In 2019, the U.S. Food and Drug Administration (FDA) issued a new guidance document that featured significant contributions from DCRI pediatricians. The guidance document provides the most up-to-date data and information for conducting research in a traditionally challenging population—newborns.

The DCRI Pediatrics group developed the data that contributed to this FDA guidance over a decade of novel research conducted in conjunction with the Pediatric Trials Network (PTN), a nationwide research network focused on making drugs safer and more effective for children. The PTN is coordinated by the DCRI and funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

“We are pleased that our thought leadership and expertise was reflected in this critical FDA guidance document,” said Micky Cohen-Wolkowiez, MD, PhD, one of the DCRI pediatricians who led this effort. “By sharing knowledge that helps to bring clarity to an area where there previously may not have been clear guidance, we can have a significant impact on pediatric drug development, which will help pediatricians everywhere improve care for our most vulnerable patients.”

Since its inception in 2010, the PTN has provided data that have contributed to 15 FDA label changes, meaning that the prescribing information was updated to include pediatric dosing guidelines.

“Through the PTN’s research, we are providing much-needed data to the FDA and really moving the needle on drug safety and effectiveness for children.”

Kanecia Zimmerman, MD, MPH

“The work of the PTN is so critical because as clinicians, we often don’t know the proper dosages for children, and we have to make inaccurate estimates based on adult dosages,” said DCRI pediatrician Kanecia Zimmerman, MD, MPH, chair of the PTN steering committee. “Through the PTN’s research, we are providing much-needed data to the FDA and really moving the needle on drug safety and effectiveness for children.”
Informing FDA Decision-Making

In addition to pediatric research, DCRI thought leadership has been considered by the FDA in many other efforts, such as refining the agency’s guidance on collection of real-world evidence.

“Over the years, the DCRI has established itself as an objective resource for generating and interpreting evidence,” said DCRI Executive Director Adrian Hernandez, MD, MHS. “DCRI faculty are known for their ability to identify next steps and determine a path forward.”

In 2019, results from a DCRI-led patient preferences survey were presented to an FDA advisory committee tasked with deciding whether esketamine should be approved for use in treatment-resistant depression. The survey, which was designed by DCRI’s Preference Evaluation Research (PrefER) group, assessed individuals’ willingness to accept certain risks associated with taking the treatment in exchange for certain benefits. When the FDA ultimately approved the treatment, several of the panelists noted that the evidence generated by the survey helped to inform their decision.

“Studies such as these can be helpful to reviewers who are charged with making value judgements about benefit-risk tradeoffs on behalf of patients,” said Shelby Reed, PhD, who led the study and serves as DCRI therapeutic area lead for Population Health Sciences Research. “In this instance, the impact of this survey and its results prove the importance of taking patient preferences into account.”

Breaking Down Siloes Locally

Another collaborative project led by a DCRI pediatrician aims to design and implement a new care delivery and payment model for children’s health at the state level. The goal of the project, which is called North Carolina Integrated Care for Kids (NC InCK) model and funded by the Centers for Medicare & Medicaid Services, is to partner with communities to support and bridge services where children live, learn, and play.

The initiative, a joint effort between Duke University, University of North Carolina at Chapel Hill, and the North Carolina Department of Health and Human Services, will serve Medicaid-insured children in five central North Carolina counties from birth up to age 20. The effort will span a wide range of services, including physical and behavioral health, housing and food security, schools, early care and education, child welfare, mobile crisis response services, public health, juvenile justice, and legal services.

“The NC InCK model is a tremendous opportunity for us to transform how we support the well-being of children and their families by breaking down siloes and working together across many different systems,” said DCRI’s Charlene Wong, MD, MSHP, executive director of the initiative. “By establishing partnerships, linking data, and better integrating services, we hope to address some of the root causes of poor health and help the state better serve the children it seeks to help.”
Ultimately, findings from the project will be leveraged to create innovative and sustainable pediatric alternative payment models under the state’s Medicaid program. The project, which was funded in late 2019, is in the planning phase, with five years of implementation set to begin in 2022.

Enabling Discoveries by Sharing Data

In addition to conducting its own impactful research, the DCRI bolsters the research of others by making efforts to improve open science. DCRI’s Supporting Open Access for Researchers Initiative (SOAR) oversees all DCRI data sharing activities.

