OUR MISSION
To develop and share knowledge that improves the care of patients around the world through innovative clinical research.

OUR VISION
To be the leading academic clinical research organization in the world.

OUR VALUES
Integrity   |   Excellence   |   Respect   |   Innovation   |   Teamwork

At the DCRI, our values—a common set of core beliefs—honor our history and represent how we see ourselves and how we want to be seen. They guide our actions and daily decisions and help us define what it means to be successful—as an organization and as individuals.
The world of clinical research is constantly changing. Even as new discoveries are translated into usable therapies for patients, DCRI faculty, fellows, and staff members are looking for the next breakthrough. From innovative study design and operations to thoughtful analytics and a commitment to rapid knowledge generation and dissemination, the DCRI is always redefining what we do and how we do it.

In this report, you'll gain insights into some of the creative new studies our faculty and operations teams are undertaking. These include new therapies for conditions such as Alzheimer's disease and heart failure, and new tools for conducting clinical trials that are keeping the DCRI on the cutting edge of research and patient care.

I would like to thank all the DCRI faculty members, operational personnel and support staff, and collaborators around the world who make this work possible. It takes an amazing team to accomplish all we have done and to set us up for all we will do in the years to come.

Eric D. Peterson, MD, MPH
Executive Director, Duke Clinical Research Institute
Professor of Medicine, Cardiology
Fred Cobb, MD, Distinguished Professor of Medicine
DCRI AT A GLANCE

DCRI PUBLICATIONS

FY17
1239 total publications
222 high impact factor (IF) publications

- Total number of publications
- Number of high IF publications

Fiscal Year


STUDY PHASE

- Registry 17%
- Networks 15%
- Phase IV 10%
- Other 16%
- Phase III 27%
- Phase I 3%
- Phase II 12%

STUDY POPULATION

- Adult 87%
- Adolescent 3%
- Pediatric 7%
- Pre/Neonatal 1%
- Geriatric 2%

STUDY SIZE

- Small 36%
- Large 17%
- Medium 26%
- MEGA 21%

STUDY REVENUE SOURCE

- Industry 55%
- Government 45%

*High impact factor = journals with an impact factor of 10 or higher
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WHAT’S KNOWN:
HOW HAS THE DCRI CHANGED PATIENT CARE AND CLINICAL RESEARCH?
Boehringer Ingelheim Pharmaceuticals, Inc. and the DCRI are expanding the Idiopathic Pulmonary Fibrosis – PROspective Outcomes (IPF-PRO) Registry, a patient registry developed to uncover insights into IPF, a rare and serious lung disease. The IPF-PRO Registry was launched in June 2014 as the nation’s first multicenter longitudinal registry focused specifically on IPF. Based on the registry’s initial success, Boehringer Ingelheim and the DCRI agreed this year to expand the IPF-PRO Registry from 300 patients enrolled at 18 study sites to more than 1,500 patients from approximately 45 sites. When completed, IPF-PRO will be the largest registry of IPF patients in the world.

“Expanding the IPF-PRO Registry is important to the IPF community because it will substantially advance the understanding of this rare and fatal lung disease,” said Scott Palmer, MD, director of Respiratory Medicine at the DCRI.

“In collecting data from a larger, more diverse group of patients from multiple centers nationwide – all of whom are newly diagnosed with IPF – this registry will allow us to better assess the impact of the disease over time on clinical and patient-centered outcomes.”

One element of the IPF-PRO Registry is a bio-repository of blood samples that provide patient genetic material that may help to better explain the relationship of various biomarkers to patient outcomes. The registry expansion will substantially increase the size of the bio-repository, creating additional opportunities for future translational research and the identification of novel biomarkers that may be predictive of disease outcomes or individual patient treatment responses.

In addition to Palmer, the DCRI IPF-PRO team includes Jamie Todd, MD; Laurie Snyder, MD; Emily O’Brien, PhD; Megan Neely, PhD; Kevin Anstrom, PhD; Eric Yow, MS; Linda Davidson-Ray, MA; Rosalia Blanco; Tara Melton; and Laura Drew.

IN COLLECTING DATA FROM A LARGER, MORE DIVERSE GROUP OF PATIENTS FROM MULTIPLE CENTERS NATIONWIDE – ALL OF WHOM ARE NEWLY DIAGNOSED WITH IPF – THIS REGISTRY WILL ALLOW US TO BETTER ASSESS THE IMPACT OF THE DISEASE OVER TIME ON CLINICAL AND PATIENT-CENTERED OUTCOMES.

SCOTT PALMER, MD
Providing fewer total opioids over a longer period of time is associated with lower overall costs and better outcomes for hip surgery patients, according to DCRI researchers.

