ASKING THE RIGHT QUESTION DOESN’T JUST REVEAL THE ANSWER
IT LEADS TO WHAT’S NEXT

LETTER FROM THE EXECUTIVE DIRECTOR

Clinical research begins by asking the right question. But it doesn’t end simply by finding the answer. Rather than be satisfied with what we’ve done, we are always looking to what’s next. We challenge the status quo, because we know the solutions we find have the power to spark other discoveries.

At the DCRI, we’re not afraid to ask questions that lead to more questions. By peering into the unknown, we discover innovations that transform clinical research and allow findings to be brought more rapidly into clinical practice.

Since the founding of the Duke Databank for Cardiovascular Disease at the Duke School of Medicine more than 40 years ago, we have constantly sought new ways to improve the lives of patients around the world. Today that work goes on as we find new ways to move scientific discovery to patient care, rethink how clinical trials should be run, share valuable sources of data, and use new technologies to connect patients to researchers and caregivers.

Working with our partners, we are committed to discovering what’s next in the world of clinical research.

Eric D. Peterson, MD, MPH, FAHA, FACC
Executive Director, Duke Clinical Research Institute
Professor of Medicine, Cardiology
Fred Cobb, MD, Distinguished Professor of Medicine
MISSION AND VALUES

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.
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Translational Science: Bridging the Gap Between Basic and Applied Science

LEADING THE WAY

One of the DCRI’s larger projects is the Antibacterial Resistance Leadership Group (ARLG), which is funded by a 6.5-year, $62 million grant from the National Institutes of Health and headed by the DCRI’s Vance Fowler, MD, MHS. Each year in the United States, at least 2 million people become infected with bacteria that are resistant to antibiotics, and at least 23,000 people die as a result of these infections.

Treating resistant infections costs the U.S. healthcare system $21–34 billion each year.

Treating resistant infections costs the U.S. healthcare system $21–34 billion each year. Antibacterial resistance is attributed to the overuse and misuse of antibiotic medications, as well as a lack of new drug development by the pharmaceutical industry due to reduced economic incentives and challenging regulatory requirements. The ARLG’s mission is to prioritize, design, and execute clinical research that will reduce the public health threat of antibacterial resistance.

“At the ARLG, we’ve created an operational scaffolding around four priority areas of unmet need: infections caused by gram-negative bacteria, infections caused by gram-positive bacteria, antimicrobial stewardship, and diagnostics,” Fowler said. “Scientific subcommittees have been set up for each topic, involving some of the best and brightest investigators in the country, to evaluate projects with potential to transform medical practice for funding by the ARLG.”

The DCRI is the operations center, coordinating and orchestrating the grant and dozens of subcontracts, clinical trial agreements, and consultancy agreements. Among current ARLG collaborations are joint projects with the Clinical Trials Transformation Initiative (CTTI) at the DCRI, ongoing discussions with more than 10 therapeutics companies and 30 diagnostics firms, and initiation of a joint working group involving ARLG scientists, physicians, U.S. Food and Drug Administration (FDA) representatives, and companies. The DCRI ARLG Site Network provides flexible, on-demand agreements for each study, with 80 sites currently active on ARLG/CTTI studies, and more than 430 feasibility surveys completed by additional sites. To date, 289 rapid-start master agreements have been executed, reducing study startup times by an average of two months.

“We are privileged to be able to host such a critical network.”

Heather Cross, D.Phil, Program Leader, ARLG

“Antimicrobial resistance can be viewed as a ‘social disease,’ with elements involving science, evolution, economics, and geography,” Fowler said. “Resistant bacteria don’t need a passport to travel and can potentially affect anyone. Action is urgently needed, and the DCRI is playing an absolutely essential role in operationalizing the ARLG’s efforts.”
FINDING NEW WAYS TO PROTECT THE BRAIN

Researchers at the Duke Clinical Research Unit (DCRU) are taking the first steps toward a new treatment for acute brain injury. If their efforts are successful, it could be the first treatment of its kind.

Treatment options for patients with acute brain injuries, such as those resulting from car accidents or combat situations, have been limited to surgery to reduce pressure inside the skull and the use of medications to prevent seizures and limit fluid retention. But a new discovery might lead to a treatment that could allow the brain to protect itself from the most severe effects of these types of injuries.

“No pharmacological agent to date has ever been shown to reduce brain injury,” said the DCRI’s Daniel Laskowitz, MD, MHS. “What we have done is create a potential therapy for acute brain injury based on a naturally occurring protein that seems to modify outcomes for patients with brain injuries.”

Laskowitz and his colleagues have evaluated the mechanisms by which different isoforms of apolipoprotein E (ApoE) can influence patient outcomes after acute brain injury. Variants of ApoE have previously been linked to Alzheimer’s disease and various cardiovascular ailments. The Duke researchers have spent more than 20 years examining how this protein can also affect the brain’s response to injury.

The culmination of this research is CN-105, a small peptide derived from the receptor-binding region of ApoE. The peptide is already known to improve outcomes in a number of animal models of brain injury. CN-105 is believed to work by blocking the brain’s inflammatory response to injury, and the researchers think the peptide could be used to treat intracranial hemorrhage, stroke, and other forms of acute brain injury.

