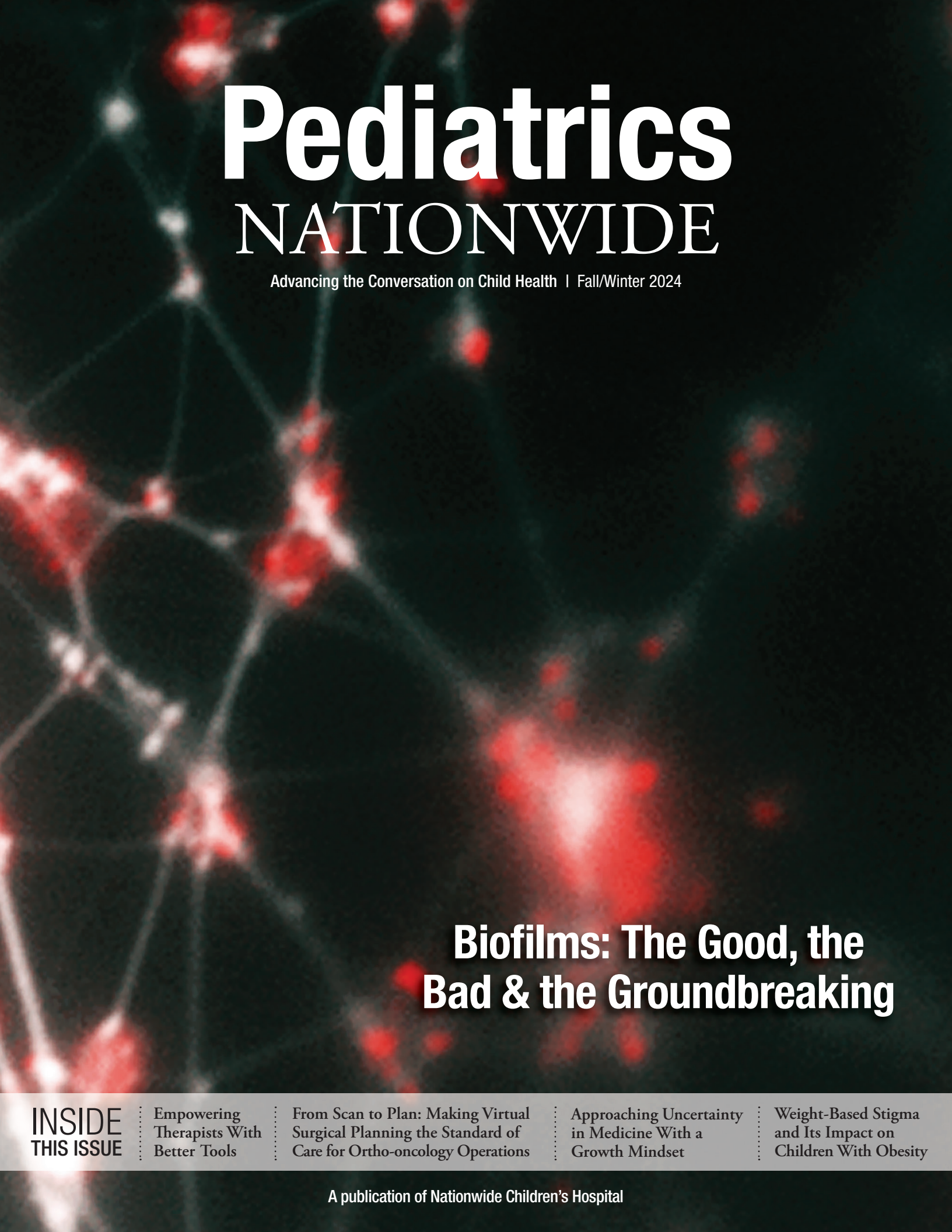

Pediatrics NATIONWIDE

Advancing the Conversation on Child Health | Fall/Winter 2024

Biofilms: The Good, the Bad & the Groundbreaking

INSIDE THIS ISSUE

A publication of Nationwide Children's Hospital

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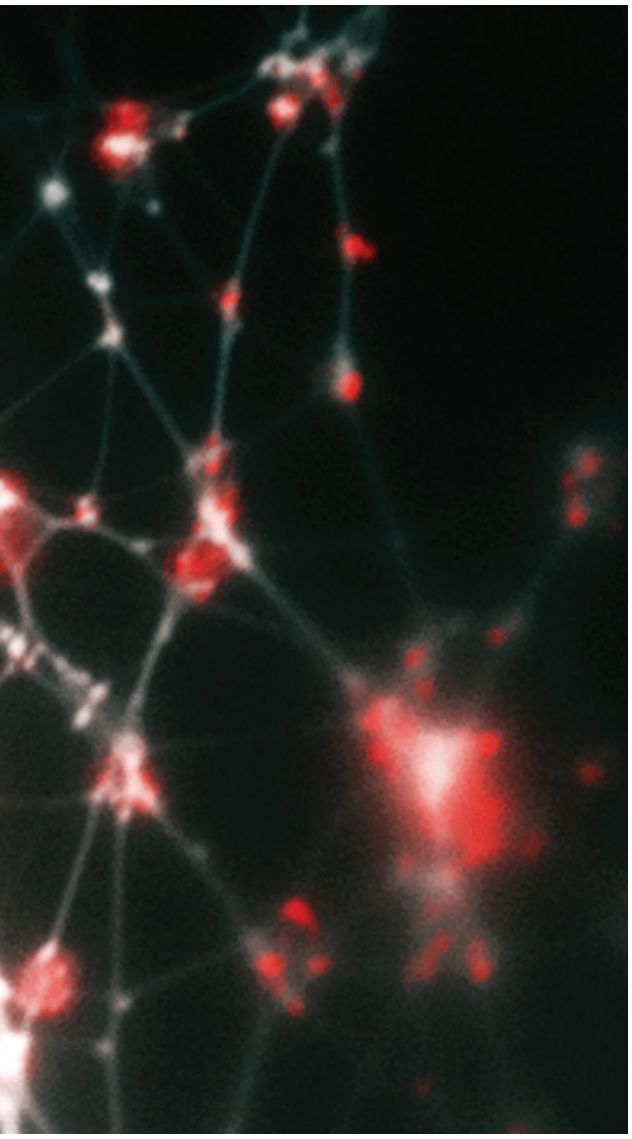
Biofilms: The Good, the Bad & the Groundbreaking



Originally published in:

Goodman S, Obergfell K, Jurcisek J, Novotny LA, Downey JS, Ayala EA, Tjokro N, Li B, Justice SS, Bakaletz LO. Biofilms can be dispersed by focusing the immune system on a common family of bacterial nucleoid-associated proteins. *Mucosal Immunology*. 2011;4:625–637.

Biofilms are naturally formed communities of bacteria that construct a web-like matrix inside the body using extracellular DNA from both the host and the bacteria. They physically shield the bacteria from immune cells, medications, adverse environments, and DNA-destroying enzymes.

The lattice of the biofilm structure (shown at left) is made of DNA fibers. The vertices form a cross that is stabilized by DNABII proteins. The vertices can create a variety of interconnected polygons that resemble a three-dimensional spider web.

Over the past few decades, researchers at Nationwide Children's Hospital have chipped away at understanding the biochemical and structural elements of these biofilms. Read the feature on page 18 to learn how they are combating the bad, harnessing the good, and making groundbreaking discoveries in biofilm science.

DEPARTMENTS

FEATURES

> If you can't use whatever we develop from a research perspective for assessment or treatment — if it isn't functional in a typical clinical setting — you haven't done much good."
>
> *– Mary A. Fristad, PhD, ABPP, director of Academic Affairs and Research Development at Big Lots Behavioral Health Services at Nationwide Children's Hospital*

> We deal in rarities. When you consider that across the entire U.S. population, we have between 2,500 and 3,000 cases of primary malignant bone tumors each year, and only half of those are kids, every case requires unique consideration and planning."
>
> *– Thomas Scharschmidt, MD, director of the Pediatric Orthopedic Oncology Program at Nationwide Children's Hospital*

Delivering Implicit Bias Training for Health Care Providers – Via Smartphone

A Virtual and Augmented Reality Implicit Association Training (VARIAT) app developed by investigators from Nationwide Children's Hospital and The Ohio State University leverages mobile technology to bring implicit bias training to the hands of Medicaid clinicians.

Everyone has implicit biases that manifest as favorable or unfavorable perspectives about race, gender, sexual orientation and/or socioeconomic status, among other factors. For clinicians, these biases can unintentionally affect medical decision making and the quality of care provided. To mitigate implicit bias in medicine, it is important for health care providers to be educated about cultural competency.

"When starting this project, we asked, 'How do we reach a large population of practicing health care providers of all different disciplines, in a way that fits their busy schedule?' and 'How can we maximize learner engagement?' Since everyone's on their phone, which is both accessible and portable, we came up with the idea of developing an app," says Tensing Maa, MD, medical director of the Simulation Program at Nationwide Children's and clinical professor in Pediatrics for The Ohio State University College of Medicine.

Dr. Maa and colleagues partnered with the technology company LittleSeed to create a mobile app through which implicit bias training could be delivered. VARIAT comprises two interconnected modules focusing on sexual orientation/gender identity and race/socioeconomic status. Each scenario has a duration of 5 to 10 minutes and is followed by a module debriefing and quiz. VARIAT can be completed in on-demand, brief periods of time, or all at once. The intended audience is Medicaid providers in Ohio, and this Medicaid Equity Simulation Project was funded by the Ohio Department of Medicaid and administered by the Ohio Colleges of Medicine Government Resource Center.

VARIAT was evaluated in a study published in *JMIR Serious Games*, in which 18 Medicaid providers used the app and were surveyed about their experience.

The study participants were majority White, women, fully credentialed physicians or social workers and worked in a hospital.

Participants reported that VARIAT training was relevant to their job and they had positive feelings about being in the simulation. Most participants thought completing both modules would improve their relationship with their patients, improve delivery of tailored care and avoid undesirable events. In addition, most thought the sexual orientation and gender identity module would improve patient satisfaction and that the race and socioeconomic status module would improve community resources.

All quiz scores increased from pretest to posttest, however, no changes reached significance.

Dr. Maa concluded, "I think that there is a lot of potential for this type of technology, that it could be updated or expanded with other modules." VARIAT is available for free in the App store.

Shen J, Clinton AJ, Penka J, Gregory ME, Sova L, Pfeil S, Patterson J, Maa T. Smartphone-based Virtual and Augmented Reality Implicit Association Training (VARIAT) for reducing implicit biases toward patients among health care providers: App Development and Pilot Testing. *JMIR Serious Games*. 2024 Mar 7:12:e51310.

— Jessica Nye, PhD

Tissue-Engineered Vascular Grafts Resist Calcification

Dystrophic calcification is the biggest reason for prosthetic biomaterial failure.

Compared to expanded poly(tetrafluoroethylene) (PTFE) grafts, tissue-engineered vascular grafts (TEVGs) exhibited superior durability, including reduced late-term calcification, according to a study published in *Nature Communications*.

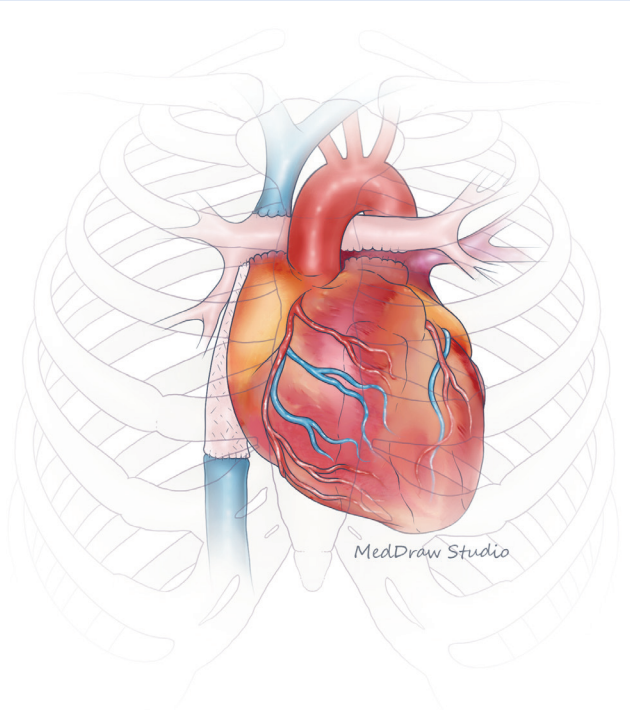
"All of the biomaterials we routinely use for cardiovascular surgery are susceptible to dystrophic calcification," says Christopher Breuer, MD, pediatric surgeon and director of the Center for Regenerative Medicine at Nationwide Children's Hospital. "This biomineralization reduces the function of the material, whether it is functioning as a vessel or valve, and can ultimately lead to the need for replacement of the prosthetic."