With opioid overdoses and abuse a subject of growing concern for public health agencies, the Centers for Disease Control and Prevention issued a series of guidelines in 2016 intended to improve communication between clinicians and patients about the risks and benefits of opioid drug therapy. Although these guidelines included recommendations for acute, general surgery opioid management, there has been little research into management strategies for intermediate- to long-term post-surgical musculoskeletal pain.

In an observational cohort study, the DCRI’s Chad Cook, PhD, and his colleagues sought to analyze post-operative opioid prescription strategies and measure direct and indirect healthcare utilization and costs in individuals undergoing non-arthroplasty orthopedic hip surgery.

Using data from the Military Health System Data Repository (MDR), which serves as the centralized data repository for all Defense Health Agency corporate healthcare data, the researchers identified 1,219 patients who received hip surgery between 2003 and 2015.

Using cluster analysis, Cook and his study team then identified two distinct post-operative opioid prescription subgroups: patients who received a high total number of opioids over a short period of time, and those who received fewer total opioids over a longer period of time. The researchers then used linear mixed effects modeling to examine opioid prescription pattern subgroups and identify subgroup differences in healthcare utilization and costs. They found that patients who received more opioids over a shorter period of time generally had more complications, opioid prescriptions, and total days of opioid pain medications.

While these findings suggest that the lower, longer strategy may be superior, Cook emphasized the need for future randomized trials to better understand the effectiveness of opioid prescription patterns on reducing side effects and minimizing the chances of opioid abuse.

“We need to start looking at patterns of treatment,” he said. “We couldn’t find anything in the literature about other musculoskeletal conditions or post-surgical conditions. This topic is essentially unstudied.”
CHOLESTEROL CONFUSION

A study by DCRI researchers is the latest attempt to resolve the confusion surrounding dueling guidelines for the use of statins to prevent cardiovascular disease.

If all doctors followed advice from the U.S. Preventive Services Task Force (USPSTF), 9 million fewer adults would be taking the drug than if they adhered to the American College of Cardiology (ACC) / American Heart Association (AHA) recommendations, the researchers found. The analysis also found that most of those who would be dropped from the USPSTF guidelines are younger adults.

“Having multiple guidelines out there for cholesterol-lowering drugs can be confusing to physicians and patients,” said the DCRI’s Neha J. Pagidipati, MD, lead author of the study. “Until we get more definitive answers about the optimal approach, the best we can do is understand the pros and cons of each set of guidelines. Our study adds some of that context.”

Pagidipati and colleagues—including senior author Michael J. Pencina, PhD, director of biostatistics at the DCRI—analyzed the most recent six-year data from the National Health and Nutrition Examination Survey, a representative sample of U.S. residents that provides key health statistics over time.

The researchers estimated that, if fully implemented, the USPSTF recommendations would result in a 15.8 percent rise in the use of statins among U.S. adults aged 40 through 75 with no prior cardiovascular disease.

Those newly recommended for statins would be in addition to the 21.5 percent of U.S. adults already taking the lipid-lowering therapy. By comparison, the ACC/AHA guidelines would result in an additional 24.3 percent of U.S. adults beginning on statins.

“We estimate there could be 9 million fewer individuals recommended for statin therapy under the USPSTF recommendations compared with the ACC/AHA guidelines,” Pagidipati said.

The Duke researchers found that of those who are recommended to receive statins by the ACC/AHA but not the USPSTF, over half are younger adults aged 40 to 59 years, and over one-quarter are people with diabetes.

“Even though younger people have a modest short-term risk of developing cardiovascular disease in 10 years, the risk escalates over 30 years,” Pencina said. “Half of all cardiovascular events in men and one-third in women occur before the age of 65 years, so reliance on 10-year risk could miss many younger people who could potentially benefit from long-term statin therapy.”

UNTIL WE GET MORE DEFINITIVE ANSWERS ABOUT THE OPTIMAL APPROACH, THE BEST WE CAN DO IS UNDERSTAND THE PROS AND CONS OF EACH SET OF GUIDELINES. OUR STUDY ADDS SOME OF THAT CONTEXT.

NEHA J. PAGIDIPATI, MD, MPH
In 2006, the Cardiac Safety Research Consortium (CSRC) was launched under the U.S. Food and Drug Administration’s Critical Path Program as a public-private partnership. The mission of the CSRC was to establish a neutral, transparent organization that could bring together thought leaders across the stakeholder spectrum—patients, physicians, manufacturers, regulatory authorities, professional societies, and academics—to identify cardiovascular safety barriers to therapeutic innovation and develop pragmatic, innovative solutions to lowering or removing those barriers as a means to enhance regulatory science.

