ABIGAIL WEXNER RESEARCH INSTITUTE

DISCOVER
A NEW ERA IN PEDIATRIC RESEARCH

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.
The Abigail Wexner Research Institute (AWRI) at Nationwide Children’s Hospital is a dynamic, collaborative, state-of-the-art environment for world class, child health research. More than 170 scientists on the Nationwide Children's Hospital campus work to advance child health and pediatric medicine using the resources and expertise of the Research Institute.

In 2020, we welcomed 12 new research-focused faculty, nine of whom are women. Maryam Fouladi, MD, a renowned brain tumor expert, joined us as co-executive director of the Neuro-Oncology Program. With her arrival, the international consortium for neuro-oncology clinical trials, CONNECT, will now be based at Nationwide Children's.

Two of our faculty have been elected to the National Academy of Medicine: Elaine Mardis, PhD, co-executive director of the Steve and Cindy Rasmussen Institute for Genomic Medicine and a past president of the American Association for Cancer Research, and Jerry Mendell, MD, principal investigator in the Center for Gene Therapy and one of the lead scientists behind the first systemic gene therapy approved by the Food and Drug Administration (FDA).

Our translational work to discover, test and deliver new cures to children throughout the world is exemplified by the newest recipient of the Allen Distinguished Scholar Award. Lauren Bakalertz, PhD, and her collaborators have gone from the basic science discoveries about biofilm structures to a novel platform technology. Through the support of the Office of Technology Commercialization, this biofilm-disrupting technology has been licensed to the start-up company Clarametix, who will support the first-in-human clinical trial in 2021. To date, there are 16 active startup companies that have been developed based on Nationwide Children's discoveries.

Our commitment to diversity, inclusion and health equity from the lab to the clinic and beyond has grown even deeper with a rededicated Center for Child Health Equity and Outcomes Research. Under the leadership of Deena Chisolm, PhD, our acclaimed health equity research is focused on reducing health disparities to create better solutions and best outcomes for all children and families. Part of that work was recognized in 2020, when Nationwide Children’s Healthy Neighborhoods Healthy Families initiative was awarded the prestigious Hearst Health Prize.

In the pages that follow, we invite you to learn more about the teams, resources and culture that make the tremendous work of AWRI possible.

Sincerely,

John A. Barnard, MD
President

Dennis R. Durbin, MD, MSCE
Chief Scientific Officer
Lauren Bakaletz, PhD, is named the 2021 Allen Distinguished Scholar in Pediatric Research

Lauren Bakaletz, PhD, director of the Center for Microbial Pathogenesis in the Abigail Wexner Research Institute (AWRI) at Nationwide Children's, is named the 2021 Allen Distinguished Scholar in Pediatric Research. The award is given in honor of former Nationwide Children's CEO, Steve Allen, MD, and his role in growing the AWRI into a preeminent research institution.

“It is an incredible honor to receive the Allen Distinguished Scholar award for my work,” Dr. Bakaletz says. “I’m thrilled to be recognized in this way.”

She and her team study the molecular mechanisms that underlie polymicrobial infections of the respiratory tract, including otitis media, or middle ear infections. Otitis media affects more than 90% of children by the time they are 3 years old.

While working to create a novel vaccine candidate for otitis media (which is still in development), she and her team made a discovery that would change how we understand and approach biofilms — the extracellular fortresses that shield and protect bacteria from the immune system and antibiotics. This discovery led to a platform technology that has been shown to be effective against biofilms of all kinds in preclinical studies. A clinical trial is anticipated in the next year.

“As a basic scientist, being able to discover something fundamental about a microorganism and to use that new knowledge to develop a platform technology and shepherd it all the way to human trials is a tremendously gratifying and educational experience,” she says.

Dr. Bakaletz is also the Tillie E. Coleman Endowed Chair in Pediatric Research and vice president for Basic Sciences Research at Nationwide Children’s, as well as a professor of Pediatrics and Otolaryngology at The Ohio State University. In total, Dr. Bakaletz’s research has led to 43 patents, and she is a scientific founder of Scioto Biosciences and Scientific Advisory Board Co-chair for Clarametyx Biosciences. She was named an Ohio State University College of Medicine Distinguished Professor in 2013, a lifelong honorific distinction. In 2020, she was named a Fellow of the American Academy of Microbiology.

About the Allen Scholar Award
In nearly 13 years as CEO, Steve Allen, MD, helped build Nationwide Children’s into a renowned pediatric research institution, including overseeing an increase from $41.7 million to $105.9 million in external research awards. Nationwide Children’s is currently ranked sixth in the country for National Institutes of Health funding among freestanding children’s hospitals.

In recognition of Dr. Allen’s role in the evolution of Nationwide Children’s as a leader in pediatric research and health care, Nationwide Children’s has established the Steve Allen, MD Distinguished Scholar in Pediatric Research. The award is given to a preeminent Nationwide Children’s senior researcher for scientific innovation and achievement advancing the understanding, diagnosis, treatment and prevention of childhood disease.
Following a national search, Katherine Deans, MD, MHSc, co-director of the Center for Surgical Outcomes Research at Nationwide Children’s Hospital and a professor of Surgery at the Ohio State University, has been appointed to the new position of chief clinical research officer at Nationwide Children’s. She began the role on September 1, 2020.

In her new role, Dr. Deans is focused on the development and oversight of clinical research operations across Nationwide Children’s. She will oversee the full life cycle of the clinical research process, with an emphasis on increasing quality, compliance, and efficiency along with promoting a culture of excellence among investigators and clinical research staff. The Biostatistics Core and Clinical Research Services at Nationwide Children’s now report to Dr. Deans as part of this new role.

