE. Identifying adverse events in pediatric surgery: comparing morbidity and mortality conference with the NSQP-Pediatric system. *Journal of the American College of Surgeons*. 2017 May;224(5):945-953.

— Kevin Mayhood

Children With Autism and Abdominal Pain Have Distinctive Bacterial Profiles

The microbiome may harbor causes of abdominal and behavioral issues and potential targets for relief.

Children with autism spectrum disorder (ASD) and functional abdominal pain may have a distinct microbiome-neuroimmune profile compared to kids with gastrointestinal disorders (GI) and those with no GI illness.

Building on others' research showing that *Clostridia* bacteria in the gut are altered in children with ASD, a team from six institutions shows the organisms interact with intestinal mucosa and are associated with altered neuroimmune signaling, indicated by changes in inflammatory cytokine, tryptophan and serotonin levels.

The findings add to the growing evidence demonstrating the brain-gut microbiome complex plays a significant role in ASD.

“The study gives a hint we might be able to identify certain biomarkers and bacterial profiles that are associated with abdominal pain in children with ASD,” says Kent Williams, MD, an attending gastroenterologist, investigator at The Research Institute at Nationwide Children’s Hospital and senior author of the study, published recently in *Cellular and Molecular Gastroenterology and Hepatology*.

“The big idea is if we can identify some way to manipulate the microbiome, we might be able to manipulate and improve children’s behaviors – providing not only relief from gastrointestinal issues but also improvement in oppositional and rigid behaviors,” Dr. Williams says.

The researchers analyzed rectal biopsies and blood from 14 children with ASD and functional gastrointestinal disorder (FGID), 15 typically-developing children with FGID and six typically-developing children without it.

They found a marked increase in mucosa-associated *Clostridiales* bacteria species and decreases in *Blautia*, *Dorea* and *Sutterella* among the ASD-FGID group. Within the group, multiple organisms correlated significantly with cytokines, tryptophan and serotonin but at differing levels among the children who reported pain versus those who didn’t, giving each subgroup a unique profile.

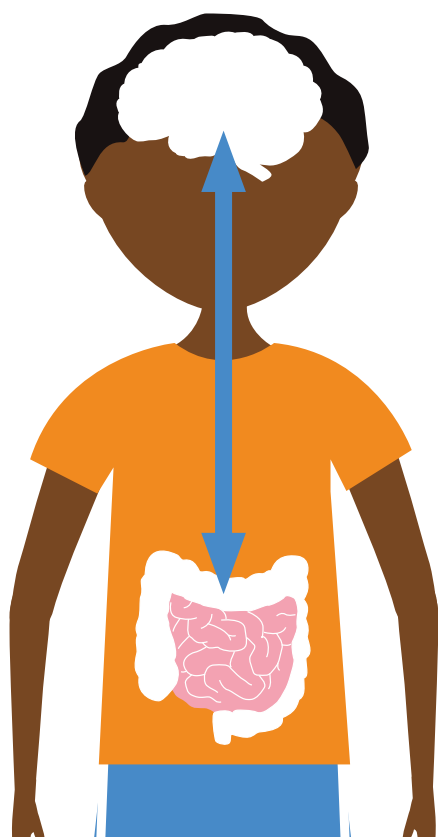
Ruth Ann Luna, PhD, director of Medical Metagenomics at the Texas Children’s Microbiome Center at Texas Children’s Hospital and lead author of the study, has also found the recurrence of many of the same organisms in increased abundance in the stools of a child with ASD.

“In the related study, we were also able to layer on changes in the microbiome with changes in GI symptoms and changes in behavior,” Dr. Luna says.

She and Dr. Williams are now involved in a 300-child study in which they hope to verify their findings and reveal biomarkers that may be used to identify specific subtypes of autism and potential targets for therapy. They are also looking for markers they can use to help identify which nonverbal children with ASD have abdominal pain.

Luna RA, Owzguen N, Baldeeras M, Venkatachalam A, Runge JK, Versalovic J, Veenstra-VanderWeele J, Anderson, GM, Savidge T, Williams KC. Distinct Microbiome-Neuroimmune Signatures Correlate With Functional Abdominal Pain in Children With Autism Spectrum Disorder. *Cellular and Molecular Gastroenterology and Hepatology*. 2016 Dec 11;3(2):218-230.

— Kevin Mayhood



How to Reduce Unnecessary Antibiotic Use for UTI in Urgent Cares

A quality improvement project shows children with negative urine cultures take antibiotics they don't need.

Even before a urine culture confirms the diagnosis, urgent care physicians often prescribe antibiotics when children present with symptoms of urinary tract infection (UTI).

Early treatment is important for relief of symptoms and prevention of complications. But what if the urine culture comes back negative as many as 48 hours after the urgent care visit? The patient has already been exposed to unnecessary antibiotics. In an era of increasing antimicrobial resistance, the patient should be stopped from taking any more.

A quality improvement project by physician-researchers at Nationwide Children's Hospital, recently reported in *Pediatrics*, showed that the implementation of a relatively simple protocol in urgent cares can substantially reduce unnecessary antibiotic exposure after a negative urine culture.

"Urgent cares and other acute care settings often do not have culture follow-up mechanisms, in part because they do not have a relationship with a patient or family that a primary care provider does," says Joshua Watson, MD, an Infectious Diseases specialist at Nationwide Children's and senior author of the publication. "It means that acute care settings are excellent for this kind of QI intervention."

When planning for the project began in September 2013, urgent cares within Nationwide Children's system did not have a process for telling patients with presumed UTI to discontinue antibiotic use when urine cultures were negative. There was also little documentation when follow-up did occur.

So the authors designed a protocol:

- A nurse reviews the urine culture result
- If negative, the result is forwarded to a clinician
- The clinician makes a determination to discontinue (if appropriate)
- A nurse notifies the parent or caregiver to discontinue the medication; if phone calls on two consecutive days fail, a letter is sent
- The clinician documents discontinuation in the electronic medical record

Before the study began, a mean of only 4 percent of patients prescribed antibiotics for UTI, who then had a negative culture, were documented to have discontinued their medication. During the study period, 910 patients were covered under the protocol, and documented antibiotic discontinuation rose to a mean of 84 percent.

The protocol saved 3,429 (40 percent) of a possible 8,648 "antibiotic days." As familiarity with the protocol grew, and a lab nurse position was dedicated to the task of follow-up, 60 percent of days were saved.

The project drew attention to other antimicrobial stewardship opportunities, says Dipanwita Saha, MD, director of Urgent Care Quality Improvement at Nationwide Children's and lead author of the publication. The protocol is now used in the Emergency Department; Urgent Care physicians are trying to determine if all presumed cases of UTI require an initial antibiotic prescription; and an overuse of broad-spectrum antibiotics for UTIs has been discovered, leading to an additional QI project already having a major impact.

"We have been contacted by physicians in the United States and internationally who are interested in this work," says Dr. Saha. "It's humbling to see that our efforts here are being noticed elsewhere."

Saha D, Patel J, Buckingham D, Thornton D, Barber T, Watson JR. Urine culture follow-up and antimicrobial stewardship in a pediatric urgent care network. *Pediatrics*. 2017 Apr; 139(4):e20162103.

—Jeb Phillips



“Impatient” Therapy: Physicians Too Aggressive in Treatment of ITP

Despite guidelines that advocate watching and waiting, physicians are still treating most patients with immune thrombocytopenia.

When a child presents with easy bruising or bleeding, red skin spots and fatigue – symptoms similar to those for leukemia – families seek evaluation immediately. However, more often these cases are pediatric immune thrombocytopenia (ITP), an acquired disorder that destroys blood platelets and is most common in 2- to 5-year-olds. Historically, the disorder has been treated pharmacologically to increase platelet count until the illness resolves.

In 2011, the American Society of Hematology (ASH) published new treatment guidelines for pediatric ITP that recommended a watchful waiting strategy in children with mild or no bleeding, regardless of platelet count. A multicenter cohort study recently published in *Pediatric Blood and Cancer* shows that the changes may not have been widely implemented.

“Given the guidelines, patients newly diagnosed with ITP should only be admitted to the hospital and given pharmacological treatment for clinically significant bleeding,” says Sarah O’Brien, MD, principal investigator in the Center for Innovation in Pediatric Practice in The Research Institute at Nationwide Children’s Hospital and an author of the retrospective study. “But we found that even after the guidelines, admission frequency was about the same, and 86 percent of patients admitted did not have any diagnostic codes consistent with bleeding. Most of these patients received treatment.”

The team looked at data from almost 5,000 ITP primary admission patients across the United States between the ages of 6 months and 18 years between 2008 and 2014 to determine whether pharmacologic therapy for

pediatric patients without significant bleeding symptoms had decreased.

The study found that in the three years following the publication of the new guidelines, only about 14 percent of patients had documented bleeding complications due to ITP, but 93 percent of patients received pharmacological treatment. These treatments, including intravenous immunoglobulin and corticosteroids, can be expensive and have side effects such as fever, nausea and aseptic meningitis.

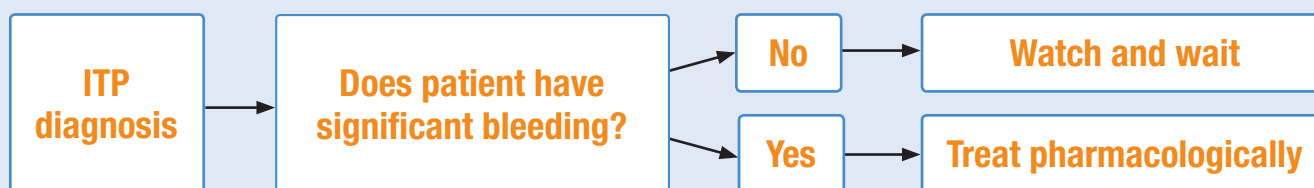
“We’re currently working to determine whether new ITP patients admitted to the hospital and patients that leave the emergency department and go home for observation are significantly different symptomatically from each other. The retrospective study focused exclusively on patients that have already been admitted to the hospital, not necessarily those seen in the ED or in a hematology clinic,” adds Dr. O’Brien, also a physician in the Division of Hematology, Oncology & Blood and Marrow Transplant.

Dr. O’Brien and her colleagues still have a lot of questions about the trends observed in the data.

“What are we missing in this drive to treat? Clearly, treatment is not associated with reducing bleeding, as most patients receiving treatment have little to no bleeding at all. To understand the discrepancy between what the guidelines say and what we practice, we need to understand what’s causing the variation.”

Witmer CM, Lambert MP, O’Brien SH, Neunert C. Multicenter cohort study comparing U.S. management of inpatient pediatric immune thrombocytopenia to current treatment guidelines. *Pediatric Blood & Cancer*. 2016 Jul;63(7):1227-1231.