Over the last 10 years, the CSRC has supported ongoing efforts to address key areas of cardiac safety concern, including the need for more efficient means of detecting proarrhythmia; considerations for blood pressure and biomarker monitoring, cardiac imaging, and cardiac safety in special populations, such as diabetics and women; and an expanded program focused on pediatric cardiovascular safety.

Some recent areas of great interest and current exploration include enhanced electrocardiographic algorithmic detection of prolonged QTc and QT syndromes; antidotes for novel oral anticoagulant agents; cardiac safety concerns with biologics; enhanced clinical science processes, including registry-based randomized trials; development of a standardized cardiac event reporting structure; use of social media for safety surveillance; and the role of event adjudication for cardiac safety events.

“Over the past decade, the relationships and level of trust among CSRC members have matured enormously,” said the DCRI’s Mitchell Krucoff, MD, one of the CSRC’s co-directors. “Our working processes have increased in resilience, and today we have a robust track record of projects and publications.”

“I’m also happy to see a progressive increase in the involvement of young people with new ideas, while keeping the founding leadership group together. I’m pleased with this ability to keep making progress while staying open to new ideas. This is proof that the CSRC is very much a living organization.”

**HEART PARTNERS**

**OVER THE PAST DECADE, THE RELATIONSHIPS AND LEVEL OF TRUST AMONG CSRC MEMBERS HAVE MATURED ENORMOUSLY. OUR WORKING PROCESSES HAVE INCREASED IN RESILIENCE, AND TODAY WE HAVE A ROBUST TRACK RECORD OF PROJECTS AND PUBLICATIONS.**

MITCHELL KRUCOFF, MD
THINK DIFFERENT

Tackling today’s healthcare problems requires cooperation from every stakeholder, from clinical researchers to regulators to industry executives. The mission of the DCRI Think Tank program is to address the most critical gaps in clinical research by convening leaders across the healthcare industry to map the way forward in designing, conducting, and implementing high-quality, evidence-based research.

“We’re taking this successful existing initiative, set up more than two decades ago by DCRI founder Rob Califf, and adding a renewed focus on impact and sense of urgency,” said Carolyn Moore Arias, MPH, associate director of the DCRI Think Tank Program. “Looking ahead, the DCRI aims to partner with all types of 21st-century healthcare stakeholders—including technology companies, payers, and associations—giving the initiative an even more strategic and influential role.”

The Think Tank program fits within the DCRI’s extensive range of activities aimed at shepherding scientific insights into clinical practice. The meeting format is a one-and-a-half-day meeting with a suite of five-minute talks by industry, academic, and government leaders with demonstrated expertise and a commitment to making an impact. These experts frame the various perspectives on a problem with the intent to provoke meaningful conversation and debate.

“These meetings demonstrate what is possible when you bring smart people together to tackle the biggest challenges in clinical research,” said DCRI Executive Director Eric Peterson, MD, MPH. “From cardiovascular diabetes to the Pediatric Rule to the Modern Data Monitoring Committee, these meetings are about creating pathways to useful, focused discussions across the healthcare continuum and then moving consensus to action.”

Recent Think Tank meetings include:
• Heart Failure with Preserved Ejection Fraction, led by Michael Felker, MD, MHS, and Margaret Redfield, MD (Mayo Clinic)
• Advancing Care and Clinical Trials through Digital Health, led by Eric Peterson, MD, MPH; Robert Harrington, MD (Stanford University); and Zubin Eapen, MD (CareMore Health System)
• Issues in Pediatric Cardiovascular Drug Development, led by Jennifer Li, MD, MHS, and Prince Kannankeril, MD, MSc (Vanderbilt)

Over the past 22 years, the DCRI has convened 84 Think Tank meetings involving 45 Duke directors, 250 academic institutions, and almost 4,000 attendees. At least 51 publications and four alliances have resulted.
WHAT’S NEW:
HOW IS THE DCRI AFFECTING PATIENT CARE TODAY?
Researchers from the DCRI and Mercy Health are making vital contributions toward the adoption and use of unique device identifiers (UDIs) to transform and streamline medical device evaluation and surveillance.

A study by the DCRI’s James Tcheng, MD, and Mercy Health’s Joseph P. Drozda, MD, highlights the informatics aspects of the U.S. Food and Drug Administration (FDA)-funded Mercy Demonstration Project. The project was primarily conducted in the Mercy Health System in St. Louis, where prototype UDIs were incorporated into the enterprise’s electronic information systems.

