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- New Faculty
- Executive Leadership
- Operational Leadership
The Duke Clinical Research Institute is dedicated to advancing clinical research through innovation, education, sharing knowledge, designing scientifically rigorous studies, and conducting operationally efficient clinical trials across multiple therapeutic areas. We conduct amazing clinical research, from the smallest pilot study to global megatrials. Our experience covers all phases of evaluation, from initial, proof-of-concept studies to multinational, late-phase trials, postapproval registries, and outcomes studies.

We embrace the concept that integration of biostatistical, clinical, site and data management, and project management expertise is essential for successful clinical research. Physician-investigators with extensive knowledge in many specialties provide critical leadership and input on study design to create more robust endpoints as well as more efficient, practical, and clinically relevant research. Our faculty and staff are devoted to understanding the causes, prevention, and treatment of human disease. The DCRI continues to lead the way in utilizing risk-based monitoring to ensure operational efficiency, subject protection, and the overall integrity of the data that will be used to make important decisions.

Our operational focus encourages innovation, quality, expertise, efficiency, and diversification of clinical trials. With increased emphasis on patient-centered and registry-based research, we are leading the push to implement personalized medicine as a way to develop effective therapies that reach patient populations sooner. Transformative research using electronic medical records and population screening allows us to more efficiently identify potential patients for enrollment, thus speeding the process of conducting pragmatic, meaningful, and efficient studies to discover answers sooner and share the knowledge gained from these models of trial conduct.

This report highlights a few of the projects in which we are integrating components of translational research—including genetic analysis, gene expression, advanced imaging, and immune monitoring—with clinical research, transforming the conduct of clinical trials and development of registries, bringing the promise of personalized medicine to reality, turning data into knowledge, and applying that knowledge to improve the lives of patients everywhere. It also illustrates how a thriving organization made up of creative and diverse individuals, learning from one another, can produce important and innovative discoveries that involve and extend the capacity of our international partners while improving the care and lives of people around the world. The future of research, discovery, and global health improvement is bright indeed.

Our Mission

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

The Duke Clinical Research Institute is dedicated to advancing clinical research through innovation, education, sharing knowledge, designing scientifically rigorous studies, and conducting operationally efficient clinical trials across multiple therapeutic areas. We conduct amazing clinical research, from the smallest pilot study to global megatrials. Our experience covers all phases of evaluation, from initial, proof-of-concept studies to multinational, late-phase trials, postapproval registries, and outcomes studies.

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

Since its inception in 1969, the Duke Databank and the DCRI have:

- Conducted studies at more than 37,500 sites in 65 countries
- Completed more than 970 phase I-IV clinical trials, outcomes studies, and comparative effectiveness analyses
- Enrolled more than 1.2 million patients in DCRI studies
- Published more than 8,300 papers in peer-reviewed journals

The DCRI:

- Is the largest academic research organization in the world, employing more than 1,100 employees, including more than 200 faculty
- Developed national and international education programs
- Coordinates projects in 19 therapeutic areas

In 2013, the DCRI:

- Managed five national registries comprising 1,003,000 patients at 3,532 inpatient and outpatient sites
- Managed or monitored six megatrials across 4,000 sites, enrolling more than 250,000 patients in more than 50 countries
- Provided site management and monitoring services for studies comprising 1,130 unique investigators across 970 unique sites, with more than 8,000 subjects enrolled
Core Capabilities

As the world’s largest academic research organization, we combine the clinical expertise and academic leadership of a premier teaching hospital with the full-service operational capabilities of a major contract research organization.

Our leaders are some of the world’s foremost authorities on the science, study, and application of clinical research, making them uniquely positioned to understand the operational, financial, and regulatory implications of numerous project designs.

The close integration of clinical faculty and operational experts into the design, conduct, and interpretation of clinical trials contributes to the DCRI’s unique success. Our faculty are practicing physicians in these specialties, applying cutting-edge research in their own patient practices. Their informed input on study design and interpretation creates more efficient, practical, and credible research.

- **Advanced biomarkers**
  - Integrates the characterization of disease into caring for patients and understanding how they respond to novel agents

- **Biostatistics**
  - Full-service statistical operations for multicenter trials
  - Analyses for secondary interests
  - Assistance with interpretation of results

- **Clinical events classification (CEC) and adjudication/safety surveillance**
  - Expedites adverse event reporting to provide trial endpoint data
  - Integrates CEC and safety surveillance services for streamlined workflow and processing

- **Clinical helpline**
  - Centralized, rapid access to physicians with expertise in diseases and clinical trial protocols

- **Data management**
  - Full data collection and query resolution
  - Expertise with multiple clinical data management systems on a full range of studies in all phases and therapeutic areas

- **Electrocardiography (ECG)**
  - A unique blend of ECG analyses, platforms, and software to provide the gold standard in ST recovery analysis, arrhythmia diagnosis, and cardiac safety monitoring

- **Global health outreach**
  - Coordinates studies through an integrated, global, academic collaborative network to conduct and manage global trials, allowing for maximum creativity and flexibility in protocol development, site start-up activities, and regulatory submissions

- **Imaging**
  - Experienced oversight and independent management of all imaging for all phases of clinical trials

- **Medical communications**
  - Newsletters and trial-related communications
  - Publications management and research results dissemination
  - Patient recruitment and retention tools

- **Pharmacometrics**
  - Applied pharmacometrics and academic leadership to improve quality and efficiency in all phases of drug development to support programs from industry, government, and independent investigators

- **Outcomes, health outcomes, and quality-of-life studies**
  - Collection and analysis of data for clinical research, the conduct of comparative effectiveness studies, and the development of decision models

- **Project leadership**
  - Operational partners for the principal investigator for each project
  - Site contract and payment negotiation
  - Site collaboration and communication
  - Coordination of activities with other coordinating centers, service providers, and subcontractors

- **GI/PI educational interventions**
  - Wide array of quality and performance improvement educational offerings for healthcare, pharmaceutical, and device industry professionals in both the certified and non-certified space

- **Regulatory services and medical writing**
  - Regulatory document collection and review
  - Protocol and clinical study report writing services
  - Drug and device clinical trial application preparation, regulatory filing, and maintenance

- **Site management and clinical monitoring**
  - Overall project and site management throughout all phases of the study
  - Site/investigator selection, qualification, and regulatory compliance
  - Investigative site start-up and training
  - Good Clinical Practice-trained monitors

- **Thought leadership**
  - Authorities on the science, study, and application of clinical research
  - Leaders who develop ideas and protocols for clinical research projects designed to maximize efficiencies
  - Influencers who sit on clinical guideline committees and U.S. Food and Drug Administration (FDA) and National Institutes of Health (NIH) panels, hold leadership roles in specialty societies, serve as journal editors, and prolifically publish original clinical research articles
Manuscript Productivity

Published Papers

- 1997: 159
- 1998: 170
- 1999: 232
- 2000: 258
- 2001: 280
- 2002: 327
- 2003: 483
- 2004: 490
- 2005: 538
- 2006: 511
- 2007: 621
- 2008: 653
- 2009: 784
- 2010: 939
- 2011: 784
- 2012: 948

High impact manuscripts published in journals with an impact factor greater than 10.0 (<2% of all indexed journals)

- 1997: 5
- 1998: 11
- 1999: 11
- 2000: 35
- 2001: 11
- 2002: 8
- 2003: 99
- 2004: 12
- 2005: 2
- 2006: 4
- 2007: 7
- 2008: 16
- 2009: 4
- 2010: 194
- 2011: 39
- 2012: 39

Trials Experience by Phase and Size

- Phase I: 3%
- Phase II: 12%
- Phase III: 20%
- Phase IV: 18%
- Other/Registry: 20%

- Small (<1,000 patients): 45%
- Medium (1,000–4,999 patients): 18%
- Large (5,000–10,000 patients): 6%
- Mega (>15,000 patients): 27%

Project Portfolio: 1 July 2013–30 June 2014

- Commercial: 62.3%
- Government: 36.7%
What Sets Us Apart?

Building on more than 40 years of experience in innovative approaches to analyze the impact of various therapies on patient outcomes, the DCRI offers full clinical trial services as well as substantial resources dedicated to outcomes research and assessments, clinical database design and management, and medical education.

Our faculty are practicing physicians in these specialties, applying innovative research findings in their own patient care. Their informed input on study design and interpretation creates more efficient, practical, and compelling research.

The differentiators?

- We are the world’s largest academic research organization, distinguished by our medical and scientific knowledge combined with cutting-edge statistics and operational expertise.
- We are driven by our desire to both define new knowledge and speed adoption of this knowledge into routine clinical practice.
- We focus strongly on disseminating research results, publishing more than 600 articles per year in peer-reviewed journals. Their effects on patient care and the state of medicine are felt around the world.
- We believe fully in achieving our goals through collaboration.
- We are committed to constantly evolving and improving.
Advances in technology and healthcare knowledge in recent years have led to an increase in individually designed patient-centered treatment solutions. Through advances in diagnostic capabilities and the use of linked electronic health records (EHRs), physicians now have better access to their patients’ overall medical histories and can more quickly assess their future medical needs. They can therefore more accurately make treatment recommendations that address their patients’ specific circumstances. This personalized approach to medicine crosses all therapeutic areas and has been a focus for many of the research projects conducted at the DCRI.