“Kate is passionate about the mission of Nationwide Children’s and believes that best outcomes are achievable through scientific innovation and its translation into a wide range of interventions that improve access to evidence-based patient care,” says Dennis Durbin, MD, MSCE, chief scientific officer, at the Abigail Wexner Research Institute at Nationwide Children’s. “We are excited to have an accomplished clinician and scientist to serve as our first chief clinical research officer to lead our clinical research into a new era.”

“I am incredibly excited for the opportunity to lead the next stage of our growth in clinical research,” says Dr. Deans. “The new Office of the CCRO will help Nationwide Children’s to develop and support one of the most diverse, innovative and patient-focused pediatric research portfolios of any children’s hospital in the country by facilitating impactful clinical research throughout the organization.”

Dr. Deans has been a faculty member at Nationwide Children’s since 2011. She is a Fellow of the American College of Surgeons and an assistant editor for the *Journal of Pediatric Surgery*. As an educator, Dr. Deans has trained more than 20 pediatric surgery residents and fellows; served as a preceptor for 12 fellows in minimally invasive and colorectal surgery; and supervised more than 15 post-doctoral research fellows and medical students.

During her career, Dr. Deans has published more than 190 peer-reviewed papers, book chapters and abstracts and has received over $10 million in research funding.

To learn more about clinical research at Nationwide Children’s visit: NationwideChildrens.org/research/clinical-research
Katherine Deans, MD, MHSC
The Center for Innovation in Pediatric Practice at Nationwide Children’s has a new name: Center for Child Health Equity and Outcomes Research.

“Over the years the focus of our research and the need for research devoted to health equity has grown,” says Deena Chisolm, PhD, vice president of Health Services Research and director of the center. “With the new name comes the opportunity to renew our mission to advance child health and well-being through research in and across clinical care, health services, health policy and community initiatives.”

The work of the center encompasses clinical innovations and outcomes, social and community factors and their influence on health; health disparities; health policy and Medicaid; and more. Over the years, members of the center have become leaders in pushing the discussion of health equity on the national stage.

“Health equity and outcomes research is an integral part of the clinical and translational science being conducted across Nationwide Children’s Hospital,” says Dennis Durbin, MD, MSCE, chief scientific officer at the Abigail Wexner Research Institute at Nationwide Children’s. “We anticipate this center to be an integral part of supporting and connecting researchers who are asking these important questions.”

By working with internal and external partners, and using the broad portfolio of resources available, researchers aim to reduce health disparities, support vibrant communities with flourishing families and, most importantly, achieve best outcomes for all children.
ABIGAIL WEXNER RESEARCH INSTITUTE LEADERSHIP

John A. Barnard, MD
President

Dennis R. Durbin, MD, MSCE
Chief Scientific Officer

Katherine J. Deans, MD
Chief Clinical Research Officer

Lauren O. Bakaletz, PhD
Vice President, Basic Sciences Research

Deena Chisolm, PhD
Vice President, Health Services Research

Amy J. Roscoe
Vice President, Strategic Planning and Finance

William E. Smoyer, MD
Vice President, Clinical Research

Veronica J. Vieland, PhD
Vice President, Computational Research
Nationwide Children’s strategic plan is aptly named *Journey to Best Outcomes*. It is the journey that each clinician, researcher, family and patient strives for in and through every interaction with the institution. The Abigail Wexner Research Institute supports the pillars of the *Journey to Best Outcomes*.

This year, 2021, is the last year of the *Journey to Best Outcomes* strategic plan. A new strategic plan will be rolled out this year, and the strategic focus of AWRI will continue to align with that of Nationwide Children’s.

**OUR STRATEGIC PLAN**

**Vision**

BEST OUTCOMES

for Kids Everywhere

**Core Strategies**

- One Team Values
- Core Strategies
- Growth & Partnerships
- Operational Excellence
- Education

**ACCELERATORS**

- GOAL
  - Pre-eminent Clinical & Research Programs
- ACCELERATORS
  - Quality, Safety & Service
  - Behavioral Health
  - Genomics
  - Wellness/Population Health

**Strategic Plan Accomplishments in Research**

The following list is just a few of our accomplishments during this strategic period:

- Partnering with The Ohio State University, we announced a new Proton Therapy Center to be located on Ohio State’s Wexner Medical Center’s West Campus.
- Zolgensma® (spinal muscular atrophy gene therapy) received FDA approval — the first ever gene therapy for a terminal disease approved by the FDA.
- Two Cancer Moonshot Grants were awarded to AWRI principal investigators including Stephen Lessnick, PhD, Timothy Cripe, MD, and Elaine Mardis, PhD.
- The Institute for Genomic Medicine implemented several genomic protocols in rare diseases, cancer, neonatology and behavioral health, bringing genomics into the clinic.
- A study from the Center for Suicide Prevention and Research helped compel Netflix to edit the first season of its series “13 Reasons Why.”
- In collaboration with OSU, we established the Cellular Therapy and Cancer Immunotherapy Program with Dean Lee, MD, PhD, as director.
- Extensive growth and expertise in vector production led to the creation of Andelyn Biosciences, a Nationwide Children’s affiliate company manufacturing gene therapy products for the biotechnology and pharmaceutical industries.
- The Center for Injury Research and Policy is a Centers for Disease Control-recognized Injury Control Research Center (CDC ICRC), which has been funded continually since 1999.
FACULTY RECRUITMENT SUMMARY

2018 to 2020

37 TOTAL RESEARCH INTENSIVE FACULTY RECRUITED

11 of 13 RESEARCH CENTERS WITH NEW RECRUITS

17 COLLABORATIVE RECRUITS WITH A CLINICAL DEPARTMENT/DIVISION

20 WOMEN / 17 MEN

16% UNDER-REPRESENTED MINORITIES
2020 PERFORMANCE INDICATORS

GROWTH OF EXTERNAL RESEARCH FUNDING AT NATIONWIDE CHILDREN’S

2018 2019 2020

Principal Investigators* 195 207 208
Research Fellows 81 71 71
Graduate Students 42 38 42
Employees 1238 1583** 1534
Publications 1583 1357 1600

RESEARCH BY THE NUMBERS

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<tr>
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*Includes faculty from the Abigail Wexner Research Institute and faculty from Nationwide Children’s Hospital with $50,000 or more in research funding support.