Dr. Breuer and his team have spent nearly three decades developing TEVGs that use a biodegradable scaffold seeded with the patient's own cells. As the scaffold degrades, it is replaced with native tissue, resulting in a vessel that functions and grows with the patient — an important aspect for young patients who undergo surgery for congenital heart disease.

Their TEVG is currently the only one in clinical trials in the United States evaluating their technology in children and has recently been granted Breakthrough designation by the U.S. Food and Drug Administration (FDA). The latest study evaluates the long-term performance of the grafts compared to graft options currently in the marketplace.

Utilizing natural history data from expanded PTFE grafts, which are the most frequently used vascular conduits, and retrospective data from clinical trials and ovine model studies of TEVGs, the researchers evaluated the formation of dystrophic calcification and other biomechanical properties, including compliance mismatch. Compliance describes the change in vessel diameter over a change in pressure. Compliance mismatch refers to the difference between the compliance of the native vessel and the graft. The team then validated the findings through computational modeling.

TEVGs resisted dystrophic calcification when used as extra-cardiac conduits in the Fontan procedure (a common surgery used to treat single-ventricle disease in children). Additionally, TEVGs had better compliance matching, which allowed the graft to act more like the native vessel.



Stenosis, or narrowing of the vessel, is another risk associated with vascular grafts. The researchers used computational modeling to show that better compliance matching also prevented the formation of stenosis.

"This study further demonstrates the promise of tissue-engineered vascular grafts as long-term solutions in congenital heart surgeries," says Dr. Breuer. "We continue to work to try to bring tissue engineering technology to the clinic in an attempt to improve outcomes for children born with congenital heart disease."

Turner, ME, Blum KM, Watanabe T, Schwarz EL, Nabavinia M, Leland JT, Villarreal DJ, Schwartzman WE, Chou T-H, Baker PB, Matsumura G, Krishnamurthy R, Yates AR, Hor KN, Humphrey JD, Marsden AL, Stacy MR, Shinoka T, Breuer CK. Tissue engineered vascular grafts are resistant to the formation for dystrophic calcification. *Nature Communications*. 2024;14:2187.

— Abbie Miller, MWC

Health-Related Quality of Life in Pediatric Cancer Survivors: Assessing the Impacts

Family factors have a significant impact on health-related quality of life.

Childhood cancer is a life-changing diagnosis for children and their families. Children undergoing cancer treatment often experience impairment in health-related quality of life compared to children from healthy populations. The severity of impact can depend, in part, on social determinants of health, such as the family's sociodemographic background.

In a recent study, published in *Pediatric Blood & Cancer*, from the lab of Cynthia Gerhardt, PhD, principal investigator in the Center for Biobehavioral Health at Nationwide Children's Hospital, researchers examined how family factors such as stress and communication, affected long-term health-related quality of life (HRQOL) in survivors of pediatric cancer, in combination with pre-existing sociodemographic factors, such as family income, education, race and number of children living in the household.

While this topic has been studied previously, "most research has focused on the role of diagnosis or side effects from treatment that influence HRQOL in survivors," says Valdeoso Patterson, previous clinical research coordinator for the Gerhardt Lab and lead author of the study. "Few studies have identified early family factors that may be related to long-term quality of life."

Researchers hypothesized that, when analyzed alongside cancer-related stress and parent-adolescent communication, greater cumulative sociodemographic risk would result in lower levels of HRQOL in survivors. However, findings showed that sociodemographic risk was not a significant predictor of HRQOL when combined with the family factors examined.

"Findings demonstrated the importance of more proximal family factors in relation to long-term quality of life in survivors of pediatric cancer and their families," says Patterson.

"Our lab is interested in a variety of individual, family, medical and environmental factors that may increase risk or promote resilience in children with cancer," says Cynthia Gerhardt, PhD, who is also the chief clinical research officer at Nationwide Children's. "The goal is to learn what hinders and what helps children adapt to adversity so we can develop better interventions and provide better care."

The team's findings have helped support that goal, with suggested implementation starting early in treatment, as their study examined variables measured near initial diagnosis that predicted HRQOL five years later.

"Regardless of known sociodemographic risk factors that often affect health, health care professionals should focus on early interventions that reduce family stress and strengthen parent-adolescent communication to improve HRQOL in survivors and their families," says Patterson. "Clinicians should assess family stress and facilitate open and honest communication among parents and children to optimize well-being."

The Gerhardt Lab is currently developing and testing several digital health interventions to promote positive parenting, self-care and coping strategies like problem solving in families of children with cancer and young adult survivors.

Patterson V, Olsavsky A, Garcia D, Sutherland-Foggio M, Vannatta K, Prussien KV, Bemis H, Compas BE, Gerhardt CA. Impact of sociodemographic factors, stress, and communication on health-related quality of life in survivors of pediatric cancer. *Pediatric Blood & Cancer*. 2024;71(7):e31001.

— Madison Storm

Good Intentions but Low Adherence for Safe Sleep Guidelines

Although mothers are aware of the Safe Sleep Guidelines developed by the American Academy of Pediatrics, they frequently deviate from them to try to help their babies sleep better and longer.

Research recently published in *Pediatrics* and conducted by Lara B. McKenzie, MA, PhD, FAAHB, principal investigator in the Center for Injury Research and Policy at Nationwide Children's Hospital, and her team revealed the tension mothers feel between following Safe Sleep guidelines established by the American Academy of Pediatrics (AAP) and getting their babies to sleep.

The guidelines, known as the ABCs (Alone, Back, Crib) of Safe Sleep, aim to reduce the risk of sudden and unexpected infant death (SUID).

Although guideline awareness is high, adherence remains stubbornly low.

From November 2022 to March 2023, the researchers interviewed 25 mothers via five 90-minute virtual focus groups (VFGs). Eligible mothers had infants younger than 6 months old and placed them in a non-recommended sleep position or location at least twice in the past week.

The mothers completed surveys on their demographics and infant's sleep. VFG transcripts were analyzed to extract major themes. Most of the mothers were White and were married or living with a partner. The infants woke up approximately twice per night and napped about three times a day.

Five major themes arose from the VFGs:

1. *Universal knowledge of the AAP Safe Sleep guidelines.* All mothers were aware of the guidelines via multiple sources.

2. *Challenges regarding infant sleep*. One mother noted, "He doesn't want to just lay down on his crib or bed or wherever I try to let him sleep. So, I have to hold him."

3. *Deviations from the ABCs.* "Moms deviate from the guidelines to help their infants sleep," says Dr. McKenzie. Deviations included placing the infant in a non-recommended sleep location, such as the couch.

4. *Justifications for not following the ABCs.* The mothers believed the guidelines were unrealistic. Some followed alternative sleep guidelines, while others prioritized minimizing lesser sleep-related injury risks.

5. *Low self-efficacy with getting the infant to sleep following the guidelines.* "If I had to follow the [guidelines]…I don't think she would get much sleep, nor would I, so I don't feel confident in that," noted one mother.

Mothers were generally unconcerned about SUID risk. "There may be some distance between recognizing what the guidelines are for and SUID's relative rarity," explains Dr. McKenzie.

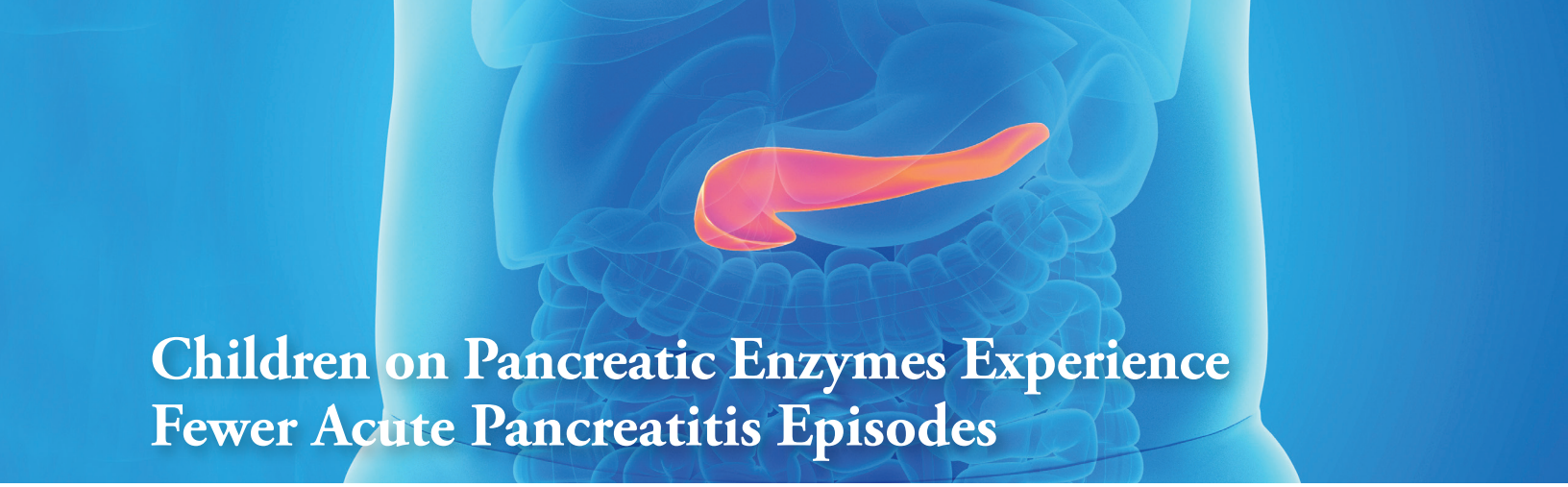
"Our group wants to help parents bridge the gap between understanding the guidelines and implementing them to help their babies sleep soundly," she says.

Dr. McKenzie explains that she and her team plan to combine safe sleep education with preventive sleep education, which is reportedly effective in improving infant sleep.

"We recognize the extreme challenge mothers face in helping their infants sleep," says Dr. McKenzie. "Our ultimate goal is to help babies sleep safely and soundly, ensuring that babies and their families get adequate sleep."

Moon RY, Mindell JA, Honaker S, Keim S, Roberts KJ, McAdams RJ, McKenzie LB. The tension between AAP Safe Sleep Guidelines and infant sleep. *Pediatrics.* 2024:153(4).

— Joanna Pendergrass, DVM



Children on Pancreatic Enzymes Experience Fewer Acute Pancreatitis Episodes

Pancreatic enzyme therapy benefitted patients with pancreatic-sufficient acute recurrent pancreatitis and chronic pancreatitis.

A new study shows that children with both acute recurrent pancreatitis and chronic pancreatitis had significantly lower incidence of acute pancreatitis episodes per year after starting pancreatic enzyme therapy. The findings support the need for a clinical trial to determine the treatment's efficacy in pediatric patients.

Children with acute recurrent pancreatitis (ARP) or chronic pancreatitis (CP) can experience acute pancreatitis (AP) episodes that are painful, require hospitalization and contribute to disease complications and progression. There are currently no interventions to prevent AP episodes or delay disease progression in children or adults with ARP or CP.

For the new study, researchers leveraged data from the INSPPIRE (INternational Study Group of Pediatric Pancreatitis: In Search for a CuRE) study, an international consortium of 22 tertiary care centers for pediatric pancreatitis.

Lead author A. Jay Freeman, MD, medical director of Pancreatic Care for the Pancreas and Liver Care Center at Nationwide Children's Hospital, had noticed an interesting trend in the INSPPIRE database: Although evidence supporting the efficacy of pancreatic enzyme therapy in children with pancreatic-sufficient ARP and CP is lacking, the treatment is not uncommon.

"There was a significant number of patients who did not have exocrine pancreatic insufficiency yet were given pancreatic enzymes, either in hopes of modifying their pain or gaining some other clinical benefit," he says.

To investigate further, Dr. Freeman and colleagues conducted a retrospective cohort study assessing the impact of pancreatic enzyme therapy on clinical outcomes among children with pancreatic-sufficient ARP or CP in the INSPPIRE dataset.

The researchers found that nearly 17% of children with pancreatic-sufficient ARP and CP were treated with pancreatic enzymes. Children started on pancreatic enzyme therapy experienced fewer AP episodes annually, and approximately 40% of children on pancreatic enzyme therapy had no additional AP episodes over approximately two years of follow-up. Children with a SPINK1 mutation and those with ARP (compared with CP) were less likely to have an AP episode after initiating pancreatic enzyme therapy.