**On Target**

**Targeting genes to improve treatment of hepatitis C**

Clinicians have long suspected that if they could unlock the mysteries within genes, they would have answers to curing or treating countless diseases that remain resistant to current therapies. In a revolutionary step towards achieving this goal, in May 2013, clinicians from the DCRI and around the world announced the results of the first clinical trial to successfully use gene-targeting therapy for the treatment of hepatitis C (HCV) in humans.

DNA and RNA are biological molecules that are necessary for life in all organisms. While DNA is used for the long-term storage of genetic information, RNA’s role is to transfer and regulate this code within a cell to control protein production. In this trial, clinicians specifically sought to manipulate small, noncoding RNA molecules called microRNA (miRNA) through a process called antisense therapy. When implementing...

**Keyur Patel, MD**

Associate Professor of Medicine, Gastroenterology

Continued on following page
On Target (cont.)

antisense therapy, clinicians develop a complementary genetic strand that will bind to a specific genetic sequence and influence its functionality.

According to the DCRI’s Keyur Patel, MD, this recent antisense therapy trial started with the identification of the miRNA molecule miR-122. Patel explained that miR-122 makes up around 70 percent of the miRNA found in liver cells. Researchers discovered, through animal testing, that these molecules play a crucial role in the spread of HCV’s genetic materials within the liver. With this discovery, the biopharmaceutical company Santaris Pharma has developed a compound called miravirsen, which targets and deactivates miR-122. The DCRI joined the project in 2010 to develop safety monitoring protocols and data monitoring procedures for human trials.

The results of the trial, the first ever in humans to target miRNA in a disease state, showed clearly that the greater the dosage of miravirsen, the more significant the decline in HCV. Perhaps most important for this trial, however, is the fact that the therapy appears to have no significant short-term safety risks. This finding, said Patel, could potentially revolutionize not only the way HCV patients are treated, but also could provide relief for patients suffering from autoimmune disorders, cardiovascular disease, cancer, and countless other ailments.

“The far-reaching implications of these findings are huge,” said Patel. “In the future, we can extend this treatment method beyond HCV. The fact that this compound or similar technologies can target microRNA in a safe way means it will open up potential therapies for many disease states.”


First in Class

The Duke Clinical Research Unit is the DCRI’s state-of-the-art early-phase unit

The DCRI’s early-phase unit, Duke Clinical Research Unit (DCRU), is one of just a handful of state-of-the-art hospital-based early-phase research units in the country. The DCRU enables Duke investigators to conduct proof-of-concept research, including efforts to identify and validate novel biomarkers, while leveraging advances at the forefront of technology. In addition to early-stage investigator-initiated studies and NIH-funded research, Duke researchers also work with pharmaceutical, biotechnology, and medical device companies to generate data.

DCRU researchers have more than 20 years of early-phase clinical trial experience and have successfully conducted more than 150 early-phase studies, including 80 phase I studies. Their experience, support systems, and infrastructure enable the DCRU to provide the highest level of program management and services for early-phase clinical trials, including quality processes, accurate reporting, and regulatory expertise. Expert teams are able to advance a product through development and approval on time and within a sponsor’s budget.

Collaborating with similar ultra-modern, early-phase units, DCRU works with the recently established Medanta Duke Research Institute (MDRI) in New Delhi, India, and the early-phase research unit in Singapore General Hospital through a collaboration with the Duke-National University of Singapore Graduate Medical School. Building on the strength of Duke’s thought leadership, therapeutic expertise, patient base, and access to the latest technologies, the DCRU is a critical component of the DCRI’s efforts to speedily translate new laboratory discoveries into treatments for patients.

Barry Mangum, PharmD
Associate Professor of Medicine, Clinical Pharmacology
Director of Clinical Pharmacology, Duke Clinical Research Unit
GUIDE-IT: Personalizing approaches for better heart failure care

In GUIDE-IT (Guiding Evidence Based Therapy Using Biomarker Intensified Treatment), led by Michael Felker, MD, MHS, researchers are examining the biomarker N-terminal prohormone of brain natriuretic peptide (NT-proBNP, a blood marker of disease severity in heart failure). The idea is to compare standard care versus a strategy of titrating therapy to achieve a desired level of NT-proBNP that has been associated with improved outcomes.

The standard drug regimens for heart failure patients have grown in complexity as new therapies have been found to be effective. The ongoing validation of biomarkers that provide objective evidence of a patient’s disease state has given clinicians a better understanding of how treatments might be personalized to be the most effective for individual patients.

“The idea is to use a personalized approach to find the best combination of drugs and therapies that improve outcomes and allow patients to live longer,” said Felker. “We are trying to apply the same level of rigor as would apply to a new drug study to test a strategy for heart failure care.”

Michael Felker, MD, MHS
Associate Professor of Medicine, Cardiology

Molecular testing to evaluate and predict treatment options

The Endocrine Neoplasia Health Services Research Group was formed in January of 2013 when Julie Ann Sosa, MD, MA, arrived at Duke to head the Section of Endocrine Surgery in the Department of Surgery and the Endocrine Neoplasia Diseases Group at the DCRI and the Duke Cancer Institute (DCI). The research group is intended to be transdisciplinary, with members from the DCRI; the DCI; the Center for Clinical and Genetic Economics; and the endocrine surgery, endocrinology, and biostatistics departments in the Duke School of Medicine.

Research is focused in several areas, including understanding the application of molecular testing in the evaluation of the indeterminate thyroid nodule and predictors of its diffusion as a novel technology in the United States, along with patient and physician preferences surrounding its application. This has important public health implications, since between 5 and 50 percent of Americans have a thyroid nodule, and nearly 30 percent of those undergoing biopsy will have indeterminate results.

Julie Ann Sosa, MD, MA, FACS
Professor of Surgery
DCRI Endocrine Neoplasia Disease Program
Monitoring is a significant part of clinical trials, but there is often little science to drive individual trial-monitoring plans. The DCRI, however, has found a way to leverage existing data into an effective monitoring strategy. Monitoring refers to the methods used by sponsors and clinical research organizations (CROs) to oversee the conduct of and reporting of data from clinical trials. This oversight includes communication with the investigators and study site staff, review of the study site’s processes, procedures, and records; and verification of the accuracy of data submitted to the sponsor. The DCRI has been a leader in this field, utilizing risk-based monitoring in every large trial since GUSTO-I in 1990.

“This has always been our standard approach on the international megatrials managed by the DCRI, but more recently it has been incorporated into smaller phase-II and phase-III trials,” said John Alexander, MD, MHS, director of cardiovascular research at the DCRI.

Studies have found that risk-based monitoring is actually more likely than routine visits to clinical sites and full data verification to ensure subject protection and overall study quality. A recent review of onsite monitoring findings collected during a multicenter international trial determined that centralized monitoring activities could have identified more than 90 percent of the findings identified during onsite monitoring visits. Risk-based monitoring is important because it does not monitor everything equally but rather monitors things that are truly important to trial safety and efficiency, Alexander said.

“We should only be monitoring when there is risk to things we care about: the protection of human subjects and the integrity of the data that will be used to make important decisions,” said Alexander.

Renewable Resources

RENEW: Offering hope to patients with heart disease

Routine activities can be challenging for people with refractory angina, as they typically experience angina-related chest pains daily and find their normal activities severely limited by the pain. Those with advanced ischemic heart disease are often already taking as much medication as they can tolerate and have to learn to live with their symptoms.

A new therapy currently being tested at the DCRI could offer hope to these patients. Researchers conducting the RENEW (Efficacy and Safety of Targeted Intramyocardial Delivery of Auto CD34+ Stem Cells for Improving Exercise Capacity in Subjects With Refractory Angina) trial are testing the use of autologous stem cells (CD34+ cells) to create individualized treatments for patients with advanced ischemic heart disease.

The DCRI is leading the design and implementation of this phase III trial to develop a treatment that could become the first stem cell therapy to be approved for managing this disease. If the treatment benefits observed in the phase II trial are confirmed in the RENEW trial, the treatment, which uses a patient’s own cells, could significantly improve quality of life for these patients and allow them to be more active.

Thomas J. Povsic, MD, PhD
Associate Professor of Medicine, Cardiology

(Not So) Risky Business

The DCRI leads the way with risk-based monitoring of its clinical trials

Monitoring is a significant part of clinical trials, but there is often little science to drive individual trial-monitoring plans. The DCRI, however, has found a way to leverage existing data into an effective monitoring strategy.

Monitoring refers to the methods used by sponsors and clinical research organizations (CROs) to oversee the conduct of and reporting of data from clinical trials. This oversight includes communication with the investigators and study site staff; review of the study site’s processes, procedures, and records; and verification of the accuracy of data submitted to the sponsor.

Effective monitoring of clinical investigations by sponsors is critical to the protection of human subjects and the conduct of high-quality studies. However, the sheer size and scope of many clinical trials make in-person inspections of every site and complete verification of every piece of data impractical. For that reason, many sponsors and CROs are now turning to risk-based monitoring. This approach, which is based on draft guidelines released by the FDA, incorporates centralized monitoring practices to ensure the quality of clinical trial data. The DCRI has been a leader in this field, utilizing risk-based monitoring in every large trial since GUSTO-I in 1990.