**In 2020, Andelyn Biosciences became a separate entity, resulting in approximately 100 employees moving from Nationwide Children’s to Andelyn Biosciences.
RESOURCES AND CORES

Abigail Wexner Research Institute at Nationwide Children’s Hospital has a wealth of resources available to ensure researchers have the tools they need to advance the hospital’s mission. From core facilities to computational resources and regulatory offices, researchers have the support to enhance the health of children by engaging in high-quality, cutting-edge research according to the highest scientific and ethical standards.

**Clinical Research Services (CRS)** Clinical Research Services is designed to be a portal through which clinical investigators access streamlined coordination of services necessary to initiate clinical research projects, regardless of funding source. Support is provided for all types of clinical research studies from initiation to completion according to Good Clinical Practice and federal, state and institutional regulations and policies. Nationwide Children’s is accredited by the Association for the Accreditation of Human Research Protection Program (AHRPP). This accreditation highlights clinical study participant safeguards that surpass state and federal requirements.

**Good Manufacturing Practices (GMP)** AWRI is home to a current Good Manufacturing Practices (cGMP) Clinical Manufacturing Faculty that operates according to FDA cGMP Guidelines to ensure the safety of manufactured biologic products. The CMF space is 9000-sq ft space. It consists of a 7500-sq ft. clean room suite with ISO Class 5/7/8 spaces and 1500-sq ft. of quality control lab and research production spaces. The cGMP facility is operated by Andelyn Biosciences, a for-profit spin-off of Nationwide Children’s.

**Research Information Solutions and Innovation (RISI)** The mission of RISI is to collaborate and innovate on impactful health IT solutions combining data analytics, technological intervention and user experience designs. As an agile group, they accelerate innovation through wide array of services. Collaboration is fundamental to RISI’s high resolution imaging facility to the organization and patients.

The **Animal Resources Core** facilitates preclinical research by providing the highest quality animal husbandry, veterinary care and technical support in an ethical and compliant manner. The high resolution imaging facility provides a centralized imaging suite for *in vivo* studies in small animals.

The **Behavioral Outcomes Core** assists investigators incorporating behavioral assessments in their research, which can add a practical or applied aspect to research by defining meaningful outcomes from a patient-centered perspective.

The **Biopathology Center (BPC)** serves as a biospecimen processing and storage core for projects sponsored by Nationwide Children’s Hospital investigators as well as a large number of national cancer research consortia. The BPC is the repository for many National Cancer Institute-sponsored biorepository-based efforts, including the Children’s Oncology Group, the Gynecologic Oncology Group, SWOG (formerly the Southwest Oncology Group), and the Cooperative Human Tissue Network.

The **Biostatistics Resource at Nationwide Children’s Hospital (BRANCH)** provides assistance to researchers in study design, data analysis and interpretation of statistical results.

The **Cell Line Core** processes human subject samples and provides the researcher with cell lines or DNA appropriate for applications in human and molecular genetic studies.
The **Flow Cytometry Core** offers several platforms for performing flow analysis and cells sorting.  

**Genomics Services** offers advanced sequencing technologies to provide high quality genomics as a critical clinical and research resource.

The **Morphology Core** provides services in histology, electron microscopy, confocal and laser scanning microscopy and atomic force microscopy.
The Institutional Animal Care and Use Committee reviews all research activities involving the use of animals and operates in full accordance with the Animal Welfare Act and the Health Research Extension Act to ensure the humane treatment of animal subjects in research.

The Institutional Biosafety Committee is responsible for evaluating and approving all research involving infectious or potentially infectious agents, recombinant DNA or RNA, and biological toxins. The committee ensures compliance with current safety regulations and guidelines as issued by the U.S. departments of Health and Human Services and Agriculture, the NIH, and the Centers for Disease Control and Prevention.

International Employee Resources provides expertise in key regulations and procedures, international paperwork and green cards required for employment to ensure a mutually productive and valuable experience.

The Institutional Review Board (IRB) provides oversight of all research involving human subjects. For more than a decade, the IRB has received full accreditation from the Association for the Accreditation of Human Research Protection Programs.

The Office of Finance and Sponsored Projects supports grant and contract funding from the start of a search for funding through the closeout of a project. The department offers expertise in federal and state regulatory requirements.

The Office of Research Compliance and Integrity ensures all research is conducted according to the highest scientific and ethical standards and in compliance with regulations from the NIH, FDA and all other government agencies with authority over research activities.

The Office of Research Regulatory Affairs assist medical faculty and investigators in traversing various regulations that govern the conduct of preclinical and clinical trials. The FDA closely regulates human participation in clinical trials involving new drugs and devices and the Office of Research Regulatory Affairs guides investigators through this complex submission, review and approval process.

“The breadth and impact of our researchers’ discoveries would not be possible without the support of many research cores and services and our outstanding research administration team holding it all together. From basic science to clinical research core services and cutting edge regulatory and administrative support that ensure the highest level of ethical and scientific standards are met, we have a framework for discovery that allows our researchers to excel.”

– John Barnard, MD, president of the Abigail Wexner Research Institute
PARTNERSHIPS

Life-changing research is a team effort. Collaboration is as essential outside of the organization as it is within it. Some key partnerships between the Abigail Wexner Research Institute and other entities include the following.

OHIO STATE UNIVERSITY
The Ohio State University’s Wexner Medical Center and seven health science colleges and Nationwide Children’s have come together to form the OSU Center for Clinical and Translational Science. Nationwide Children’s receives funding annually in support of CCTS activities and are eligible to compete for pilot and training grants through CCTS.