Safety surveillance of medical devices has been a top priority of the FDA, but there has been no universal mechanism for identifying these devices across healthcare. This lack of standardization has been a barrier to efficient business processes and device safety surveillance in the past. Therefore, the FDA, along with the European Commission and other regulators, devised the UDI system as a framework for identifying medical devices using an alphanumeric barcode system that can be applied globally. The demonstration project goes a step further by testing the implementation of UDIs in electronic health data, which, according to Tcheng, is a key priority for the FDA.

“Via the Demonstration Project, we set out to build and implement prototype UDIs for coronary stents across all electronic health information systems, using Mercy Health’s information systems as the test bed,” he added.

The demonstration project involved multiple stakeholders, including the FDA, the American College of Cardiology’s National Cardiovascular Data Registry, various departments across Mercy Health, manufacturers, health system partners, professional societies, and information system vendors.

During the course of the project, the researchers created both a UDI reference database containing device characteristics and a UDI research and surveillance database containing the connected clinical and device data, facilitating longitudinal assessment of device performance. The UDI prototype database has since evolved into a product that is now available from the FDA: the Global Unique Device Identification Database (GUDID), which will serve as a reference catalog for every device with a UDI.

“[This work] represents a major milestone in developing a device evaluation system, serving as the framework for what’s going to be put in place nationally for device surveillance,” Tcheng said. “UDI implementation will improve patient safety, modernize device post-market surveillance, and facilitate medical device innovation.”

UDI IMPLEMENTATION WILL IMPROVE PATIENT SAFETY, MODERNIZE DEVICE POST-MARKET SURVEILLANCE, AND FACILITATE MEDICAL DEVICE INNOVATION.
COSTLY CARE

Most prescriptions for a class of drug that was heralded as a game-changer for people with stubbornly high cholesterol are going unfilled because of high out-of-pocket costs and challenges by pharmacy benefit managers.

DCRI researchers found that less than one-third of patients prescribed a PCSK9 inhibitor—injectable drugs designed to lower cholesterol levels—actually got the drug.

Two factors limited access: lack of insurance approval for the prescription and high copays. Less than half of patients prescribed a PCSK9 inhibitor ever received approval for the drug by their insurer.

Even after approval, one in three patients failed to fill their prescription. Sticker shock was a key factor. A quarter of patients had copays over $300 per month for therapies that cost about $14,000 per year. The net result was that just 31 percent of patients who were initially prescribed a PCSK9 inhibitor ever received the therapy, the researchers found.

“This study basically reveals a system of rationing by roadblocks,” said lead author Ann Marie Navar, MD, PhD. “Access comes down to patients whose doctors are persistent enough to win payer approval through multiple appeals, and patients who can afford the out-of-pocket costs.”

In their study, Navar and colleagues analyzed a large database of pharmacy claims that included more than 45,000 prescriptions for PCSK9 inhibitors. These drugs work by blocking a protein in the liver called proprotein convertase subtilisin kexin 9 (PCSK9), setting off a chain of events that breaks down low-density lipoprotein cholesterol, the “bad cholesterol” that causes heart disease.

In the first year after the drugs’ approvals, the researchers found that nearly 80 percent of doctors’ prescriptions were rejected by pharmacy benefit managers that govern drug coverage for health insurance plans. Most of the requests (73.5 percent) were resubmitted, but only 47.2 percent eventually won approval.

The median time between initial submission and approval was about four days, but some patients waited nearly three months for therapy.

“The current system we have is at best a very blunt instrument to restrict use of high-cost therapies to those who need it most,” said DCRI Executive Director Eric Peterson, MD, MPH, a co-author of the study. “We need to figure out a better way to contain costs. We also need to better identify which patients are the best candidates for prescribed therapies, so we can apply the same approval criteria across the board.”

ACCESS COMES DOWN TO PATIENTS WHOSE DOCTORS ARE PERSISTENT ENOUGH TO WIN PAYER APPROVAL THROUGH MULTIPLE APPEALS, AND PATIENTS WHO CAN AFFORD THE OUT-OF-POCKET COSTS.

ANN MARIE NAVAR, MD, PHD
PERFECTING POLICY

As the costs of healthcare rise, the need to understand and quantify the value of various therapeutics becomes more urgent. Yet without standards for measuring cost effectiveness, it is difficult for analysts to accurately benchmark the value of a particular therapy.

In September 2016, the Second Panel on Cost-Effectiveness in Health and Medicine updated 20-year-old guidelines and recommendations. The updates guide decision makers in the use of new methods for analyzing evidence, reporting standardized results, incorporating both healthcare system and societal perspectives, and weighing ethical issues in using cost-effectiveness analysis. These build on the work of the 1996 Panel on Cost-Effectiveness in Health and Medicine convened by the U.S. Public Health Service.