Intracerebral hemorrhage, or bleeding within or around the brain, accounts for between 8 and 13 percent of all strokes and is more likely to result in death or major disability than ischemic stroke or subarachnoid hemorrhage. Intracerebral hemorrhage and accompanying edema can also disrupt or compress adjacent brain tissue, leading to severe neurological dysfunction.

A team of researchers is beginning the first in-human trials of CN-105 to see if the peptide could be a viable treatment for these patients. Although there is still much work to do, Laskowitz is optimistic that the years of research will eventually pay off.

“This would be the first neuroprotective drug of its kind,” he said. “Our hope is that we will finally have something to help people who otherwise would have very few options.”

“FINDING NEW WAYS TO PROTECT THE BRAIN”

Translational Science: Bridging the Gap Between Basic and Applied Science

DANIEL LASKOWITZ, MD, MHS
MAKING TRIALS MORE EFFICIENT

Researchers at the DCRI and Vanderbilt University Medical Center (VUMC) recently received a major federal grant to study how multisite clinical trials of new drugs and therapies in children and adults can be conducted more rapidly and efficiently.

“This is an unprecedented opportunity to change how we conduct clinical trials and improve patient care around the world.”

Lori Poole, Project Leader, Trial Innovation Center Study Design Core

The seven-year, $26.5 million grant for a joint Trial Innovation Center (TIC) is supported by the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH).

The center will be a key component of the Trial Innovation Network, which is the newest part of the Clinical and Translational Science Award (CTSA) Program.

Daniel Benjamin, Jr., MD, MPH, PhD, faculty associate director of the DCRI, is one of the grant’s principal investigators.

“The DCRI and Vanderbilt partnership is a perfect fit for the TIC,” said Benjamin. “The academic research organization model at the DCRI and Vanderbilt’s informatics and central institutional review board model are poised to immediately contribute to the NIH’s vision of high-functioning networks for clinical research.”

SPOTLIGHT: ASSURING HIGH-QUALITY CLINICAL STUDIES

The DCRI’s Clinical Events Classification (CEC) group plays a crucial role at the institute, bringing diversification, innovation, and thought leadership to the review of cases and operational processes. The team has processed more than 36,000 adjudications and 8,000 safety events across more than 84 active studies this year. CEC has expanded its role beyond the traditional cardiovascular studies and has diversified into emerging areas for adjudication, including respiratory medicine, infectious diseases, gastrointestinal and liver disease, kidney disease, and pediatrics.

“We have experienced tremendous growth this year,” said Renato Lopes, MD, MHS, PhD, co-director of the CEC group. “Our exceptional faculty and operational teams work together in a close, cohesive way to achieve impressive results for our sponsors. Our group is also well-positioned and highly respected by other academic groups, sponsors, and regulatory agencies.

“Importantly, we are strategically leading advances in the field at the same time that we are seen as an example by other CEC and safety groups globally.”

A recent example of the high-quality work done by the CEC group was the EUCLID trial. This was the largest study of peripheral artery disease completed to date, enrolling more than 13,500 patients at more than 800 sites in 28 countries. The DCRI CEC and Safety clinical program for EUCLID was a team effort that incorporated multiple aspects of clinical event surveillance and adjudication, with over 11,000 triggers completed.

“I think the most impressive accomplishment of the CEC group has been the commitment to measuring quality in adjudication and improving our processes, as seen by the EUCLID experience,” said Schuyler Jones, MD, the CEC’s other co-director and EUCLID CEC principal investigator.
DESIGNING STUDIES THAT DO MORE THAN GATHER DATA THEY UNVEIL TRUTHS
Clinical Trials: Research Designed to Shape the Clinical Standards of Tomorrow

A SMALL STUDY WITH BIG IMPLICATIONS

Not all clinical trials are the same. At the DCRI, we uniquely design each trial—from small pilot studies to global megatrials—based on the question that needs to be answered.

A small but innovative DCRI study is breaking new ground while trying to find a treatment for children with attention deficit hyperactivity disorder (ADHD).

The Software Treatment for Actively Reducing Severity of ADHD (STARS-ADHD) study is examining whether a new digital intervention can benefit young patients with ADHD.

“This is a very sophisticated therapy,” said the DCRI’s Scott Kollins, MS, PhD, the study’s principal investigator. “It’s effectively a task disguised as a high-action, consumer-grade video game.”

ADHD is one of the most common neurobehavioral disorders among young people. Children with ADHD often have trouble paying attention, controlling impulsive behaviors, or staying still. The condition, which can last into adulthood, is estimated to affect approximately 6.4 million (11 percent) of American children 4–17 years of age.

ADHD has traditionally been treated with medication and behavioral therapy, but these approaches have their limitations. Medications have side effects, Kollins noted, while some patients do not respond to behavioral therapy. If the digital intervention Kollins and his colleagues are studying eventually becomes an approved treatment for ADHD, it would be among the first of its kind.

The intervention at the center of STARS-ADHD is a software program developed by Akili Interactive Labs and based on research conducted at the University of California-San Francisco. The Akili scientists were inspired by studies suggesting that action video games can stimulate cognitive function.