The association with ARP suggests that pancreatic enzyme therapy may be more effective for preventing AP episodes early, before the disease progresses to CP. However, the researchers emphasize that a randomized, placebo-controlled clinical trial is necessary to evaluate the true impact of pancreatic enzymes for these patients — and they are currently working to make that happen.

"We would like to see if pancreatic enzyme therapy helps prevent the progression of ARP to CP, or the sequelae of CP," says Dr. Freeman, who is also a professor of Pediatrics at The Ohio State University College of Medicine.

"If the clinical trial is positive, this would be the first drug that we have that shows clinical efficacy in treating ARP and CP and potentially helps these patients."

Freeman AJ, Ng K, Wang F, Abu-El-Haija MA, Chugh A, Cress GA, Fishman DS, Gariepy CE, Gief-er MJ, Goday P, Gonska TY, Grover AS, Lindblad D, Liu QY, Maqbool A, Mark JA, McFerron BA, Mehta MS, Morinville VD, Noel RA, Ooi CY, Perito ER, Schwarzenberg SJ, Sellers ZM, Wilschanski M, Zheng Y, Yuan Y, Andersen DK, Lowe ME, Uc A; Consortium for the Study of Chronic Pancreatitis, Diabetes, and Pancreatic Cancer (CPDPC). Pancreatic enzyme use reduces pancreatitis frequency in children with acute recurrent or chronic pancreatitis: a report from INSPPIRE. *American Journal of Gastroenterology*. 2024 Apr 18. Online ahead of print.

— Mary Bates, PhD

CSPINE Injury Prediction Rule Could Decrease Radiographic Imaging Exposure in Children

A new study shows that implementing the rule can reduce CT scans by more than 50% without missing clinically significant injuries.

While cervical spine injuries (CSI) are uncommon in children, they can be potentially devastating, resulting in quadriplegia — paralysis below the neck affecting both arms and both legs. Detecting CSIs in a clinical setting often requires imaging such as X-rays and computed tomography (CT) scans, both of which expose children to radiation, which can cause other health issues over time.

In a study published in *The Lancet Child & Adolescent Health*, researchers in the Pediatric Emergency Care Applied Research Network (PECARN) — led by Julie Leonard, MD, MPH at Nationwide Children's Hospital — created a highly accurate cervical spine injury prediction rule. When applied, the rule decreases the use of CT by more than 50% without missing clinically significant injuries or increasing normal X-ray use.

"Emergency medical professionals prioritize thoroughness to ensure no serious injuries are overlooked, a crucial aspect in caring for every trauma patient," says Dr. Leonard, an emergency medicine physician at Nationwide Children's. "However, we also understand the age-related radiation sensitivity and malignancy risk caused by use of CT, and we're very encouraged that this new prediction rule could reduce some of that unnecessary exposure."

More than 22,000 study participants were enrolled at 18 children's hospitals over three years. The resulting PECARN CSI prediction rule is easy for physicians to use, relying solely on a child's symptoms and physical examination upon arrival in the emergency department. The prediction consists of nine clinical findings, four of which designate a child as "high-risk" for CSI and appropriate for initial screening with CT.

The risk factors, identified solely through the child's physical complaints and examination, are Glasgow Coma Score (GCS) score of 3–8; unresponsive on the

Alert, Verbal, Pain, Unresponsive scale (AVPU); abnormal airway, breathing, or circulation; focal neurological deficit including paresthesia, numbness, or weakness; altered mental status (GCS score of 9–14, verbal or pain on the AVPU, or other signs of altered mental status); neck pain; posterior midline neck tenderness; substantial torso injury; and substantial head injury.

"More research needs to be completed to determine how best to implement this rule into community emergency department settings, where most children are evaluated after trauma," says Dr. Leonard, who is the principal investigator of the Great Lakes Atlantic Children's Emergency Research node (GLACiER) of the PECARN. "We look forward to continuing the implementation work to improve care for children affected by traumatic injuries."

Leonard JC, Harding M, Cook LJ, Leonard JR, Adelgais KM, Ahmad FA, Browne LR, Burger RK, Chaudhari PP, Corwin DJ, Glomb NW, Lee LK, Owusu-Ansah S, Riney LC, Rogers AJ, Rubalcava DM, Sapien RE, Szadkowski MA, Tzimenatos L, Ward CE, Yen K, Kuppermann N. PECARN prediction rule for cervical spine imaging of children presenting to the emergency department with blunt trauma: a multicentre prospective observational study. *Lancet Child & Adolescent Health*. 2024;8(7):482-490.

— Katelyn Scott

Weight-Based Stigma and Its Impact on Children With Obesity

by Alaina Doklovic

More children in the United States live with obesity than any other chronic condition. The obesity rate among U.S. children and teens has more than tripled since 1980, according to the Centers for Disease Control and Prevention (CDC). Although there are numerous efforts underway to help children and adults reach and maintain a healthy weight, many efforts do not address the social consequences of obesity, specifically weight stigmatization and bias.

Weight stigma refers to the societal devaluation of a person because he or she has overweight or obesity, says Eileen Chaves, PhD, pediatric psychologist at Nationwide Children's Hospital. Common stereotypes portray patients with obesity as lazy, unmotivated or lacking in discipline. In reality, obesity is a complex disease that has many different causes, including nutrition and eating patterns, medicinal side effects, physical activity levels, irregular sleep patterns, genetics and emotional stress.

Weight stigma and discrimination are often tolerated in society because of beliefs that stigma and shame will motivate people to lose weight. However, research shows that stigma further contributes to damaging psychological, social and physical health consequences. Because weight stigma occurs in nearly every setting, it is important for medical providers and pediatricians to provide a safe space for patients with overweight or obesity and establish a positive relationship with the patient. Dr. Chaves and her team are looking at how to improve the therapeutic relationship between a patient and their medical team, one of few modifiable factors of obesity.

"The therapeutic alliance of patient, provider and caregiver is powerful," Dr. Chaves says. "Managing this alliance right away increases rates of patient retention and engagement. Our work aims to teach clinicians how to build a strong medical rapport that can help combat weight stigma and bias, starting with the first interaction."

The Psychological, Social and Physical Health Consequences of Weight Stigma

Experiences of weight stigma dramatically impair quality of life for children with obesity. A landmark study by Schwimmer and colleagues revealed that children and adolescents with severe obesity had quality-of-life scores that were worse than children of the same age with cancer. With research showing that 70% of patients with obesity have experienced weight bias, this is a large population at risk of numerous psychological and physical health conditions.

Patients who face weight stigma and bias often have higher levels of depression, anxiety, substance use, suicidal thoughts and self-harm behaviors. They are also more likely to experience disordered eating, social isolation, decreased physical activity and avoidance of healthcare services — often contributing to weight gain and fueling cycles of worsening behaviors and comorbidities.

"It's important to note that obesity doesn't cause depression or anxiety," says Dr. Chaves. "It's the experience of weight bias and stigma as a person who lives life in a larger body that causes these psychological disorders."

While patients with overweight or obesity are in the clinic, it's important for medical providers to assess what comorbidities may be present. If any psychological, social or physical health consequences are indicated, pediatricians should provide resources and treatment options available to the patient such as mental health resources, support groups or therapy.

The Clinical Setting and Broaching Topics for Change

Primary care settings are important for overweight and obesity management, yet many primary care providers do not feel equipped to address obesity. The 5 As, which was initially developed by the U.S. Department of Health and Human Services for smoking cessation, is an effective tool for addressing obesity in the clinic.

The 5 As (Ask, Assess, Advise, Agree, Assist) are rooted in behavior change theory and are key recommendations for pediatricians to follow when discussing a patient's weight during an appointment. This method of intervention takes a person-centered approach that improves patient autonomy and helps develop a positive relationship between the patient and caregiver.

Pediatricians and medical providers can also address weight stigma in the clinic by paying attention to their clinical setting, using patient-first language, increasing patient autonomy, and advocating for more training in residency and medical school courses.

"There is not just one thing we can do to tackle childhood obesity," says Stephen Cook, MD, who joined Nationwide Children's in August 2024 as chief of the Center for Healthy Weight and Nutrition. "We need to think globally and act locally. We need to have conversations about health at all sizes. Every corner of the community plays a role, and if we aren't doing our part, starting right here in the clinic, then we are just getting farther behind."

The Clinical Setting

Creating a safe, welcoming space for patients is essential to ensure patients feel comfortable when coming to the clinic to receive care. Hospitals and clinics should include comfortable seating and appropriately sized equipment, such as gowns or blood pressure cuffs, to accommodate patients of diverse body sizes. Additionally, marketing materials and other images throughout the hallways and appointment rooms should be inclusive and representative of the entire patient population.

The 5 As for Obesity Counseling

ASK
Ask permission to discuss weight and explore the patient's readiness to change behaviors. Be sure to affirm you hear what the patient says and acknowledge any concerns. Ask: "Would it be alright if we discussed your weight today?" If you are met with a no, acknowledge the boundary, and ask permission to ask about this again at the next visit.

ASSESS
Assess health status, BMI, potential root causes of weight gain and effects of weight on psychosocial functioning. Explore the drivers and complications of excess weight.

ADVISE
Advise about the risks of obesity and explain the benefits of modest weight loss and the need for long-term strategies. Explore all treatment options. Ask: "Now that we have a better understanding of your situation, can we explore and come up with a plan of action to improve things?"

AGREE
Agree on realistic weight loss expectations and targets, behavioral changes using SMART (specific, measurable, attainable, relevant, time-bound) goals and specific details of the treatment options. Treatment plans should use effective behavior modification principles such as goal setting and behavior shaping.

ASSIST
Address facilitators (motivation, support) and barriers (social, medical, emotional, and economic) that make weight management challenging. The clinician's role is to identify, educate, recommend and support. Arrange regular follow-ups.

"Managing this alliance right away increases rates of patient retention and engagement. Our work aims to teach clinicians how to build a strong medical rapport that can help combat weight stigma and bias, starting with the first interaction."

— *Eileen Chaves, PhD, pediatric psychologist at Nationwide Children's Hospital*

When discussing weight-based topics with patients, medical providers should ask patients what words they prefer to use when talking about their bodies and their weight. Use neutral terms like 'growth' or 'weight' if you are not sure what the patient prefers. People-first language, which places the individual before the medical condition or disability, should be standard (i.e. a person with obesity or a child with overweight). Providers should pay attention to the language used on patient-facing clinical documentation (i.e. post-visit documentation). Rather than focusing on what the patient is doing wrong, pediatricians should acknowledge behaviors the patient is doing well.

Training the Future

Recognizing and acknowledging the complexity of the etiology of obesity early on in a medical provider's training works to dispel common blame stereotypes. Pediatricians should advocate for additional weight stigma training and education in medical schools, residency programs and continuing medical education programs. If weight bias and stigma are addressed before medical professionals even treat a patient, they will be more equipped with the resources to eliminate bias before it happens.

"If we start training residents at the very start of their training, the hope is they will be able to recognize their own implicit biases and the biases they see around them," says Dr. Chaves. "I often say to other providers, it's not 'if' you are going to see a patient with overweight or obesity, it's how many times a day. Making sure you understand where your own biases are coming into play and addressing those before you even enter the clinic will go a long way." ■

Pont SJ, Puhl R, Cook SR, Slusser W; Section on Obesity; Obesity Society. Stigma experienced by children and adolescents with obesity *Pediatrics*. 2017 Dec;140(6):e20173034.

Vallis M, Piccinini-Vallis H, Sharma AM, Freedhoff Y. Clinical review: modified 5 As: minimal intervention for obesity counseling in primary care. *Canadian Family Physician*. 2013 Jan;59(1):27-31.

Do you have questions about GLP1-inhibitors for youth with obesity?

Check out this recent article and practice tool from our experts.
PediatricsNationwide.org/GLP1s

Patient Perspective: Living With Weight-Based Stigma

In 2019, 15-year-old Paige watched her father die from a disease that was consistently ignored, and his symptoms repeatedly blamed on his weight. He had stage 4 cancer by the time he was properly diagnosed.

Shortly after his death, her mother had a 40-pound cyst removed, a surgery that she and other doctors believe could have been prevented had her medical providers looked past her weight and listened to her concerns.

Now, Paige faces the same stigma in the clinic. For years she has been experiencing knee pain. She says that physicians constantly blame the pain on her weight, even though her pain has gotten progressively worse since she lost weight.

Every time she goes into a doctor's appointment, she repeats this mantra: "My symptoms are valid, and my weight does not define me."