John H. Alexander, MD, MHS, FACC
Faculty Associate Director; Director, DCRI CV Research
Associate Professor of Medicine, Cardiology
Measure by Measure

Personalizing drug doses for the most vulnerable patients

The Pediatric Trials Network (PTN), led by the DCRI’s Daniel Benjamin, MD, PhD, MPH, is an alliance of clinical research sites located around the United States that are cooperating in the design and conduct of pediatric clinical trials to improve health care for the youngest patients.

Children are not simply “little adults” who respond to drugs according to scale. Rather, developing organs and changes in metabolism throughout infancy and childhood affect how drugs are processed by immature or maturing bodies. This often results in guesswork, giving a “ballpark dose” rather than dosing based on evidence-based science. “Ballparks are great to communicate budget estimates, but not therapeutics,” Benjamin said.

To fill this gap, the PTN is studying the formulation, dosing, efficacy, and safety of drugs, as well as the development of medical devices, used in pediatric patients. Data collected from PTN trials will help regulators to revise drug labels for safer and more effective use in infants and children.

For example, the PTN recently completed an open-label study to describe the pharmacokinetics of acyclovir in premature infants. Acyclovir is a drug used to treat herpes simplex virus (HSV) infections in infants. HSV infection in children younger than 6 months can be extremely dangerous, often resulting in death or profound intellectual disability. This study examined acyclovir levels in the blood of premature and full-term infants who received the drug to treat a suspected HSV infection. Investigators found that infant maturity as measured by post-menstrual age is associated with the body’s ability to clear the drug. The investigators determined that less frequent dosing is needed in younger infants to achieve optimal therapeutic benefit.

Daniel K. Benjamin, Jr., MD, PhD, MPH
Faculty Associate Director
Kiser-Arena Distinguished Professor of Pediatrics

“The far-reaching implications of these findings are huge.”

— Keyur Patel, MD
Targeting genes to improve treatment of hepatitis C
INNOVATION IN RESEARCH AND OPERATIONS

To produce meaningful and impactful clinical research, it is vital to embrace innovation on both the ideological and methodological levels across a diversified portfolio of therapeutic areas. Key to the DCRI’s success is the ability to find new and more effective approaches to treating disease, improving patient care, and processing medical data. The DCRI’s thought leaders often provide insights that forever transform standards for patient care and clinical research best practices.

Bug Hunt

Reducing the public health threat of drug-resistant bacteria

In an effort to combat the increasing problem of antibacterial resistance, investigators from Duke Medicine and the University of California San Francisco (UCSF) have been allocated up to $62 million to form a national research program. The goal, which will be executed through funding provided by the NIH’s National Institute of Allergy and Infectious Diseases, is to establish an Antibacterial Resistance Leadership Group (ARLG) to prioritize, design, and execute clinical studies that will reduce the public health threat of multidrug-resistant pathogenic bacteria.

Since the 1940s, clinicians have successfully used antibacterial treatments to inhibit the growth of pathogenic bacteria, but in recent decades, many previously effective antibacterial
Bug Hunt (cont.)

medications have become less effective. The problem lies in bacteria’s innate ability to mutate its genetic makeup in response to the antibacterial medication’s targeted attacks. Overuse of antibacterial treatments has led to increased resistance in pathogenic bacteria and has forced physicians to turn to alternative medications, which are often more expensive and sometimes less effective and more toxic to patients.

The DCRI helps run the ARLG, which works under the centralized leadership of an executive committee and two principal investigators. The DCRI’s Vance Fowler, MD, MHS, will focus primarily on operations; Henry ‘Chip’ Chambers, MD, of UCSF will focus largely on the scientific agenda. The DCRI is uniquely qualified to house the ARLG, Fowler said, because of its experience with other large research partnerships.

“You have to have the platform to conduct complex clinical trials over multiple countries, and perhaps more than any other institute in the country, the DCRI is poised to do that,” Fowler said. “The track record that the DCRI brings to the table for NIH-funded networks is unprecedented.”

A Different Approach

Breaking new ground in cardiac research focused on women

The Study of Access Site for Enhancement of Percutaneous Coronary Intervention for Women (SAFE-PCI for Women) trial, led by Sunil Rao, MD, found that using the radial approach (via the wrist) over the femoral approach (via the groin) significantly reduced bleeding or vascular complications for female patients undergoing cardiac catheterization or percutaneous coronary intervention (PCI). Since its start in 2011, SAFE-PCI for Women has been breaking new ground in the United States both in its focus on radial catheterization, which is commonly used in Europe but not as often in the United States, and also by targeting female patients, who have traditionally made up less than 30 percent of participants in previous trials and have a higher bleeding risk. The findings are particularly significant because, until now, there have been little viable data on women with ischemic heart disease.

“Our findings are consistent with other data that have been gathered on lower-risk patients,” said Rao. “The results suggest that an initial strategy of wrist access is reasonable and may in fact be preferred in women, with the recognition that a portion of them will need to be converted to the traditional leg access.”

SAFE-PCI for Women was also a proof-of-concept study for the first use of the National Cardiovascular Research Infrastructure (NCRI). The NCRI is a partnership between the DCRI and the American College of Cardiology Foundation to develop a clinical investigator network based on the data collection activities of the National Cardiovascular Data Registry’s CathPCI Registry. Through this infrastructure, the DCRI was able to provide sites with resources for recruitment, education, data collection, data standards, and guideline development, resulting in a more streamlined site enrollment process.


Sunil Rao, MD
Associate Professor of Medicine, Cardiology
Around the World

The DCRI conducts two global studies of diabetes medications

The DCRI is currently investigating the effects of diabetes medication with two global trials.

The Exenatide Study of Cardiovascular Event Lowering (EXSCEL) trial is designed to test the superiority of the drug exenatide in addition to current care for glycemic control versus current care alone on cardiovascular-related outcomes in patients with type 2 diabetes. In working on this study, the DCRI became the first academic research organization to manage a trial mandated by the FDA under the new guidelines for post-marketing safety surveillance for drugs in diabetes.

Exenatide, a glucagon-like peptide-1 (GLP-1) agonist, has already been shown to result in improved glycemic control, an improved cardiovascular risk profile, and weight loss. This trial, however, is one of the first studies to examine the long-term effects of exenatide on rates of mortality, myocardial infarction, and stroke. GLP-1 agonist drugs like exenatide have novel properties beyond controlling glucose levels, but their effects have not yet been fully explored.

The DCRI provides global project oversight for EXSCEL, in collaboration with the Diabetes Trial Unit at Oxford University. Our operations group is responsible for North American site management and monitoring, global data management, statistics safety surveillance, and clinical event adjudication. In addition, the DCRI coordinates a health economics study, and the collection and management of a biorepository for a subset of EXSCEL patients.

Another study, the Trial to Evaluate Cardiovascular Outcomes after Treatment with Sitagliptin (TECOS), aims to assess the risk of heart attack and stroke in patients with type 2 diabetes receiving the drug sitagliptin in addition to their usual care. Adults with diabetes are two to four times more likely to have heart disease or a stroke than adults without diabetes. In addition, concerns about the cardiovascular safety of diabetes medications have further complicated diabetes management.

The trial began in 2008 and has enrolled more than 14,700 people aged 50 years or older with cardiovascular disease and inadequately controlled type 2 diabetes from 39 countries. TECOS researchers conducted follow-up visits with each of these patients at four-month intervals during the first year and then twice yearly, with additional interviews conducted by telephone. Follow-up will continue until 1,300 confirmed primary cardiovascular endpoint events occur.

A primary strength of TECOS is the length of time each patient received treatment and follow-up care, said the DCRI’s Jennifer Green, MD.

“The patients will have been in the trial and on their treatment assignment longer than we’ve seen in similar trials,” she said. “This will contribute in a meaningful way to our assessment of the safety and perhaps the potential benefits of this treatment.”

Jennifer B. Green, MD
Associate Professor of Medicine, Endocrinology and Metabolism

Adaptive Technology

Digitalized informed consent aids patient understanding

Patients being recruited to participate in a clinical study often lack an understanding of the study’s objectives, and therefore are not sure what they are consenting to do as a potential participant in the study. In addition, communicating the medical risks and procedural specificities of a clinical trial in a way that is clear to enrolling patients is often difficult and time-consuming, and can hinder a patient’s willingness to participate. However, a recent initiative within the DCRI to digitize the informed consent process could lead to a more intuitive, dynamic, and efficient process, and thus improve the patient’s understanding of the goals of the study.

In the traditional study consenting process, patients receive a lengthy document that they must read and sign; however, there are no measures currently in place to ensure that patients clearly understand the trial in which they are agreeing to participate. The challenge, explained Zubin Eapen, MD, director of education IT innovations, is how to transition from a dense, paper-based consent form that patients don’t receive a signed copy of the consent as well as the information needed to easily withdraw consent should they decide to do so.

Taking advantage of the latest technologies allows for a more adaptable system that is easily tailored to address the needs of a research study and the targeted patient groups. The goal is to enable a “re-livable” consenting process whereby patients can access the video instructions as often as needed to aid understanding. This interaction reduces the burden on the study coordinators to walk through the entire explanation of the study with the patient multiple times.

The concise sections and interactivity of the system allow clinicians to gather metrics to further improve the enrollment process. With this completely digital process, once a patient has completed the consent process, the system automatically generates the necessary regulatory documents for inclusion in the electronic health record. The patient receives a signed copy of the consent as well as the information needed to easily withdraw consent should they decide to do so.