The program, called Project: EVO, allows players to engage in a mobile video game interface deployed on an iPad. Project: EVO monitors the user’s movements and adjusts its difficulty automatically. Using the program engages the prefrontal cortex, the part of the brain associated with higher-order mental functions, including those that regulate attention and behavior. Researchers believe that ADHD is related to changes in the prefrontal cortex, although the exact nature of that relationship remains unclear.

Kollins and his colleagues hope that STARS-ADHD will expand their understanding of the condition and how to treat it. The trial, which is being conducted at eight sites across the United States, has already enrolled nearly 50 patients. The research team hopes to enroll at least 300 patients in total. Meanwhile, the researchers are exploring similar treatments for other neurological conditions such as autism, depression, and Alzheimer’s disease.

“We’re optimistic that this could be a game changer for ADHD treatment,” Kollins said. “This is the cutting edge of clinical research.”
PASSING THE TEST

The process of moving scientific discoveries from the laboratory into the examination room is often expensive and time-consuming. At the DCRI, we’re driven to find efficiencies and shorten the timeline so that new treatments can find their way to patients more quickly and affordably. Two studies led by Pamela Douglas, MD, highlight the DCRI’s commitment to this process. They focused on this question: How can the diagnosis of patients with potential cardiac disease be improved?

Computed tomographic angiography (CTA) and stress tests are regularly used to evaluate the more than 4 million U.S. cases per year of newly symptomatic patients with no previous diagnosis of heart disease. In the Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) study, Douglas led a robust head-to-head comparison of health outcomes for stable outpatients with suspected coronary artery disease (CAD).

“The results of PROMISE are very meaningful, since this is the first large randomized clinical trial for imaging modalities in patients with chest pain, involving 10,003 patients at 193 centers,” Douglas said. “Early signals are that the results will change testing for patients with chest pain, establishing CTA as a viable alternative to stress testing in this patient population.

The study also provides new assurance for patients and their physicians that both methods result in low rates of serious outcomes—around 3 percent over two years—which is great news.”

In the Prospective Longitudinal Trial of FFRCT: Outcome and Resource Impacts (PLATFORM) study led by Douglas, a diagnostic strategy using CTA to measure fractional flow reserve (FFRCT) was evaluated in patients with suspected CAD. Patients with chest pain, a symptom of CAD, are often sent to a cardiac catheterization lab directly or after stress testing for an invasive procedure to detect blockages.

“PROMISE is important because we are not just looking at a single step but an entire process. We are evaluating not just a test but a new approach for diagnosing symptoms and choosing a treatment plan.”

Beth Martinez, Project Leader, PROMISE

However, cardiac catheterization can be avoided in many patients, according to new findings from PLATFORM. FFRCT analysis uses supercomputers to model blood flow and helps determine whether a blockage is significant enough to require an invasive treatment. PLATFORM findings indicate that this diagnostic strategy can triage patients with suspected CAD more effectively for invasive procedures than usual care, with no increase in the occurrence of major cardiac events.
PUSHING PAST THE LIMITS

The DCRI is helping coordinate a global megatrial that may change how doctors treat patients with high levels of low-density lipoprotein (LDL, or “bad”) cholesterol.

Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab (ODYSSEY Outcomes) is a randomized double-blind trial being conducted in more than 50 countries that compares alirocumab, a novel lipid-modifying anti-PCSK9 monoclonal antibody, with placebo in patients who have experienced a recent acute coronary syndrome and have residual elevated LDL levels despite statin therapy.

ODYSSEY OUTCOMES

18,000 enrolled patients around the world
2,000 ODYSSEY centers worldwide

Alirocumab was approved in 2015 by the FDA for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of LDL cholesterol. Initial approval of alirocumab was based on its lipid-lowering efficacy, but the results of ODYSSEY Outcomes will help determine the drug’s cardiovascular efficacy on clinical outcomes—reducing an individual’s risk of having a heart attack or stroke.

“This treatment has the potential to reduce LDL levels to very low values that previously were not possible,” said Matthew Roe, MD, MHS, who is working with Megatrials Project Leader Kirby Quintero to coordinate the DCRI’s activities for this trial.

“No one likes injections,’ said Kirby Quintero. ‘Enrolling in the study took persistence from the sites to find the right patients willing to have injections and participate in a long-term outcomes study. This success is a testament to the dedication and enthusiasm of our investigators and study coordinators.”

Kirby Quintero, Project Leader, ODYSSEY Outcomes

ODYSSEY Outcomes, which has enrolled 18,000 patients around the world, is part of a larger series of ODYSSEY phase III trials conducted at more than 2,000 centers worldwide. Once completed, it is expected that 25,000 patients will be evaluated in ODYSSEY trials.

“The hope is that this degree of LDL lowering will contribute to a substantial reduction in the risk of cardiovascular ischemic events after acute coronary syndromes.”