— Brianne Moore



How to Improve Apparent Cause Analyses and Reduce Error Recurrence

A quality improvement team embarks on a project focused on the accuracy of future quality improvement initiatives.



An apparent cause analysis (ACA) is a process used to investigate the cause or causes of a medium- or low-risk safety event. Designed as a quality improvement measure, ACAs are used to explain in detail why an issue or near miss occurs and then to correct the issue and prevent its recurrence by making an action plan. Ideally, an ACA should serve as a learning tool that allows the institution at large to improve practice and reduce error recurrence, leading to safer patient care.

A recent quality improvement initiative published in *Pediatric Quality and Safety* paves the way for other institutions to reduce preventable harm by improving ACAs.

ACAs are only as helpful as they're constructed to be, so when a single institution found that its ACA reliability was only 86.4 percent, it was clear that changes needed to be made.

"As the new director of patient safety, I reviewed the prior year's completed ACAs and found that the analysis and action plans weren't constructed well. This led to gaps in learning, frustration from faculty and

error recurrence, which all contributed to relatively low reliability," says Kristen Crandall, MSN, RN, CPN, director of patient safety at Children's National Health System in Washington, D.C., and lead author of the study. "Seeing a low reliability score drove us to develop a project to increase ACA reliability."

The team utilized the model for improvement and engaged experts to identify potential weaknesses in the current ACA structure. From there, they developed interventions to implement. Following the implementation of the interventions, all ACAs were a minimum of 95 percent reliable and were turned around nearly five days earlier. Stakeholders also showed a significant increase in satisfaction with the new ACAs they were utilizing.

"The high reliability toolkit we created, which links every action item or intervention to a calculable percentage of reliability, was the most impactful part of the intervention," adds Crandall. "It gave us an objective scoring system and shifted the focus of our organization's safety culture to quality and reliability."

Having improved the reliability of a key quality improvement measure, the team plans to administer and review a safety culture survey to determine the effect of this reliability increase on the safety culture at their institution.

"While we're not currently able to measure effectiveness in terms of outcome, utilizing this toolkit and strengthening action plan development should decrease error recurrence and improve patient, family and staff safety," says Crandall. "In the future, we need a multi-center study of ACA effectiveness and quality to continue reducing repeat safety events. The peer-reviewed literature on this topic is lacking, and patients' safety should come first."

Crandall KM, Sten, MB, Almuhan, A, Fahey, L, Shah, RK. Improving apparent cause analysis reliability: A quality improvement initiative. *Pediatric Quality and Safety*. 2017 May/June;2(3):e025.

— *Brianne Moore*

Cannabidiol May Reduce Drug-Resistant Seizures by Half

Two studies demonstrate clinically significant response to oral liquid cannabidiol over placebo.

Two recent studies – one published in *The New England Journal of Medicine* and one presented at the 2017 American Academy of Neurology annual meeting – indicate that a new plant-based, cannabis-derived treatment may be able to decrease the incidence of seizures in two complex childhood epilepsy disorders, Dravet syndrome and Lennox-Gastaut syndrome.

“If this medication is approved, it will become the only FDA-approved treatment for Dravet syndrome in the United States,” says Anup Patel, MD, a member of the Division of Neurology at Nationwide Children’s Hospital and an author of the two studies. “And while there are FDA-approved treatments for Lennox-Gastaut syndrome, we’re adding to the literature and hope to make another treatment option available that works for patients.”

Cannabidiol is a purified derivative from the cannabis plant, without any of the psychoactive properties normally associated with the plant. Both studies demonstrated that at least 40 percent of participants taking oral doses of liquid cannabidiol experienced more than a 50 percent reduction in seizures compared to participants on placebo.

“Until now, there’s never been a double-blind placebo controlled study that showed effectiveness for children and adolescents with Dravet syndrome. The vast majority of kids and families from these trials have voluntarily transitioned into an open-label study, meaning they’ve seen enough benefits in their kids to continue the treatment they received during the trial,” says Dr. Patel, who is also an associate professor of Clinical Pediatrics and Neurology at The Ohio State College of Medicine.

“Greenwich Pharmaceuticals, the developer of cannabidiol, plans to submit a New Drug Application to the Food and Drug Administration so that cannabidiol can be prescribed to any patient with Lennox-Gastaut syndrome or Dravet syndrome. We want families to have another potential helpful kind of option,” adds Dr. Patel.

Overall patient conditions in the Dravet syndrome study improved in 62 percent of cases where the patient was taking cannabidiol, according to the Caregiver Global Impression of Change scale. While most Lennox-Gastaut syndrome and Dravet syndrome patients have developmental delays due to their high incidence of seizures, parents reported that their children were more alert, calmer and paid more attention.

Dr. Patel and his team are currently studying cannabidiol effects on infantile spasms in children 2 years of age and younger. They’ve recently started to enroll patients.

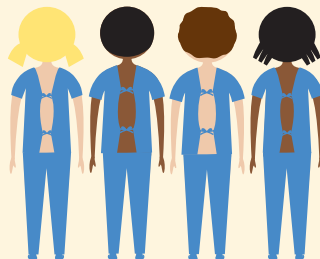
“We hope that the work we’re doing here will lead to a safe and consistent medicine that providers and parents can believe in, that won’t require desperate parents to go outside the medical community for treatment,” says Dr. Patel. “I think that’s really why we did what we did. If this gets FDA approved, these kids and their parents have a lot to be proud of as they helped make this a reality.”

Patel, A, Devinsky O, Cross JH, Villanueva V, Wirrell E, VanLandingham K, Roberts C, Checketts D, Zuberi S. Cannabidiol (CBD) significantly reduces drop seizure frequency in Lennox-Gastaut syndrome (LGS): results of a dose-ranging, multi-center, randomized, double-blind, placebo-controlled trial (GW-PCARE3). American Academy of Neurology 69th Annual Meeting; 2017 April 18; Boston.

Devinsky O, Cross JH, Laux L, Marsh E, Miller I, Nabbout R, Scheffer IE, Thiele EA, Wright S; Cannabidiol in Dravet Syndrome Study Group. Trial of cannabidiol for drug-resistant seizures in the Dravet syndrome. *The New England Journal of Medicine*. 2017 May 25;376(21):2011-2020.

— Brianne Moore

40% of
participants
taking the drug



saw
> 50% reduction
in seizures



Mapping the Journey to Optimal Health for NICU Graduates



BABIES BORN PRETERM NEED ONGOING, SPECIALIZED CARE TO HELP THEM THRIVE AFTER DISCHARGE FROM THE HOSPITAL. INNOVATIVE PROGRAMS ARE BEING DESIGNED TO ENSURE THEY GET THAT CARE.

by Jeb Phillips

In the early 1980s, only 10 percent of infants born before 28 weeks of gestational age survived to be discharged from the hospital. By 2015, 65 percent of babies born before 27 weeks were surviving.

Those statistics and others like them speak to remarkable advances in neonatal intensive care. But they have also led to an increasingly urgent question:

What should we do after a critically ill infant survives and is discharged from the hospital?

Since the 1970s, when graduates of neonatal intensive care units (NICUs) were first followed in specialized programs, it has become clear that they face more future difficulties than their full-term peers. Many have sensory processing or language problems. Half of children with cerebral palsy are born preterm, for example. Preterm babies with bronchopulmonary dysplasia (BPD) have trouble eating early in their lives and are at greater risk of asthma and obstructive lung disease later.



Nathalie Maitre, MD, with patient Taryn Cook and her family.

Despite calls from the Eunice Kennedy Shriver National Institute of Child Health, the American Academy of Pediatrics, the American College of Obstetrics and Gynecology and others for NICU follow-up best practice guidelines, no consensus about how to handle these children exists.

“A variety of studies across medical fields tells us that clinical practice lags 10 to 20 years behind research,” says Iona Novak, PhD, head of research at the Cerebral Palsy Alliance Research Institute, University of Sydney (Australia), who has helped create international early detection and intervention guidelines for cerebral palsy. “That’s a whole childhood. There are so many barriers: time, knowledge, funding, training. That’s why what Nathalie Maitre is doing at Nationwide Children’s Hospital is so important. She’s leading an international change in practice.”

Nathalie Maitre, MD, PhD, is a neonatologist and director of NICU Follow-up Programs at Nationwide Children’s. When she took the position in 2015, she began a large-scale project to implement the use of evidence-based care and tools for infants at risk for

developmental problems. More than two years later, the protocols, best practices and “journeys” that she and her colleagues have created and implemented are helping NICU graduates every day.

“NICU follow-up is not the most glamorous job, and it’s not a revenue generator for a hospital,” says Dr. Maitre. “The people involved in it come home with gummed-up Cheerios in our hair from administering the Bayley Scales of Infant and Toddler Development and spit-up on our clothes from working with toddlers who have feeding aversions. We are passionate, though, because we know we can change the trajectories of these kids for the better.”

And it is possible for others to do it too.

BUILDING AN INNOVATIVE NICU FOLLOW-UP PROGRAM

NICU Follow-up Programs at Nationwide Children’s have more than 5,000 patient visits every year in three large outpatient clinics: the Early Developmental Clinic, the BPD Clinic and the Neonatal Abstinence Syndrome Clinic. Each child has unique challenges, but Dr. Maitre



“Follow-up really can be the happy part after the NICU – children have survived, and you can help them develop as normally as possible and reach their highest potential. You cannot do that unless you have a firm grasp of best practices and how your program can implement them.”

– Teresa Borghese, CNAP-AC, Nationwide Children's

wanted to create a “common developmental journey” for them that would allow for best outcomes.

“‘The Journey to Best Outcomes’ is actually this hospital’s overall strategic plan, and we have always been supported in bringing the philosophy of comprehensively caring for these high-risk infants and their families into our follow-up programs,” she says.

Dr. Maitre began with 11 working groups. Each conducted a rigorous review of an aspect of Nationwide Children’s NICU follow-up – how neurodevelopmental exams are administered or the resources a “complex care” child might need outside of the hospital – and reported on what was working and what needed to change.

It was a time-consuming process, says Teresa Borghese, CNAP-AC, who helped create the guidelines for complex care follow-up.

“Follow-up really can be the happy part after the NICU – children have survived, and you can help them develop as normally as possible and reach their highest potential,” she says. “You cannot do that unless you have a firm grasp of best practices and how your program can implement them.”

Certain changes came quickly. Like many other hospitals, Nationwide Children’s was following children until they were 2 years of age. Dr. Maitre extended it to 3. That extra 12 months is often when autism, attention deficit hyperactivity disorders, problems with emerging

executive function and other developmental issues become obvious. Continued surveillance allows the specialized NICU follow-up team to intervene and refer children as soon as those conditions emerge.