Zubin J. Eapen, MD
Assistant Professor of Medicine, Cardiology
Expert Opinion

Creating opportunities for critical conversations

The DCRI convenes think tanks across a variety of topics to provide an opportunity for leading academic, industry, and government experts in clinical research to discuss alternative approaches to study design and trial conduct, as well as policy and regulatory issues related to drug or device development and use in routine clinical practice. Agendas focus on the essentials (e.g., agreeing on definitions, current status and supporting literature, a review of recommendations) with time for discussion during the program.

Attendees participate in thought-provoking debate from a variety of perspectives, build collaborative relationships, and, in some cases, develop alliances to pursue specific issues highlighted in the think tank. Often the discussions and approved recommendations at the think tanks result in the development and publication of white papers. For instance, the Medication Adherence Alliance was formed after the initial think tank, and has subsequently submitted three manuscripts for publication.

Over the past five years, 14 think tanks have convened, resulting in papers published or in progress from each of these critical conversations. Recent DCRI think tanks include Transforming Professional Medical Education, Resistant Hypertension, Cancer and Thrombosis, Medication Adherence, Statin Intolerance, and Rescuing Clinical Trials in the U.S.


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

Picture Perfect

Providing imaging quality control measures to inform results

The research conducted by the DCRI allows for transformative changes across many different therapeutic areas. In a recent study led by Pamela Douglas, MD, director of the DCRI Imaging Program, researchers developed a set of processes to optimize the acquisition and analysis of echocardiograms for the Placement of Aortic Transcatheter Valves (PARTNER) I trial of percutaneous aortic valve replacement for aortic stenosis. Upon reviewing the images captured during PARTNER I, Douglas and her colleagues concluded that it is possible to implement stringent quality control measures in clinical trials to ensure high image measurability and reproducibility. Given that these images play an outsized role in trials, such as PARTNER I, where the results are based directly on echocardiographic data, the existing protocols and processes should be widely adopted for future studies.


Going Global

Largest study to date for PAD patients features collaboration among diverse specialties

The EUCLID (Examining Use of Ticagrelor in PAD) trial recently completed patient enrollment approximately four months ahead of schedule, randomizing more than 13,500 patients with peripheral artery disease (PAD).

PAD causes the arteries in legs to narrow, restricting blood flow to the leg muscles. It is typically caused by a buildup of plaque in the arteries, and symptoms of PAD likely mean that a person has plaque buildup in other areas of the body. Patients with PAD are at greater risk for heart attack and stroke.

EUCLID is designed to evaluate the effects of ticagrelor compared with clopidogrel on cardiovascular events and safety in patients with PAD. Clopidogrel is typically used to treat PAD by preventing dangerous blood clots. Ticagrelor is currently not approved for the treatment of patients with PAD. Patients in the study will be randomized to receive daily doses of ticagrelor or clopidogrel, and the study team will follow them for three or four years.

“This is an often overlooked population of patients,” said Manesh Patel, MD, the DCRI’s lead investigator for EUCLID and chair of the study’s Global Steering Committee. “This is the largest trial aimed at patients with PAD to date."

EUCLID is part of the long-term research program, PARTHENON, funded by AstraZeneca. PARTHENON leaders plan to eventually study the impact of ticagrelor in more than 50,000 patients worldwide with different cardiovascular diseases.

William Hiatt, MD, of the University of Colorado School of Medicine, and Professor Gerry Fowkes of the University of Edinburgh in the United Kingdom are the co-principal investigators. CPC Clinical Research, affiliated with the University of Colorado, and the DCRI are partners in the EUCLID study.

“The unique aspect of this study is the collaboration between many different specialists, including vascular surgeons, vascular medicine physicians, cardiologists, and general medicine physicians,” Patel said. “We hope that this trial will increase awareness of this significant disease."

Patient-minded

Putting patients with familial hypercholesterolemia in the driver’s seat of their care

A new national registry, Cascade screening for Awareness and Detection of Familial Hypercholesterolemia (CASCADE-FH), seeks to identify people with familial hypercholesterolemia (FH) and help prevent serious cardiac events in this underdiagnosed and undertreated population. CASCADE-FH was designed with the patient in mind to make it easy to enroll, share information with clinicians, and identify other patients. People can enroll in the registry through participating clinics, or they can quickly enroll online themselves.

Patients who participate in the registry will receive regular education about the importance of maintaining their prescribed medications and treatments and will be notified about clinical trials that might be of interest.

FH is an inherited disorder that can be life-threatening if patients don’t receive preventive care, but 90 percent of people who have FH have not been diagnosed. The registry combines data entered from both physicians and patients; information on clinical care and quality-of-life measures will be collected on a long-term, ongoing basis. Patients will be empowered to better manage their own care and will be encouraged to have family members screened for the disease. Data from the registry will drive new clinical research and improve gaps in knowledge.

“There are many treatments available that would help patients with FH,” said Emily O’Brien, PhD, one of the co-investigators for the study and whose mother has the disease. “Once people are aware that they have the disease, their doctors can direct them to the appropriate treatments. The registry will allow us to track the real-world effects of these therapies, not just the clinical outcomes, but also the patient’s side effects and quality of life. This will help us develop best practices for treating these patients.”
A Breath of Fresh Air

PFF Registry: Building a knowledge center of research on pulmonary fibrosis

The DCRI’s Pulmonary Research group is engaged in start-up activities to support two novel US-based registries for interstitial lung disease. Last year, the Pulmonary Fibrosis Foundation (PFF) chose the DCRI to serve as the data coordinating center for the newly launched PFF Patient Registry. The registry will eventually be the largest database of pulmonary fibrosis (PF) patient records with the furthest demographic reach in the country. It will provide data essential for improving understanding of the epidemiology, incidence, prevalence, natural history, and other clinical characteristics of PF. The registry will use consistent data-gathering methodology so that the information obtained will be useful to all clinicians and researchers seeking to better understand the disease and develop new therapies for PF.

“We are proud to be a central part of such an important initiative,” said DCRI Director Eric Peterson, MD, MPH. “The PFF Patient Registry extends the DCRI’s commitment to PF research. We are pleased to be part of a national effort to collect data that is often critical for developing more effective treatments for PF.”

The DCRI’s Scott Palmer, MD, is also spearheading the creation of the Idiopathic Pulmonary Fibrosis Prospective Outcomes Registry. This registry will collect data on the strategies used to achieve a diagnosis of idiopathic pulmonary fibrosis (IPF) and the treatment and management efforts applied throughout study follow-up, clinical outcome events, and patient-reported outcomes data. Researchers will also gather blood specimens periodically throughout the study for use in future research efforts.

Scott M. Palmer, Jr., MD
Associate Professor of Medicine, Pulmonary, Allergy, and Critical Care Medicine
Director, DCRI Pulmonary Research

—we are proud to be a central part of such an important initiative."

— Eric Peterson, MD, MPH

PFF Registry: Building a knowledge center of research on pulmonary fibrosis
TURNING DATA INTO KNOWLEDGE

One of the biggest dilemmas in clinical care, and a main driver of clinical research, is the uncertainty about the right treatment to use for a particular patient. Patients, their families, and their providers try to make the most informed decisions possible, but clear answers aren’t always obvious. Making trials easier and faster to conduct, deploying innovative tools to monitor treatment activity, and developing models to test best practices all contribute to getting meaningful data into the hands of providers sooner, enabling the care team to make the best decisions about appropriate treatment options.

Model Behavior

Creating data models to develop best practices

The DCRI’s Ziad Gellad, MD, MPH, is partnering with Javad Taheri, PhD, an industrial engineer from NC State University, to use discrete event simulation modeling to improve the efficiency of hospital-based gastrointestinal (GI) endoscopy units. The researchers hope to produce a set of recommendations related to best practices and changes that would result in maximum efficiency, improved patient satisfaction, and a better understanding of this healthcare delivery system.

Discrete event simulation is an operations research methodology that has been used in manufacturing for many years to design and analyze complex systems and predict the effect of changes on that system. Gellad explained that it is often hard for one person within the system to understand how the larger process works.

“We usually focus on a specific task at hand and don’t often think how our actions could affect someone further down the line,” he said. “These models will allow researchers to step back from the minute details of the process and look at the whole system.”

Ziad Gellad, MD, MPH
Assistant Professor of Medicine, Gastroenterology
Guiding Lights

DCRI researchers study how new guidelines will affect patients with hypertension and high cholesterol

Two recent studies by DCRI and Duke researchers illustrate how new guidelines for physicians could affect the lives of millions of Americans.

A recent analysis by the DCRI’s Ann Marie Navar-Boggan, MD, PhD, and Michael Pencina, PhD, in collaboration with researchers at McGill University, found that new guidelines that ease the recommended blood pressure goals could result in 5.8 million U.S. adults no longer needing hypertension medication.

The findings are the first peer-reviewed analysis to quantify the impact of guidelines announced in February 2014 by the Eighth Joint National Committee. In a divisive move, the committee relaxed the blood pressure goal in adults 60 years and older to 150/90, instead of the previous goal of 140/90. Blood pressure goals were also eased for adults with diabetes and kidney disease.

According to the study, one in four adults over the age of 60 is currently being treated for high blood pressure and meeting the stricter targets set by previous guidelines.

