

# Research Highlights

## 2016



Carolinus HealthCare System





To our community of patients, providers, researchers and supporters:

On behalf of Carolinas HealthCare System, it's my privilege to share some of the exciting advances we have been able to achieve across our growing and diverse research programs in this 2016 research report.

Since 2015, the number of clinical research studies across the system has grown by over 30 percent – arguably the largest annual growth for Carolinas HealthCare System in recent years. Our work is deeply collaborative and rooted in a desire to improve patient care and outcomes in our communities and beyond.

Our success, I believe, is due in large part to the quality and commitment of our clinicians and the size and scope of the patient community we serve. Our clinical experience informs our research, and our research in turn translates into better care in the clinic. Our drive to constantly delve deeper is what keeps Carolinas HealthCare System at the forefront of science and medicine.

For example, our ability to perform sophisticated genetic analyses in the lab recently allowed us to accurately diagnose a 10-year-old girl with a rare form of cancer – the first known pediatric case in the world. The genomic profiling we performed helped determine the most effective treatment regimen for her disease – stem cell transplantation – and today she is alive and doing well (see page 15).

As a leading accrual center for many large, multi-center studies, we are helping to define and improve the standard of clinical care. For example, we took a leading role in the SPRINT study, a randomized clinical trial to evaluate standard versus intensive blood pressure control, which showed that setting more stringent targets for blood pressure lowering can dramatically improve patient survival and allay concerns around overmedicating patients.

Through our health outcomes research, we have developed pioneering apps that are allowing surgeons to mine a wealth of patient data, which is allowing us to deliver better care (see page 36).

Since arriving, I've been continually humbled and awed by the commitment Carolinas HealthCare System has made to support and expand the scope and depth of our research programs. I hope you enjoy reading this report and learning about some of the many accomplishments of the research programs at Carolinas HealthCare System. I know it gives me a deep sense of pride and inspiration, and we look forward to future research endeavors.



With warm wishes,  
George McLendon, PhD  
Vice President of Therapeutic Research and Development  
Carolinas HealthCare System

# Carolinas HealthCare System Research and Expertise by the Numbers



More than  
**1,100** active trials underway



**360** publications in peer-reviewed articles –  
research that helps guide treatment and patient care



**30%** Carolinas HealthCare System's active research  
portfolio growth in 2016 over the previous year



Attracted attention from clinicians nationally and internationally  
who made site visits to Carolinas HealthCare System to learn  
from our research and techniques



Nearly  
**50** facilities in our system offering clinical trials, allowing  
trials to be available closer to home.

**56%**  
Neurology  
and  
Neuroscience

**38%**  
Surgical

**36%**  
Pediatric

Rise in active trials across some  
of our clinical programs in 2016

## Table of Contents

|   |    |
|---|----|
| Research Operations .....                                       | 4  |
| Levine Cancer Institute Research Endeavors.....                 | 12 |
| Levine Children's Hospital Research Endeavors .....             | 18 |
| Neurosciences Institute Research Endeavors .....                | 24 |
| Sanger Heart & Vascular Institute Research Endeavors .....      | 30 |
| Surgery Research Endeavors.....                                 | 36 |
| Other Division and Department Research Highlights .....         | 42 |
| Division of Hepatology.....                                     | 44 |
| Liver Pathobiology Research Laboratory .....                    | 45 |
| McColl-Lockwood Laboratory for Muscular Dystrophy Research..... | 46 |
| Physical Medicine & Rehabilitation Research.....                | 47 |
| Department of Obstetrics and Gynecology.....                    | 48 |
| Department of Orthopaedics.....                                 | 49 |
| Department of Oral Medicine.....                                | 50 |
| Division of Pediatric Nephrology & Hypertension .....           | 52 |
| Department of Emergency Medicine.....                           | 53 |
| Department of Family Medicine .....                             | 54 |
| Carolinas Simulation Center.....                                | 55 |
| Center for Outcomes Research and Evaluation.....                | 56 |
| Selected Publication Listing .....                              | 59 |



# Research Operations

Building capacity and propelling research and therapies forward



*"We help keep our research safe and compliant, and can also bring innovative research opportunities to our clinicians. It's truly the foundation upon which our research studies occur and excel."*

*– Christine Becker, PhD, MBA, RN  
Director of Research*

According to the National Institute on Aging, although most babies born in 1900 did not live past age 50, life expectancy at birth now surpasses 80 years in many developed countries. Advances in therapies and disease prevention have also translated into better quality of life. Clinical trials are crucial to expanding the clinical armamentarium of evidence-based medicine, transforming healthcare and making yesterday's "fatal diseases" today's "chronic conditions."

"Every drug and device that is currently approved or marketed began as part of a clinical trial," said Mark J. King, assistant vice president, Carolinas HealthCare System Enterprise Research. "Without clinical trials and the patients who volunteer to participate in them, there would be no new therapies and we would not be able to fulfill the mission of Carolinas HealthCare System to improve health, elevate hope and advance healing – for all."