Over months, the work groups helped develop what they came to call “journeys.” Those are the paths – the appointments, screenings and possible referrals – that every child was likely to need, along with the duties that each member of the team was expected to perform.

The default journey involves appointments with neurological exams; in addition, there is a General Movement Assessment (GMA) at 3 to 4 months, and the Bayley Scales of Infant and Toddler Development (BSID) at 9 to 12 months, 22 to 26 months and 33 to 36 months.

That’s only the default journey of assessments. A child’s family may need a social worker’s help to access community services. A child with BPD may need appointments to address feeding and medication. An early abnormal GMA triggers an extra visit to the Early Cerebral Palsy Program, in an effort to diagnose and intervene as soon as possible. BSID scores can trigger referrals to occupational, speech and physical therapists.

An operations manual lays all of this out. It continues to change as new research becomes available, and it now runs to 300-plus pages. The clinic team plans to publish it in a peer-reviewed journal so others can benefit from it as well.

“The journey is not necessarily guided by a child’s medical condition, though that is part of it,” says Dr. Maitre. “It is guided by who they are as a child in the context of their family and community. We need to understand and address all of that to give children a chance at the best outcome.”

Dr. Maitre also worked on developing or strengthening relationships with other hospital subspecialties, so families could feel secure in their transitions of care to neurologists, pulmonologists, behavioral health experts and others.

A child’s best journey occurs when families are comfortable and care appears seamless to them, Dr. Maitre says.

TARYN’S JOURNEY

Taryn Cook was delivered at 27 weeks gestational age, to a birth mother who did not feel she could care for a baby with special needs. Taryn had experienced the most severe type of intraventricular hemorrhage and was diagnosed with BPD, retinopathy of prematurity, apnea of prematurity and, ultimately, cerebral palsy.

Taryn was adopted by Sarah and Doug Cook, who brought her to central Ohio and the Nationwide Children’s care area after her NICU discharge at about 14 weeks of age. For many reasons, Taryn’s care was disjointed in her first months.

“I had this huge list on a legal pad of everyone I needed to contact and all the services I needed to coordinate in order to care for a special needs baby,” says Sarah. “We were relying in part on Taryn’s original hospital for care as well. It wasn’t until we found a pediatrician who was comfortable caring for her and working with Nationwide Children’s clinics that we really felt nothing was going to fall through the cracks.”

Sarah says she began to feel a “regularity of care:” appointments not based on problems, but when Taryn needed them developmentally; information and education given in a planned, progressive way at those appointments; encouragement that, as Taryn’s parents, Sarah and Doug could make (and were making) important contributions to their child’s health.

A particular point of demarcation was Taryn’s diagnosis with cerebral palsy at about 12 months of age. Sarah was told by others that it was too early for such a diagnosis, but research in the last few years shows that diagnosis as early as 6 months is possible. It can also help a family access needed services earlier.

A COMPLEX JOURNEY

The operations manual for Nationwide Children’s NICU Follow-up Programs maps out many possible “journeys” that patients can take. Here is an example of the appointments a complex care patient may need.

2-4 WEEKS AFTER DISCHARGE

Medical and neurological exams; nutrition assessment; social work evaluation for family resource needs

3-4 MONTHS OF AGE

Med and neuro exams; Test of Infant Motor Performance (TIMP) and General Movements Assessment (GMA); referrals and evaluations as needed

9-12 MONTHS

Med and neuro exams; Bayley Scales of Infant and Toddler Development III (BSID)

18 MONTHS

Med and neuro exams; therapy evaluation

22-26 MONTHS

Med and neuro exams; BSID and Child Behavior Checklist (CBCL)

30 MONTHS

Med and neuro exams, therapy evaluation

33-36 MONTHS

Med and neuro exams; BSID and CBCL; last opportunity for social work assessment

Even though an official transition to Nationwide Children's Comprehensive Cerebral Palsy program won't occur until Taryn turns 3, Dr. Maitre and others have begun preparing the Cooks. Taryn also has been able to enroll in one of several National Institutes of Health-funded cerebral palsy research studies at Nationwide Children's (see sidebar).

"We have already seen improvement, especially in the way Taryn uses her left arm and hand," Sarah says. "She is doing wonderfully, and we firmly believe it is because of the care she has received."

WHAT INSTITUTIONS CAN DO

Nationwide Children's and other large tertiary care pediatric hospitals have an advantage in infrastructure and staffing when trying to create a multidisciplinary NICU follow-up program.

Even if there's no broad national agreement on best practices, every institution should consider standardizing their practices internally, says Andrea Duncan, MD, medical director of the Neonatal High-Risk Clinic at University of Texas at Houston McGovern Medical School. Dr. Duncan, inspired in part by Dr. Maitre, is now working on her institution's NICU follow-up manual.

"Depending on what the program looks like, it could be 20 pages with one journey," says Dr. Duncan. "If you want to set your people up for success, if you want evidence-based practice, you have to say, 'this is what we do and this is why we do it.'"

Dr. Maitre and her colleagues say following a few other basic steps can start any institution on their own journey:

- **Find a champion.** A person who realizes the complexities of neonatal follow-up care is likely already at your institution. Give that person the opportunity to research best practices and lead colleagues.

- **Identify providers.** Pediatricians, nurse practitioners, and therapists often can provide specialized care if they demonstrate interest in the complexities of neonatal follow-up. Large institutions can provide additional training to medical professionals to foster this.
- **Use what you have.** A pediatric institution likely houses many subspecialties. The NICU follow-up champion should try to build bridges with them for optimal care inside the follow-up program and to make sure that families are comfortable once the inevitable transition of care happens.

None of this is exactly easy, and it does take a commitment of resources, Dr. Maitre emphasizes. But any number of studies show that appropriate early management of these high-risk children can actually reduce the need for further hospitalization and other expenditures.

Besides, it's the right thing to do.

"It's really our responsibility to give these children their best chance at a good life," says Dr. Maitre.

Gong A, Johnson YR, Livingston J, Matula K, Duncan AF. Newborn intensive care survivors: a review and a plan for collaboration in Texas. *Maternal Health, Neonatology, and Perinatology*. 2015 Oct 19; 1:24.

Novak I, Morgan C, Adde L, Blackman J, Boyd RN, Brunstrom-Hernandez J, Cioni G, Damiano D, Darrah J, Eliasson AC, de Vries LS, Einspieler C, Fahey M, Fehlings D, Ferriero DM, Fetters L, Fiori S, Forssberg H, Gordon AM, Greaves S, Guzzetta A, Hadders-Algra M, Harbourne R, Kakooza-Mwesige A, Karlsson P, Krumlinde-Sundholm L, Latal B, Loughran-Fowlds A, Maitre N, McIntyre S, Noritz G, Pennington L, Romeo DM, Shepherd R, Spittle AJ, Thornton M, Valentine J, Walker K, White R, Badawi N. Early, Accurate Diagnosis and Early Intervention in Cerebral Palsy: Advances in Diagnosis and Treatment. *JAMA Pediatrics*. 2017 Jul 17. [Epub ahead of print]

Maitre NL. Neurorehabilitation after neonatal intensive care: evidence and challenges. *Archives of Disease in Childhood Fetal and Neonatal Edition*. 2015 Nov; 100(6): F534-40.

Chorna O, Heathcock J, Key A, Noritz G, Carey H, Hamm E, Nelin MA, Murray M, Needham A, Slaughter JC, Maitre NL. Early childhood constraint therapy for sensory/motor impairment in cerebral palsy: a randomised clinical trial protocol. *BMJ Open*. 2015 Dec 7; 5(12).

"We are not just a research program that documents outcomes. We are a clinical program that fully integrates research into our journeys."

— Nathalie Maitre, MD, PhD, neonatologist and director of NICU Follow-up Programs at Nationwide Children's

Integrating Research Into the “Journeys”



Along with their work to build an innovative follow-up program, Nationwide Children’s faculty and staff members are international leaders in NICU follow-up research.

A number of foundation and National Institutes of Health-funded follow-up studies are housed entirely or in part at the hospital, and The Research Institute at Nationwide Children’s is one of 17 member centers of the Eunice Kennedy Shriver Institute of Child Health and Human Development Neonatal Research Network.

The research is important on its own, but it also helps ensure that a clinic is using the most up-to-date, evidence-based care, says Nathalie Maitre, MD, PhD, a principal investigator in the Center for Perinatal Research at Nationwide Children’s in addition to her leadership role in the follow-up programs.

“There is a constant systematic review of evidence that must occur for these trials and studies to take place at the highest level,” says Dr. Maitre. “It is a key element of success; we can be a great clinical program in part because we are also doing this research.”

Taryn Cook, a toddler who has benefitted from the clinical care at Nationwide Children’s, is enrolled in the prospective interventional study “Early Childhood Constraint Therapy in Cerebral Palsy” (R01HD081120-02) with Dr. Maitre as principal investigator. It involves a soft mitt constraint on a young child’s more affected hand and bimanual exercise to improve brain and motor function. It’s called the

“APPLES” study around the hospital, short for “A Positive Parent-focused training for upper Limb Experience with Sensory-motor feedback.”

“We were told of the opportunity to enroll in studies right away, and we wanted to participate because it could benefit Taryn and others,” says Sarah Cook, Taryn’s mother.

Among the other studies involving NICU follow-up at Nationwide Children’s are:

- **“Omega Tots: A Randomized, Controlled Trial of Long-chain Polyunsaturated Fatty Acid Supplementation of Toddler Diets and Developmental Outcomes”** (NCT01576783), led by Sarah Keim, PhD, principal investigator in the Center for Biobehavioral Health
- **“Daily and Weekly Rehabilitation for Young Children With Cerebral Palsy (DRIVE)”** (NCT02857933) to help determine optimal frequency of rehabilitation, led by Jill Heathcock, PhD, a co-investigator at the Center for Perinatal Research and director of the Infant Lab at The Ohio State University Wexner Medical Center
- **“An Implementation Network for Early Recognition and Intervention of Cerebral Palsy”** involving seven academic centers, led by Dr. Maitre and recently funded by the Cerebral Palsy Foundation

“We are not just a research program that documents outcomes,” says Dr. Maitre. “We are a clinical program that fully integrates research into our journeys.”

TAKING INNOVATION TO HEART: Next Gen Interventions in Heart Valve Disease

From bioengineers to interventional cardiologists, molecular biologists to cardiothoracic surgeons, experts with diverse backgrounds are focusing on the problem of heart valve disease in children.