“This study reinforces how many Americans with hypertension fall into the treatment ‘gray zone’ where we don’t know how aggressively to treat and where we urgently need to conduct more research” said Eric Peterson, MD, MPH, director of the DCRI.

Another study by DCRI researchers found that revised guidelines for using statins to treat high cholesterol and prevent cardiovascular disease are projected to result in 12.8 million more U.S. adults taking the drugs, most of whom would be people older than 60.

The findings for the first time quantify the impact of the American Heart Association’s new guidelines, which were issued in November 2013 and generated both controversy and speculation about who should be given a prescription for statins.

“We sought to do a principled, scientific study to try to answer how the new guidelines might affect statin use, particularly as they focused eligibility on patients with an increased risk of developing cardiovascular disease,” said lead author Michael Pencina, PhD, director of biostatistics at the DCRI.

“By our estimate, there might be an uptake in usage as a result of the guidelines, from 43.2 million people to 56 million, which is nearly half of the U.S. population between the ages of 40 and 75.”

Those most affected by the new recommendations are older men who are not on statins and do not have cardiovascular disease. Under the earlier guidelines, about 30.4 percent of this group of men between the ages of 60–75 were recommended for statin use. With the new guidelines, 87.4 percent of these men would be candidates for the therapy. Similarly for healthy women in this age group, the percentage for preventive statin use is projected to rise from 21.2 percent to 53.6 percent.

Dynamic Data

Identifying more specific methods of liver injury prevention and treatment

For the past decade, the DCRI has served as the data coordinating center for the National Institute of Diabetes and Digestive and Kidney Diseases’ Drug Induced Liver Injury Network (DILIN). Over time, the data collection and statistical processing capabilities of the DCRI have continued to expand and diversify. Paper data collection systems have now moved to electronic data capture platforms, expediting the data analysis process and providing more accurate results. DILIN was originally established in 2003 to study drug-induced liver injuries. The network has recently been renewed for another five years with Huiman Barnhart, PhD, MA, continuing to serve as the principal investigator. Barnhart explained that in this third iteration, the network will focus on patients with more acute liver damage. Investigators hope that by collecting samples closer to the time of the liver injury, they will be able to better identify causality. This knowledge can then be used to develop specific methods of prevention and treatment.

Huiman Barnhart, PhD, MA
Professor of Biostatistics and Bioinformatics


Healthy Hearts

Studying new therapies in real-world practice

The TRANSLATE-ACS (Treatment with ADP Receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events after Acute Coronary Syndrome) study, led by Tracy Wang, MD, MHS, MSc, and DCRI Director Eric Peterson, MD, MPH, examines the treatment and long-term outcomes of contemporary patients with myocardial infarction (MI) managed with percutaneous coronary intervention (PCI).

TRANSLATE-ACS enrolled and followed more than 12,000 patients with MI from 233 hospitals in the United States, making it the largest longitudinal registry of its kind in the nation. A dedicated team of DCRI interviewers conducted telephone follow-up interviews starting from 6 weeks to 15 months post-discharge. These interviews permitted assessment of both clinical events and patient-reported outcomes such as angina symptoms, quality of life, perceived care quality, and adherence to treatment.

“These kinds of patient-reported outcomes are key in the current era of clinical research,” Wang said.

For sites already submitting data to the American College of Cardiology’s National Cardiovascular Data Registry (NCDR), many of the TRANSLATE-ACS data elements were automatically imported from NCDR, thereby reducing the redundancy of data collection and entry. TRANSLATE-ACS also provided feedback on post-discharge outcomes (such as 30-day readmissions) to participating sites, allowing iterative quality assessment and improvement benchmarked to peer performance.

The design of TRANSLATE-ACS has several notable features, Wang said. It uniquely embedded a randomized substudy within an observational registry design to investigate the impact of bedside platelet function testing on routine physician practice and patients outcomes. It also allowed the integration of health economics with clinical endpoint data collection. These innovations allowed researchers to promote research efficiency and productivity, while enhancing the quality of cardiovascular care delivery. This approach, Wang said, may serve as a template for future cardiovascular studies.

Live Long and PROSPER

Developing tools to enable patients to evaluate the best treatment approach

The PROSPER (Patient-Centered Research Into Outcomes Stroke Patients Prefer and Effectiveness Research) study, a Patient-Centered Outcomes Research Institute-funded project, led by the DCRI’s Adrian Hernandez, MD, MHS, will combine data from the American Heart Association’s (AHA’s) Get With The Guidelines (GWTG)-Stroke registry with Medicare claims to track long-term clinical outcomes. It will also track patient-reported outcomes and quality-of-life concerns.

Although stroke is the fourth leading cause of death in the United States and many studies have been conducted to examine different treatment options to prevent stroke, there are limited data about the benefits and risks of the most common treatments among patients who are at least 65 years old, female, or minorities. PROSPER will develop online tools highlighting the benefits and risks of different treatments to enable patients who have had a stroke to evaluate the treatment approach that suits them best.

“This will be an incredible opportunity to leverage our research experience while working alongside patients to address the most important questions about stroke care and outcomes,” said Hernandez. “We hope this study will not only improve decision making for patients but also serve as a model for how the DCRI can conduct research in partnership with patients to answer the difficult questions they face every day.”
Rehabilitating Care for Stroke Survivors

Learning to manage the effects of a stroke

Of the 7 million adult stroke survivors, most need help after the acute event. Rehabilitation care after stroke is the prime healthcare service for reducing disability and learning to manage the effects of a stroke, yet the risks and benefits of certain types of rehabilitation services, as well as the options that best support each individual’s unique needs, are unknown.

Approximately 60 percent of stroke survivors older than 65 years receive some form of rehabilitation. The most common services for those patients who remain hospitalized are inpatient rehabilitation or skilled nursing, and the most common services for those who leave the hospital are home health and outpatient care.

The research team, led by Janet Prvu-Bettger, ScD, is using data from seven primary sources to compare these rehabilitation options in hopes of guiding individual decisions, as well as improving future practice, policy, and patient-centered outcomes.

Janet Prvu-Bettger, ScD
Assistant Professor, Duke University School of Nursing
DCRI Health Services Researcher

Safety First

Assessing the safety of novel oral anticoagulants

An older registry recently entered a new phase. The Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) won a recent contract renewal and will continue into a second phase with ORBIT-AF II. This multicenter, prospective outpatient registry of patients with incidental or prevalent atrial fibrillation (AF) will continue to be used to analyze treatment patterns and outcomes in patients with AF in the United States.

ORBIT-AF II has a target enrollment of 15,000 patients from approximately 300 sites in the United States and will provide post-marketing surveillance data needed for assessing the safety of novel oral anticoagulants when used in broader patient populations and community practice settings. ORBIT-AF II will include patients who were newly diagnosed with AF along with those who have been recently started on a target-specific oral anticoagulant agent.
Big Time

Transforming how trials are conducted with “big data” and EHRs

One of the hottest trends in clinical research today is the use of electronic health data to improve how trials are conducted and better inform clinical care decisions. The amount of available data increases as the number of hospitals, medical centers, and clinics using electronic health records (EHRs) continues to grow, paving the way for a “big data” push in clinical research.

Trials are often conducted in parallel to clinical care and are not integrated into typical workflows. This results in inefficiency, often leading to duplication of effort and data. It also makes it more difficult to translate research findings into improved patient care.

EHRs present an opportunity to better integrate trials and patient care. They can capture a significant amount of patient data that include demographics, details about healthcare encounters, and billing. They can be used to help identify patients for upcoming clinical trials, allowing doctors to discuss the trial with eligible patients during office visits. Patient screenings for trials can add significant cost and delays to trial startup, and EHRs can make it easier to identify potential participants. EHRs can also aid in study follow-up and quality assessment work.

Perhaps most importantly, EHRs can capture “real-world” data on patients who more accurately represent the typical patient seen in a clinic. Clinical trials often enroll a very specific subset of patients, so it is often unclear how the results of a trial apply to patients who are sicker, have more coexisting health conditions, or don’t meet the trial entry criteria. EHRs can be used in outcomes research to learn how medications and devices actually perform in the general population.

However, there is still work to be done to make the best use of EHRs and to capture the most meaningful data. As part of the DCRI’s mission to improve patient care through innovative clinical research, the DCRI’s Lesley Curtis, PhD, directs the Center for Pragmatic Health Systems Research (PRAGMATIC-HSR), a relatively new center within the DCRI, to develop innovative methods to use electronic health data created from clinical care to conduct high-impact, pragmatic clinical research studies.

PRAGMATIC-HSR develops and tests approaches to integrating electronic health data from various sources across the healthcare delivery system into a sustainable platform for clinical research, providing guidance about how different types of electronic health data can best be used to answer critical research questions. The center closely collaborates with and complements research activities within the DCRI’s clinical trials and health services research domains. PRAGMATIC-HSR also partners with industry leaders to develop tools to help researchers conduct robust observational studies and pragmatic trials using electronic health data platforms.

— Ziad F. Gellad, MD, MPH

Creating data models to develop best practices
In recent years, medical registries have played an increasingly important role in clinical research, helping to answer comparative effectiveness questions. The DCRI is a leader in this growing field, with a number of registry-based trials that are providing new insights into patient care.

It takes an average of 17 years for 14 percent of original research findings to lead to changes in care that benefit patients.