THE OHIO STATE UNIVERSITY COMPREHENSIVE CANCER CENTER – ARTHUR G. JAMES CANCER HOSPITAL AND RICHARD J. SOLOVE RESEARCH INSTITUTE
A collaborative agreement among Nationwide Children’s Hospital and OSU CCC broadens the study of childhood cancers and accelerates the transfer of key research findings to the clinical setting. The unique relationship among the institutions is stimulating novel research and developing collaborations in pediatric cancer-related studies that will also have applications to adults. Among the innovative outcomes of this collaboration are the Cellular Therapy and Cancer Immunology Program and the proton therapy facility that is expected to open in 2021.

OHIO PERINATAL RESEARCH NETWORK (OPRN)
AWRI, Nationwide Children’s, Wexner Medical Center and OSU have developed the OPRN, a research collaborative dedicated to better understanding preterm birth and its complications. A major effort of OPRN is a research repository for clinical data and specimens from infants delivered preterm and their mothers. Additional collaborating institutions include Ohio-Health, Mt. Carmel and community partners in the Ohio Better Birth Outcomes (OBBO) project aimed at mothers and physicians to prevent preterm births.

REV1 VENTURES
Nationwide Children’s is a sustaining member of Rev1 Ventures, an organization created to accelerate innovation, business growth, job creation and prosperity in the 15-county region of central Ohio. Rev1Ventures works to create new companies, strengthen existing businesses, open doors to technology resources and support the attraction and retention of technology-based businesses.

NATIONWIDE PEDIATRIC INNOVATION FUND
Established in 2014 by the Nationwide Foundation, the Nationwide Pediatric Innovation Fund has now contributed more than $50 million. This fund supports pediatric research and innovative projects to advance the science and practice of pediatric health care. Innovation Fund investments are directed long-term to both clinical and research program development and recruitment in areas of greatest priority.

ADDITIONAL VENTURES
AWRI is the recipient of a $1 million Innovation Fund, gifted by the nonprofit foundation: Additional Ventures. In receiving this funding, AWRI will join four other research institutions in a large-scale coordinated research effort centered on identifying new avenues to functionally cure patients with single ventricle heart defects (SVDs).

PEDSNet
PEDSNet is a large, national community of hospitals and health care organizations, researchers and clinicians, and patients and families. Nationwide Children’s is a founding member of this multi-specialty network that conducts observational research and clinical trials across multiple children’s hospital health systems.

AND MANY MORE
Nationwide Children’s also collaborates with OSU through their joint Muscle Group and the Center for Microbial Interface Biology, with Battelle Memorial Institute and with many other partners. Researchers at AWRI also collaborate with a variety of institutions, present at national meetings, publishing in highly respected journals and earning research grants to further their fields of study.
Research education and training are vital to the mission of Nationwide Children’s, with the outstanding faculty at the Abigail Wexner Research Institute dedicated to training and mentoring the next generation of scientists in pediatric research. Investigators at AWRI are teaching faculty in various departments at The Ohio State University College of Medicine. As a result, a large number of students and trainees are based at AWRI. This includes undergraduates, residents and fellows in pediatrics and pediatric surgery, graduate students, postdoctoral fellows and high school students. Instruction occurs in informal and formal didactic sessions, one-on-one interactions and hands on laboratory training.

Research Institute Trainee Association (RITA)
RITA was formed to help train and prepare young scientists for careers in research. All trainees are welcome to participate, including graduate students, postdoctoral scientists and fellows. It is modeled after guidelines established by the National Postdoctoral Association, of which the AWRI is a member. RITA is led by a team of trainees nominated and elected by their peers. They receive guidance and assistance from an advisory committee of faculty co-advisors and administrators.

FUTURES MATTER PROGRAM
The Futures Matter Program is an eight-week, paid summer research experience on the AWRI campus. High school students with an interest in biomedical research careers have an opportunity to work with researchers for hands-on science experience, while learning about different professional pathways in biomedical research.

INTERNSHIPS FOR HIGH SCHOOL AND UNDERGRADUATES
Beyond the Futures Matter Program, opportunities for paid or for-credit internships are available through the different research centers. The Summer Scientist Education Series is a summer seminar series designed to expose all interested high school and early college students to the scientific method and careers in medical research. This lecture series is open to the public.

“As the chair, I am committed to keep all trainees’ engaged in RITA activities and to ensure everyone benefits from provided career development trainings. Also, I believe this is an excellent opportunity to gain leadership experiences.”

– Afrooz Rashnonejad, PhD, postdoctoral scientist in the Center for Gene Therapy and 2021 RITA chair
Nationwide Children’s Hospital has a remarkable track record of moving discoveries into the marketplace. The hospital’s Office of Technology Commercialization facilitates the transfer of new technologies, research and innovations to outside partners to benefit patients, the local community and the general public.

Discoveries and inventions ranging from new therapeutics — including the recently approved, first-of-its-kind gene therapy Zolgensma — to biomarkers, diagnostic tools and clinical tools — such as the Comfort Collar, designed to prevent pressure wounds around tracheostomy tubes — are supported through the expert team.

“People might not intuitively think of a nonprofit hospital like Nationwide Children’s as a hotbed for technology commercialization. They should. Just like universities, we make substantial investments in commercialization of new discoveries and create job-producing startup companies. But even more importantly, we’re able to expand the benefits of innovation to improve the care and lives of children who may never set foot in our hospital.”

— Matthew McFarland, RPh, PhD, vice president, Commercialization and Industry Relations at Nationwide Children’s

Please note the following start-ups have been acquired: AveXis by Novartis, Myonexus by Sarepta, and Celenex by Amicus.
TECHNOLOGY COMMERCIALIZATION AT NATIONWIDE CHILDREN’S: BY THE NUMBERS

DISCLOSURES

ISSUED PATENTS

U.S. PATENT APPLICATIONS FILED

LICENSES/OPTIONS
OUR CENTERS AND INSTITUTES

The Abigail Wexner Research Institute is organized into centers of emphasis and the Institute for Genomic Medicine, all of which facilitate interdisciplinary team science by transcending traditional academic boundaries. The structure supports discovery, enabled by outstanding shared resources. Each center or institute is home to talented faculty members, staff, graduate students, residents, postdoctoral fellows and other students.