..... by Abbie Roth

Hear valve disease affects more than 5 million Americans. And while acquired disease in the adult population certainly accounts for much of this, children with heart valve disease face multiple surgeries, procedures and morbidities over the course of their lives.

Pediatric heart valve disease can present at any age. Some infants have valves that need to be treated early on. Some children with bicuspid aortic valves may not even know they have a congenital heart defect until adolescence or adulthood. Each case of congenital heart valve disease is unique, making standardized treatments more difficult to come by.

Heart valve replacement is lifesaving but it is invasive. And the associated morbidity and mortalities of existing treatments for heart valve disease are trade-offs. Despite efforts to treat symptoms with medication or repair the valve through surgery, treatment for children often arrives at heart valve replacement.

Now, surgeons, tissue engineers and interventional cardiologists are tackling heart valve replacements with an aim to improve the outcomes for these children. And molecular biologists, geneticists and engineers are working to understand how these heart defects form in the first place. With rapidly advancing science and technology, and a spirit of collaboration and innovation among scientists, big changes are on the horizon for the millions of patients with heart valve disease.

TO REPAIR OR REPLACE? THE FIRST QUESTION OF HEART VALVE SURGERY

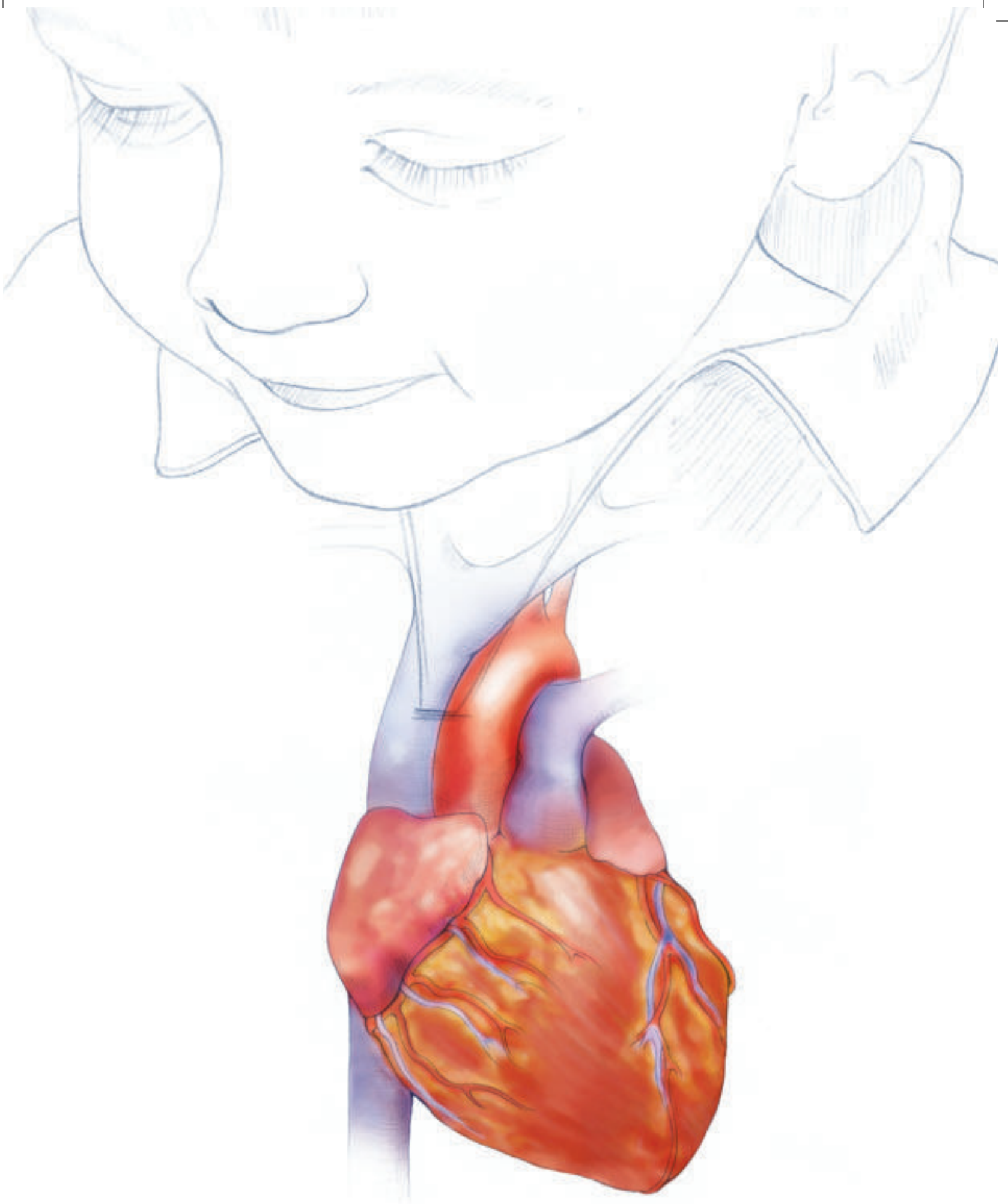
The only options when the valve ceases to function properly are surgical attempts to repair the leaflet or annular region and to replace the valve entirely. “While repairs can sometimes delay the need for a full valve replacement, the choice ultimately becomes, how many more surgeries do we want this child to face?” says Patrick McConnell, MD, pediatric cardiothoracic surgeon in The Heart Center at Nationwide Children’s Hospital.

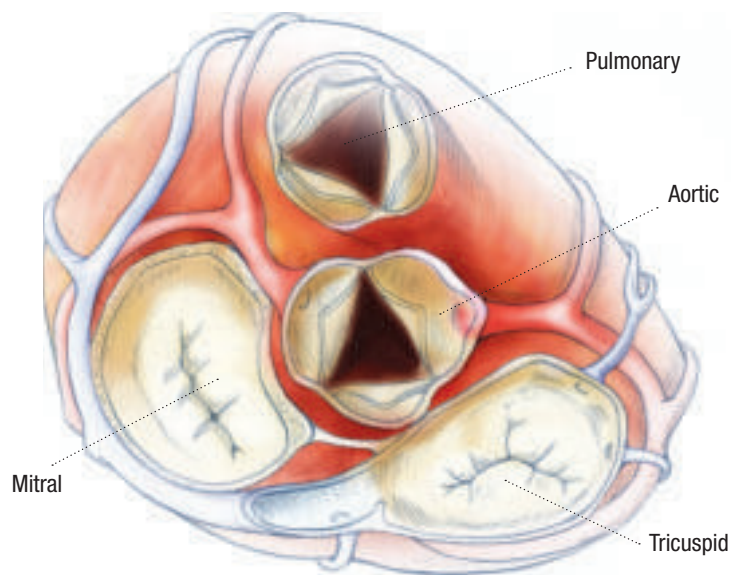
“Even a busy surgeon will only do pediatric heart valve repair a couple times a year,” he says. “Each child has his or her own unique heart valve problem, unlike adults whose pathology tends to remain pretty similar across patients and for whom replacement is more standardized and durable.”

When each case is a special one, and the cases are few and far between for an individual surgeon or center, developing standardized treatments is difficult.

“Repair of pediatric heart valves has not seen an epiphany like it has in adult valve surgery,” elaborates Dr. McConnell, who is also an assistant professor of Surgery at The Ohio State University College of Medicine. “Standard procedures don’t exist for pediatrics, in part because the anatomy of each pediatric case is unique and we are more often starting with too small of a valve where options are far more limited.”

And while Dr. McConnell says that repair is almost





The heart's four valves – the aortic and mitral on the right side and the pulmonary and tricuspid on the left side – ensure the unidirectional flow of blood through the heart. Acquired and adult heart valve disease are mostly concentrated in the left side of the heart. Pediatric valve dysfunction also involves the left side but the right side is impacted more often than in adults.

always attempted, it has to be balanced with the goal of reducing the number of times the patient and family need to see a surgeon. And so, ultimately, a patient with heart valve disease will be facing the prospect of heart valve replacement.

For pediatric patients, this involves at least one open heart surgery. For most pediatric patients, it means multiple surgeries over the course of their lives. Infants who need a heart valve replacement face three to four surgeries from infancy to adolescence to upsize the valve as the child grows. Issues with the durability of the replacement valves often result in the need for additional procedures.

Two types of prosthetic valves – mechanical and biological – are used in replacements. In children, mechanical valves are rarely used for two main reasons. First, they don't grow and can't be stretched or enlarged, meaning another surgery is always required. Second, the anticoagulant therapy required for mechanical valves, regardless of placement, involves higher risks and more severe side effects for children than it does for older adults.

Biological valves may be constructed from animal tissues (pig or cow) or cadaveric valve tissue and do not require anticoagulation. The drawbacks of biological valves include potential immune-incompatibility and the speed with which the leaflets degenerate.

As any parent knows, kids are hard on things. They wear out clothes and shoes and toys – and replacement heart valves.

“Children aren't just out-growing their valves. That's certainly a factor, but it's not the whole story,” says

Dr. McConnell. “They tend to tear through their replacement valves, and we can't easily predict why or how or who will be most affected.”

The issue of durability of the valve in children may be related to the unique biomechanical forces the valve is exposed to in a growing child as well as the immune response of the growing child.

Heart valve researchers are now taking aim at these factors and collaborating with bioengineers to develop better solutions for congenital heart valve disease (CHVD).

“The outcomes of pediatric heart valve replacement are some of the worst results you would ever encounter in the adult world,” says Dr. McConnell. “But they are the reality in pediatrics. We cannot accept the reality that the best we can do for some of these children is six months between procedures. It's a struggle to reduce morbidity and mortality for these kids. We have to do better.”

USING A CATHETER TO REPLACE VALVES

The invention of the Medtronic Melody transcatheter pulmonary valve replacement on a stent in 2000 – treating both stenosis and valve regurgitation without open heart surgery – created a big shift in thinking.

“Now, heart valves do not always need to be put in by a surgeon with a patient on bypass. This is huge,” explains John P. Cheatham, MD, interventional cardiologist and co-director of The Heart Center at Nationwide Children's. “The risks associated with cardiopulmonary bypass compound with repeated open heart surgeries. But with the transcatheter approach, you can come in the morning, get a new valve and go home the next day.”

“Pediatric patients will almost always still need an open heart surgery first,” says Dr. Cheatham, who holds the George H. Dunlap Endowed Chair in Interventional Cardiology. “But if we can reduce the number of open heart procedures over the child’s lifetime by giving them a transcatheter option that is equal to or better than surgery, we’ll be making a huge improvement in morbidity and mortality.”