Mission: Improvable

Implementing proven findings

The goal of educating and organizing caregivers to more quickly implement proven clinical findings is at the heart of the AHA’s Mission: Lifeline initiative. Mission: Lifeline seeks to establish higher standards of patient care based on best practice guidelines from the AHA and American College of Cardiology. The DCRI’s Christopher Granger, MD, is the principal investigator for Mission: Lifeline’s STEMI (ST-segment elevation myocardial infarction) System Accelerator program, wherein advisors work with 17 regional healthcare systems to more fully and successfully implement Mission: Lifeline strategies.

Christopher Granger, MD
Professor of Medicine, Cardiology
Mission: Improvable (cont.)

In the past five years, the program has influenced more than 480 hospitals and around 150,000 patients across 46 states. Granger explained that Mission: Lifeline has led to dramatic improvements, including a 50 percent decrease in patients not being treated, a doubling in the use of ECGs by emergency medical service workers, and substantial reductions in the time it takes to open blocked arteries in patients experiencing a heart attack.


Lay My Burdens Down

Relieving the symptom burdens of sickest heart failure patients

An essential part of advancing clinical care is finding new and more effective ways to relieve heavy symptom burdens in the sickest patients. In Palliative Care in Heart Failure (PAL-HF) the DCRI’s Joseph Rogers, MD, is seeking to address this need in the growing population of patients with heart failure for whom aggressive therapies like transplantation or mechanical circulatory support are unlikely to improve either the length or quality of life. In PAL-HF, clinicians will work closely with patients to honor their wishes regarding end-of-life care and resuscitation preferences.

“One of the most important outcomes of this study,” explained Rogers, “is the knowledge the heart failure care providers will gain about the symptom relief options they should focus on as they care for this very sick patient group.”

Rogers further stressed that it is not just about external symptoms; these patients also have emotional concerns that need to be addressed.

Joseph Rogers, MD
Associate Professor of Medicine, Cardiology
Patient Power

Establishing evidence-based options for end-of-life care

The Center for Learning Health Care (CLHC), under the leadership of Amy Abernethy, MD, PhD, develops and tests practical solutions to facilitate learning care delivery systems and evidence-based patient-centered care. One of its projects is the Palliative Care Research Cooperative (PCRC) Group, which is establishing more evidence-based recommendations to improve end-of-life care. To do this, PCRC established a research cooperative group focused solely on end-of-life care research.

To help raise awareness around the financial toxicity, stress, and fatigue experienced by many cancer patients, the CLHC is also developing a web-based tool that assesses patient-reported financial stress as part of a routine collection of patient data. The web-based program will generate customized information and education for patients, and the information will also allow providers to better address financial concerns with their patients before the stress can impact the patient’s health. The CLHC has also developed Pillars4Life, an online educational program that teaches coping skills to cancer survivors and their caregivers. It is a solution-focused, educational course that patients and caregivers can participate in without the need to travel to a support group.

Portal to Knowledge

New online delivery system revolutionizes continuing medical education

Using the vast resources available at the DCRI, Zubin Eapen, MD, is leading several initiatives that are revolutionizing medical education and clinical practice. By embracing and advocating new technologies, Eapen and his colleagues hope to further enhance both clinical care and the effectiveness by which new discoveries are disseminated to the medical community. One example of this push for technological advancement is the newly developed Education Gateway. This novel, continuing medical education delivery system is a centralized, easily navigated online portal that provides access to on-demand, high-quality medical and health education programming. The platform makes it simple to create a personalized education package for each individual or group. Students, medical trainees, and healthcare providers from across the globe can have instant access to learn from Duke faculty.

Amy Abernethy, MD, PhD
Director, Duke Center for Learning Health Care
Director, Duke Cancer Care Research Program

“The Education Gateway will give users access to a comprehensive library of what the DCRI has to offer and allow medical practitioners and researchers to self-direct their continuing medical education,” said Eapen. “We are hoping to leverage all the existing CME content that we already deliver live, such as grand rounds. This system is a new platform to offer this content online and on mobile devices.”

The Education Gateway will offer online lectures and presentations spanning numerous therapeutic areas, including cardiovascular medicine, oncology, and gastroenterology.
Foreign Affairs
Partnering to improve and develop clinical research initiatives in China

As the Chinese economy continues to grow exponentially, so concomitantly does the prevalence of heart disease and stroke among its more than 1.3 billion inhabitants. As China’s leading cardiovascular treatment centers struggle to respond to this epidemic, some are now turning to the DCRI to provide guidance and big-picture solutions.

The DCRI’s Ying Xian, MD, PhD, has been working alongside Eric Peterson, MD, MHS, Matthew Roe, MD, MHS, and John Alexander, MD, MHS, to implement and provide support for a number of different information architecture and quality improvement initiatives that have already enjoyed marked success in the past few years.

Working in collaboration with Fu Wai Hospital, the largest heart center in China, the DCRI has helped set up a nationwide registry in cardiovascular disease. The registry is comprised of the following smaller registries, each addressing different cardiovascular related issues: 1) acute myocardial infarction, 2) heart failure, 3) arrhythmia, and 4) cardiovascular surgery. Since its launch last year, the nationwide registry has already enrolled more than 13,000 patients from nearly 200 hospitals.

In another collaborative effort, the DCRI is working with the Capital Medical University Beijing Tian Tan Hospital, the largest neural center in China. Together they are conducting quality improvement initiatives and cluster randomized control trials, with the goal of improving adherence to guideline-recommended intervention in stroke care. The program has already enrolled more than 150 hospitals.

Through the George Institute for Global Health, the DCRI has received a series of grants to explore the issues associated with providing care for China’s rural population. Although in big cities, like Beijing or Shanghai, there are already many state-of-the-art healthcare facilities, in many remote areas there are much more limited resources for healthcare treatment. Since approximately 80 percent of China’s population still lives in rural areas, these crucial studies are exploring alternative intervention programs that account for these limited resources and still improve patient outcomes.

Room for Improvement
Voluntary quality-improvement program an overall success

The first quality assessment of the Get With The Guidelines (GWTG) – Resuscitation registry found noted improvements in hospitals adhering to recommended treatments for sudden cardiac arrest, with greater performances the longer that hospitals participated in the program.

To researchers’ surprise, the only quality measure that did not see any significant improvement with participation in the GWTG program was initial time to defibrillation. Studies have found that if an automatic external defibrillator is not used within the first two minutes of sudden cardiac arrest, a patient’s chance of survival drops significantly. More research is needed to determine why participating hospitals have not improved their initial use of defibrillators during this crucial time period, said Monique Anderson, MD, lead author of the study.

GWTG – Resuscitation is a voluntary quality improvement program with more than 450 hospitals currently participating. Hospitals in the program are given regular feedback about how well they are using recommended therapies for patients experiencing sudden cardiac arrest. Researchers analyzed data from 2000 to 2012 and found that the longer a hospital has participated in the program the more their overall composite scores improved. Most hospitals had composite scores between 80 and 90 percent, meaning that 80 percent of the time they are meeting the recommended care guidelines.

Improvements in resuscitation quality of care were generally observed regardless of hospital location or size, with the exception of rural hospitals, which showed no benefit. There was a significant interaction between hospital volume and time in GWTG – Resuscitation such that the largest (>500 beds) benefited the most from participation in the quality improvement program.

“Our study shows that participating in a quality improvement program such as GWTG – Resuscitation can help hospitals improve their performance,” said Anderson. “In coming years, there will be national performance measures for sudden cardiac arrest and hospitals will have to report on their processes of care and outcomes. While there was overall improvement in resuscitation quality of care, there were still areas for improvement with individual measures such as time to defibrillation.”

Monique Anderson, MD
Medical Instructor, Department of Medicine, Cardiology

Ying Xian, MD, PhD
Assistant Professor of Medicine, Clinical Pharmacology
Check It, Change It
Community-based blood pressure intervention

Check It, Change It was launched in Durham County, NC to help a targeted community (about 74 percent African American) maintain healthy blood pressure. The program combined the use of a web-based tracking tool, Heart360®, with access to remote monitoring, health mentoring, and guidance from physician assistants as needed.

The DCRI’s Bimal Shah, MD, MBA, Kevin Thomas, MD, and Eric Peterson, MD, MPH, headed up this program. Study findings showed that the number of participants with healthy blood pressure (readings of less than 140/90) increased by 12 percent in the six months between the first and last readings. The number of participants who had high blood pressure in the range of 140–149/90–99 decreased by 4.7 percent, and those with readings in the higher range of 150/100 or above decreased by 8.2 percent. The study concluded that a program that follows this type of approach can improve blood pressure across a diverse or high-risk community.

Check It, Change It was developed through a collaboration of the American Heart Association and Durham Health Innovations. Novartis Pharmaceuticals Corporation provided the full funding for this initiative and is recognized for their participation and support.


Kevin L. Thomas, MD
Assistant Professor of Medicine, Cardiology

“One of the most important outcomes of this study is the knowledge the heart failure care providers will gain.”

— Joseph Rogers, MD
Relieving the symptom burdens of sickest heart failure patients
The DCRI is recognized around the world as a leader in clinical research, having conducted studies at more than 37,000 sites in 65 countries. A core part of the DCRI’s mission is to share knowledge that will improve the care of patients everywhere.