“With healthcare costs continuing to increase sharply, the new recommendations offer a transparent framework for comparing the value of various healthcare interventions from multiple perspectives,” said panel co-chair Gillian D. Sanders Schmidler, PhD, professor in the Duke Department of Population Health Sciences and a member of both the DCRI and the Duke-Margolis Center for Health Policy. “Cost-effectiveness analysis can help decision makers to use healthcare resources wisely; our recommendations provide guidance for the next generation of practitioners and consumers. Such analyses can also inform policy decisions.”

Key changes include:
- Broadening the perspectives of the Reference Cases, which describe standard methodology that should be followed to ensure quality analysis by creating comparable measurements
- Including both costs reimbursed by third-party payers and those paid for out-of-pocket by patients in healthcare sector analyses
- Using an “impact inventory” table that lists the health and non-health effects of a healthcare intervention to ensure that all consequences are considered
- Including a reporting checklist and guidelines for transparency that include assumptions in any analysis and the disclosure of potential conflicts of interest

The 16-member panel led by Schmidler and Peter Nuemann from Tufts Medical Center was primarily funded by grants from the Robert Wood Johnson Foundation and the Bill & Melinda Gates Foundation. Cost-effectiveness analyses informed by the new recommendations should be considered in potential replacements for the Affordable Care Act, Schmidler said. Such analyses could take into account the impacts of interventions that are most important to patients and other stakeholders and present the costs, benefits, and harms of alternative strategies using transparent and evidence-based methods.

WITH HEALTHCARE COSTS CONTINUING TO INCREASE SHARPLY, THE NEW RECOMMENDATIONS OFFER A TRANSPARENT FRAMEWORK FOR COMPARING THE VALUE OF VARIOUS HEALTHCARE INTERVENTIONS FROM MULTIPLE PERSPECTIVES.

GILLIAN D. SANDERS SCHMIDLER, PHD
SAFE AT HOME

Every year, medical technology companies roll out new products designed to address all manner of diseases and conditions. Yet few of these items undergo empirical testing to determine their effectiveness. Now the DCRI and Reflexion Health, Inc. have teamed up to conduct Virtual Exercise Rehabilitation In-home Therapy: A Research Study (VERITAS), which is designed to evaluate the cost and outcomes of using a virtual rehabilitation platform to deliver physical therapy following total knee replacement (TKR) surgery.

According to the Centers for Disease Control and Prevention, 700,000 TKRs are performed each year in the United States. TKR is the most frequently performed procedure in the hospital and is more common among women than men. The average Medicare expenditure for surgery, hospitalization, and recovery ranges from $16,500 to $33,000 across geographic areas. With a significant growth in TKRs among younger adults with knee osteoporosis, an aging population working longer, and a shift to value-based care, the demand for TKR surgery is expected to exceed three million by the year 2030, while at the same time, healthcare systems will continue to optimize costs.

“Physical therapy is often a critical component of care for patients who have TKR surgery,” said Janet Prvu Bettger, ScD, associate professor with the Duke Department of Orthopedic Surgery and principal investigator for the study at the DCRI. “Digital health technology, including virtual and telehealth options, may increase access, improve quality, and lower healthcare costs. Extending the reach of physical therapists into the home using a digital healthcare platform like VERA™ can provide remote guidance and supervision for a home-based therapy program; however, implementation in the U.S. has not been widely evaluated until now.”

VERITAS is a multicenter, randomized controlled trial and will enroll approximately 300 adult participants scheduled for TKR surgery at six U.S. sites. The treatment group will include 150 adults who will receive Reflexion Health’s proprietary virtual exercise rehabilitation assistant, VERA™, both pre- and post-surgery, compared with a control group of 150 adults who will receive traditional in-home or clinic-based physical therapy at participating sites. Clinical outcomes, health service use, and costs will be examined for three months after surgery.

THE AVERAGE MEDICARE EXPENDITURE FOR SURGERY, HOSPITALIZATION, AND RECOVERY RANGES FROM $16,500 TO $33,000 ACROSS GEOGRAPHIC AREAS.

THE DEMAND FOR TKR SURGERY IS EXPECTED TO EXCEED THREE MILLION BY THE YEAR 2030.

JANET PRVU BETTGER, SCD
EARLY WARNING

A new DCRI-led program is looking for ways to improve systems of stroke care across North Carolina and beyond.

Stroke kills more than 130,000 Americans each year, making it the fifth-leading cause of death in the nation. Every year, more than 795,000 people in the United States have a stroke. Many of these strokes occur in the southeastern United States, in an 11-state region known as the “stroke belt.” North Carolina, which occupies the middle of this region, is sometimes described as the “buckle” of the belt.