Nationwide Children’s, in an effort led by Dr. Cheatham, was one of five sites in the United States to test the Melody TPV. This study led to the approval by the Food and Drug Administration (FDA) in 2010 for valve replacement in pulmonary outflow tracts that have a surgically placed conduit; that is, for patients who have already had at least one pulmonary valve replacement with a conduit. This patient population accounts for approximately 20-25 percent of people who have had surgery in that area.

The Medtronic Harmony transcatheter pulmonary valve, which is now in clinical trial, was designed using the same concept as the Melody valve but to fit in patients who did not receive a surgical conduit – approximately 75 percent of the people who have had surgery in this area. Historically, patients with congenital heart disease who had narrowing around the pulmonary valve and artery had a transannular patch inserted to widen the area, and the valve was sacrificed. Because the patients appeared to do well after the surgery, even without their pulmonary valve, it was generally believed that it wasn’t absolutely necessary to replace the pulmonary valve in these cases, explains Dr. Cheatham, who is also a professor of Pediatrics and Internal Medicine at The Ohio State University College of Medicine.

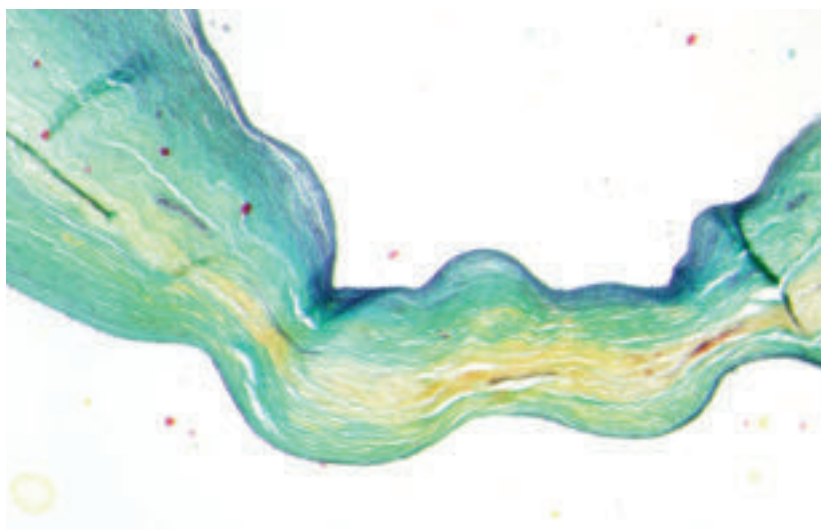
Nationwide Children’s was one of three sites worldwide to test this new valve in the FDA’s first early feasibility study, led locally by Dr. Cheatham. Now, Dr. Cheatham serves as the national principal investigator for the pivotal trial.

“Now that these patients are living longer, we are learning that going along without a pulmonary valve is really not good for the long term. Patients may survive initially, but eventually, we’re seeing that the regurgitation into the pumping chamber is causing heart failure,” says Dr. Cheatham. “Adults with CHD who had this surgery in childhood are having to go back for open heart surgery to place a conduit or pulmonary valve. The Harmony is designed to be a transcatheter option for this group.”

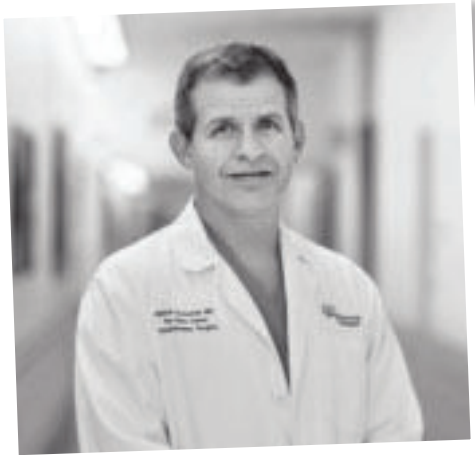
While advances in transcatheter approaches are promising, each size of transcatheter valve and conduit requires additional engineering and clinical study before it can be made available to the public. Additionally, researchers are following patients who have had transcatheter valve replacements to understand what impact, if any, leaving the diseased valve or the worn-out replacement valve in the body has.

And durability is still a huge issue. The valves delivered by transcatheter approach are still biologic valves without growth potential and prone to degradation and calcification.

“In the future, we’d like to have a better valve to implant with the transcatheter approach,” says Dr. Cheatham. “A tissue engineered valve made from the patient’s own cells that could grow and remodel, delivered without surgery – now that would be a game changer.”



In a healthy valve, the leaflets are comprised of extracellular matrix and a layer of endothelial cells. These thin leaflets are the “doors” to the four chambers of the heart. A heart valve will open and close billions of times in an average lifetime, so durability is an essential feature. Pictured at left: Pentachrome staining of pulmonary valve leaflet cross section to show organized layers of extracellular matrix.



“Children aren’t just out-growing their valves. That’s certainly a factor, but it’s not the whole story. They tend to tear through their replacement valves, and we can’t easily predict why or how or who will be most affected.”

– Patrick McConnell, MD, pediatric heart surgeon at The Heart Center at Nationwide Children’s

“Using a transcatheter approach to fix a fetal heart valve *in utero*, using a tissue engineered valve, could result in a baby that would have faced a lifetime of procedures being born with no defect and no need for additional surgery,” adds Dr. Cheatham. “This is an exciting opportunity, and I think we’re just beginning to see how fetal heart catheterizations can be used.”

DESIGNING A TISSUE ENGINEERED HEART VALVE

Tissue engineered heart valves (TEHVs) have been teetering between the bench and the bedside for the last 20 years since Christopher Breuer, MD, and Toshiharu Shinoka, MD, PhD, co-directors of the Tissue Engineering Program at Nationwide Children’s, created the first TEHV at Harvard University.

“Our first heart valve was a scaffold seeded with cells that formed a functioning valve that was alive and could grow and remodel,” says Dr. Breuer, who holds the Nationwide Endowed Chair in Surgical Research. “As we turned our focus to moving tissue engineered vascular grafts into the clinic, others carried the torch of the TEHV.”

According to Drs. Breuer and Shinoka, the investigation into TEHV follows two fundamental approaches. In the first approach, a biodegradable polymer scaffold is seeded with cells from the patients. The cells then make their own extracellular matrix (ECM) before and after implantation. In the second approach, researchers start with an established ECM – for example a decellularized donor valve. Then cells are added *in vitro* or the ECM acquires cells *in vivo*. Neither of these approaches has resulted in reliably good clinical results, but the research is moving forward.

In June 2017, experts from around the world gathered at Nationwide Children’s to discuss the state of tissue engineered vascular grafts and valves at the International Society for Vascular Tissue Engineering Symposium. There, John Mayer Jr., MD, senior associate in cardiovascular surgery at Boston Children’s Hospital and professor of surgery at Harvard Medical School, gave a special presentation about the past, present and future of TEHV.

During his talk, he called for investigation into the mechanical and microenvironments of the cells involved in the scaffold or ECM. Dr. Mayer suggests that creating a multilayered scaffold and refining ways to test the valve before placing it in the animal model should be the next steps toward a clinically useful TEHV.

COLLABORATING WITH ENGINEERS

In a lab at the Dorothy M. Davis Heart and Lung Research Institute at The Ohio State University, associate professor of biomedical engineering and surgery Lakshmi (Prasad) Dasi, PhD, leads a team in the application of engineering principles to heart valves. At the heart of his lab is a bioreactor that can do just what Dr. Mayer suggests.

“My lab is focused on understanding the role of valve mechanics on the initiation of native valve diseases or performance of novel prosthetic valves. While we are currently focused on calcific aortic valve disease, you could use a similar system to model the conditions of any valve,” says Dr. Dasi. “The engineering side of this project studies detailed blood flow patterns through the valve, how the leaflets open and close in response to these patterns, and what mechanical signals could trigger disease processes.”

To learn about how mechanics impact disease, Dr. Dasi and his team have designed an incubator-sized bioreactor system that enables them to control and measure nearly every variable influencing the valve.

“The bioreactor system serves as a model in which we can change local aortic root anatomy, heart rate, cardiac output, systolic durations and even coronary flow rates,” says Dr. Dasi.

The applications of this tool extend far beyond testing tissue engineered valves for durability. In one project, Dr. Dasi’s team is collaborating with Dr. Cheatham, using the flow setup to test new designs for catheter-deliverable valves. From altering the ring shape to using different polymers in the stent and finally altering the leaflet materials, researchers are working to move the needle on the durability of valves.

WHAT ROLE DOES BIOMECHANICS HAVE IN CALCIFICATION?

In a new collaboration with Joy Lincoln, PhD, principal investigator in the Center for Cardiovascular Research in The Research Institute at Nationwide Children’s, Dr. Dasi and his team are aiming to use the bioreactor to study how fluid mechanics influence the onset and progression of calcific aortic valve disease (CAVD).

CAVD is the most prevalent valvular disorder in the United States. While it has long been considered an adult disease, increasing evidence suggests that the disease has its origins during embryonic development.

In the collaboration, they will use 3D printed models of patients with CAVD to characterize the flow patterns

and pressures experienced by the cells. “By comparing healthy and sick patients, we’re trying to see what’s different in terms of cellular experience,” elaborates Dr. Dasi. “Then we can take living valves in the bioreactor to learn about biological signals in response to the mechanics.”

Dr. Lincoln has studied CAVD *in vitro*, with cell culture models and *in vivo* using small animal models. The next step in that process is going *ex vivo*, in Dr. Dasi’s lab where she and her team can work with whole pieces of tissue or whole aortic valves.

“We’re trying to explore the geometries and hemodynamic parameters that affect the valve short-term,” says Dr. Lincoln, who is also an associate professor of Pediatrics at The Ohio State University College of Medicine. “We also want to look for biomarkers or molecular indicators of early stages of calcification to prevent progression to end stage valve failure.”

Through her work *in vivo* and in animal models, Dr. Lincoln has teased out some of the signaling pathways involved in calcification.

By understanding the mechanisms of calcification, she hopes to find strategies or drugs to slow or eliminate the calcification process, thus providing a pharmaceutical option for the treatment of CAVD.

Dr. Lincoln is testing one such drug in animal models. The phase 1 clinical trial drug – KPT-330 – is currently being tested for cancer treatments. And based on her *in vitro* studies, it looks promising to treat or prevent calcification as well.

“Now, heart valves do not always need to be put in by a surgeon with a patient on bypass. This is huge. The risks associated with cardiopulmonary bypass compound with repeated open heart surgeries. But with the transcatheter approach, you can come in the morning, get a new valve and go home the next day.”