Future Researchers

Providing practical clinical research experience to future researchers

The North Carolina Collaborative (NCC) Summer Research Experience Program, held annually at the DCRI, is designed to attract high school and college students to careers in science by providing practical experience in clinical research. The program capitalizes on world-renowned training programs in place at Duke University, and is led by Daniel Benjamin, MD, PhD, MPH, Vivian Chu, MD, and Kristen O’Berry. The team of instructors includes adult medicine and pediatrics faculty members, a writing instructor, a statistician, and operations staff. Students are given opportunities to actively participate in NIH-sponsored research in clinical pharmacology, therapeutics, trials, and pharmacoepidemiology.

The eight-week program is funded by a grant from the Eunice Kennedy Shriver National Institute of Child Health and Human Development. Each student is paired with a faculty mentor and works on a pharmacoepidemiological research project, culminating in a written thesis and formal presentation. By the end of the course, the goal is that every student should be qualified for co-authorship on a peer-reviewed publication. The program's first year was a great success, with students and teachers from Duke, North Carolina Central University, the Medical University of South Carolina, and Durham Public Schools coming together for a unique learning opportunity in the field of clinical research.

“All the planning that went into developing this unique and meaningful research experience created a wonderful program for the outstanding participants who were selected among all the applicants,” said Chu, the administrative director for the program. “We look forward to continuing to grow this program and help educate the next generation of clinical researchers.”
Clinical Research 101

Teaching the basics of clinical research to a global audience

The DCRI, in partnership with Kaplan EduNeering (now UL), has developed a unique curriculum called CREATe (Clinical Research Education and Training) to teach the basics of clinical research that meet United States regulatory standards while also addressing local and cultural requirements of other countries.

Clinical trials in other parts of the world are often conducted with vastly different approaches to patient privacy, ethics, regulatory standards, and data monitoring. Trials that originate in the United States and have sites in different countries are set up to meet United States regulatory standards, but those that originate in other countries and want to be approved here can face significant challenges. In order for therapies to be approved for use in the United States, trials must comply with FDA standards. The DCRI saw an opportunity to help standardize the conduct of international trials and simultaneously improve the overall quality of research.

CREATe launched as an online tier-based learning system in China and India, two countries with the greatest assessed need for standardizing research. These countries have significantly different regulatory frameworks and have lacked the infrastructure to support clinical research.

“The benefit of CREATe is that it helps to provide a common understanding across different cultures and countries, and it will help these countries meet basic standards of research, allow them to participate more in global trials, and provide high-quality data to meet the standards for global regulatory approval,” said John Sundy, MD, PhD, director of the Center for Educational Excellence, which supports this initiative. “It centralizes education for sites participating in clinical trials about how to conduct better research.”

CREATe is still in its early stages, but it will eventually expand to include more countries, with a focus on developing nations.

“The DCRI is a renowned, trusted expert in conducting clinical trials, and CREATe will help change how research is conducted around the world for the better,” said Sundy.

Taking the Initiative

Reaching out to the community to improve outcomes for diabetic patients

The Southeastern Diabetes Initiative (SEDI), led by the DCRI, the Duke Translational Medicine Institute, and the University of Michigan’s National Center for Geospatial Medicine, is taking a multi-tiered community approach to improving outcomes for high-risk patients with diabetes.

Diabetes is one of the biggest health epidemics facing the United States, and it increases the risk for many other serious health problems. The Centers for Medicare & Medicaid Services, in collaboration with Bristol-Myers Squibb Foundation, launched SEDI to improve patient outcomes in communities with high rates of uncontrolled diabetes. Traditional approaches to patient care have not been able to successfully reverse the epidemic.

This unique community intervention program is based in five diverse regions, including Durham and Cabarrus Counties in North Carolina; Camden, New Jersey; Mingo County in West Virginia; and Quitman County in Mississippi. These areas, despite being geographically diverse and having significantly different populations, all have epidemic rates of diabetes.

"Changing the course of the diabetes epidemic requires a radically new approach," said Robert Califf, MD, principal investigator for the project. “By combining the modern technology of electronic records and geospatial mapping with a new workforce of community-based healthcare professionals, we believe we can achieve the triple aim of better outcomes, better health care, and lower costs.”

The program identifies people in the communities who have diabetes and other risk factors associated with poor clinical outcomes, such as high blood pressure and high cholesterol. Staff at Duke and the DCRI built a predictive algorithm that indicates which people are at the greatest risk, and the outreach efforts focus on those patients. Using a multi-tiered approach that includes home visits and educational outreach, the program aims to reduce the rates of stroke, heart attack, and other serious complications in this population.

The program is a true multidisciplinary, cross-institutional approach to treating diabetes. It involves community health workers, statisticians, cardiologists, nephrologists, internists, and information technology staff, as well as the geospatial mapping team at the University of Michigan, notes Bimal Shah, MD, MBA, one of the DCRI investigators involved with the project. Geospatial mapping allows the researchers to identify particular neighborhoods with the highest-risk populations where additional outreach can have the most impact. The goal is to expand the program further if SEDI can successfully improve outcomes in these communities with diabetes epidemics.
Collaborate and Listen

Transforming clinical research with data

The use of electronic health records (EHRs) to identify or define appropriate patient populations for specific studies continues to transform and bring innovation to the practice of clinical research. In September of 2012, the DCRI was chosen to serve as the coordinating center for the NIH’s Health Care Systems Research Collaboratory. This joint venture is intended to improve the way clinical trials are conducted by creating a new infrastructure for collaborative research. Robert Califf, MD, the Collaboratory’s principal investigator and Vice Chancellor for Clinical Research at Duke, explained that the goal is to compile trial best practices and guidelines into a comprehensive living textbook and online portal that includes everything researchers need to know to conduct pragmatic health system-based clinical research using EHRs. This textbook will outline the most effective ways to use readily available clinical evidence, but at the same time reduce the cost of clinical research.

Robert Califf, MD, MACC
Professor of Medicine, Cardiology
Vice Chancellor for Clinical Research

Down South

Seeking solutions to the global health threat of cardiovascular disease

The DCRI also extends its global reach by working with partner institutions around the world. One of our key partners is the Brazilian Clinical Research Institute (BCRI), founded in 2009 by DCRI faculty member Renato Lopes, MD, PhD, MHS. Lopes is also the executive director of the BCRI and a faculty member at that institution. Many DCRI faculty members are part of the BCRI’s advisory board.

The BCRI, which is affiliated with the Federal University of São Paulo – Paulista School of Medicine, was founded with the objective of helping to advance clinical research in South America and Brazil. The concept of an academic research organization is new to South America, where clinical research has traditionally been conducted as a business by contract research organizations. When it launched, the BCRI was the first academic research organization in the country.

The DCRI and BCRI have partnered on a number of clinical trials, including APPRAISE-2, ARISTOTLE, TRACER, and BRIDGE-ACS. The latter was the first trial for which all research efforts were led and conducted in Brazil by the BCRI and another research institute there.

Cardiovascular disease, particularly acute coronary syndrome (ACS), is a global health threat and, in many countries, it is the leading cause of death. Despite the proven effectiveness of evidence-based treatments, studies have

Continued on following page

Renato Lopes, MD, PhD, MHS
Associate Professor of Medicine, Cardiology
Director, DCRI Clinical Events Classification
Real-time Research

Building knowledge using data collected in real time from clinics and practices

PCORnet, the National Patient-Centered Clinical Research Network, was founded, in part, to facilitate the shift from researcher-driven to patient-centered health research. The Patient-Centered Outcomes Research Institute (PCORI) created PCORnet in 2013 to enable providers to obtain answers to pressing clinical questions more quickly and efficiently. The intent is to reduce the time and effort it takes to launch new clinical studies while focusing on the questions and outcomes that are most important to patients.

The DCRI, with Harvard Pilgrim Health Institute, is coordinating the activities of PCORnet. PCORnet will build on data collected in real time from clinics and practices, rather than relying on the traditional, highly constructed clinical trials with patients who often are not representative of those seen daily by local providers. PCORnet will take a unique approach to conducting studies by involving patients and other stakeholders in all aspects of the research process, from determining which research topics and outcomes should be studied to helping develop and conduct the studies to sharing the results.

Down South (cont.)

found that adherence to these treatments drops significantly in low- to middle-income countries, or even in poorer parts of the United States.

Findings from the BRIDGE-ACS study, for instance, demonstrated how a simple, low-cost intervention program significantly increased hospitals’ rates of adherence to evidence-based therapies for patients with ACS.

“Guideline therapies work if given to the right patients in time, yet studies highlight gaps between guidelines and what physicians do in practice – not just in Brazil but in the United States, Europe, Australia, and elsewhere,” said BRIDGE-ACS co-chair Otavio Berwanger, MD, PhD, director of the Research Institute HCor (Hospital do Coração) at the Cardiac Hospital of São Paulo.

“BRIDGE-ACS is an exciting trial because our results could be applied wherever ACS is undertreated, such as in lower-income countries and lower-income areas of the United States,” said Lopes. “The results reinforce the idea that a simple, feasible educational intervention, combined with evidence-based treatments, is effective and can make a significant difference in patient care.”