Early action is important for improving outcomes for stroke patients. Patients who arrive at the emergency room within three hours of their first symptoms often have less disability three months after a stroke than those who received delayed care. Ensuring rapid care in North Carolina is particularly difficult, however, as there are only four certified comprehensive stroke centers in the state.

The IMPROVE Stroke Care program was created to develop a regional integrated stroke system in North Carolina that identifies, classifies, and treats patients with acute ischemic stroke more rapidly and effectively with reperfusion therapy.

Based on similar programs developed to improve systems of care around heart attacks, IMPROVE Stroke Care will develop a network of stroke centers and other hospitals to implement best practices and integrate state-of-the-art technologies into regional systems of stroke care.

The DCRI’s Bradley Kolls, MD, PhD, and Carmelo Graffagnino, MD, medical director of the Duke Comprehensive Stroke Center, will serve as principal investigators for the project.

One of IMPROVE Stroke Care’s novel elements is the use of new data capture technologies. Key data elements will be defined, collected, and fed back in real time to drive practice improvement. Participating centers will have real-time feedback on their performance metrics, utilizing novel data capture methods and mobile applications that operate independently of existing electronic health records or primary databases but are able to interact with them.

“We’ve come up with an innovative way of capturing data automatically through the Telestroke Network,” Kolls said. “This is a new strategy for collecting data on the systems of care throughout the state.”

STROKE KILLS MORE THAN 130,000 AMERICANS EACH YEAR, MAKING IT THE FIFTH-LEADING CAUSE OF DEATH IN THE NATION. EVERY YEAR, MORE THAN 795,000 PEOPLE IN THE UNITED STATES HAVE A STROKE.

BRADLEY KOLLS, MD, PHD
WHAT’S NEXT: HOW WILL THE DCRI CHANGE CLINICAL RESEARCH?
The DCRI has been named the coordinating center of a $157-million federal initiative involved in studying how environmental factors affect childhood health.

The grant from the National Institutes of Health (NIH) will fund the organizational framework of the Environmental Influences on Child Health Outcomes (ECHO) initiative. The DCRI has been awarded $14.7 million in fiscal year 2016. This award is a seven-year grant with a total value of $119 million.

As the coordinating center for the research initiative, the DCRI will provide support to the study’s steering committee, lead site training for participating research teams, develop common rules and standard procedures, monitor quality controls, and establish and maintain websites and other communications tools.

The ECHO coordinating center at the DCRI will also include an Opportunities and Infrastructure Fund to support pilot projects, encourage development of junior investigators, and introduce new tools and technologies in the context of the ECHO program.

“We are certainly honored to be selected as the coordinating center for this important research initiative at the NIH,” said principal investigator Brian Smith, MD, a Duke neonatologist and faculty member of the DCRI. “This builds on a number of our strengths in clinical research, notably in pediatric clinical research, where we have developed specific expertise.”

The awards will build the infrastructure and capacity for the ECHO program to support multiple longitudinal studies that extend and expand existing studies of mothers and their children. ECHO research will focus on factors that may influence health outcomes around the time of birth as well as into later childhood and adolescence, including:

- Airway diseases such as allergies and asthma
- Obesity and nutrition
- Pregnancy and childbirth
- Brain and behavioral development

In addition to Smith, the DCRI’s ECHO leadership includes co-principal investigators L. Kristin Newby, MD, MHS, and Daniel Benjamin, Jr., MD, MPH, PhD, as well as Program Director Lila Schweins.
The DCRI has teamed up with Stanford Medicine and Verily Life Sciences to launch Project Baseline, a longitudinal study that will collect broad phenotypic health data from approximately 10,000 participants who will be followed for at least four years. The study is designed to develop an in-depth “baseline” for a person that may be used to better understand the transition from health to disease. Project Baseline will also test and develop new tools and technologies to access, organize, and activate health information.

Each site will gather deep datasets that include clinical, imaging, self-reported, physical, environmental, behavioral, sensor, molecular, genetic, and other health-related data. The participants will also provide daily information via a wrist-worn investigational device and other sensors, as well as completing interactive surveys and polls conducted through a smartphone, computer, or call center.

One of the focus areas of the Project Baseline study is participant involvement, which includes development of a participant committee and the option to receive certain health data and test results, participate in conference calls with members of the study team, and evaluate new tools and technologies.

“Through the Project Baseline study, we are aiming to engineer a true 21st-century approach to health—in a preventive and personalized way,” said the DCRI’s Adrian F. Hernandez, MD, MHS.