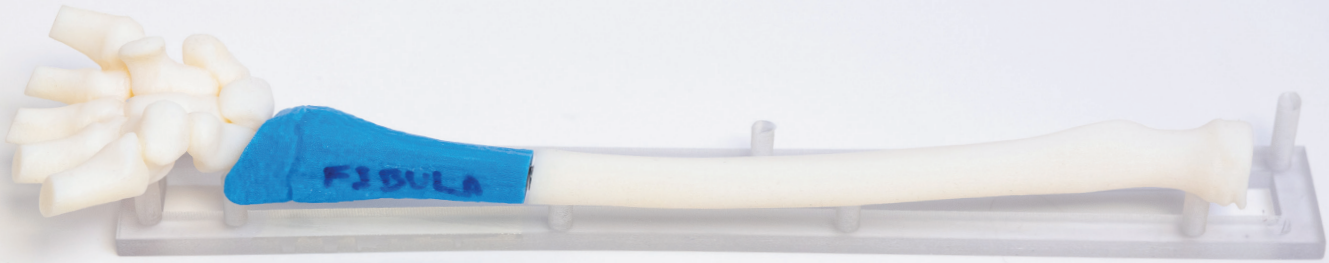
The stigma she, her family, and patients just like her have experienced has taken a toll on her mental health and well-being. She says she experiences it in the clinic where she works — in addition to times when she's the patient.

Now that she's working with the team at the Center for Healthy Weight and Nutrition at Nationwide Children's Hospital, Paige is focusing on her whole health — physical and mental. She's also become a champion for meeting weight-based discrimination head-on and challenging stigmas associated with body size. Talking about what she and her family have experienced is just the first step.

"Dr. Chaves has been an amazing part of helping me learn to respect myself and stand up for myself in the clinic. It's amazing how much progress I've made in the last three years," she says. "She taught me that just because you live life in a larger body, that does not mean that's all you are. Advocate for yourself and stand against the discrimination. Know your rights as a patient and know that you deserve to be treated with respect."

"Dr. Chaves has been an amazing part of helping me learn to respect myself and stand up for myself in the clinic. It's amazing how much progress I've made in the last three years."

— *Paige, patient at the Center for Healthy Weight and Nutrition at Nationwide Children's Hospital*



From Scan to Plan: Making Virtual Surgical Planning the Standard of Care for Ortho-oncology Operations

by Abbie Miller, MWC

"We deal in rarities," says Thomas Scharschmidt, MD, director of the Pediatric Orthopedic Oncology Program at Nationwide Children's Hospital and professor of Orthopedics at The Ohio State University. "When you consider that across the entire U.S. population we have between 2,500 and 3,000 cases of primary malignant bone tumors each year, and only half of those are kids, every case requires unique consideration and planning."

While in the past nearly every patient with a bone tumor would be facing amputation, modern limb salvage techniques combined with improving survival rates make orthopedic oncology an expanding field.

According to Dr. Scharschmidt, caring for children with sarcomas, the largest category of tumor seen by ortho-oncology experts, is a "team sport." At Nationwide Children's the sarcoma team includes representatives from orthopedic surgery, medical oncology, surgical oncology, plastic surgery, radiology, pathology, radiation oncology, physician assistants and nurse practitioners, as well as the legion of nurses and other clinicians supporting all of these areas.

The team also includes Jayanthi Parthasarathy, BDS, MS, PhD, manager of the 3D Printing and Innovations Lab in the Department of Radiology at Nationwide Children's. Dr. Parthasarathy is bringing the transformational impact of 3D printing and virtual modeling to patients across the hospital. Her collaboration with Dr. Scharschmidt has made it the standard of care for sarcoma patients.

Virtual Surgical Planning (VSP)

"The best analogy I can think of is this: We never get on a plane without a pilot who has a flight plan completely mapped out and in place before we get on the plane," says Dr. Scharschmidt. "But I think we often do the opposite in surgery. We have a general idea of where we are going, but we do a lot of figuring out how to get there in the operating room. The idea behind VSP is to use the tools at our disposal to have that complete flight (surgical) plan in place for us, the families and the trainees, before going to the operating room. This makes the surgery more efficient — and safer for the patient."

The first step to building the virtual model is to obtain magnetic resonance imaging (MRI) and computed tomography (CT) scans. The scans need to be taken on the same day with imaging markers placed to help guide image layering. The size of the image slices must also be 1 mm or smaller to ensure the accuracy of the resulting model.

"In the transition to making this part of our standard of care, we've moved the orders for these images into our electronic medical record," says Dr. Parthasarathy. "This ensures every person, from the ordering physician to the technologists and radiologists, knows the requirements for a successful model."

If the surgeons want to plan for a reconstruction using bone from another body part, the patient will also have a CT scan of that area.

Once she has the images, Dr. Parthasarathy builds the 3D virtual model and calls in the surgeons.

"We tend to see anatomy in 3D, and surgeons are very hands-on people," says Dr. Scharschmidt. "Using the virtual model, we're able to see that three-dimensional anatomy and plan our surgical margins more precisely."

Once the surgeons have made their plan and marked their margins, Dr. Parthasarathy begins work on the physical models.

3D Printing: Reference Models

"Our multicolored, 3D printed models enable physicians to see a physical representation of their plan," says Dr. Parthasarathy.

With sarcoma surgeries, surgeons are always removing part of the body — even in the case of limb salvage, she says. "This is hard for the patients. The models can help them see what will happen and why."

"It's really powerful for families and patients to see the planning," agrees Dr. Scharschmidt. "It helps them better understand our goals of surgery before we get into the operating room."

When it comes time for surgery, the 3D model heads to the operating room with the surgeon. While it stays outside the sterile field, it's there as a reference if needed.

"When figuring out resections and reconstructions in the operating room, there's usually longer surgical time, with associated risks of higher anesthetic times and increased infection risk," says Dr. Scharschmidt. "By utilizing VSP and 3D printing, we've shown we can do it better."

In addition to the reference model, the VSP process enables the creation of custom implants and tools.

"We work with a vendor to use our models to create custom tools, such as cutting jigs to guide resections or custom implants," says Dr. Parthasarathy. "The implants may include 3D printed metal components to replace portions of the pelvis or shoulder — complex areas where a patient-specific approach is essential."

Proof Points

In 2022, Drs. Parthasarathy and Scharschmidt published a proof-of-concept description of their VSP and 3D printing process. The paper, published in the *International Journal of Computer Assisted Radiology and Surgery*, showed that the accuracy of the resections and the model predictions were within –0.29 to 0.45 mm (mean –0.09).

Since then, the team has continued to improve their process.

"We verify models by CT scanning the printed models," Dr. Parthasarathy says. "In testing, we've shown a 0.01 to 0.05 mm range of variance — our models are incredibly accurate."

The team has also continued to track the accuracy of the models for resection and reconstruction.

"To have the best possible impact on patient outcomes and surgical processes, we need to know if our models are accurate — not just anatomically accurate — but did we follow the plan we set, and if not, why?" says Dr. Scharschmidt. "This is an ongoing area of study, and we expect to publish our latest data toward the end of this year." ■

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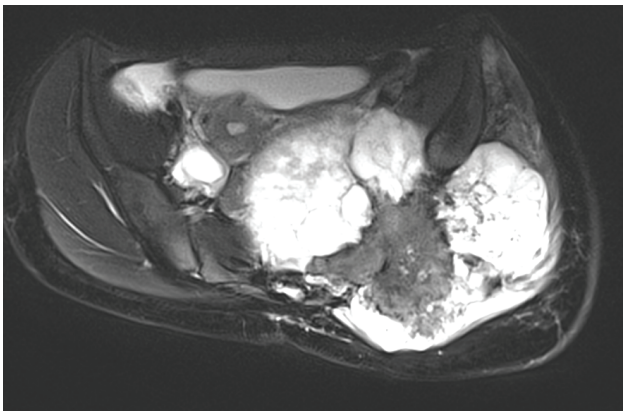
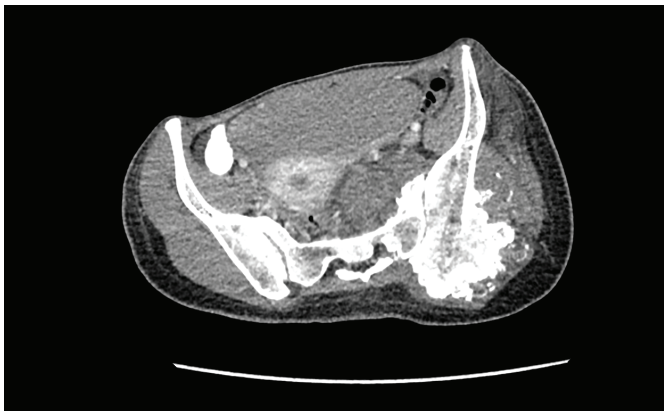
Thomas Scharschmidt, MD, director of the Pediatric Orthopedic Oncology Program at Nationwide Children's Hospital and professor of Orthopedics at The Ohio State University

Jayanthi Parthasarathy, BDS, MS, PhD, manager of the 3D Printing and Innovations Lab in the Department of Radiology at Nationwide Children's