– John Cheatham, MD, interventional cardiologist and co-director of The Heart Center at Nationwide Children’s



– Joy Lincoln, PhD, principal investigator in the Center for Cardiovascular Research in The Research Institute at Nationwide Children’s

– Vidu Garg, MD, director of the Center for Cardiovascular Research at The Research Institute and a pediatric cardiologist in The Heart Center at Nationwide Children’s

“Now we’re doing some high throughput screening to try and work out how exactly the drug is working, as well as *in vivo* studies to rescue mouse models of calcification with the drug,” she says.

Parallel molecular studies are also ongoing to determine the molecular mechanisms by which KPT-330 can treat CAVD.

Another avenue of research in Dr. Lincoln’s lab is studying the development of heart valves in the embryo. “There’s still so much to learn about how the valves form *in utero*, what signaling pathways are important, how the leaflets form,” she says. “If we can understand this, it will open new avenues of research and understanding how the leaflets repair and remodel over the course of a lifetime.”

USING GENOMICS TO UNCOVER THE ORIGINS OF HVD

In the 1990s, mouse knockout technology enabled the study of the function of genes in an animal model. In the case of cardiovascular diseases, researchers identified numerous genes, which, when knocked out or deleted in the mouse, would result in the lethality of the embryo often due to improper heart development.

“While we figured out that it was due to defective heart development, these findings did not translate into the patients we see with congenital heart disease, because they’re born alive,” explains Vidu Garg, MD, director of the Center for Cardiovascular Research at The Research Institute and a pediatric cardiologist in The Heart Center at Nationwide Children’s. “That’s what stimulated me to look at this question starting from a

human genetics approach. We’ve always thought there were genetic contributors, and so that’s why we began collecting DNA samples from patients with congenital heart disease.”

Dr. Garg’s research focuses on the genetic origins of bicuspid aortic valve disease, which affects adults and children alike. “With bicuspid aortic valve disease, there’s a spectrum,” he explains. “You may have a thickened dysplastic valve that presents on day one. Others may not present until much later.”

Interestingly, bicuspid aortic valve runs in some families. “As such, it’s one of the congenital heart defects that we’ve been able to find a genetic basis for,” says Dr. Garg, who holds the Nationwide Foundation Endowed Chair in Cardiovascular Research.

The first causative gene that was discovered is NOTCH1. “We found that mutations in NOTCH1 cause bicuspid aortic valve and calcific aortic valve disease in families,” says Dr. Garg. “This finding opened the door to study how mutation of NOTCH1 can cause bicuspid aortic valve and predispose an individual to valve calcification. This has allowed for the development of mouse models with mutations in NOTCH1 that display both bicuspid aortic valve and calcification.

“Currently, we know that mutation of NOTCH1 is implicated in the defect and potentially in the development of valve calcification, but we don’t know how or why exactly. There’s a lot of controversy in this area,” says Dr. Garg. “Many researchers are focusing on the abnormal flow across the bicuspid valve. My bias as a geneticist is that the aortic valve cells are going to be abnormal, as many of the genes, including NOTCH1, expressed in development are expressed in adulthood. It’s not a far stretch to say that the cells aren’t normal, even if they may look normal, because the cells contain a gene that is mutated.”

Bicuspid aortic valve is also associated with getting an aneurysm of the ascending aorta, and researchers are currently studying if loss of NOTCH1 plays a role in this process.

“If we can understand how the genetic mutations are impacting the cellular pathways and processes to cause bicuspid aortic valve and its complications of valve calcification and aortic aneurysm, we could potentially unlock the underlying mechanisms for these associated diseases,” he explains.

As CHD care continues to improve and more people with CHD live longer and have babies, physicians and geneticists will get a clearer genetic picture of the heritable pattern of specific types of CHD. Ultimately, the goal is to allow for more personalized care so that physicians and patients can know the risks of future complications and what to look for. “By understanding the genetics and underlying mechanisms of valve disease, we hope that it will ultimately lead to new therapies,” Dr. Garg says.

Another interesting area of Dr. Garg’s research looks at environmental attributes that influence genes during development and disease. For example, in developing more accurate animal models of valve disease, he and his collaborators discovered that exposure to nitric oxide influences the phenotype in models with mutations in NOTCH1.

“We think that the interactions of genes and environmental stressors are likely key in the development of heart disease – including valve disease – and this occurs even in the growing fetus,” says Dr. Garg. “If we know that there’s a certain environmental attribute that influences an important cardiac molecular pathway, why can’t we alter that?”

Dr. Garg suggests that by more closely monitoring genetic susceptibility to environmental risk factors in pregnancies we could prevent CHD for some babies.

“But we’re still trying to identify all the genetic players,” Dr. Garg adds.

BRINGING IT ALL TOGETHER

Because of the collaborative work being done across the spectrum of HVD research, the future for treatment is likely to be multifaceted – full of innovations from many diverse areas of science and clinical care.

“Looking to the future, our goal is to find ways to prevent HVD where we can offer multiple choices for treatment – pharmaceuticals, surgery or catheterization procedures – to fix valves that are not properly developing,” says Dr. Garg. “Each of these three areas, supported and integrated by biomechanical and tissue engineering, is critical to the long term success for heart valve patients.”

Dasi LP, Grande-Allen J, Kunzelman K, Kuhl E. The pursuit of engineering the ideal heart valve replacement or repair: A special issue of the *Annals of Biomedical Engineering*. *Annals of Biomedical Engineering*. 2017 Feb;45(2):307-309.

Kerstjens-Frederikse WS, van de Laar IM, Vos YJ, Verhagen JM, Berger RM, Lichtenblet KD, Klein Wassink-Ruiter JS, van der Zwagg PA, du Marchie Sarvaas GJ, Bergman KA, Bilardo CM, Roos-Hesselink JW, Janssen JH, Frohn-Mulder IM, van Spaendonck-Zwarts KY, van Melle JP, Hofstra RM, Wessels MW. Cardiovascular malformations caused by NOTCH1 mutations do not keep left: data on 428 probands with left-sided CHD and their families. *Genetic Medicine*. 2016 Sep;18(9):914-923.

Koenig SN, Bosse K, Majumdar U, Bonachea EM, Radtke F, Garg V. Endothelial Notch 1 is required for proper development of the semilunar valves and cardiac outflow tract. *Journal of the American Heart Association*. 2016;5:e003075.

Lincoln J, Garg V. Etiology of valvular heart disease. *Circulation Journal*. 2014 Aug;78:1801-1807.

Mayer JE. Making progress toward a tissue engineered heart valve. *The Journal of Thoracic and Cardiovascular Surgery*. 2016;152(4):1165-1166.

Shinoka T, Miyachi H. Current status of tissue engineering heart valve. *World Journal for Pediatric and Congenital Heart Surgery*. 2016;7(6):677-684.

“Looking to the future, our goal is to find ways to prevent HVD where we can offer multiple choices for treatment – pharmaceuticals, surgery or catheterization procedures – to fix valves that are not properly developing. Each of these three areas, supported and integrated by biomechanical and tissue engineering, is critical to the long term success for heart valve patients.”

– Vidu Garg, MD



CREATIVE REALITY

Collaboration and innovative thinking result in a new technology platform to improve the patient experience.

..... by *Abbie Roth*

Amy Dunn, MD, had a problem. Some of her patients in the hematology clinic at Nationwide Children's Hospital receive hundreds of needle sticks each year.

"Needle phobia is very real for these patients and their families," says Dr. Dunn, director of Pediatric Hematology at Nationwide Children's. "In some cases, ports need to be implanted so that these children can get the medicine they need. In every case, appointments and infusions are filled with stress, anxiety and discomfort for everyone involved."

When Dr. Dunn approached the User Experience team – which works with researchers to create people-friendly health technology solutions – about this problem, the team started on a journey of "what could be."

AN UNCONVENTIONAL TEAM FOR AN UNCONVENTIONAL SOLUTION

An artist, designer, gamemaker and doctor work at a hospital... It may sound like the beginning of a really confusing joke, but in this case, it's the beginning of a story about innovation. About a team that is working to create a new reality of how technology, clinical research and patient care can intersect.

The solution Dr. Dunn and the User Experience team created is a suite of virtual reality games, named Voxel Bay, built entirely in-house with evidence-based research as the cornerstone. Additionally, they solved the problem of getting a child-sized, affordable, clinically appropriate virtual reality headset by building their own.

So what makes Voxel Bay and its creators unique? Certainly, virtual reality has been explored in medicine previously. One of the most successful uses of virtual reality in the medical setting is for burn victims during dressing changes. Studies have shown that virtual reality experiences during dressing changes result in a decrease in required pain medication and psychological distress. But most of that work has been done in adults.

"Every component of Voxel Bay and the headset was designed with the needs and goals of the pediatric patient with hemophilia in mind," says Jeremy Patterson, lead for User Experience Technology Research and Development at Nationwide Children's. "The true magic of Voxel Bay is in the entire experience that was crafted around a specific problem—a targeted experience that was designed and created in tandem with clinical expertise and research."

"We now have an in-clinic experience that begins when the patient is handed the headset and then transitions into the meat of the experience, which is the games and activities," he elaborates. "This is exactly the tactic employed by Disney World for their iconic experience. We have brought a rich experience like this into a pediatric clinic; and this is a big deal. This is what resonates with people, and most importantly with our patients and families."

This bench-to-bedside effort exemplifies the results that can be obtained when the clinical staff and the design team work closely together.

"We wanted to do more than make something fun and cute," says Dr. Dunn, who is also a professor of Pediatrics at The Ohio State University College of Medicine. "The aspect of clinical utility is paramount, and we were able to conduct a clinical trial with the system to measure the impact it had on our patients. We were able to show that we could incorporate our virtual reality platform into a busy hemophilia clinic without lengthening time in clinic. Additionally, the medical team, parents and children really saw what a difference Voxel Bay made in the patient experience."

According to Charmaine Biega, RN, nurse clinician and leader of the clinical trial, the feedback from clinic staff, patients and parents has all been positive.

"The time difference for blood draws and factor infusions after adding Voxel Bay to the clinic visit was

"The true magic of Voxel Bay is in the entire experience that was crafted around a specific problem—a targeted experience that was designed and created in tandem with clinical expertise and research."

– Jeremy Patterson, lead for User Experience Technology Research and Development at Nationwide Children's

less than one minute,” she says. “But the difference in patient experience was dramatic. It was a 180-degree change for some of our most challenging patients.”

Voxel Bay was presented at Association of Computing Machinery (ACM) SIGGRAPH 2016 – an international conference and exhibition on computer graphics and innovation techniques.

Since then, the program has caught the attention of others. Voxel Bay has been the recipient of several honors and awards, including being a nominated finalist at South by Southwest (SXSW) Interactive for 2017, receiving the #WhatsGood award at SXSW, being named the Children’s Miracle Network Achievement of the Year and being a 2017 Most Wired Children’s Hospitals Innovation Finalist.