• Battelle Center for Mathematical Medicine
  Veronica Vieland, PhD, Director

• Biobehavioral Health
  Cynthia Gerhardt, PhD, Director

• Biopathology Center
  Nilsa Ramirez, MD, Director

• Cardiovascular Research
  Vidu Garg, MD, Director

• Childhood Cancer and Blood Diseases
  Stephen Lessnick, MD, PhD, Director

• Clinical and Translational Research
  William Smoyer, MD, Director

• Gene Therapy
  Kevin Flanigan, MD, Director

• Child Health Equity and Outcomes Research
  Deena J. Chisolm, PhD, Director

• Injury Research and Policy
  Gary Smith, MD, DrPH, Director

• Microbial Pathogenesis
  Lauren Bakaletz, PhD, Director

• Perinatal Research
  Lynette K. Rogers, PhD, Interim Director

• Regenerative Medicine
  Christopher Breuer, MD, Director

• Vaccines and Immunity
  Christopher Walker, PhD, Director

• The Steve and Cindy Rasmussen Institute for Genomic Medicine
  Richard Wilson, PhD, Executive Director
  Elaine Mardis, PhD, Co-executive Director

At the Abigail Wexner Research Institute, collaboration, discovery, translation and team science define us. They are our foundation as we seek answers on behalf of children everywhere. Our researchers’ dedication and commitment to the common goal of improving the health and quality of life for children and their families enable them to work together to accomplish more than could be imagined independently. In the pages that follow are stories about the tremendous progress made possible by our culture, resources and integration with our world-class clinical teams.
Increases in Number and Severity of Suicide-Related Calls to U.S. Poison Control Centers Involving Over-the-Counter Pain Relievers

Researchers at the Center for Injury Research and Policy and the Central Ohio Poison Center at Nationwide Children’s Hospital have analyzed the 549,807 calls made to Poison Control Centers (PCCs) in the U.S. for suicide-related cases involving OTC analgesics from 2000 through 2018 in a new study, published in *Pharmacoepidemiology and Drug Safety*. They found that both the overall number and rate of these cases increased significantly (by 57% and 34%, respectively) during this period. This trend was driven primarily by the increasing exposures among 6-19-year-old females.

According to the study, children between the ages of 6 and 19 years accounted for half of all suicide-related OTC analgesics cases (50%) and females represented 73% of cases among individuals of all ages.

In addition to the increase in the number and rate of cases, there was also an increase in the severity of the exposures. The proportion of calls resulting in a serious medical outcome or admission to a health care facility increased significantly (a 64% increase and 29% increase, respectively) over the study period. The proportion of cases resulting in a serious medical outcome or admission also increased with increasing age.

“An important first step to reduce the suicidal use of over-the-counter analgesics would be to require unit-dose packaging, or ‘blister packs,’ for all solid forms of acetaminophen and aspirin sold to consumers. Because suicidal ingestion is often a highly impulsive act, this would deter overdoses by limiting the amount of medication that can be extracted at one time,” says Gary Smith MD, DrPH, senior author of the study and director of the Center for Injury Research and Policy at Nationwide Children’s. “In addition, the U.S. should follow the lead of other countries that have successfully reduced suicidal ingestions of these medications by limiting the package size and quantity that can be purchased by an individual at one time.”

Dr. Smith adds, “Remarkably, the top three substance categories associated with suicide-related ingestions in the U.S. are antidepressants, over-the-counter analgesics and antipsychotics, and of these, over-the-counter analgesics is the only one readily available without a prescription or other restrictions.”

Data for this study were obtained from the National Poison Data System, which is maintained by the American Association of Poison Control Centers (AAPCC). The AAPCC receives data about calls to regional poison control centers that serve the United States and its territories.

Does TEVG Stenosis Spontaneously Resolve?

THE COMPLICATION THAT HALTED A CLINICAL TRIAL FOR TISSUE-ENGINEERED VASCULAR GRAFTS FOR CHILDREN WITH CONGENITAL HEART DISEASE MAY REVERSE SPONTANEOUSLY WITHOUT CLINICAL COMPLICATIONS.

Based on promising modeling of a biodegradable scaffold seeded with a patient’s own cells, a clinician-scientist research team now based at Nationwide Children’s Hospital initiated a pediatric tissue engineered vascular graft (TEVG) trial in Japan for children requiring the Fontan procedure for univentricular hearts. After its high success rate — with only one in 25 patients developing serious stenosis, which was successfully treated — the group launched a similar study in the United States.

When three of the first four patients developed postoperative stenosis requiring balloon angioplasty, the study was terminated. All patients were safely treated and remain well several years after the trial.

To find out why the U.S. trial’s results differed, the investigators initiated robust computer modeling and found a surprising suggested explanation: early stenosis may reverse on its own. Tests on sheep confirmed that stenosis reversed spontaneously in time, without clinical complications.

The research showed that when the TEVG is implanted, stenosis develops due to inflammation, as the body recruits cells and builds new tissue on the scaffold. When the immune reaction calms, stenosis resolves, and the graft is replaced with a new, natural blood vessel that is virtually indistinguishable from native tissue.

“It’s possible that this exact phenomenon occurred in the Japanese trial, but was largely missed due to post-surgical imaging timing and different criteria for angioplasty,” says Christopher Breuer, MD, director of the Center for Regenerative Medicine and Endowed Chair in Surgical Research at Nationwide Children’s and director of Tissue Engineering at The Ohio State University Wexner Medical Center.