Virtual Surgical Planning for Musculoskeletal Oncology

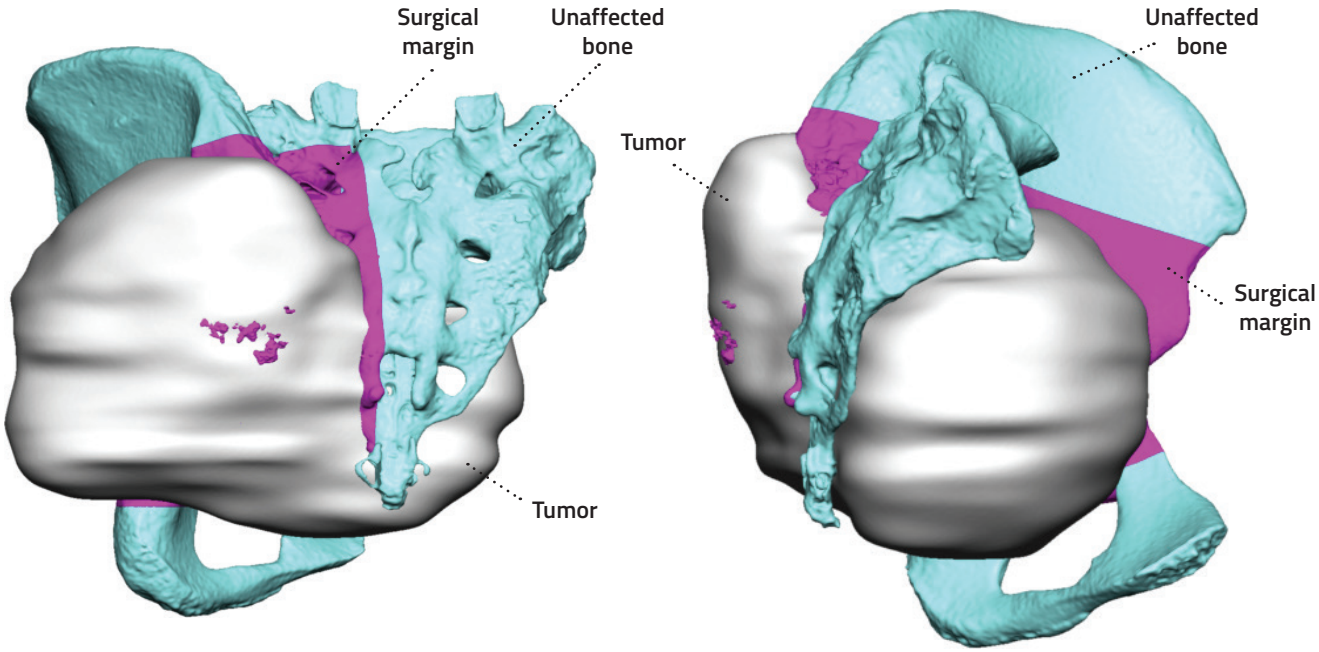


MRI of pelvis showing tumor

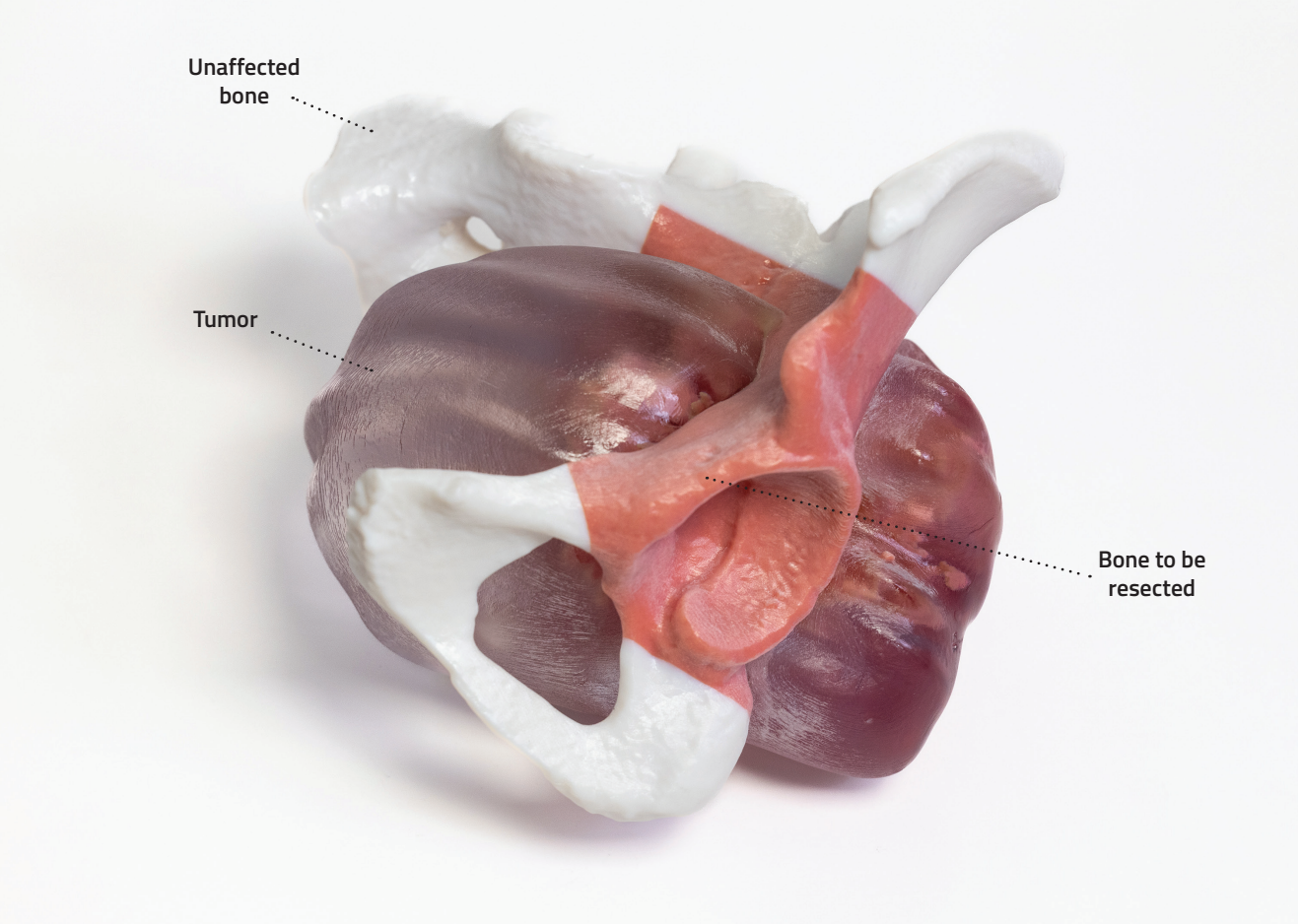


CT of pelvis showing tumor

1. Data acquisition: Computed tomography and magnetic resonance images are obtained during the same visit with markers used to help align the scans to create the composite image. That composite is used to develop the virtual model.



2. The 3D Printing and Innovations Lab maps out the anatomy and tumor location, resulting in 3D virtual models. Based on the virtual model, surgeons plan the surgical margins and reconstruction.



3. The 3D model is printed in house, using different colors and textures to show cutting margins, tumors and tissues.

4. The 3D models are used to educate families, trainees and the surgical team before, during and after the procedure.

5. Quality assurance: After the procedure, the resected tumor and postoperative scans are compared against the models to assess accuracy.

Visit PediatricsNationwide.org/Virtual-Surgical-Planning for more examples.

BIOFILMS:
The Good, the Bad & the Groundbreaking

Decades of research into the structure and function of bacterial biofilms have begun to pay off in the form of imminent clinical applications capable of harnessing both the protective and problematic aspects of this universal phenomenon.

by Katie Brind'Amour, PhD, MS, CHES

Imagine a hospital emergency department filled with patients — those with painful ear infections, recurrent urinary tract infections, fevers and swelling after surgery, signs of infection at the site of a wound. Then picture the hospital's inpatients — a child with cystic fibrosis, an elderly patient with pneumonia, a patient with a drug-resistant skin rash.

Now imagine all of these patients have essentially the same problem.

And the solution is on the horizon.

A BIOFILM PRIMER

Nearly 5 million people die every year due to bacterial infections that resist antimicrobial therapies — accounting for almost 1 in every 10 deaths worldwide. Approximately 70% of these deaths are attributable to just seven pathogens, which together go by the moniker ESKAPEE: *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter spp.* and *Escherichia coli.*

ESKAPEE pathogens, at the root of many of the familiar infections affecting the patients described above, often "escape" traditional pathogen-specific antibiotics or even high-dose, broad spectrum antimicrobial therapies. They linger on surfaces and resist both our immune system's defenses and aggressive medical therapies, either becoming recalcitrant, life-threatening infections or subsiding only to recur over time.

The reason? Biofilms.

About 80% of bacterial infections in humans involve biofilms — naturally formed communities of bacteria that construct a web-like matrix inside the body using extracellular DNA (eDNA) from both the host and the bacteria. The resultant film physically shields the bacteria from immune cells, medications, adverse environments and even DNA-destroying enzymes.

The protected bacteria become more than 1,000 times as resistant to antibiotics as their free-floating counterparts in the blood. Protected by the biofilm, they can thrive without wasting energy on additional defense mechanisms or extensive cell division.

Over the past few decades, researchers at Nationwide

> We have identified what we believe is the Achilles heel common for all biofilms, regardless of which organisms produce them. By targeting that Achilles heel, we can rapidly force the bacteria out of the biofilm."
>
> — Lauren Bakaletz, PhD, director of the Center for Microbial Pathogenesis at the Abigail Wexner Research Institute at Nationwide Children's Hospital

Children's Hospital have chipped away at understanding the various biochemical and structural elements of these biofilms.

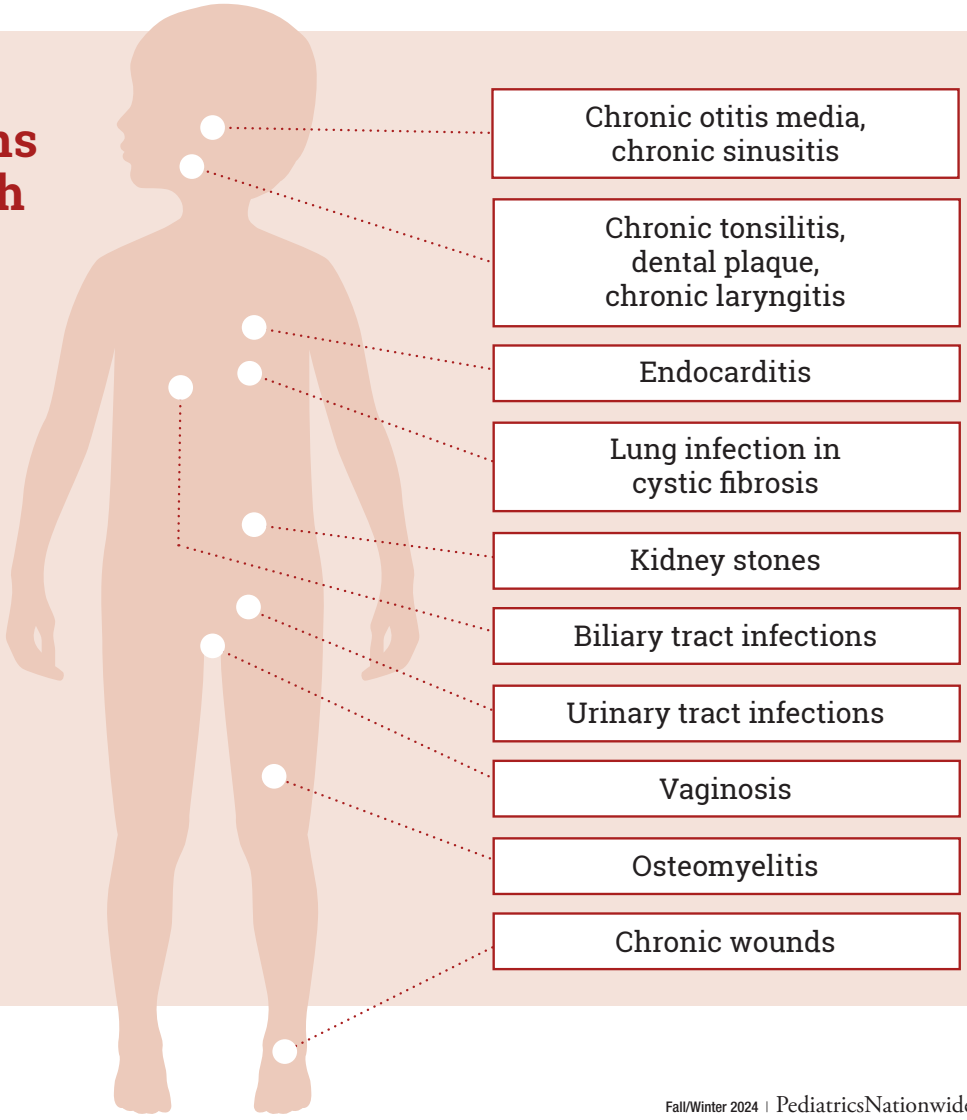
For example, they discovered that biofilms form when eDNA is wrapped into a rare, enzyme-resistant configuration known as Z-DNA.

More importantly, however, they found the linchpin protein for virtually every biofilm: DNABII. This protein family holds the matrix together — making it a prime target to literally make biofilm walls come tumbling down.

TARGETING THE UNDERLYING THREAT

"We have identified what we believe is the Achilles heel common for all biofilms, regardless of which organisms produce them," says Lauren Bakaletz, PhD, director of the Center for Microbial Pathogenesis at the Abigail Wexner Research Institute (AWRI) at Nationwide Children's and one of the two leading biofilm experts who helped reveal the role of DNABII.

Tissue Infections Associated With Biofilms



Dr. Bakaletz and colleagues designed a humanized monoclonal antibody, called HuTipMab, that recognizes and binds to the critical DNABII proteins. As DNABII becomes increasingly unavailable to the biofilm, this DNA-dependent shield quickly weakens and collapses.

"By targeting that Achilles heel, we can rapidly force the bacteria out of the biofilm," Dr. Bakaletz explains. "There is a period of time — a really important, opportunistic period of time — where they have what we call the newly released or NRel phenotype, when they are incredibly sensitive to antibiotics and our immune system."

Dr. Bakaletz's long-term research colleague and fellow discoverer of biofilm's DNABII-dependence, Steven Goodman, PhD, principal investigator in the Center for Microbial Pathogenesis at AWRI, likens the NRel phenotype to the sluggish, discombobulated state most people would be in upon a midnight wake-up call followed by a push out the door to run a marathon. This period of shock lasts about 6 to 12 hours, during which the NRel bacteria are nearly defenseless.

This is another potential win for patients and antimicrobial stewardship, as much smaller doses of antibiotics may be required, and — when coupled with the immune system — should result in total eradication of these newly released pathogens.

Even better, DNABII proteins are pathogen-agnostic, meaning HuTipMab works regardless of the primary bacteria at play. HuTipMab even disrupts biofilms formed by the notorious ESKAPEE pathogens, making them extremely susceptible to even small doses of common antibiotics. These findings, published in *Frontiers in Microbiology*, represent exciting progress toward a possible solution to the global antimicrobial resistance crisis.

The real test, of course, comes in the form of *in vivo* studies and clinical trials, and so far, all signs point to "go."

PARADIGM-SHIFTING CLINICAL PROMISE

"Lauren's preclinical models are spectacularly accurate when it comes to results that are applicable to human beings, which is hard to find," says Dr. Goodman. Distinct models of human infection — middle ear, necrotizing enterocolitis, periodontal disease and lung infections — complement dozens of *in vitro* and biospecimen studies for biofilm-associated problems.

To facilitate the advancement of HuTipMab, Drs. Bakaletz and Goodman became the scientific co-founders of a company called Clarametyx Biosciences and licensed the technology — now called CMTX-101 — to them to accelerate its development.

"CMTX-101 represents a potentially transformative therapy to combat difficult-to-treat bacterial infections," says Chuck McOsker, PhD, co-founder and chief scientific officer for Clarametyx. "Overall, we are hopeful that our therapeutic antibody can reduce the frequency, severity and duration of bacterial infections, resulting in a significant improvement in the quality of life for patients and their families."