MANAGING RISK

The lessons for innovation gleaned from the creation and development of Voxel Bay resonate with innovators everywhere: Take calculated risks, think big, use your resources, start, fail forward and keep going. Let your passion fuel you.

“In my mind, our biggest risk was the risk of failure,” says Dr. Dunn. “Many times along the way we ran into obstacles that could have derailed the project. But we have a team of people who are really passionate about making a difference in the lives of our patients, and we were determined not to give up.”

But it’s not just hammering away at the problem until something gives. “There’s a methodology to our brand of innovation,” explains Patterson. “The key is taking informed and calculated risks. You can fail, but you need to set yourself up for graceful failure. This comes

through informed, strategic bets on how to move forward in such a way that if you fall down, you are at least falling in the right direction.”

By introducing this concept and way of working to the institution, the User Experience team has contributed to the innovation culture in a way that sets the stage for continued innovations beyond Voxel Bay.

“This level of innovation at a pediatric institution is unique, but it shouldn’t be. This collaboration across divisions, departments and specialties should be the norm,” says Robert Strouse, MFA, User Experience Designer, Research Information Solutions & Innovation at Nationwide Children’s. “Why can’t this happen everywhere? My thought is that it can. And it should.”

One example of the method described by Patterson is the iterative design process that led to the creation of the clinic-friendly virtual reality headset.

“When we started this project, we started with a commodity headset, an Oculus Rift dev kit to be exact. But when doing an initial test of the games with some children at a hemophilia fundraising event, we realized that the headset was a major pain point for us when setting things up and for the kids playing,” says Patterson. “We saw that the games were fun, the breath controls were working, but the headset needed help. That’s when we knew we needed to design our own headset.”

By continually learning from their collective experiences, the team continued to find a way forward.

“Version 14 of the headset finally made it into the clinic,” says Strouse, lead designer of the headset. “We’re now on version 18, which is a headset that looks like the



“I think we should always strive to find new and better ways to help our patients. My best advice is to really think about the challenges faced in the care of patients and then work collaboratively to come up with new ways to overcome those challenges.”

– Amy Dunn, MD, director of Pediatric Hematology at Nationwide Children’s



Left: Jeremy Patterson with patient Jackson, who was part of the clinical trial. Jackson is wearing the latest version of the headset. Right: The early versions of the headset were constructed of cardboard.

dragon in the game and is made entirely out of the same material as a stress ball. Despite our forward progress, we continue to learn from our patients and evolve the headset – as well as the entire system – to meet the needs of patients, parents and practitioners.”

Part of managing risk and utilizing resources includes managing the financial picture. Innovative projects like this one cost money, and funding is certainly a concern for researchers, clinicians and institutions alike.

“We have had a series of grants to help along the way, starting with an internal technology development grant, a Clinical and Translational Science Voucher from The Ohio State University and Nationwide Children’s, a grant from the National Hemophilia Foundation and, most recently, a grant from the Department of Education – ICORP@Ohio,” says Dr. Dunn.

Beyond the financial support of grants, Dr. Dunn also credits the institution for having the infrastructure to accommodate innovative projects like this.

“The hospital was instrumental in setting up and funding User Experience from the beginning; I think this was incredibly forward thinking and unique among children’s hospitals,” she says.

WHAT’S NEXT?

“A lot of people we’ve talked with are excited about what could be next,” says Dr. Dunn. “If you think about how

we can take what we’ve done, what we’ve learned, and expand it to other parts of the hospital or other parts of the patient experience, it’s a really exciting prospect.”

An exciting prospect that takes time, effort and funding to do it right. According to Dr. Dunn, the Voxel Bay team is actively pursuing partnerships and clinical research funding to explore the use of the platform to help patients in a variety of clinical situations.

And for other clinicians, researchers and innovators who want to blaze their own trails, Dr. Dunn and her team are enthusiastic supporters.

“I think we should always strive to find new and better ways to help our patients,” says Dr. Dunn. “My best advice is to really think about the challenges faced in the care of patients and then work collaboratively to come up with new ways to overcome those challenges.”

Strouse agrees. “Identify what gets in your way the most. Don’t edit it, don’t try to solve it, just identify it and name it. Then, look for the people who can help. Maybe they’re in another department, another building or another institution. Reach out. This is the beginning of the path from health care provider to health care innovator.”



For videos, pictures and more about Voxel Bay, visit PediatricsNationwide.org/More-Voxel-Bay



CAN BEHAVIORAL ECONOMICS HELP PEOPLE ADOPT BETTER HEALTH HABITS?

Simple incentives may nudge patients, caregivers and clinicians to make more healthful choices.

..... by Kevin Mayhoo
.....

Behavioral economics has helped electricity customers cut down on usage, new employees to start setting aside money for retirement from day one and, more recently, to change health care provider and patient behaviors.

The practice combines insights from psychology, economics and marketing to improve decision-making by individuals, says Jack Stevens, PhD, a clinical psychologist and principal investigator at the Center for Biobehavioral Health at Nationwide Children's Hospital.

"In the health care field, certainly there are concerns about finding ways to save money and prevent unnecessary or ineffective care, but also concerns about optimizing people's well-being," says Dr. Stevens, an associate professor of Pediatrics at The Ohio State University College of Medicine and author of a commentary on behavioral economics in *Pediatric Quality and Safety*. "This can promote both objectives."

Behavioral economics provides low-intensity nudges to help people make better decisions and avoid poor ones. But rather than dictate, the nudges include some degree of freedom of choice and control.

So far, most research has been done with adults, but Charlene Wong, MD, assistant professor of pediatrics and a health services/health policy researcher at Duke University, believes incentives that work in pediatric medicine may prove to be the most impactful.

"Disease starts before adulthood. If we're able to help kids develop healthier habits or take better control of their chronic diseases, that would have implications for population health and costs for the health care system," says Dr. Wong, whose practice focuses on adolescent health. "To prevent disease, even better."

"We have a real opportunity to improve health for many, many years," she says.

Unlike traditional economics, which assumes people always make decisions in their own best interest, behavioral economics assumes people frequently make biased decisions that are not always in their best interest. For example, many people opt for the immediate gratification of overeating and don't consider the long-term damage of obesity.

Interventions – nudges – that address common decision errors can make it harder for people to make bad decisions and easier to make better choices, researchers say. A variety of strategies are showing promise.

For example, a common problem among patients is their failure to take medications consistently, even when they're aware of the benefits. Typically, doctors suggest to patients that they set a daily reminder.

“Behavioral economics ups this by asking the patient to set the reminder before leaving the office,” Dr. Stevens says. Or, even stronger, the office will set it up and the doctor tells the patient to expect automatic reminders. In either case, the patient can disregard or discontinue the reminders.

Dr. Wong has completed a study using financial incentives to encourage adolescents with type 1 diabetes to check their glucose at least four times a day. “We were using the behavioral economics principle of loss aversion, which is that people are more motivated by losses than gains. Participants would lose money from a virtual account if they failed to monitor their glucose appropriately,” she says. “We found that daily loss aversion financial incentives got them to check their glucose more.”

Among providers, a study published in the *Journal of the American Medical Association*, used different nudges to reduce inappropriate prescriptions for antibiotics. Sometimes, “patients are miserable and expect or demand an antibiotic, and the doctor gives the prescription,” Dr. Stevens says.

But when a clinician entered the diagnostic code for a viral infection such as influenza in the electronic medical record and prescribed an antibiotic, the clinician immediately received a message saying the prescription may be inappropriate. The clinician was

then asked to write a sentence or two to explain why this prescription was ordered. And, the clinician knew others may see the record. “These nudges decreased the likelihood that a clinician would prescribe an inappropriate antibiotic,” Dr. Stevens says.

Drs. Wong and Stevens say more research is needed to determine whether behavioral economics will work in pediatrics.

“Incentivizing parents for their children's health or young people themselves is a different construct, both in the parent/child dyad and neurodevelopmentally, than designing these interventions for adults,” Dr. Wong says. “We're also targeting behaviors like physical activity and healthy eating, which in many cases, have benefit much further down the road than reduced hospitalization. However, the pay-off is significant and multiplied by many more years of health.”

Most studies have been short-term and Drs. Stevens, Wong and some colleagues question whether the incentive effect of nudges diminishes over time. Nudges, may become ignored as patients or physicians become accustomed and tune them out, they say.

But if the incentive wears off, evidence of improved health may be enough to encourage a patient, parent or provider to continue down the path, Dr. Stevens says.

Another hurdle, according to Dr. Stevens, is that health care professionals may consider the strategies too unsophisticated to change behavior and dismiss them out of hand. “We don't expect a panacea,” he says. “But if it's low-cost and has a meaningful benefit, it's worth doing.”

Both researchers warn that interventions won't work on people who have no interest in changing. Learning to identify those who are willing or want to change will be critical to efficiently using strategies and resources. In all cases, Stevens says, the use of interventions must have a compelling and ethical rationale – such as to increase vaccination rates and to protect children.

Stevens J. The promising contributions of behavioral economics to quality improvement in health care. *Pediatric Quality and Safety*. 2017 May/Jun;2(3): e023.

Meeker D, Linder JA, Cox CR, Friedberg MW, Persell SD, Goldstein NJ, Knight TK, Hay JW, Doctor JN. Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices: A randomized clinical trial. *Journal of the American Medical Association*. 2016 Feb 9;315(6): 562-570.



For extended content, including practical strategies for incorporating behavioral economics principles, visit [PediatricsNationwide.org/Behavioral-Economics-Strategies](https://www.pediatricsnationwide.org/Behavioral-Economics-Strategies).

Bouncing Back: Overcoming Physician Burnout with Resilience

By Suzanne Reed, MD, Assistant Professor of Clinical Pediatrics, Hematology/Oncology/BMT;
and John Mahan, MD, Professor of Pediatrics, Pediatric Nephrology

Physician burnout is becoming increasingly recognized as an extensive and debilitating reality. Present in specialties across the spectrum of medicine, most disciplines report burnout rates of 50 to 60 percent or more, and these rates have been increasing over the last several years. Pediatrics alone demonstrated a more than 16 percent increase in burnout, up from 35 percent in 2011 for general pediatricians. Burnout has been defined as a “state of mental and physical exhaustion related to work or care-giving activities.” The Maslach Burnout Inventory, the reference standard for measuring burnout, utilizes three domains in describing and characterizing burnout: high emotional exhaustion, high depersonalization and low sense of personal accomplishment.

The consequences of burnout are significant, from professional consequences such as poorer patient outcomes; for example, increased medical errors and lower quality of care; to personal problems such as inability to cope, leading to increased rates of substance abuse and death by suicide.