Dr. Breuer and Toshiharu Shinoka, MD, PhD, co-director of the Tissue Engineering Program at Nationwide Children’s, lead the team that designed the TEVG, ran the trials and published the latest results. When the team reexamined imaging from the Japanese trial, they found a few cases where narrowing was observed but monitored via imaging only.

The team has launched a new TEVG trial, with different stenosis monitoring and intervention criteria designed to accommodate the likely scenario of temporary, asymptomatic narrowing with spontaneous resolution.


Can Complications For a Baby Born Preterm Be Predicted?
A PILOT STUDY LOOKS TO ASSESS THE ROLE OF GENETICS IN THIS QUESTION.

Complications from being born preterm are the number one cause of death in the world for children under the age of five, says Leif Nelin, MD, division chief of Neonatology at Nationwide Children’s Hospital and professor of Pediatrics at The Ohio State University. But why do some babies born preterm develop complications while many others seem to thrive? And what if we could predict through genetics who was much more likely to have those preterm complications?

“It has been believed that complications were a matter of chance but the thought here was what if it wasn’t the case?” says Dr. Nelin, senior author of the recent pilot study published in *Pediatric Research*. “This study’s data strongly suggests that there are genetic influences on these complications of being born preterm. If we can predict it then we may sometimes be able to treat the issue even before the baby is born.”

The study sequenced 182 exomes from infants with gestational ages ranging from 26 to 31 weeks, with a polygenic risk score for the top 10 genes used to predict complications. The study used the Perinatal Research Repository at Nationwide Children’s Hospital.

Dr. Nelin says the hope for future studies is to have a larger sample size that included significant numbers of infants in it from ethnicities other than what is categorized as non-Hispanic white.

“The non-Hispanic Black numbers in our studies were lower (at 51 infants) and when analyzed separately it didn’t come out to be significant,” he says. “But we think the pilot data strongly suggest that if there’s a bigger sample size that it would find what was found in non-Hispanic Whites. It’s also reasonable to assume it will hold true for other ethnicities but in order to know for sure we have to expand the study.”

Among the technology utilized, Churchill, developed by Peter White, PhD, and his team in the Institute for Genomic Medicine, was used for secondary analysis.

As noted in *Pediatric Research*, to the study authors’ knowledge, this is the first ever whole-exome sequencing study focused on genetic differences in neonatal complications. To Dr. Nelin, it is a chance to make history in an even more important way.

“If we can get a handle on those complications and be able to predict them early and maybe even before they are born, we could have targeted therapies that could truly change the complications,” he says.

Three Projects Targeted at Single Ventricle Heart Defects Funded Through Additional Ventures Award

In January 2020, the Abigail Wexner Research Institute at Nationwide Children’s Hospital announced that it was the recipient of a $1 million Innovation Fund, endowed by the nonprofit foundation: Additional Ventures. In receiving this funding, AWRI joined four other research institutions in a large-scale coordinated research effort centered on identifying new avenues to functionally cure patients with single ventricle heart defects (SVDs).

“Our goal is to provide a platform for scientists and clinicians to test bold, transformative ideas, and then the space to come together and share their learnings. By attracting these world-class experts and incentivizing risk-taking, we believe we can make a significant impact for these kids in a short amount of time,” says Kirstie Keller, PhD, director of Scientific Programs at Additional Ventures.

In June, Nationwide Children’s awarded funding to the following three projects under the Additional Ventures Innovation Fund.

**Elucidating Mechanisms of Ventricular Hypoplasia in PA-IVS Using Patient-Derived iPSCs**
Co-principal investigators for the project are Vidu Garg, MD, PhD, director of the Center for Cardiovascular Research at The Heart Center, and Mingtao Zhao, DVM, PhD, principal investigator in the Center for Cardiovascular Research.

**Development of a Protocol to Risk Stratify Individuals With Single Ventricle Congenital Heart Disease Using Deep Phenotyping and Genome Sequencing**
Co-principal investigators for the project are Kim McBride, MD, MS, division chief of Genetic and Genomic Medicine, and Peter White, PhD, senior director of Computational Genomics.

**Unlocking Our Regenerative Capacity: Elucidating the Role of LYST on Neotissue Formation in Tissue Engineered Constructs**
Co-principal investigators for the project are Chris Breuer, MD, director of the Center for Regenerative Medicine, and Rick Wilson, PhD, co-executive director of the Institute for Genomic Medicine.

“These projects represent some of the innovative and exciting research happening at AWRI,” says Dr. Durbin. “It’s an honor to be able to partner with Additional Ventures to fund projects that could change the way we understand and treat congenital heart defects.”
In a new proof-of-concept study, researchers used CRISPR/Cas9 technology to genetically modify natural killer immune cells, which are then able to address a recognized hurdle in immunotherapy of multiple myeloma.

“It was an amazing feeling when we saw the first result,” says Meisam Naeimi Kararoudi, DVM, PhD, a principal investigator in the Center for Childhood Cancer and Blood Diseases at Nationwide Children’s and lead author of the study. “The ability to easily genetically engineer these cells will usher in a new era in cancer immunotherapy.”

NK cells are historically resistant to conventional methods of gene editing that use viral vectors. But because the CRISPR/Cas9 system does not use viral transduction, Dr. Naeimi Kararoudi used this approach to create short pieces of RNA and protein to intentionally knock out specific genes.

Then, the team focused on a protein called CD38. A monoclonal antibody targeting CD38, daratumumab, is used to treat patients with multiple myeloma; however, the response is transient in most cases. One problem is that daratumumab binds to the CD38 protein on NK cells as well as multiple myeloma cells, resulting in the NK cells killing each other.

“When we used CRISPR to knockout CD38 from the surface of NK cells, we found they did not kill each other at all anymore; they killed significantly more cancer cells,” says Dr. Naeimi Kararoudi.