The DCRI operational teams are responsible for site management and monitoring for participating sites in the United States, coordinating the study’s collaborations among academic leadership committees and global academic research organizations, as well as clinical events classification (across all ODYSSEY trials in the program).
BRINGING ORIGINAL THINKING TO PATHWAYS ALREADY EXPLORED AND NEW PERSPECTIVES YET TO BE FORGED
Open Science: Making Data Public and Purposeful

OLD DATA, NEW SOLUTIONS

Clinical research generates a tremendous amount of data. However, for decades much of this information has been siloed, hidden, or otherwise made unavailable to the larger community of researchers. As a result, its potential has been reduced tremendously. By opening these vast warehouses of data, we open a new world of possibilities in which the search for new cures and treatments is advanced.

The DCRI is at the forefront of efforts to proactively engage in data sharing and transparency. In an initiative with analytics leader SAS, we are the first academic group to share our own data. Together, we will provide researchers worldwide with data management and analytics tools to explore 45 years of cardiovascular patient data collected by the Duke University Health System. Through greater transparency and openness in research, our goal is to find new ways to treat heart disease, the leading cause of death in the United States.

For the DCRI, the collaboration with SAS is a milestone for the broader data access initiative called Supporting Open Access for Researchers (SOAR). SOAR is a collaborative effort between academia and private industry to open clinical research data for the benefit of the broader research community.

SOAR

The dataset of SOAR is part of the Duke Databank for Cardiovascular Disease (DDCD), which includes de-identified records for patients treated at Duke between 1969 and 2013. The database includes details of more than 100,000 procedures on more than 50,000 unique patients, including patient demographics, cardiac medical history, other conditions occurring simultaneously, final impressions, and subsequent treatments. DDCD can be used to test clinical hypotheses, develop clinical trial protocols, and help researchers assess long-term outcomes and trends.

Another aspect of the SOAR initiative is a collaboration between the DCRI and Bristol-Myers Squibb aimed at facilitating open sharing of Bristol-Myers Squibb trial data with interested researchers. Key features of the data-sharing model include an independent review committee run by the DCRI that ensures expert consideration of each proposal, stringent data de-identification/anonymization and protection of patient privacy, requirement of pre-specified statistical analysis plans, and independent review of manuscripts before submission for publication. DCRI Executive Director Eric Peterson, MD, MPH, and Director of Biostatistics Michael Pencina, PhD, will oversee the independent review process.

“We believe that these approaches will promote open science by allowing investigators to verify trial results as well as to pursue interesting secondary uses of trial data without compromising scientific integrity,” said Brian McCourt, director of Clinical Research Informatics at the DCRI.
Numbers reflect DCRI faculty and staff collaborations in FY2016.
Each circle's size and position reflects an index that weighs the number of jointly authored papers combined with the number of co-authorships on those papers.

the number of jointly authored papers combined with the number of co-authorships on those papers.
The goal of the Academic Research Organization Consortium for Continuing Evaluation of Scientific Studies—Cardiovascular (ACCESS CV) is to provide avenues for the sharing of data from cardiovascular clinical trials while minimizing risks and unintended consequences.

Spearheading the ACCESS CV project at the DCRI is Manesh Patel, MD. Patel is working with a wide range of experts from academic research organizations (AROs) to build portals and other ways to share data and to aggregate and provide access to data in a structured and safe way. A key goal is to increase publication of analyses of shared data.

“The new consortium has proposed a secure method of sharing sensitive patient data that balances the legitimate desire of the scientific community for data access with the responsibility to ensure high-quality analyses and protection of patients’ expectation of privacy,” Patel said. “The goal of data sharing is at the core of the DCRI’s mission to develop and share knowledge that improves the care of patients around the world through innovative clinical research.”

ACCESS CV will work to operationalize proposals on clinical trial data sharing from two major bodies: the Institute of Medicine (IOM), which has called for a multistakeholder effort to develop the culture, infrastructure, and policies to foster responsible sharing; and the International Committee of Medical Journal Editors (ICMJE), which has proposed sharing of clinical trial data as a prerequisite for publication in ICMJE journals. These include such prestigious titles as the New England Journal of Medicine, the British Medical Journal, and The Lancet.
PREDICTING PATIENT BEHAVIOR

The DCRI has found a new way to transform data sources into practical tools for patients and physicians. More than 29 million Americans have diabetes, which is the seventh-leading cause of death in the U.S. It also results in annual costs of over $245 billion, including direct medical costs and reduced productivity. Studies indicate that recommended glycemic goals are achieved by less than 50 percent of patients, which may be associated with poor adherence to therapies. To help address this issue, an interdisciplinary team from the DCRI is collaborating with Sanofi U.S. on a pilot study to create tools to predict how people with type 2 diabetes adhere to medication.

Led by Michael Pencina, PhD, of the DCRI’s Center for Predictive Medicine, the initiative aims to develop data-driven solutions to improve adherence at the individual, clinic, community, and eventually even national levels.

“The DCRI’s collaboration with Sanofi has the potential to transform chronic disease population management by analyzing how predictive analytics—big data—might forecast medication adherence and result in more personalized patient adherence programs,” said Pencina.

The DCRI team includes faculty and operational experts from the DCRI, Duke Translational Research Institute, Duke School of Nursing, Duke Department of Electrical and Computer Engineering, and Duke Health Technology Solutions. The DCRI is using novel machine learning methods to extract meaningful patient insights based on large-scale use of anonymized individual patient-level data, adhering to strict privacy standards.