Causes of burnout fall into three main categories: systems issues, such as bureaucratic overload; divisional/local issues, such as difficult patients; and personal issues, such as family stressors and lack of self-compassion and self-care. Burnout is more prevalent in female physicians across subspecialties, and they report less happiness at work than male physicians, as well.

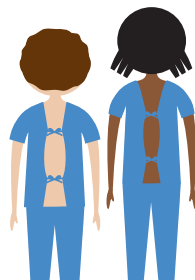
Resilience is the ability of an individual to respond to stress in a healthy, adaptive way so that personal goals are achieved at reasonable psychological and physical costs, and we believe it is the primary protection against burnout. The nature of medicine is to care for vulnerable individuals and cope with illness and undesired outcomes; resilience allows physicians to withstand and “bounce back” from the challenges associated with these duties.

As physician-educators, we endorse multiple complementary methods to promote resilience, such as (1) attending to self-awareness, self-care, optimism, gratitude, mind-body skills and (2) pursuing enhanced support and community-building for physicians. Mitigating burnout is best addressed through a multifaceted professional and personal approach. Professionally, we must prioritize balancing excessive workload and improving efficiency for physicians in their clinical work. Promoting physician autonomy by valuing input and facilitating engagement can be very powerful. Personally, encouraging efforts at work-life balance, or rather work-life integration, can foster the healthy proportion of work and life and acknowledge the interconnectedness of our relationships, roles and responsibilities in all facets of our lives. Balance implies competition between the elements of work and life, or at least their independent existences. In today’s technological age, the boundaries of our work and lives increasingly overlap, and healthy work-life integration is a more realistic and useful goal.

Consequences of Burnout for Patients and Physicians

PROFESSIONAL (PATIENT) COSTS

- Increased medical errors
- Communication problems
- Decreased quality of care
- Patient dissatisfaction



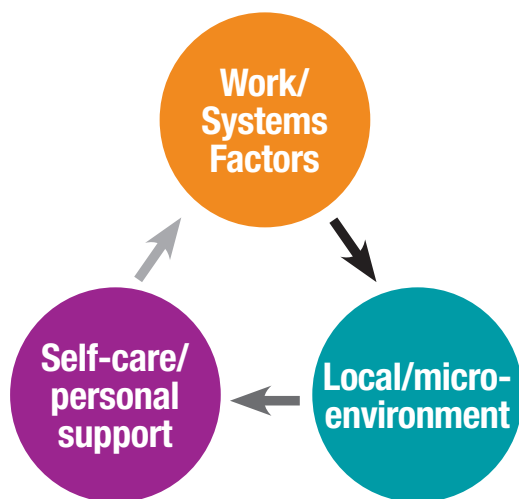
PERSONAL (PHYSICIAN) COSTS

- Job dissatisfaction
- Decreased job tenure
- Relationship problems
- Poor coping
- Depression
- Substance abuse
- Suicide



Suzanne Reed, MD and John Mahan, MD

Influencers of Burnout/Resilience



An essential facet of healthy work-life integration is uncovering, re-establishing and maintaining the intrinsic and extrinsic meaning in our work. It is that which, for most of us, compelled us to become physicians, and that which defines our work as not simply a job, but a calling.

Institutions must work to improve and optimize work environments to promote institutional physician resilience. On a local level, leaders can develop more effective team functions to better support physicians and other team members. Focused rewards and recognition of accomplishments can promote a cohesive, supportive local environment and foster resilience.

It is important to recognize that work on systems and local environments are only part of the path to resilience. Personal growth and development are arguably as important and certainly under the control of the individual physician. Mindfulness and meditation have been shown to enhance resilience in physicians. Purposeful focus on gratitude, such as keeping a gratitude journal, and maintaining a healthy perspective are other routines associated with wellness. Positive thinking is another life practice that fosters resilience;

it describes the ability to experience both negative and positive emotions in difficult situations and the capacity to find redeeming value in the challenges. Notably, these are all skills that can be learned by anyone with proper instruction and, most importantly, deliberate practice. Additionally, adequate sleep, exercise and a healthy diet are so basic (and so often neglected), yet so essential to personal wellness and enhanced resilience.

It is insufficient to only understand and acknowledge burnout. Cultivating true resilience in physicians through system changes and promoting wellness and self-care is the path beyond burnout. It will require a concerted and integrated effort between systems, leadership and individual physicians to create and enforce a culture which develops and values resilience. This requires a paradigm shift for the medical profession and necessitates the letting go of long-held professional norms that have implicitly expected physicians to simply work on, work harder, and endure. Resiliency allows physicians to flourish while staying connected with their own missions, values and priorities at work and in life. The stakes and rewards for our patients and our society will be profound.

Connections

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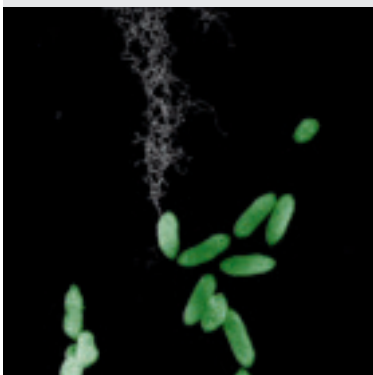


Could Nutritional Supplements Impact Autism Symptoms in Toddlers Born Preterm?

by Rachael Hardison

Delay in language development is often an early indicator in children at risk for developing autism spectrum disorder (ASD), yet clinicians are still trying to understand the best practices for how and when to implement early intervention strategies. In a pilot study, recently published in the *Journal of Autism and Developmental Disorders*, a team of researchers found that supplementation with omega-3 and -6 fatty acids had positive effects on language development in preterm toddlers at risk for developing ASD.

PediatricsNationwide.org/Omega-3-6-Autism



Mechanism for Expulsion of DNA From NTHI Described

by Abbie Roth

Nontypeable *Haemophilus influenzae* (NTHI) bacteria, a common culprit in otitis media, are known for their ability to create dense biofilms. These biofilms are part of an elaborate defense system that enables the bacteria to persist despite attack from antibiotics and the immune system. A scaffold of extracellular DNA and DNABII proteins comprise the central structure of the biofilm. In a paper recently published in *Proceedings of the National Academy of Science*, Lauren Bakaletz, PhD, and her team describe the mechanism by which NTHI eject DNA for the purpose of creating the biofilm matrix.

PediatricsNationwide.org/NTHI-DNA-mechanism



How to Advocate for Patients With Legislators

by Steve Allen, MD

Perhaps now more than ever, the health care community has come together to advocate for their patients regarding specific legislation. As subject matter experts, health care professionals have perspectives on issues that government officials do not. It is a privilege and obligation to advocate on behalf of patients, and there are some simple tips and tactics to consider when reaching out to legislators.

PediatricsNationwide.org/How-To-Advocate-With-Legislators

“ You cannot get through a single day without having an impact on the world around you. What you do makes a difference, and you have to decide what kind of difference you want to make. ”

– Jane Goodall

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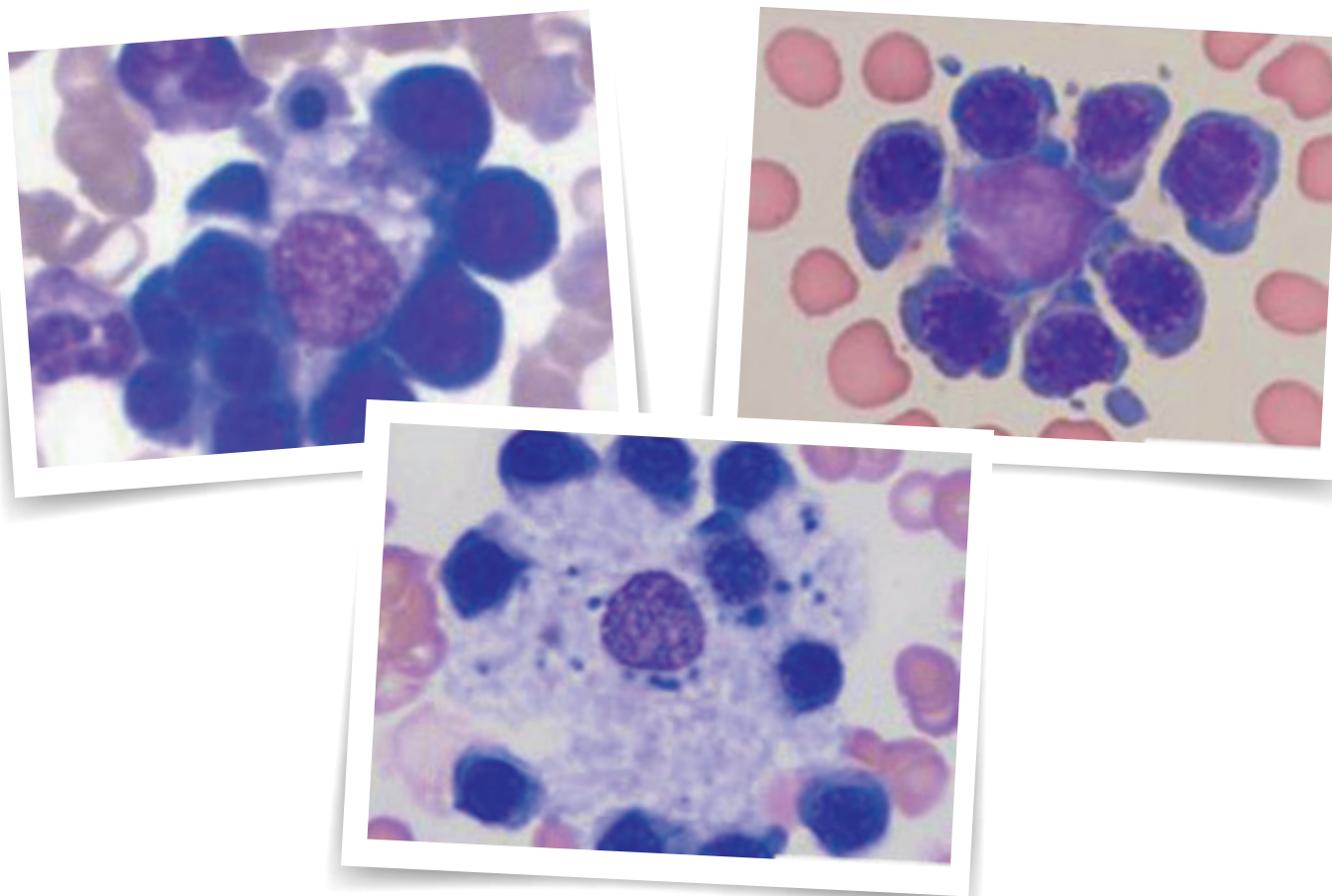


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