The findings provide proof-of-concept that adoptive immunotherapy using these knockout NK cells has the potential to strengthen the therapeutic effect of daratumumab against multiple myeloma.

The approach for engineering NK cells was licensed by Kiadis Pharma. It also caught the attention of Sanofi, which has its own FDA-approved CD38 monoclonal antibody therapy. Sanofi sublicensed the protocol to use these CD38 knockout NK cells with their therapy for multiple myeloma and subsequently bought Kiadis.

“This particular knockout is applicable to other types of leukemia and lymphoma, but our study is also proof-of-principle for knocking out any gene in NK cells,” says co-author Dean Lee, MD, PhD, director of the Cellular Therapy and Cancer Immunology Program at Nationwide Children’s and The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute.

“We are working on how to move this CRISPR-edited CD38 knockout NK cell into the clinic,” he says. “It is very likely that we will do that manufacturing here in our new cell therapy manufacturing space.”

Facioscapulohumeral muscular dystrophy (FSHD) arises from genetic and epigenetic changes that result in expression of the DUX4 gene in muscle. DUX4 is a developmental gene that is normally off in healthy muscle. When expressed in FSHD muscle, DUX4 activates pathways involved in cell death, oxidative stress, impaired muscle differentiation, immune responses and muscle atrophy.

FSHD affects up to 870,000 individuals worldwide, with no treatments to alter the course of this progressive, lifelong disease available.

Researchers in the lab of Scott Harper, PhD, principal investigator in the Center for Gene Therapy, have been dedicated to understanding the role of DUX4 in FSHD and developing potential therapies. In their recent publication in *Molecular Therapy: Nucleic Acids*, they describe three U7 small nuclear RNA antisense expression cassettes (U7-asDUX4) as a way to silence DUX4 expression in human cells, including those derived from FSHD patient muscles.

“These noncoding RNAs inhibit the production or maturation of the full-length DUX4 pre-mRNA by masking either the DUX4 start codon, the splice sites or the polyadenylation signal,” says Dr. Harper. “Targeting these sites enables us to stop the production of DUX4 protein.”

The U7-asDUX4 cassettes act similarly to the previously described antisense oligonucleotides, but with the added advantage of a potential one-time delivery approach.

“With antisense oligonucleotides, uptake into the muscles is poor, and we need repeated, lifelong dosing,” says Dr. Harper. “With U7-asDUX4, though, we can use a gene therapy vector for delivery, and one dose might be sufficient for sustained silencing.”

The team demonstrated the ability of the U7-asDUX4 constructs in cotransfected cells and myotubes derived from individuals with FSHD. The study serves as a proof of concept for the potential therapy. Translation of this approach will require safety and efficacy studies in the Harper Lab’s TIC-DUX4 mouse model, which are currently ongoing.

“We believe that this approach has the potential to be a new therapeutic option for individuals with FSHD,” Dr. Harper says. “We expect that these could be used in combination with RNAi therapy to maximize DUX4 silencing, or even as a standalone therapy. We look forward to seeing the translation of this therapy through preclinical studies and the prospect of future clinical studies.”

In 2015, a research team led by Octavio Ramilo, MD, chief of Infectious Diseases, Asuncion Mejias, MD, PhD, attending physician in Infectious Diseases, and Mark Peeples, PhD, all principal investigators in the Center for Vaccines and Immunity at Nationwide Children’s, received a $6.75 million grant from the National Institutes of Health to study immune responses to respiratory syncytial virus — with the ultimate goal of developing a vaccine candidate.

With the help of collaborators across the nation, including Jianrong Li, DVM, PhD, and Stefan Niewieski, DVM, PhD, from The Ohio State University, and Michael Teng, PhD, from University of South Florida, the team has published more than 35 peer reviewed publications based on research funded by the grant.

“Thirty-five papers from our team — all with at least two of the six principal investigators in the group — is a remarkable feat,” says Dr. Ramilo. “Many of these papers have been in high impact journals, and some describe research that has led to patents. We have been able to greatly add to the knowledge about RSV and immune responses in infants.”

The researchers say the key to their success has been to dig into understanding the immune profiles of infants affected by RSV — especially those who have mild disease compared with those who develop severe disease.

“By defining what a protective immune profile looks like, we can better design the vaccine candidate to mimic that response,” says Dr. Mejias. “For example, we know based on in vivo and in vitro studies that higher levels of IL-6 indicate a more severe illness. But higher levels of IP-10 are protective. Understanding the ‘safe and protective’ immune response is critical to our success in developing an effective vaccine.”

Their recent publication in Journal of Virology, describes the live attenuated RSV vaccine strain developed by the team as a vaccine candidate.

“While we are very excited about what we’ve developed so far, we also have ideas about how to make our vaccine candidate even better,” says Dr. Peeples. “Our next steps include applying what we’re learning about the immune response of children and including critical proteins from both strains of RSV to make the best possible vaccine candidates, comparing them in cultured cells from the airways and in cotton rats to identify the best candidates before moving into human trials.”


When children are born prematurely, they miss the opportunity to receive key nutrients and fats from their mothers during the late stages of fetal development. Studies show that preterm infants who may not get enough docosahexaenoic acid (DHA) naturally can benefit from supplements of the nutrient soon after birth.

To evaluate whether DHA would be beneficial for these babies as they reached toddlerhood, Sarah Keim, PhD, principal investigator in the Center for Biobehavioral Health in the Abigail Wexner Research Institute, and her team studied 377 toddlers who had been treated in the Neonatal Intensive Care Unit at Nationwide Children’s Hospital, were born at less than 35 weeks’ gestation and were now, at the time of the study, one year old. The “Omega Tots” were administered either a daily DHA supplement or a placebo, corn oil.

The initial results of this study, published in JAMA Pediatrics in 2018, showed that the supplement didn’t seem to improve these aspects of development compared to the placebo. Dr. Keim says that after this study, it did not seem warranted to offer DHA supplements to toddlers who were born preterm. But she and her team thought there might still be potential benefits that this initial analysis did not examine.