The initiative involves collaboration with Lincoln Community Health Center in Durham, NC, which serves 40,000 patients per year. It will provide sociogeographic data to help understand how physical environment, social and economic conditions, and health and lifestyle behaviors can affect medication adherence.

“This initiative is a striking example of team science,” said Bradi Granger, MSN, PhD, RN, professor at the Duke University School of Nursing and director of the Duke Heart Center Nursing Research Program. “In this pilot project, the expertise of multidisciplinary collaborative groups is being tapped to help resolve a major public health problem.”
PEERING INTO THE UNKNOWN ISN’T UNNERVING IT’S EXHILARATING
Innovations: Technologies That Seamlessly Connect Researchers with Patients

GETTING HEART SMART

As part of the larger Duke Health System, the DCRI has the opportunity to partner with physicians from across the system to recruit patients for its studies. Duke is a participating site in the Centers for Medicare and Medicaid Services (CMS) Million Hearts® Cardiovascular Disease (CVD) Risk Reduction Model study. The Duke Heart Center and researchers at the DCRI—including Executive Director Eric Peterson, MD, MPH; Ann Marie Navar, MD, PhD; and Cary Ward, MD—are working with Duke primary care clinics to improve delivery of cardiovascular preventive care using electronic health records (EHRs).

The Million Hearts® CVD Risk Reduction Model proposes an innovative way to lower the risk of heart attacks and strokes, a leading cause of death and disability. About 610,000 people die from heart disease in the United States every year, accounting for one in every four deaths and costing $315.4 billion annually, according to the Centers for Disease Control and Prevention.

Cardiovascular disease is the number-one cause of death in the United States. CMS is determining whether utilizing incentives at the system level can lead to improved delivery of preventive care to its highest-risk patients. A key component of the Million Hearts® model is patient and provider shared decision making, using personalized risk scores and modification plans for patients. The model will operate for five years and aims to enroll more than 300,000 Medicare beneficiaries and 720 diverse practices.

“This partnership between researchers at the DCRI and the Duke Health System highlights our mission not just to improve care nationally, but also in our own health system,” Navar said. “Our work on the Million Hearts® initiative demonstrates the diversity of research at the DCRI and the growing role for implementation science to test and evaluate the effectiveness of quality improvement initiatives.”

“”We’re excited to be part of a multidisciplinary team across the health system, all focused on the same goal of improving care for patients at Duke. If the approach is effective, we hope to expand it beyond patients in the Million Hearts® project to all patients cared for at Duke who are at risk for cardiovascular disease.”

ANN MARIE NAVAR, MD, PHD
Another first-of-its-kind study being conducted by the DCRI is the 6th Vital Sign. The study asks volunteers to download a free ResearchKit app from the Apple iTunes Store, answer some questions, and then take a two-minute stroll. The app securely uploads walking speed captured on a phone along with demographic data to calculate a reliable and personalized health measure.

“Walking speed is recognized, yet underutilized, as a measure and predictor of a person’s health. It can be used as a vital sign much like blood pressure, temperature, heart and breathing rate, and pain,” said study team leader Janet Prvu Bettger, ScD.

“Mobility, or a person’s ability to move, reflects the health of all of our body’s systems,” Bettger said. On the other hand, immobility impacts a person’s muscles, heart, digestive system, joints, and even mood.

“As a sixth vital sign, walking speed can be used to track a person’s recovery from illness or injury, declines in health, or even risks for falls, or depression,” Bettger said. “Among older adults, we know that walking speed can even be used to predict survival.”

“Mobility, or a person’s ability to move, reflects the health of all of our body’s systems.”

This research app allows us to create new mobile phone-based standards and norms for walking speed for people, first around the U.S. and eventually around the world,” Bettger said. “The more people who participate in the study, the more representative our findings. This will help us create more accurate predictions of future health and measurement-based action plans to promote health, recovery from an injury, and prevention of falls. And because smartphones are so common among people of all ages, there is a great potential to engage an unlimited population in research and create new knowledge for entire populations.”
MAKING AN IMPACT

DCRI researchers are also exploring new ways to treat persistent problems. In the United States, there are about 5 million patients with atrial fibrillation (AF), the most common type of cardiac arrhythmia. Worldwide, the number of people with AF is estimated at 34 million. The most serious consequence of AF is stroke, which is five times more common in patients with AF.

Although oral anticoagulation has proven effective in preventing stroke related to AF, only about half of patients with AF are being treated in high-income countries, and many fewer in lower-income counties. Thus there are hundreds of thousands of preventable strokes occurring worldwide each year, with the bulk of these occurring in low- and middle-income countries.

The International Multicenter Clustered Randomized Controlled Trial to imProve Treatment With AntiCoagulanTs in Patients With Atrial Fibrillation, or IMPACT-AF, seeks to change this by means of an innovative study design. In this trial, centers in Argentina, Brazil, China, India, and Romania will be randomized to an experimental or a control group. The intervention consists of patient measurement and feedback tools and education programs for patients and providers to increase the use of oral anticoagulation for patients with AF at risk of stroke.