“Instead of having the annual physical exam that has not changed in decades, we’re hoping to develop new platforms that will discover changes in health as they happen in meaningful and actionable ways. To do this successfully, we will partner with participants to learn and deliver the best approaches for every aspect of the study.”

ADRIAN F. HERNANDEZ, MD, MHS
Making a Connection

Heart failure remains a major issue, affecting 5.7 million Americans and contributing to one in nine deaths. Clinical trials have shown that new drugs can reduce mortality and hospitalizations and increase quality of life in participants with heart failure, yet uptake has been poor.

To respond to this issue, the Care Optimization through Participant and Hospital Engagement Clinical Trial for Heart Failure (CONNECT-HF) trial is enrolling high-risk hospitalized participants with acute heart failure and reduced ejection fraction. This large-scale, pragmatic, cluster-randomized trial is evaluating two heart failure quality improvement initiatives: one that targets health systems and one that engages participants through mobile health applications. In terms of numbers of hospitals involved, this will be the largest-ever quality improvement trial in heart failure, with 160 hospitals and 8,000 participants.

“There has been a lot of enthusiasm for this study, both at the health system level and among participants, and we’re really happy with progress so far,” said the DCRI’s Adam DeVore, MD, MHS, principal investigator for CONNECT-HF. “This large-scale and pragmatic study has enrolled more than 60 sites and over 100 participants to date.”

“This study provides a unique opportunity to incorporate patient engagement, mobile health innovations, and quality improvement methods aimed at impacting the journey of heart failure participants,” said the DCRI’s Linda Davidson-Ray, MA, associate director of Operations Outcomes at the DCRI.

The participant engagement committee, a group of patient advisers living with heart failure called the Cardi-Yaks, has been closely involved in the trial’s design, sharing real-life experiences to help researchers design a trial that is both useful and easy for participants. The members of this group also provided “real-life” tips and testimonials to other patients.

CONNECT-HF is adopting user-facing mobile health technologies in the participant engagement intervention to help improve adherence to medication and self-care routines, including physical activity and daily weight self-monitoring. The DCRI is working in collaboration with Dan Ariely’s Center for Advanced Hindsight at Duke to incorporate behavioral economic techniques through two apps. The CONNECT-HF study is also evaluating an intervention at the hospital level to identify the greatest opportunities for quality improvement in heart failure.

“The focus is on healthcare transitions—ensuring participant-centered approaches at each step—and on health literacy-appropriate education to improve adherence to self-care routines,” said Monica A. Reed, MHA, RCIS, clinical research associate at the DCRI.

This large-scale and pragmatic study has enrolled more than 60 sites and over 100 participants to date.

Adam DeVore, MD, MHS
SMART WATER

Physicians often tell patients to increase their daily intake of water to reduce their chances of developing urinary stones, also known as kidney stones. But can smart technology help facilitate increased water consumption? Researchers are recruiting participants for a two-year clinical trial to determine whether using a high-tech water bottle will encourage people to drink more water, and therefore reduce the recurrence of kidney stones.

The trial, known as the Prevention of Urinary Stones with Hydration (PUSH) study, is being conducted as part of a five-year initiative by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to improve outcomes for patients with kidney stones. The purpose of the initiative, the Urinary Stone Disease Research Network (USDRN), is to design and conduct clinical trials in adults and children who suffer from kidney stones. The DCRI serves as the network’s Scientific Data Research Center. Charles Scales, MD, and Hussein Al-Khalidi, PhD, serve as the research center’s principal investigators.

PUSH will enroll 1,642 people, half in an intervention group and half in a control group. The study’s primary aim is to determine whether a program of financial incentives, receiving advice from a health coach, and using a smart water bottle called Hidrate Spark that monitors fluid consumption and connects to an app will result in reduced risk of kidney stone recurrence over a two-year period.

Kidney stones are small, hard mineral deposits that form inside the kidneys and can cause kidney damage and excruciating pain. Kidney stones affect about 1 out of 11 Americans. The prevalence of kidney stones among Americans has nearly doubled in the last 15 years and is increasing in both adults and children.

Kidney stones are a recurring condition for many patients. Data from the National Health and Nutrition Examination Survey show that 35 percent of participants had experienced two or more distinct episodes of urinary stones. Although the causes of kidney stone formation are relatively well-understood, there has been little clinical emphasis on preventing recurrent kidney stones. Many physicians treat kidney stones as discrete events, rather than a chronic metabolic condition resulting in painful “stone attacks.”

“If we treated people with heart disease the way we treat patients with kidney stones, we would only be treating patients with chest pain or a heart attack,” Scales said. “We wouldn’t pay attention to risk factors like smoking or cholesterol. My hope is that through the PUSH study, we can focus on stone prevention and empower patients to make the necessary lifestyle changes to avoid recurrent kidney stones.”