A secondary analysis, published in Pediatrics in September 2020, focused on social skills and emotion regulation, including behaviors typically associated with autism spectrum disorder (ASD), rather than cognitive development more broadly.

This time, the supplement did seem to have a positive impact in some ways. On a test their caregivers completed, toddlers who were given DHA supplements were less likely to meet the threshold for requiring further evaluation for ASD.

When the results are taken together, the big picture of how DHA supplements might benefit children after their first few months of life seems mixed, so Dr. Keim says that it’s especially important for them to continue researching.

“Considering the results of the Omega Tots trial, as a whole, is complicated,” says Kelly Boone, MA, CCRP, associate director of the Behavioral Trials Office at AWRI and lead author of the study. “The analysis of our main outcome in 2018 showed that DHA offered no improvement for children’s cognitive development or executive function. A 2019 study found no effect on children’s sleep. The 2020 study found no benefit for general competence or problem behaviors, but we did find that supplementation resulted in a reduced risk of displaying clinical concern for autism spectrum disorder.”

“We also do find negative effects of supplementation for certain subgroups of children,” she adds. “Without more research, we do not have strong evidence to support DHA supplementation of children born preterm during their toddler years.”


Fostering Novel Collaborations Through Research Affinity Groups

Purposeful synergy drives the most meaningful medical science. This is the philosophy behind research affinity groups in the Abigail Wexner Research Institute at Nationwide Children’s Hospital.

The Nephrology and Urology Research Affinity Group (NURAG) at AWRI was the first affinity group and has now become a model for sinterdisciplinary, innovative and collaborative science.

The group was founded by a developmental biologist and anatomist at Nationwide Children’s — Kirk McHugh, PhD, now director of the Division of Anatomy at The Ohio State University College of Medicine — eager to do something clinically useful with his newly discovered megabladder mouse model.

Since then, members of NURAG have built some of the country’s largest — and best-rated — pediatric research programs in both urology and nephrology, with research encompassing everything from mouse models to natural urinary tract infection (UTI) prevention. The collaborations involve more than just lip service to the concept of translational research, and often directly influence work done both by the group’s clinical members and bench scientists on a daily basis.

“I grew up with NURAG, so to speak,” says Brian Becknell, MD, a pediatric nephrologist and principal investigator who first experienced the group as a medical student and is now the group’s director. “It’s one of the main reasons I chose to specialize in nephrology and stay here for my residency and fellowship. I liked to see surgeons, clinicians and medical students getting together in a nonintimidating environment to share ideas. I’ve benefitted hugely from the level of support it provides.”

This cultivation of the next generation of researchers is key to NURAG’s mission. The group regularly offers all participants the option to practice their presentations or submit their written work for review, ensuring that their research products are defensible, thorough and thoughtful. The group also hires and provides travel funding for students, residents and fellows and is seeking NIH grants to begin supporting full NURAG trainee funding.

“Supporting each other and the next generation in the advancement of relevant, powerful research is the best legacy NURAG can leave,” says Christina Ching, MD, a pediatric urologist and principal investigator, who credits her series of NIH grants to close relationships with her mentors, all of whom are NURAG members. “It truly is a breeding ground for new pediatric urology and nephrology clinicians and scientists.”
**Acute Kidney Injury**
Cardiology, basic science, nephrology and chemotherapy experts collaborate to identify mechanisms of AKI and therapeutic targets for repair or prevention.
*Front Pediatr.* 2019 Nov 26;7:492

**Glomerular and Inflammatory Disease**
NURAG researchers may have identified a biomarker to predict steroid resistance in children with nephrotic syndrome.
*Kidney Int Rep.* 2019 Sep 19;5(3):81-93

**Obstruction and the Renal Urothelium**
NURAG scientists have identified cells in the renal urothelium that remodel themselves in response to urinary tract obstruction and injury.

**UTI Susceptibility and Therapy**
NURAG collaborators identified peptides that protect the urinary tract and fight infection. Now they are working on how to use them to predict and treat UTI.
*Pediatr Nephrol.* 2019 Jun 13; [Epub ahead of print]

**Megabladder Mouse Model**
This model is the first animal model of chronic renal disease and congenital obstructive uropathy. It was recently confirmed near-identical to these problems in humans.
OUR CAMPUS

RESEARCH FACILITY HIGHLIGHTS

• Wexner Institute for Pediatric Research (Research Building I) contains 136,580 sq. ft. of dedicated research space contiguous with Nationwide Children’s clinical facilities.

• Research Building II provides 164,016 square feet of additional space including a 200-seat amphitheater. It is also contiguous with the clinical facilities.

• Research Building III is 238,914 sq. ft. and includes a 75-seat conference facility. Research Building III is LEED certified for sustainable green building design.

CAMPUS HIGHLIGHTS

• 1,184,473 square feet of inpatient space on Main Campus

• 406,751 sq. ft. of outpatient space

• Largest neonatal network in the United States

• Highest volume pediatric surgery program in the nation

• The Big Lots Behavioral Health Pavilion — the largest such facility on a pediatric campus — opened in 2020.
RESEARCH BUILDING IV
Research Building IV is currently under construction. It will serve as a companion to Research Building III, and the buildings will be connected through a common entry atrium and on every floor, enabling the two buildings to function as one complex. The new building will add approximately 285,000 sq. ft. to Nationwide Children’s dedicated research space. Research Building IV is anticipated to open in 2023.

“At Nationwide Children’s we are building world-class leading edge research facilities to support our continued growth and success. Our growing facilities will help us to reach our aspirations, ultimately resulting in new life-changing therapies and best possible outcomes for children around the world.”

— Dennis Durbin, MD, MSCE, chief science officer at the Abigail Wexner Research Institute