Unlike other interventional studies that use a pre- and post-assessment model to determine the impact of the intervention, the IMPACT-AF researchers are using a cluster-randomized design to more rigorously assess the result of the implementation intervention.

The goal, said IMPACT-AF’s principal investigator, Christopher Granger, MD, is to better understand the reasons for underuse and improve the application of anticoagulation, with the goal of creating lasting improvement in the care of patients with AF.

“With this trial, we have the potential to improve stroke prevention care for atrial fibrillation on a global scale,” Granger said. “We also intend to build on this collaboration with our partners to find new ways to improve the care of patients around the world.”

SPOTLIGHT: PARTNERS FOR CHANGE

The DCRI and Duke-Margolis are partnering to provide expert perspectives for policy-focused convening activities addressing such issues as antimicrobial payment reform and innovation in clinical trials, such as surrogate endpoints in hematologic cancer trials. The centers are actively seeking collaborative activities, including an investigation of reimbursement and regulatory policy associated with biomedical innovation in the treatment of high cholesterol based on analysis of real-world evidence. The centers will convene a small informal meeting of diverse stakeholders and academic experts to outline the key areas in which healthcare providers and payers need better evidence and examine which of these questions can be answered quickly and effectively using distributed data sources.

The DCRI is partnering with the Duke-Margolis Center for Health Policy to coordinate resources across Duke and change how scientific discoveries inform policymaking. With the Center for Population Health Sciences, the DCRI and Duke-Margolis are actively pursuing acquisition of Center for Medicare and Medicaid Services (CMS) claims data that will enable faculty to investigate longitudinal outcomes for questions on clinical outcomes, population health measures, and measures of value and accountable care. Together, the centers are developing outreach, documentation, and governance to maximize access and maintain the highest levels of research integrity and academic productivity.
TURNING KNOWLEDGE INTO PRACTICE FOR REAL PATIENTS IN REAL-WORLD SETTINGS
The Patient Voice in Clinical Research: Actively Engaging Patients as Partners in Our Research

PATIENT PREFERENCES

Patients are a vital part of any clinical research project. Researchers are increasingly realizing that they can play a larger role in many clinical trials. In response to the patient-centeredness movement and regulatory interest in patient preferences, the DCRI has established the Preference Evaluation Research (PreFER) Group. Co-led by Shelby Reed, PhD, RPh, this group conducts industry-, foundation-, and government-funded studies. Although focus groups and in-depth interviews provide important qualitative information regarding the patient perspective, stated preference methods used by PreFER are more quantitative in nature.

“Through its Patient-Focused Drug Development initiative, the FDA is increasingly bringing the patient’s voice into its decision making.”

“The real advantage of these methods is that we’re able to quantify the priorities of patient groups, what benefit-risk tradeoffs they’re prepared to make, and their relative preferences for various types of medical treatments and services,” Reed said. “Through its Patient-Focused Drug Development initiative, the FDA is increasingly bringing the patient’s voice into its decision making. This is a major driver for industry to sponsor our research.”

Among topics being examined by the PreFER group are psoriasis, with a project focusing on the importance to patients of complete clearance of psoriasis plaques; Alzheimer’s disease, where the focus is on the potential risks that people would accept for possible new treatments that could intercept or slow disease progression; and a Patient-Centered Outcomes Research Institute (PCORI)-funded project in Crohn’s disease and ulcerative colitis to facilitate preference-weighted comparative effectiveness research. A project newly underway will examine benefit-risk tradeoffs in patients with mitral valve regurgitation.

PreFER investigators also are collaborating with the Duke Cancer Institute on several studies. One of these studies will examine patients’ preferences for initial treatment strategies for ovarian cancer. This study also will elucidate women’s preferences for gains in progression-free survival versus overall survival, important endpoints in evaluating new therapies. A technological platform is being developed to field preference studies with a patient registry, offering a model that could potentially be used with any of the DCRI’s registries. The PreFER group also is working to quantify patients’ perceived benefit-harm balances for ductal carcinoma in situ (DCIS) versus active surveillance management options, to better understand women’s treatment decisions in breast cancer.
As patients become more involved in clinical trials, ethicists are reassessing many of the rules that guide their participation. The Program for Empirical Bioethics carries out empirical research on ethical issues in research, using a variety of quantitative and qualitative techniques to gather data from a range of stakeholders to inform policy and practice.

“Informed consent is a major focus for us, with the goal of helping patients make good decisions about taking part in research.”

LAURA BESKOW, PHD, MPH

The program has several National Institutes of Health Research Project Grants that actively engage patients in the effort to improve informed consent. In one study, funded by the National Library of Medicine, Beskow’s team gathered data from hundreds of patients in four diverse counties around the southeastern U.S., using one-on-one interviews and focus groups to assess patient perspectives on research use of their electronic health records and acceptable approaches to consent. Later in the project, they will return to these counties to share their results and elicit policy input from community members using deliberative dialog techniques.