Clarametyx has already garnered $33 million in Series A funding to bankroll its first initiatives: a Phase 1b/2a clinical trial for the use of CMTX-101 in people with cystic fibrosis and a Phase 1 trial using CMTX-101 as an adjunct to standard-of-care antibiotics for bacterial pneumonia.

The early-phase trials should allow assessment of the antibody's safety and tolerability and provide data on opportunities to enhance timing, dosage, delivery method and future study designs.

"Developing an effective anti-biofilm treatment could dramatically increase the effectiveness of current antibiotics," says Dr. McOsker. "We see a tremendous opportunity for anti-biofilm therapies like CMTX-101 to deliver improved clinical outcomes for a wide range of additional biofilm-associated bacterial infections, including acute and chronic wounds, prosthetic joint infections [PJI] and osteomyelitis, bacterial exacerbations in chronic obstructive pulmonary disease and non-cystic fibrosis bronchiectasis, among others."

John Hamilton, MD, PhD, instructor and physician-scientist in the Department of Orthopedic Surgery at Rush University Medical Center, agrees.

"Use of anti-DNABII antibody could fill a much-needed clinical gap for preventing and treating PJI through directly targeting bacterial biofilm," says Dr. Hamilton, who reached out to Drs. Bakaletz and Goodman when he was searching for new ways to fight PJI.

Despite improvements in safety over the past couple of decades, PJIs still affect tens of thousands of patients per year in the U.S. alone and can result in life-altering

> Use of anti-DNABII antibody could fill a much-needed clinical gap for preventing and treating PJI through directly targeting bacterial biofilm."
>
> — John Hamilton, MD, PhD, instructor and physician-scientist in the Department of Orthopedic Surgery at Rush University Medical Center

sequelae, such as long periods of high-dose antibiotics, reoperation and, in severe cases, amputation. The two groups collaborated to test the anti-DNABII antibody in animal PJI studies via intravenous injection, intra-articular injection and even an anti-DNABII antibody coating directly on the orthopedic implants.

"We felt their technology was the perfect fit to test in the setting of PJI," says Dr. Hamilton. "It could substantially enhance PJI treatment success and reduce mortality, which can be as high as 25% over 5 years. It could also be added to the antibiotic and surgical treatments used currently for PJI, and perhaps even eliminate the need for surgical treatments for PJI altogether."

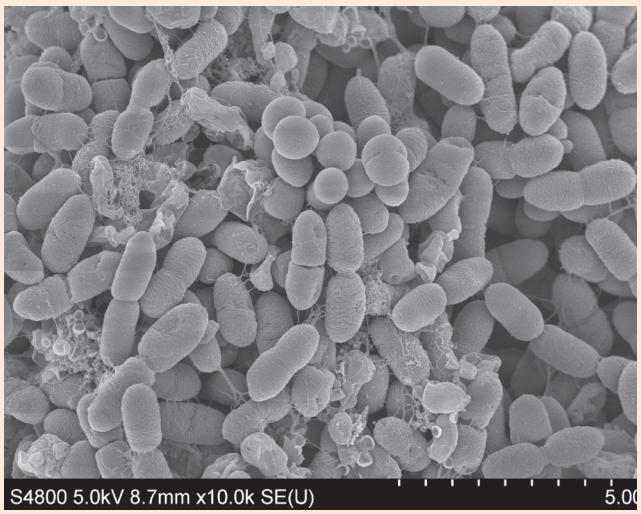
Preliminary data from the animal studies suggests the anti-DNABII antibody may effectively reduce the risk of PJIs, and Dr. Hamilton has secured funding from the National Institutes of Health (NIH) to further study these approaches.

WORK TO BE DONE

Questions that biofilm researchers still have to answer include whether therapies could have detrimental off-target effects, how often potential patients would have to be dosed, how long anti-biofilm antibodies stay in the body, and what methods of delivery are appropriate for each application.

At Nationwide Children's, early research has already confirmed that anti-DNABII antibodies administered into the middle ear via tympanostomy tubes cause less disruption to both the nasopharyngeal and gut microbiome than standard-of-care antibiotics in multiple preclinical models.

This initial work represents an important advantage compared to gold-standard treatments and is a major focus of Michael Bailey, PhD, principal investigator in the Center for Microbial Pathogenesis at AWRI. He



This figure shows a biofilm formed *in vitro* by two human respiratory pathogens — nontypeable *Haemophilus influenzae* and *Moraxella catarrhalis*. NTHI is the rod-shaped bacterium. *M. catarrhalis* are the spheres. The NTHI had never been known to completely cover the *M. catarrhalis* bacterium when they grow together. Drs. Bakaletz and Goodman posit this provides protection for both bacterial species due to unique properties of each. The more open areas are likely water channels that feed/bathe the biofilm, and the "stringy" fibers are the extracellular DNA that a portion of the bacteria put out into the extracellular environment to build the supportive structure of the biofilm matrix.

> With our studies on anti-biofilm treatments targeted at the middle ear, they look like they're leaving the body's microbiomes intact — maintaining healthy microbiomes — and not inducing dysbiosis."
>
> — Michael Bailey, PhD, principal investigator in the Center for Microbial Pathogenesis at AWRI

specializes in characterizing the microbiome and in studying possible mechanisms at play in the gut-brain connection.

"There is increasing evidence that the natural microbiota, primarily in the gut but in other areas in the body as well, contribute to overall health, and growing awareness that every time we use a medication, there is potential to disrupt the body's microbiomes," says Dr. Bailey, who explains that this is particularly true for antibiotics.

This opened up a new area for consideration: what about good bacteria? Avoiding disruption of positive microbiota is critical to both patient wellbeing and long-term utility of the antibody as a solution to the problem of antimicrobial resistance.

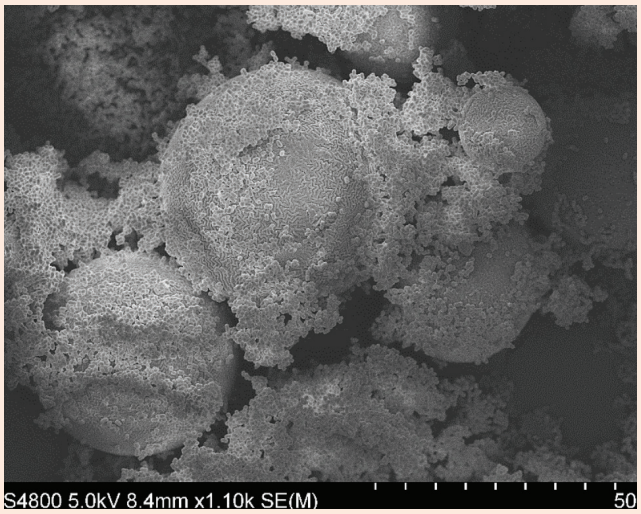
"With our studies on anti-biofilm treatments targeted at the middle ear, they look like they're leaving the body's microbiomes intact — maintaining healthy microbiomes — and not inducing dysbiosis," says Dr. Bailey of the team's work in animal models.

The multidisciplinary research team started thinking about big-picture implications of managing biofilms and the microbiome, and struck another golden idea.

PROMOTING THE GOOD

More than 10 years ago, Gail Besner, MD, chief of pediatric surgery at Nationwide Children's, gave a cross-disciplinary talk to the gastroenterology faculty about her research in necrotizing enterocolitis (NEC) and protecting the neonatal intestines from injury. After her presentation, then-president of AWRI at Nationwide Children's, John Barnard, MD, told her she needed to connect with Drs. Goodman and Bailey right away.

"When you talk to physicians and surgeons about



Limosilactobacillus reuteri forms a biofilm on maltose-filled dextranomer microspheres. When administered as a single dose to an animal model, Lr-DM-Malt reduced the incidence of NEC dramatically.

> We can induce beneficial *L. reuteri* to form a biofilm, which makes the bacteria more acid-resistant when ingested and more capable of binding to intestinal epithelial cells once they're past the stomach. Then they can actually exert their beneficial effects, because they're more able to combat the immune system of the host, they're more resistant to antibiotics and they're more capable of competing with the pathogenic bacteria around them."
>
> — Gail Besner, MD, chief of pediatric surgery at Nationwide Children's

biofilms, what immediately comes to mind is that biofilms are our enemy, because when produced by pathogenic bacteria they prevent treatment of infection," says Dr. Besner, who admits she was initially skeptical of using biofilms to treat her most vulnerable neonatal patients, but was willing to explore just about anything that could help. "I think I speak for every pediatric surgeon when I say that we would love to never have to operate for NEC in these babies again."

NEC is a problem of gut dysbiosis in premature babies, with a mortality rate as high as 50%. Severe forms can necessitate removal of large portions of the intestines, and it often causes long-term developmental delays. A lack of bacterial diversity in the gut, along with disproportionately high levels of harmful Gram-negative species, contributes to development of the disease.

For many years, neonatal intensive care units (NICUs) around the world prophylactically treated babies with daily doses of probiotics — often with *Limosilactobacillus reuteri*, a healthy bacterial species isolated from breastmilk that competes with harmful bacteria to restore and maintain balance of intestinal microbes.

Unfortunately, efficacy of this intervention has been mixed, and in September of 2023 the Food and Drug Administration issued a warning against the off-label use of probiotics for preterm infants, since the preparations used to date have not been tested for purity and are not FDA-approved.

A primary problem with traditionally administered probiotics is their durability — they often don't survive past the acidic environment of the stomach to reach their target in the intestines. Those that do make it to the gut lack staying power.

But biofilms are built to last.

Drs. Goodman and Bailey had started exploring the possibility of using biofilms to help beneficial probiotics actually reach the small and large bowel — and Dr. Barnard believed that Dr. Besner's fragile patients represented a group in great need of such an advancement.

Fast-forward several years and the team has published numerous studies in multiple animal models supporting the approach, confirming that just a single dose of *L. reuteri* administered in its biofilm state using biocompatible microspheres can dramatically reduce the incidence of NEC.

"We can induce beneficial *L. reuteri* to form a biofilm, which makes the bacteria more acid-resistant when ingested and more capable of binding to intestinal epithelial cells once they're past the stomach," says Dr. Besner of the unique probiotic technology. "Then they can actually exert their beneficial effects, because they're more able to combat the immune system of the host, they're more resistant to antibiotics and they're more capable of competing with the pathogenic bacteria around them."

The trio, together with Dr. Bakaletz, has since patented and licensed the technology to a start-up company called Scioto Biosciences.

As Scioto Biosciences and the research team of co-founders and scientific consultants examined options for their first human trial for the probiotic biofilm microspheres, they landed on a rather unexpected condition: autism.

"It has been shown in the literature that *L. reuteri* stimulates a hormone called oxytocin, which is out of balance in many people with autism spectrum disorder and may contribute to social behavioral deficits," explains Dr. Bailey.

The blinded, placebo-controlled Phase 1 safety trial revealed that not only were the *L. reuteri* microspheres safe and tolerable in a small sample of otherwise healthy adults with autism, but that there is also preliminary evidence for improvement in behavior during periods of daily supplementation.

"The only drugs approved for autism so far are high-powered antipsychotics, and here we have something with the potential for an industry-leading safety profile — we say it's like eating a protein bar," says Joe Trebley, PhD, co-founder and chief executive officer at Scioto Biosciences. The company plans to launch a larger Phase 2 autism trial in 2025. "The formulation seems incredibly promising, not just in a safety and GI sense, but also for modulating social behaviors."

NEC models from the labs at Nationwide Children's also demonstrated improved neurodevelopment and a decrease in brain inflammation, suggesting the probiotic biofilm has both GI- and neuro-protective effects.

As the team continues to collect sufficient data to justify an early-phase trial in premature infants with NEC, opportunities for alternative probiotic applications abound, from gastrointestinal disorders such as irritable bowel syndrome and *Clostridioides difficile* infections to psychiatric and immunologic conditions linked to disruptions in gut-brain balance.

MORE CONTENDERS IN THE RACE TO THE CLINIC

The research team has not stopped at just two approaches to biofilm manipulation.

Dr. Bakaletz's original foray into biofilm research involved development of a vaccine against middle ear infections. This approach uses an anti-DNABII vaccination to teach the body to prevent the formation of pathogenic biofilms in the middle ear and other sites of infection in high-risk populations, such as children with chronic or recurrent ear infections.

The technology, licensed to Clarametyx for development, is also being studied for use in pulmonary diseases such as cystic fibrosis. Preclinical data show potential for reduced antibiotic use in these populations, as well as prevention of the devastating consequences of recalcitrant infections.

In addition, the team continues to study biofilms and the way the host identifies and responds to them.