APPRAISE-2

ARISTOTLE

TRACER

BRIDGE-ACS
Teachers and Trailblazers

Partnering with colleagues in Kenya to train physicians and fight cardiovascular disease

The DCRI’s Eric Velazquez, MD, and Cynthia Binanay, BSN, MA, of the Duke Hubert Yeargan Center for Global Health, are addressing the developing epidemic of cardiovascular disease in Africa. Velazquez is principal investigator for Duke in the Academic Model Providing Access to Healthcare (AMPATH) Consortium. AMPATH is a global health partnership between 10 North American universities, the government of Kenya, Moi University and Moi Teaching and Referral Hospital in Eldoret, Kenya. Duke joined AMPATH in 2006 and received a grant from the National Heart, Lung, and Blood Institute in 2009 to establish a Cardiovascular and Pulmonary Disease (CVPD) Center of Excellence (COE) in Eldoret.

Africa’s need for trained cardiologists is acute. The continent has few trained cardiologists; Kenya has 12. Ten work in the capital city of Nairobi and two in coastal towns. Cardiovascular disease is Africa’s second leading cause of death after infectious diseases. It is the number one cause of death among adults over age 30, occurring 10 years earlier than people the same age in Europe and North America. By 2020, Africa’s cardiovascular disease rate will double, reach epidemic proportions and create staggering financial costs.

Under the leadership of Velazquez and Binanay, the COE created a competency-based clinical training curriculum for physicians, nurses, and allied health technicians. Duke faculty train local doctors to lead research and patient care programs that address the prevalence, prevention, and treatment of CVPD. Nurses and allied health technicians are trained in patient care, lab, and clinical processes.

In February 2013, the COE opened Kenya’s first cardiac care unit. More than 3,300 patients have been treated in critical care and outpatient settings. Today, Duke continues its mission at the COE by training physicians, nurses, and allied health professionals; providing global health opportunities to faculty, fellows, residents, and students; and developing innovative, locally relevant research and clinical care programs.

Additional staff and faculty members from Duke who are part of the Kenya project include Ralph Corey, MD, Gerald Bloomfield, MD, Jennifer Li, MD, and Kevin Anstrom, PhD. Other institutional partners include Brown and Indiana Universities.

Training Days

Developing the next generation of clinical investigators

Preparing and developing the next generation of clinical investigators is a key aspect of the DCRI’s mission to share knowledge. Under the direction of Matthew Roe, MD, MHS, the DCRI Research Fellowship Training Program this year includes 37 postdoctoral fellows and six medical students. While at the DCRI, fellows participate in protocol development, study operations, continuing medical education curricula development, and clinical events adjudication. In addition to managing the clinical aspects of the studies, the fellows collaborate with the teams that manage the operational functions specific to multicenter clinical research studies, including project and data management, site management, and information technology. Each fellow benefits from mentorship by a senior member of the DCRI faculty.

Matthew Roe, MD, MHS
Associate Professor of Medicine, Cardiology
Director, DCRI Commercial Megatrials
FELLOWS

From July 2012 – June 2013

- Published Manuscripts and Book Chapters – 80
- Manuscripts and Book Chapters Accepted for Publication – 27
- Abstracts Presented – 69

Second-year Fellows

1. Tariq Ahmad, MD  
   Cardiology

2. Julie Autmizguine, MD  
   Co-Chief Fellow Pediatrics, International

3. Gwen Bernacki, MD, MHSA  
   Cardiology

4. Flavio Souza Brito, MD  
   Cardiology, International

5. Cristal Brown, MD  
   Gastroenterology

6. Brian Englum, MD  
   Cardiac Surgery

7. Hyun-Jae Kang, MD, PhD  
   Cardiology

8. Prateeti Khazanie, MD, MPH  
   Cardiology

9. Matt Sherwood, MD  
   Co-Chief Fellow Cardiology

10. Ben Steinberg, MD  
    Cardiology

11. Yamini Virkud, MD, MA  
    Peds-Allergy Immunology

12. Lawrence Kuy, MD  
    Pediatric ICU

First-year Fellows

1. Axel Akerblom, MD  
   Cardiology

2. Arthur Baker, MD  
   Infectious Diseases

3. Melissa Burroughs Pena, MD  
   Cardiology

4. Adam Devore, MD  
   Cardiology

5. Michael Durheim, MD  
   Pulmonology

6. Jessica Ericson, MD  
   Pediatric Infectious Diseases

7. Rachel Greenberg, MD  
   Pediatric Neonatal Pediatrics

8. Emil Hagstrom, MD, PhD  
   Cardiology

9. Lynn Howis, MD  
   Oncology

10. Susan Hupp, MD  
    Pediatric ICU

11. Kristen Hyland, MD  
    Endocrinology

12. Larry Jackson, MD  
    Cardiology

13. Aurn Krishnamoorthi, MD  
    Cardiology

14. Robert Mentz, MD  
    Cardiology

15. Sean Pokorney, MD  
    Cardiology

16. Meena Rao, MD, MPH  
    Cardiology

17. Julius Wilder, MD, PhD  
    Gastroenterology

18. Kanecia Zimmerman, MD, MPH  
    Pediatric ICU

“We look forward to continuing to grow this program and help educate the next generation of clinical researchers.”

— Vivian Chu, MD

Providing practical clinical research experience to future researchers
NEW FACULTY: 2013

1. Monique Anderson, MD
   Medical Instructor, Department of Medicine, Cardiology

2. Laura Beskow, PhD
   Associate Professor, Medicine

3. Michaela Dinan, PhD
   Medical Instructor, Department of Medicine, Medical Oncology

4. Matthew Dupre, MD
   Assistant Professor, Community and Family Medicine, Cardiology

5. Robert Harrison, MD
   Medical Instructor, Department of Medicine, Cardiology

6. Christoph Hemlik, MD
   Assistant Professor of Pediatrics, Critical Care

7. Schuyler Jones, MD
   Assistant Professor of Medicine, Cardiology

8. Emily O’Brien, PhD
   Medical Instructor, Department of Medicine, Clinical Pharmacology

9. Michael Pencina, PhD
   Professor of Biostatistics and Bioinformatics
   DCRI Faculty Associate Director

10. Janet Prvu-Bettger, ScD
    Assistant Professor, Duke University School of Nursing
    DCRI Health Services Researcher

11. Charles Scales, MD
    Associate Professor of Surgery, Urology

12. Julie Ann Sois, MD, MA, FACS
    Professor of Surgery
    DCRI Endocrine Neoplasia Disease Program
EXECUTIVE LEADERSHIP

1. Eric D. Peterson, MD, MPH, FAHA, FACC
   Executive Director, Duke Clinical Research Institute
   Professor of Medicine, Cardiology

2. John H. Alexander, MD, MHS, FACC
   Faculty Associate Director; Director, DCRI CV Research
   Associate Professor of Medicine, Cardiology

3. Daniel K. Benjamin, Jr., MD, PhD, MPH
   Faculty Associate Director
   Kiser-Arena Distinguished Professor of Pediatrics

4. Lisa G. Berdan, PA
   Director, Global Outcomes Commercial Operations

5. Nicole Hedrick
   Chief Human Resources Officer

6. Adrian F. Hernandez, MD, MHS
   Faculty Associate Director
   Associate Professor of Medicine, Cardiology

7. Kristen O’Berry
   Director, Academic Affairs

8. Michael J. Pencina, PhD
   Faculty Associate Director; Director, Biostatistics
   Professor of Biostatistics and Bioinformatics

9. Kevin A. Schulman, MD, MBA
   Faculty Associate Director; Director, CCGE
   Professor of Medicine, General Internal Medicine

10. Michael W. Sledge
    Chief Financial Officer

11. John S. Sundy, MD, PhD
    Faculty Associate Director; Director, CEE
    Associate Professor of Medicine, Pulmonary and Critical Care Medicine
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<th>#</th>
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<tr>
<td>1</td>
<td>Connor Blakeney</td>
<td>Clinical Data Management</td>
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<td>2</td>
<td>Pamela Buchholz</td>
<td>Imaging</td>
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<td>3</td>
<td>Kaye Fendt</td>
<td>Quality Assurance and Regulatory Compliance</td>
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<td>Sherri Foster</td>
<td>Communications and Center for Educational Excellence</td>
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<td>5</td>
<td>Elizabeth Fraulo</td>
<td>Outcomes Research</td>
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<td>6</td>
<td>Debra Harris</td>
<td>Integrated Clinical Events &amp; Safety Surveillance</td>
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<td>7</td>
<td>David Howard</td>
<td>Project Management for Clinical Operations</td>
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<td>Cristine Karasek</td>
<td>Facilities Services</td>
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<td>9</td>
<td>Brian McCourt</td>
<td>Clinical Research Informatics</td>
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<td>10</td>
<td>Uduak Ndoh</td>
<td>Interim Director, Information Technology</td>
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<td>11</td>
<td>Suzanne Pfeifer</td>
<td>Business Development &amp; Contracts Management</td>
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<td>12</td>
<td>Deborah Roth</td>
<td>Interim Director, Clinical Operations</td>
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<td>13</td>
<td>Bill Shannon</td>
<td>Organizational Learning</td>
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<td>14</td>
<td>Damon Sells</td>
<td>Center for Clinical and Genetic Economics</td>
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<td>15</td>
<td>Kristina Sigmon</td>
<td>Statistical Operations</td>
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<td>16</td>
<td>David Tillotson</td>
<td>Finance</td>
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<td>17</td>
<td>Jamie Young</td>
<td>Sponsored Projects Administration</td>
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