Another study, funded by the National Human Genome Research Institute, is focused on confidentiality issues in precision medicine research. The team is investigating participants’ reactions to consent form descriptions of the benefits, risks, and protections involved in such research, including what they understand and what might be confusing.

“Part of this project is a huge legal analysis of the strengths and limitations of state and federal laws and regulations for protecting research participants,” Beskow said. “But at the end of the day, one of the most critical components is coming up with ways to simply and clearly describe these to people during the informed consent process.”

“Informed consent is a major focus for us, with the goal of helping patients make good decisions about taking part in research,” said program director Laura Beskow, PhD, MPH. “An important part of that is to ensure that consent forms are not only concise and easy to read, but also emphasize the information that is most important to patients.”
ASKING THE RIGHT QUESTIONS

New techniques and devices are not only changing the way clinicians provide care; they are also changing how researchers gather data and conduct trials. Increasingly, these researchers are relying on consumer products that their patients already own.

One study utilizing this approach is a five-year, $20 million project to evaluate the effectiveness of various treatment strategies for women with uterine fibroids. The Comparing Options for Management: Patient-Centered Results for Uterine Fibroids (COMPARE-UF) Registry will enroll more than 10,000 women at clinics affiliated with nine medical centers across the country. Participating women will be asked at annual intervals specific questions about the treatments they have elected to receive and how well the treatments seem to be working for them.

COMPARE-UF

WILL ENROLL MORE THAN 10,000 WOMEN at clinics affiliated with NINE MEDICAL CENTERS across the country

Studies will focus on symptom relief, reproductive effects, and effectiveness among different patient subgroups, including African-American women, who are disproportionately affected by uterine fibroids. Approximately three years after initial treatment, researchers at the DCRI will analyze patients’ feedback to determine which procedures provide the greatest benefit.

The study will use novel analytic methods, with patient follow-up via a web portal accessed from an iPad or smartphone. An online patient community has also been set up.

“The study will help us better understand which treatments are most effective and produce the best outcomes for symptom relief and reproductive function.”

Barbara Lytle, Project Leader, COMPARE-UF

“This is the largest and most ambitious attempt to date to gather comparative effectiveness data on treatments for uterine fibroids, a condition that affects up to 75 percent of women,” said the study’s principal investigator, Evan Myers, MD, MPH. “We are hoping that this registry will help to answer important questions and, ultimately, enable collection of data on all women undergoing treatment for fibroids.”
THE DCRI AT A GLANCE

More than 1.2 MILLION patients enrolled

Partners around the World

North America
• Canadian VIGOUR Center – Edmonton, AL
• Canadian Heart Research Centre – Toronto, ON
• CSResearch – Cleveland, OH
• Harvard Clinical Research Institute – Boston, MA
• PERFUSE Study Group – Boston MA
• Population Health Research Institute – Hamilton, ON
• Stanford Center for Clinical Research – Palo Alto, CA
• TIMI Study Group – Boston, MA
• Colorado Prevention Center – Denver, CO
• Mayo Clinic – Rochester, MN

Europe
• Cardalysis – Rotterdam, NL
• Leuven Coordinating Centre – Leuven, BE
• Uppsala Clinical Research Center – Uppsala, SE
• French Alliance for Cardiovascular Clinical Trials – Paris, FR
• Diabetes Trial Unit – Oxford, UK

South America
• Brazilian Clinical Research Institute – São Paulo, BR
• Estudios Clínicos Latinoamérica – Buenos Aires, AR
• Trials Argentine Group Organization – Buenos Aires, AR

Asia-Pacific
• Medanta – Gurgaon, India
• South Australian Health and Medical Research Institute – Adelaide, AU
• The George Institute – Sydney, AU
• Singapore Clinical Research Institute – Singapore
Study Size
- Small: 27%
- Large: 18%
- Mega: 24%
- Medium: 31%

Study Population
- Adult: 89%
- Pre/neonatal: 1%
- Pediatric: 9%
- Geriatric: 1%

Study Phase
- Phase I: 5%
- Phase II: 11%
- Phase III: 48%
- Phase IV: 5%
- Registry: 6%
- Observational/Registry: 6%
- Other: 19%

Study Revenue Source
- Industry: 65%
- Government: 35%

Duke Health faculty members leveraged on every study: 200
Experienced employees: 1,200
Phase I–IV clinical trials and outcomes, comparative effectiveness, and implementation studies: 970+
Publications in peer-reviewed journals: 10,000+
Sites in 65 countries: 37,000
THERAPEUTIC AREAS

From data gathering to data sharing, the DCRI challenges traditional approaches to clinical research across the therapeutic spectrum, because we’ve made a commitment to do whatever is needed to find the answers patients need us to find. That requires us to push beyond the expected, look at things differently, and never be willing to accept an answer just because it’s the one that everyone else has come up with. At the DCRI, our faculty members are trailblazers who eagerly and passionately search for what lies ahead, because they know that’s where they’ll find the answers that lead to better care for patients around the world.

CARDIOVASCULAR
The world looks to the DCRI as the definitive leader in cardiovascular clinical research, science implementation, and education. We look to our practicing faculty, cutting-edge analytics, and operational expertise to address the spectrum of challenges through clinical research focused on improving the care of patients with cardiovascular disease.