MY HOPE IS THAT THROUGH THE PUSH STUDY, WE CAN FOCUS ON STONE PREVENTION AND EMPOWER PATIENTS TO MAKE THE NECESSARY LIFESTYLE CHANGES TO AVOID RECURRENT KIDNEY STONES.

CHARLES SCALES, MD
In an example of successful collaboration between groups with Clinical and Translational Science Awards (CTSA) program funding at Duke and the University of Kentucky, a clinical trial in healthy volunteers has recently been completed for a novel potential therapy, TT301/MW189. Duke conducted the clinical trial, pharmacokinetic analysis, and data management, while Kentucky provided study leadership, monitoring, and statistical support.

TT301/MW189 is being studied as a possible treatment for people with different types of brain injury and neurodegenerative disease such as Alzheimer's disease, which currently lack effective therapies. The latest trial was a phase I, double-blind, randomized, placebo-controlled multiple ascending dose study to evaluate the safety, tolerability, and pharmacokinetic profile of TT301/MW189 administered intravenously to healthy volunteers. The drug had previously been given to healthy human volunteers as a single dose with no significant adverse events.

“We are excited to participate in this collaborative study between CTSA sites investigating a novel approach that offers promise in both Alzheimer’s disease and brain injury, diseases where treatment options are desperately needed,” said the DCRI’s principal investigator for this trial, Jeffrey T. Guptill, MD, MA, MHS.

“Based on available data, the drug appears safe, and we feel we have a dose that we can test in patients in future trials. The full dataset from this phase I study will be available in early 2018.” Guptill is an associate director of Duke Early Phase Clinical Research, a group that conducts a broad range of early phase, proof-of-concept, and first-in-human studies for new therapies, technologies, and device prototypes.
NEXT IS NOW: TRANSFORMING CLINICAL RESEARCH

TRADITIONAL
RANDOMIZED CLINICAL TRIAL

PATIENTS ARE RECIPIENTS OF THE THERAPY BEING STUDIED

PATIENTS ARE IDENTIFIED AND ENROLLED IN THE TRIAL AT STUDY SITES

ALL RELEVANT DATA ARE RECORDED AT STUDY SITES

INVESTIGATORS MONITOR STUDY DATA THROUGH CASE REPORTS

PATIENTS

DATA

PRAGMATIC
CLINICAL TRIAL

PATIENTS ARE PARTNERS FOR EVERY STAGE OF THE STUDY, FROM PROTOCOL DESIGN TO DATA COLLECTION TO REPORTING RESULTS

PATIENTS CAN ENROLL IN THE TRIAL ELECTRONICALLY

THE STUDY USES A COMBINATION OF EXISTING DATA AND PATIENT-REPORTED OUTCOMES FOR BASELINE CHARACTERISTICS AND FOLLOW-UP

AN INTERNET PORTAL ENABLES THE COLLECTION AND MONITORING OF STUDY DATA BY BOTH PATIENTS AND INVESTIGATORS
Since conducting the landmark GUSTO trial, the DCRI has been steadily changing the way clinical research is conducted. With new studies such as ADAPTABLE, the DCRI and its partners are finding new ways to make clinical trials faster, less expensive, and more responsive to patient needs.

**THE STUDY IS CONDUCTED IN TRADITIONAL CLINICAL SETTINGS SUCH AS HOSPITALS**

**THE STUDY COMPARES A PLACEBO TO THE THERAPY BEING STUDIED**

**INSTITUTIONAL REVIEW BOARD (IRB) FUNCTIONS, CONSENT, AND CLAIMS DATA ARE MANAGED SEPARATELY**

**THE STUDY’S FINDING IS A SURROGATE MEASURE FOR PATIENT OUTCOMES**

**THE STUDY HAS NO PLACEBO, INSTEAD TREATING PATIENTS WITH DIFFERENT DOSES OF THE THERAPY BEING STUDIED**

**IRB FUNCTIONS AND CONTRACTS, ELECTRONIC CONSENT, AND THE USE OF ELECTRONIC HEALTH RECORDS (EHRS) AND CLAIMS DATA ARE CENTRALIZED**

**THE STUDY’S FINDING ANSWERS A SPECIFIC QUESTION ABOUT PATIENT OUTCOMES**
THERAPEUTIC AREAS

- CARDIOVASCULAR
- GASTROENTEROLOGY
- INFECTIOUS DISEASES
- MUSCULOSKELETAL
- NEUROSCIENCES MEDICINE
- PEDIATRICS
- PERIOPERATIVE
- RESPIRATORY MEDICINE
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