"Something we discovered that I think will have real legs is that our immune systems actually do not try to get rid of biofilms — not because they don't want to, but because they're 'afraid' to," says Dr. Goodman. "The goal is to prevent them from proliferating, because the host has no mechanism to know how many bacteria are in the biofilm; it could be 10, or it could be 10 billion, so the immune system would rather cordon it off."

This is what happens with many infections, such as recurrent sinusitis or even tuberculosis. The immune system encapsulates the biofilm, allowing it to essentially go dormant for long periods of time. When it rears its head, treatments quiet it down again until the process repeats.

Drs. Goodman, Bakaletz and their laboratory teams discovered a protein in the innate immune system called HMGB1 that, much like antibodies to bacterial DNABII proteins, can quickly disrupt a biofilm to release the bacteria. HMGB1 typically triggers an inflammatory response, but when engineered with a single amino acid change, it keeps inflammation in check while disrupting the biofilm's structure.

Separately, DNABII antibodies and HMGB1 each collapse biofilms, enabling the host's immune response to naturally and rapidly clear large percentages of the NRel bacteria.

"When you mix them together, the biofilm infection is gone — there are no detectible bacteria at all," says Dr. Goodman. The function of HMGB1 and its combined effects with DNABII antibodies have been tested and confirmed in multiple animal models.

Dr. Goodman believes that understanding how and why the immune system largely avoids fighting biofilms could hold valuable insights both for improving biofilm-based therapeutics and for managing life-threatening infections. Controlling how many bacteria are released and when, as well as how much inflammation arises in response — enough to recruit help from the immune system but not enough to trigger sepsis — could be a game-changer in clinical care.

> When you mix [DNABII antibodies and HMGB1] together, the biofilm infection is gone — there are no detectible bacteria at all."
>
> — Steven Goodman, PhD, principal investigator in the Center for Microbial Pathogenesis at AWRI

THE FUTURE OF BIOFILM-CENTERED THERAPIES

Biofilms have the potential to recalibrate the global struggle against antimicrobial resistance, provide new tools in regulating the gut's microbiome and even transform the efficacy of over-the-counter probiotic products for general wellness.

Positioned at the cusp of this medical revolution, the research teams at Nationwide Children's continue to pour their time, effort and intellect into biofilm management, with ever-advancing goals in mind — new clinical trials, grants to study new diseases, new patents, and new discoveries in biofilm biology.

"It's really fun to see how you can move so well and so quickly when you have people who challenge each other and aren't just here to say 'good idea,'" says Dr. Bakaletz of the team's progress in the field over the past few decades. "We still have bad days when things just didn't work out. But we don't quit, we keep our eyes on the prize." ■

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> It's really fun to see how you can move so well and so quickly when you have people who challenge each other and aren't just here to say 'good idea.' We still have bad days when things just didn't work out. But we don't quit, we keep our eyes on the prize."
>
> — Lauren Bakaletz, PhD, director of the Center for Microbial Pathogenesis at AWRI

Empowering Therapists With Better Tools

New Research Director Sets Out to Improve Mental and Behavioral Health Care with Assessments

by Wendy Margolin

Providing mental or behavioral health care without simple, effective clinical assessment tools is like trying to lose weight without access to a bathroom scale, says Eric Youngstrom, PhD, the new director of the Institute for Mental and Behavioral Health Research at Nationwide Children's Hospital and an expert in clinical assessment.

Dr. Youngstrom learned this lesson early in his career when he presented his paper on a new assessment tool to his wife, Jen Youngstrom, PhD, who was then a clinical psychologist in a community health center. There was no way she'd use it.

"Come back to me when it's one page and free," she said.

That conversation about diagnostic assessments was one of many over their decades of marriage and professional collaboration. The two have spent years discussing how to:

- Make short assessment forms
- Make diagnostic tools free
- Identify and share the best tools so clinicians can find them
- Simplify scoring so clinicians can determine results and reduce errors

Today, Dr. Eric Youngstrom continues collaborating with Dr. Jen Youngstrom, now a clinical professor and director of clinic services and assessment at the University of North Carolina Department of Psychology and Neuroscience. There, she often consults her husband about referrals to determine the best diagnostic measurement tool.

"We were buying tools and expanding on a referral-to-referral basis, but the literature grows very fast, and there's no way any director could keep up with it," she says.

Jen, in turn, was shaping Dr. Eric Youngstrom's focus on research with practical clinical application.

How the Right Assessment Tools Can Improve Pediatric Mental Health Outcomes Overall

Dr. Eric Youngstrom, who is now a nationally renowned psychologist specializing in the relationship between mood and psychopathology and the clinical assessment of children and families, considers standardized assessment tools the secret sauce to achieving better behavioral and mental health outcomes. "If we get the assessment and diagnosis wrong, we have no prayer of picking the best treatment," he says.

> You'd think for the number one disability, we would send in the cavalry, but we don't. If we have good scouts and good information, there's a better chance of identifying the needs accurately and then figuring out ways to intervene appropriately."
>
> — Robert Findling, MD, MBA, pediatrician, child psychiatrist and chair of psychiatry at Virginia Commonwealth University

The challenge to assessments is identifying which tool is ideal for the symptoms with which patients present. While there are hundreds of diagnoses in the DSM-5, even a common diagnosis, like depression, has 300 different assessment questionnaires.

"A busy clinician just wants someone to identify which tools are best," says Dr. Youngstrom.

Identifying the best evidence-based screening tools is even more essential among less common diagnoses. Clinicians are experienced at recognizing typical diagnoses, such as anxiety and depression. Many clinicians could get through clinical training and even be on the job for a few years before seeing someone with rare conditions such as obsessive-compulsive disorder or emerging psychosis.

Clinicians learn about many diagnoses in graduate school, but they may not have a template for what rare disorders look like in practice.

"If you don't have a screener for those things, you could easily misattribute what you see. That's where developing a robust set of screening tools becomes helpful," says Mary A. Fristad, PhD, ABPP, director of academic affairs and research development at the Big Lots Behavioral Health Services at Nationwide Children's Hospital.

'Knocking at the Door' of Common Problems

Families often have more than one problem, says Dr. Youngstrom. They may come in asking for help with one issue, but a good assessment could uncover a different root of the problem, such as trauma, abuse or substance misuse.

Without standardized assessments, it's possible to miss important issues that can get in the way of treatment. One such case stands out for Dr. Youngstrom. A patient had mood swings and extreme irritability. Dr. Youngstrom nearly diagnosed the patient with ordinary oppositional defiant disorder but first did a trauma screening.

It turned out the patient was being sexually abused.

"I never would have asked if I wasn't using a more structured approach with a script because I already thought I had the smoking gun and knew what was going on," says Dr. Youngstrom.

That case became a lesson Dr. Youngstrom often repeats about standardizing screening and following a script to rule out other possibilities. "We have to knock at the door of those eight to 10 vital possibilities that might reveal plot twists," he says.

Bringing Big Assessment Goals to an Institute That Will Help Him Deliver

Dr. Eric Youngstrom joined Nationwide Children's Hospital in early 2024 as the inaugural director of the new Institute for Mental and Behavioral Health Research. The Institute is located in the Big Lots Behavioral Health Pavilion — home of the country's largest pediatric-affiliated behavioral health system.

"We have depth and breadth of clinical services, and the volume of clinical services is simply massive. We provide over a quarter of a million outpatient visits and over 8,000 psychiatric crisis department visits a year," says Dr. Fristad.

Affiliated partners with Nationwide Children's treat nearly half-a-million kids in 47 Ohio counties.

While Nationwide Children's mental and health care reach is wide, so is the need.

Depression is the number one cause of disability among teenagers in the United States, according to the National Institute of Mental Health.

Robert Findling, MD, MBA, a pediatrician, child psychiatrist, and chair of psychiatry at Virginia Commonwealth University, and a mentor to Dr. Youngstrom, says, "You'd think for the number one disability, we would send in the cavalry, but we don't.

If we have good scouts and good information, there's a better chance of identifying the needs accurately and then figuring out ways to intervene appropriately."

Meanwhile, there are no standardized assessment tools to diagnose even the most common pediatric diagnoses among the hundreds in the DSM-5.

"If you took your child to a therapist, they'd say what they think is going on, and if you got a second opinion, the chances that a second opinion would agree with the first one is slightly better than chance," says Dr. Youngstrom.

Evidence-based universal screeners are key to identifying the appropriate diagnoses and determining the best treatment plan. Throughout that plan, using micro assessments to measure results over time should mean kids get better faster, says Dr. Fristad.

"We want these tools to assist clinicians in diagnosis and ongoing treatment planning — without taking away decision making or clinical judgment."

Clinical judgment remains essential, but improving the assessment process can help clinicians meet the growing demand. "Everyone is so busy because there are so few of us. Anything that can facilitate that process is incredibly important," says Dr. Findling.

The Process to Standardize Assessment Tools

Identifying the best assessment tools for the hundreds of pediatric behavioral and mental health diagnoses is a massive undertaking, but Dr. Youngstrom says he is up for the task. With the help of a team of interns, he's concentrating on the vital few that meet the biggest needs of families in Ohio.

These include:

- Oppositional behavior
- Aggressiveness
- Mood problems
- Depression
- Bipolar disorder
- Anxiety
- Autism
- Sleep hygiene
- Substance misuse
- Trauma

Dr. Youngstrom and his team started by mapping what Nationwide Children's clinicians already use. A second team scores those tools to determine whether they are equally accurate for different ages and demographic groups.

Once he and his team identify the best assessment tools for common diagnoses, they plan to promote them across the clinical service line. They also hope to build the tools into MyChart, making them accessible to even more families. Eventually, the goal is to build them into the electronic health record tool Epic, which is used by hospitals across the country.

"This is the first time I've ever had the resources and institutional support to build a team and do whatever will help solve these problems faster," says Dr. Youngstrom.

Standardizing Assessment Tools Across Pediatric Mental and Behavioral Health Care

With the help of statistical research and meta-analysis, Dr. Youngstrom is confident he can make a difference in standardizing diagnostic tools. He and a team are running four meta-analyses on the following tools:

- Scales to measure therapeutic relationships
- Treatment options for bipolar disorder in kids and teenagers
- Bipolar disorder screening scales
- Depression screening scales

Dr. Youngstrom hopes to complete an assessment of ADHD screening scales and autism screening tools by the summer of 2025.

> "If you can't use whatever we develop from a research perspective for assessment or treatment — if it isn't functional in a typical clinical setting — you haven't done much good."
>
> — Mary A. Fristad, PhD, ABPP, director of Academic Affairs and Research Development at Big Lots Behavioral Health Services at Nationwide Children's Hospital

Closing the Science-Practice Divide

Dr. Youngstrom acknowledges that his roadmap at Nationwide Children's will change as he identifies clinicians' needs. "I ask them what questions they have and promise our teams in the Abigail Wexner Research Institute will take those questions seriously. If it's something I can use science to answer, I promise to try," he says.

Bringing evidence-based medicine to a traditional psychological assessment is not easy. Research typically occurs under controlled conditions, while working in a clinic can be vastly different.

"I'm not interested in doing research under best-case scenarios and pristine track conditions. I want to test in the real, much messier reality, which is where families need us," says Dr. Youngstrom.

The leadership at Nationwide Children's agrees. "If you can't use whatever we develop from a research perspective for assessment or treatment — if it isn't functional in a typical clinical setting, you haven't done much good," says Dr. Fristrad.

Dr. Jen Youngstrom, who spends her days in what she calls the "messy trenches of the real world," has high hopes for what Eric can accomplish at Nationwide Children's with the help of the team. "Having Nationwide Children's do the background work to determine what is best makes it so much easier for people to use and implement these tools," she says.

Giving Away Science to Help Kids Everywhere

While Nationwide Children's has a wide reach in central Ohio and beyond, the goal of standardizing assessment tools is to become a national model for improving diagnostic tools.

Before coming to Nationwide Children's, Dr. Youngstrom founded a nonprofit, Helping Give Away Psychological Science (HGAPS), to make the most effective assessment tools widely available to therapists who need them. With the help of student volunteers, Dr. Youngstrom identifies the best tools and builds new ones when necessary. They offer the tools for free so they're accessible to everyone.

Dr. Fristad says her goal in the next five years is for everyone in behavioral health at Nationwide Children's to feel more confident in the diagnosis and initial treatment plan they develop. If they get stuck in treatment, as everyone does with various cases over time, the assessment processes embedded into the system will help therapists identify treatment modifications.