Our cardiovascular expertise covers all research phases, from proof of concept studies to multinational late-phase trials. We also work with post-approval registries sponsored by industry, government, and professional societies. Most importantly, everything we learn is shared openly so that others can take our findings and build upon them, ensuring that the best answers to the hardest cardiovascular questions are found.

NEUROSCIENCES MEDICINE
From epilepsy to depression to Alzheimer’s, neurological conditions affect almost everyone. And people are desperately seeking solutions for themselves or someone they love. The Neurosciences Medicine (NSM) research program at the DCRI is dedicated to taking bold action to find these solutions. Driven by more than 40 psychiatry and neurology faculty, our program develops, conducts, and supports innovative phase I–IV clinical trials addressing neurological and psychiatric conditions for child, adolescent, adult, and geriatric patient populations.

PEDIATRICS
Our commitment to advance the scientific investigation of medical therapies in children begins at the bedside. We know firsthand the limits and risks of providing treatments based on evidence generated through studies carried out in adults. Through innovative design methods and data monitoring, our faculty is leading the world in expanding the impact of pediatric research.

INFECTIONOUS DISEASES
There’s no room for uncertainty in identifying infectious diseases and finding effective treatment solutions. Success requires the confidence that can only come with the experience derived from clinical practice and the deep understanding gained from repeatedly navigating the complexities of infectious disease research. This is the kind of confidence found at the DCRI. With an attentive network of key opinion leaders, site investigators, and faculty of practicing infectious disease physicians, we stand ready with insights and innovative research methods needed to understand and defeat infectious diseases.
GASTROINTESTINAL/HEPATOLOGY
Digestive disorders and diseases of the liver vary widely but share one common feature: the devastating impact they can have on a person's health and quality of life. In the DCRI's gastrointestinal (Gi) program, clinical and basic science experts come together to seek out bold and creative innovations in the treatment of these complex conditions. This partnership positions Duke University and the DCRI as one of the leading GI and hepatology research centers in the world, a distinction that can offer patients with GI and liver diseases new hope for better lives.

RESPIRATORY
For patients suffering from respiratory illnesses, every breath taken can be a struggle. At the DCRI, we're working with sponsors to apply new approaches to respiratory research—approaches that will lead to better and more effective therapies that offer both hope and relief.

Respiratory medicine at the DCRI is distinguished by world-class faculty leading cutting-edge programs in airway biology, environmental health sciences, and lung fibrosis. Our team has coordinated multicenter trials in respiratory diseases, including idiopathic pulmonary fibrosis and lung transplantation. Through Duke, we're connected to one of the largest and most successful lung transplant programs in North America.

To partner with the DCRI in respiratory research studies is to look beyond what's been done and push toward new and promising possibilities.

ORTHOPEDICS
While the DCRI is best known for its work in cardiology, we have been making great strides in expanding our impact and influence in other therapeutic areas to help improve patient care around the world. Our knowledge and experience in clinical research is now extended to the field of orthopedics.

Disorders of the musculoskeletal system are quite common, with almost every individual seeking medical care at some point during his or her life. Because of their frequency and interference with the ability to perform critical tasks of daily living, musculoskeletal disorders are a major determinant of health of both individuals and populations. The disease burden of musculoskeletal injury and arthritis alone represents an estimated 20 percent of healthcare expenditures, well ahead of cancer and cardiovascular disease. In fact, osteoarthritis alone is predicted to be the fourth-leading cause of disability by 2025. Despite the significant financial costs and health implications of musculoskeletal disease, there is little clinical research identifying population needs and trends and comparing outcomes of different treatment approaches.
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Fred Cobb, MD, Distinguished Professor of Medicine

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Reza Rostami
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Kristina Sigmon, MA
Director, Statistical Operations

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Matt Wilson, RN
Director, Clinical Events Classification — Safety Surveillance

Jamie Young
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Department of Medicine, Gastroenterology

Li-Tzy Wu, PhD, RN, ScD
Department of Psychiatry and Behavioral Sciences

FELLOWS

SECOND-YEAR FELLOWS
- Austin Chan, MD
- Meredith Clement, MD
- Daniel Friedman, MD
- Patricia Guimarães, MD
- Nancy Luo, MD
- Robert Olivo, MD
- Neha Pagidipati, MD, MPH
- Kishan Parikh, MD
- Abhinav Sharma, MD
- John Stanifer, MD, MSc
- Alice Wang, MD
- Tunde Yerokun, MD

FIRST-YEAR FELLOWS
- Andrew Ambrosy, MD
- Stephen Balevic, MD
- Emily Clausen, MD
- Morgan Cox, MD
- Samantha Dallefeld, MD
- Alex Fanaroff, MD
- Taku Inohara, MD, PhD
- Ruchir Karmali, MD
- Brystana Kaufman, MD
- Ajar Kochar, MD
- Melissa Makar, MD
- Aditya (Adi) Mandawat, MD
- John Mitchell, PhD
- Shruti Raja, MD
- Nazario Rivera Chaparro, MD
- Jay Shavadia, MMed, MRCP
- Tina Tailor, MD
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