DCRI SOAR provides an independent review committee for datasets from Bristol Myers Squibb, examining factors such as the articulation of the research question and the quality of the statistical analysis plan. Since the group’s inception in 2014, it has reviewed nearly 40 different data requests, with the number of requests increasing year-over-year. The group also makes DCRI data available for sharing, such as the Duke Cath dataset, which offers data for both educational purposes and for research. Data requests for this source have come from industry sponsors, fellow academic researchers, and nonprofit organizations.

“By making these datasets available, we’re not only encouraging transparency, but we’re helping other researchers build on work that has already been done,” said Rebecca Wilgus, RN, MSN, a DCRI clinical informatics project leader. “By enabling others to use our datasets and reviewing requests for data, we’re helping research be used for more than its original purpose, which allows us to have an even wider impact.”

DCRI faculty also contribute influential thought leadership in the data sharing space. This year, Hernandez and DCRI faculty statistician Frank Rockhold, PhD, contributed to a paper making recommendations for the National Institutes of Health (NIH)’s newly updated data sharing policy.

“By enabling others to use our datasets and reviewing requests for data, we’re helping research be used for more than its original purpose, which allows us to have an even wider impact.”

Rebecca Wilgus, RN, MSN

“While the NIH has already made significant steps in the realm of data sharing, we have provided recommendations for actions they can take to truly advance open science,” Rockhold said. “By investing the effort to create a culture of data sharing now, the NIH and other entities will be setting the stage for a future of efficient and innovative clinical research.”

Developing the Next Generation of Clinical Trials

DCRI’s impact does not stop at guiding policy and regulatory science. The Institute is also helping to shape how the next generation of research will be conducted through its role as the coordinating center for the NIH Health Care Systems Research Collaboratory.
Established in 2012, the NIH Collaboratory provides a supportive and collaborative environment in which to conduct novel research—namely, pragmatic clinical trials. Lessons learned from these trials, or Demonstration Projects, and other NIH Collaboratory work are shared publicly through several avenues: publications, webinars, training workshops, and the Living Textbook of Pragmatic Clinical Trials on the NIH Collaboratory website. Staff on DCRI’s Research Communications and Engagement team oversee these activities.

“Through the NIH Collaboratory, the DCRI is helping to guide national approaches in a key area,” said Lesley Curtis, PhD, chair of Duke’s Department of Population Health Sciences and one of three DCRI principal investigators for the NIH Collaboratory. “These Demonstration Projects are providing the blueprint that will inform how organizations can support the development of embedded, pragmatic clinical trials.”

Other DCRI projects, such as VESALIUS-EHR, are also helping to evolve research. The VESALIUS team’s goal is to facilitate incorporation of data from electronic health records (EHRs) into research through initiatives such as a framework that will help investigators transform EHR data into data that is fit-for-purpose and high quality.

“Through the NIH Collaboratory, the DCRI is helping to guide national approaches in a key area.”

Lesley Curtis, PhD

“The field has known for years that using EHRs in research has many potential benefits,” said VESALIUS-EHR principal investigator Emily O’Brien, PhD, who, like Curtis, sits both within the DCRI and Duke’s Department of Population Health Sciences. “However, there are many assumptions about using this kind of data that haven’t been well tested. We’re now testing these assumptions and answering questions such as, are EHR data actually fit for use in this specific scenario? Will the EHR data be representative of what we would see if we actually ran a trial? By answering these questions, VESALIUS-EHR will provide best practices for incorporating EHR data in a systematic, robust way while building confidence in results from EHR studies.”

A Legacy of Impact

From landmark global clinical trials to innovative approaches to research delivery, the DCRI has been leading the way forward and shaping the future of research for decades. The Institute’s legacy of impact began in 1969 with the Duke Databank for Cardiovascular Disease, which ushered in what was at the time a novel, computer-assisted, data-driven approach to generating evidence for cardiovascular clinical research studies.

“I am tremendously proud of all the work that DCRI’s people undertake on a daily basis. Their tireless efforts ensure that our thought leadership is applied directly to clinical practice.”

Adrian Hernandez, MD, MHS

DCRI’s standing as an academic clinical research organization within one of the nation’s most outstanding health care systems affords it the freedom to explore and establish innovative approaches to clinical research. And through its more than 16,000 publications since 1996, DCRI faculty help to improve health and patient outcomes around the world.

“I am tremendously proud of all the work that DCRI’s people undertake on a daily basis,” Hernandez said. “Their tireless efforts ensure that our thought leadership is applied directly to clinical practice.”