"Our goal is to help kids get better faster," she says. ■

> "I'm not interested in doing research under best-case scenarios and pristine track conditions. I want to test in the real, much messier reality, which is where families need us."
>
> — Eric Youngstrom, PhD, director of the Institute for Mental and Behavioral Health Research at Nationwide Children's

Approaching Uncertainty in Medicine With a Growth Mindset

by Abbie Miller, MWC

"In baseball, a really good batting average is .333 — which means the batter hits the ball and gets to first base a third of the time. That also means they miss — they fail — two-thirds of the time. Medical providers are expected to get things right 100% of the time," says Michael Patrick, MD, emergency medicine and urgent care attending physician at Nationwide Children's Hospital and host of PediaCast and PediaCast CME.

The idea that medical providers are expected to "get it right" 100% of the time leaves no room for uncertainty — but uncertainty in medicine does exist.

In a recent episode of PediaCast CME, a group of experts explored uncertainty in medicine and how accepting uncertainty can help everyone — patients, clinicians and trainees – move forward in ways that lead to better patient safety, increased job satisfaction and decreased burnout.

TYPES OF UNCERTAINTY

Broadly speaking, uncertainty is the "actual or perceived inability of a clinician to identify causes of symptoms, make a diagnosis, offer prognosis and outline the best course of treatment," says Anna Kerr, PhD, a health communication researcher at Ohio University.

Types of uncertainty fall into three main categories: technical, personal and conceptual.

Technical uncertainty is also sometimes called data-related uncertainty. Here, a clinician lacks knowledge, skills or certain data needed to make a diagnosis or perform a procedure. This type of uncertainty is common among trainees, says Claire Stewart, MD, critical care physician and associate program director for the Pediatric Critical Care Medicine Fellowship at Nationwide Children's. For example, they may feel uncertain about their ability to perform a specific procedure.

Personal uncertainty is also called relationship-related uncertainty. Clinicians who don't know their patient's (or patient family's) values, wishes or expectations can experience this type of uncertainty. Dr. Stewart says, in the pediatric intensive care unit (PICU), clinicians may feel personal uncertainty when a patient is nearing the end of their life — not knowing the family's values or desires for continued treatments creates uncertainty. If a clinician is unwilling to confront personal uncertainty and ask families about their wishes, shared decision-making becomes nearly impossible.

Conceptual uncertainty is application-related uncertainty. In this case, clinicians are unable to apply concrete criteria. They have knowledge and skills, but for some reason, they are not able to apply them to a specific patient or situation. This could be related to a patient's symptoms

MEET THE EXPERTS

Anna Kerr, PhD
assistant professor in the Department of Primary Care, Ohio University Heritage College of Osteopathic Medicine

Alex Rakowsky, MD
primary care physician, medical director for the Healthy Children Service Line, Partners For Kids®, Nationwide Children's Hospital

Claire Stewart, MD, MEd
critical care physician, associate program director for General Pediatrics residency and associate program director for Pediatric Critical Care Medicine Fellowship, Nationwide Children's

Charee Thompson, PhD
associate professor of Communication and Biomedical and Translational Science, University of Illinois Urbana-Champaign

not fitting into a diagnosis or a typical course of treatment not working for an unknown reason.

HARMS OF NOT ACKNOWLEDGING UNCERTAINTY

"If you don't openly discuss uncertainty in health care teams, it's to the detriment of patient care," says Charee Thompson, PhD, associate professor of Communication and Biomedical and Translational Science at the University of Illinois Urbana-Champaign.

On a population health level, uncertainty can cause harm if clinicians order unnecessary tests out of fear of missing something. Unnecessary tests may mean additional blood draws, which carry physical risks for children. Unnecessary tests and unwarranted referrals to specialists also increase the financial and time burden of care for patients and their families, explains Dr. Thompson.

"In the case of rare or undiagnosed diseases, a clinician's inability to sit with the discomfort of uncertainty can lead to premature, incorrect diagnoses," says Dr. Kerr.

UNCERTAINTY AS OPPORTUNITY

But uncertainty is not necessarily a bad thing. It can be fuel for collaboration, research, innovation and discovery. Even better — normalizing uncertainty leads to increased trust.

"When uncertainty is addressed, it can ultimately improve patient safety and care. But for positive outcomes, uncertainty needs to be discussed openly and lead to growth," says Dr. Kerr

Alex Rakowsky, MD, medical director of the Healthy Kids Service Line for Partners For Kids®, primary care clinician at Nationwide Children's and associate professor of Pediatrics at The Ohio State University, likes to share this example of how seeing uncertainty as an opportunity led to an unexpected learning.

In a primary care office, physicians were noticing higher lead levels among one-year-olds of Afghani immigrants. They started testing for lead earlier and discovered that levels were raised from infancy. After interviewing families and asking about possible sources of lead, Dr. Rakowsky reached out to the toxicology team at Nationwide Children's. Working together, they discovered the source of lead was in body paint (kohl) imported from Afghanistan, which is traditionally used around babies' eyes. The clinicians shared this information with the families, and a local store began selling lead-free kohl.

This open approach led to collaboration and contributed to the trusting patient-provider relationship among a potentially vulnerable population.

Addressing uncertainty also helps build trust among trainees and teachers.

Trainees have been ingrained to find "the" correct answer their entire academic careers, says Dr. Stewart. Then they come into the clinic and find out that's not how things work in the real world.

It's important for attendings to model how to address uncertainty among themselves, with trainees and with patients, she adds. "We must show that it's not just expressing uncertainty but identifying what we are going to do about it. We can't just leave it at 'I don't know.'"

Unaddressed uncertainty among trainees has been shown to contribute to burnout and depression, according to a study published in *Medical Teacher*. Attendings and mentors play an important role in equipping the next generation of clinicians to handle uncertainty and approach it with a growth mindset.

"Communication is a science," says Dr. Thompson. "And so we have tools that we can teach that are evidence based in how you can better communicate, because research tells us over and over that suppressing uncertainty is harmful. So the question becomes: how can we communicate uncertainty?"

Drs. Thompson, Kerr, Rakowsky and Stewart are part of a group working to develop a curriculum for medical trainees to do exactly that. Their initial work has been submitted for publication and is in press in *Hospital Pediatrics*. ■

UNCERTAINTY IN MEDICINE
is episode 100 of PediaCast CME. Tune in for your free CME credits and to hear more from these experts about the importance of addressing uncertainty in medicine.

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Lessons Learned:

From First Gen Student to Chief Scientific Officer

What inspired you to go to college and pursue a bachelor's degree in science?

When I was in school, college never came up as an option. No one in my family had been to college. It just wasn't something we knew about. My dad wanted me to run his business (a fish and chip shop) and my mum preferred that I work as a bank teller (for a good mortgage rate). Either were great safe options for them, and within their own realm of experience.

Instead of continuing to two more years of higher education, I left school at 16 (this was not unexpected in my family) to find a job in a lab because I enjoyed biology class. I worked in a variety of labs as a technician, both in research and industry, some good and some bad, for the next six years. Fortunately, all my employers supported and paid for part-time education in technical college, so I did continue my education.

My final job before college was as a lab technician at Cambridge University studying parasitic infections. When I asked the department chair if they would support my part-time education, he gently told me no. He explained that it was because he thought I should go to college. He also helped me understand how to apply, because I had no idea where to start. I wanted to study blood cells and be an immunologist because my technical career had always been in that discipline. I was accepted to Kings College in London to get my undergraduate degree in immunology.

In college, I learned that my dissatisfaction with being in school was the requirement to know something without understanding it. In college, we got to understand the why. That was rewarding to me.

Why did you decide to keep going — earning your doctorate and pursuing a career in academia?

My career path wasn't ever planned. I said yes to opportunities that came my way or leaned into the suggestions of others. My college advisor suggested I apply to graduate school, so I thought I would try that. I didn't realize that I was considered a strong student, and I only applied to a few places. I had no other big life plan.

I was awarded a prestigious Medical Research Council fellowship at the London School of Hygiene and Tropical Medicine London and joined a lab studying immunology of leprosy infection in humans. My doctoral advisor would probably describe me as strong-willed because I changed my doctoral project to study tuberculosis (TB) — a more exciting topic and a highly competitive research area. I am grateful she let me do it, and for making connections for my next career move. During my doctoral work, I also had the opportunity to work in The Gambia in West Africa for many months, studying TB patients. The experience was humbling.

Then, I took a postdoctoral position at Colorado State University using mouse models to understand mechanisms of TB infection that we could not examine in humans. I moved to the United States without really considering how big a life-changing event that was. I had one suitcase and no idea where Colorado was — I just knew it was an incredible career opportunity.

As a postdoc I published very well but hadn't considered being faculty. However, I was again surrounded by people who saw something more in me than I did and encouraged me to move up. My postdoc advisor requested a research faculty position for me because he thought I should take that career path. After two more years at Colorado State, I moved to The Ohio State University as an assistant professor where I had a successful academic career studying TB in mice and humans.

As I look back, I see that my career has been driven by scientific curiosity and the good work ethic bestowed on me by my working-class background. But it's been

Joanne Turner, PhD, chief scientific officer at the Abigail Wexner Research Institute at Nationwide Children's Hospital, shares what it's like to go from first gen college student to academic leadership.

guided mostly by an abundance of people who saw talent in me that I did not yet recognize.

When did you begin your move to leadership?

A couple of things made me consider moving into leadership. As my academic faculty position matured, I was invited to join a variety of institutional committees. I loved to see what was on the other side of the (administration) fence. In general, these experiences reminded me of my past dissatisfaction with school. As faculty, things happened at OSU but I didn't always know why. Being around leadership taught me the why and I enjoyed that — a recurring theme.

I also took on a biocontainment level 3 (BSL3) director role that made me think about billing, building controls, and biological safety. The practical and compliance side of managing a facility gave me a new and very different challenge. Similarly, as I managed my lab, I found myself more interested in mentoring. I realized that I found people and problems more interesting than the science. I didn't wake up as excited to do my science as I did to solve a problem or help someone. That's when I realized that I could have a bigger impact on the academic environment from a leadership position.

What role did mentorship play in your career?

I have been fortunate to have had many mentors or advocates who provided opportunities to progress or helped me work through a career decision. Some have been my direct supervisor or employer, and others are colleagues or friends. I have go-to colleagues who always show up for me when I need them, and they are often from unexpected connections. I value them all so much and try to pay it forward. I get a great sense of pride in seeing my own mentees be highly successful.

What advice would you give to students navigating academia as first gen scientists?

Use your life experience as a strength. You will have experienced life differently compared to many others competing with you for the same opportunities. Balance expressing what makes you different and unique with just enough alignment to the norms to fit in. I talk about my background as an asset, as it brought different creativity to my science. Now working as an administrator, that background also allows me to relate to the experiences of others in a more meaningful way. Finally, accept the support and mentoring of others. There are wonderful people around you who care about your happiness and development — let them help. ■

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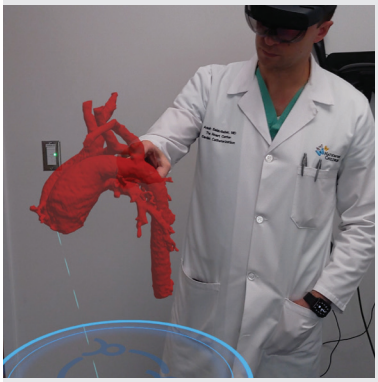
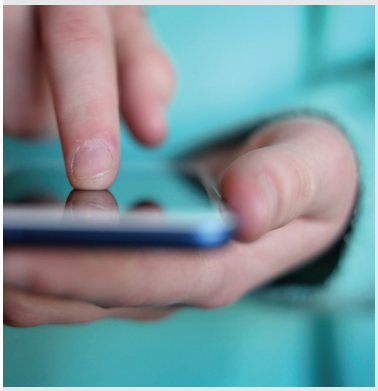


Extended Reality Offers New Ways to View Congenital Heart Disease

Take a look inside The Heart Center XR Program at Nationwide Children's Hospital. With multiple IRB-approved studies investigating clinical, training and patient education applications, Arash Salavitabar, MD, director of The Heart Center XR Program, and his collaborators are looking to bring the possibilities of XR to life.

PediatricsNationwide.org/Heart-Center-XR



Can Post-discharge Text Messages Help Teens With Suicidal Thoughts or Behaviors?

A recent publication in *JMIR Pediatrics and Parenting* looks at developing and implementing the Caring Contacts approach. Patients who received the messages overwhelmingly (92%) said they thought other kids would be helped by the messages. If given the option, 87% said they would keep receiving the messages.

PediatricsNationwide.org/Caring-Contacts

What Pediatricians Need to Know About Over-the-Counter Oral Contraception

The first over-the-counter contraceptive pill — the Opill® — is currently available in retail outlets and online. Elise Berlan, MD, and Caroline Weingart, MD, answer frequently asked questions about this new option in contraception.

PediatricsNationwide.org/Opill-FAQ

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