Groundbreaking clinical research has grown in scale, sophistication and reach over the past century. Carolinas HealthCare System has an active and dynamic research program that both traverses and connects its clinical programs systematically and geographically, and it increasingly draws international acclaim. Research Operations provides the administrative backbone and operational expertise to support effective, efficient cutting-edge research projects and partnerships across our system.



## A Valued Research Leader and Partner

Carolinas HealthCare System investigators participate in and lead Phase I to IV research, and the system is frequently sought after as a core research site for clinical trials. We have also established research collaborations with many leading academic centers across the United States and beyond, engaging in multi-center research on a national and global scale. Our investigators have published their research in leading journals, presented their findings at major symposiums, and are called upon as subject matter experts in medicine. They are also active members of disease-focused research consortia, as well as private, state and federally funded research initiatives.

Carolinas HealthCare System participates in:

- Academic research center trials
- Disease-focused consortia
- Investigator-initiated system-sponsored trials involving peer institutions
- Multi-site federally funded research, including studies supported by the National Institutes of Health and the U.S. Centers for Disease Control and Prevention
- Trials sponsored by biopharmaceutical and medical device companies

Carolinas HealthCare System is not only in demand as a clinical trial site; it has been recognized for the innovative approaches our clinicians and research teams use to advance our research mission. Many projects begin with an idea from a patient, clinician or research teammate and are piloted on a small scale before being implemented across Carolinas HealthCare System. From advancing innovative medical devices to software solutions, novel treatments and therapies that address the mind-body aspects of disease, our research operations team is helping to advance care for our patients and others around the world.

Researchers from Family Medicine and Pediatrics partnered with pediatric patients and their caregivers to develop an app called Carolinas Asthma Coach ([CarolinasHealthCare.org/AsthmaCoach](https://CarolinasHealthCare.org/AsthmaCoach)). Asthma Coach incorporates shared decision-making and decision support to help standardize care delivery and improve outcomes. All participants in a 2016 pilot study rated their experience with the Asthma Coach highly and demonstrated an improved understanding of asthma. Efforts are currently underway to integrate this innovative research product as part of pediatric asthma care across the system.

Jeko Madarov, MD, of Sanger Heart & Vascular Institute developed a longitudinal sternal device entirely within Carolinas HealthCare System. He performed the first in-person chest implantation of the device in 2016. The benefits of this FDA-approved device, as compared to rigid sternal fixation devices, include simpler design, increased stability of the sternum post-surgery, and no need for replacement.

## Coordination and Innovation to Enable Impactful Research

Our commitment is to advance patient care and provide cutting-edge experimental treatment options for our patients, while upholding the highest standards of safety, research integrity, ethics and compliance.

“We help keep our research safe and compliant, and can also bring innovative research opportunities to our clinicians. It’s truly the foundation upon which our research studies occur and excel,” said Christine Becker, PhD, MBA, RN, director of research, who oversees the Office of Clinical and Translational Research.

Carolinas HealthCare System has made great strides in its research programs in recent years. New initiatives and tools – achieved through cross-disciplinary collaboration and the dedication of clinical research teams and support functions – have bolstered our research infrastructure and enhanced the capabilities of our clinical research program. Research Operations served a lead role in efforts to improve patient access to trials, strengthen the processes to uphold study compliance and safety, and streamline operations for trial sponsors, investigators and patients.

Key operational initiatives advanced in 2016 include:

- Expanding the use of the OnCore® Clinical Trial Management System (CTMS) to seamlessly integrate research management activities across the system
- Creating a pool of trained clinical research nurses and coordinators who provide on-demand research study support
- Augmenting the training program for new clinical research coordinators
- Bolstering the training program for investigators regarding clinical trial research, human subjects protections and regulatory compliance

These programs have been energizing for clinicians across the system, whose collaboration has catalyzed the ongoing growth of the research program. On an ongoing basis, Research Operations also supports and improves essential functions such as REDCap (Research Electronic Data Capture), our centralized data collection, storage, reporting and archiving system, as well as programs to support internal monitoring, adherence and quality assurance for clinical trials.

Research across Carolinas HealthCare System is growing in scope, scale and influence. In fact, the number of trials and patients enrolled throughout the system is at an all-time high. Crucial to this growth has been a focus on the needs of our patients, for example, by addressing common barriers to enrollment such as awareness and transportation. Many Carolinas HealthCare System facilities now offer patients access to clinical trials closer to where they live, which can be critically important for people who may have limited therapeutic options or who cannot travel far for clinic visits and treatments.

“Not only are we engaging in more clinical trials research, we are offering them in more locations. Patients can participate at sites closer to home, which can make getting to and from treatments easier,” said Becker.

TO IMPROVE  
HEALTH,  
ELEVATE  
HOPE  
AND ADVANCE  
HEALING  
– FOR ALL

Research is a core mission at Carolinas HealthCare System. Clinical studies give us the ability to offer the best treatment options for our patients and continue to advance new therapies and practices. The system’s medical faculty, affiliated physicians, residents and fellows are involved in clinical research targeting specific illnesses, from cancer and neurological disorders, to pediatrics and surgery.

- More than 1,000 active clinical studies
- Translational research laboratories
- Outcomes research programs
- Investigator-initiated clinical trials
- National Institutes of Health-supported registries and interventional trials

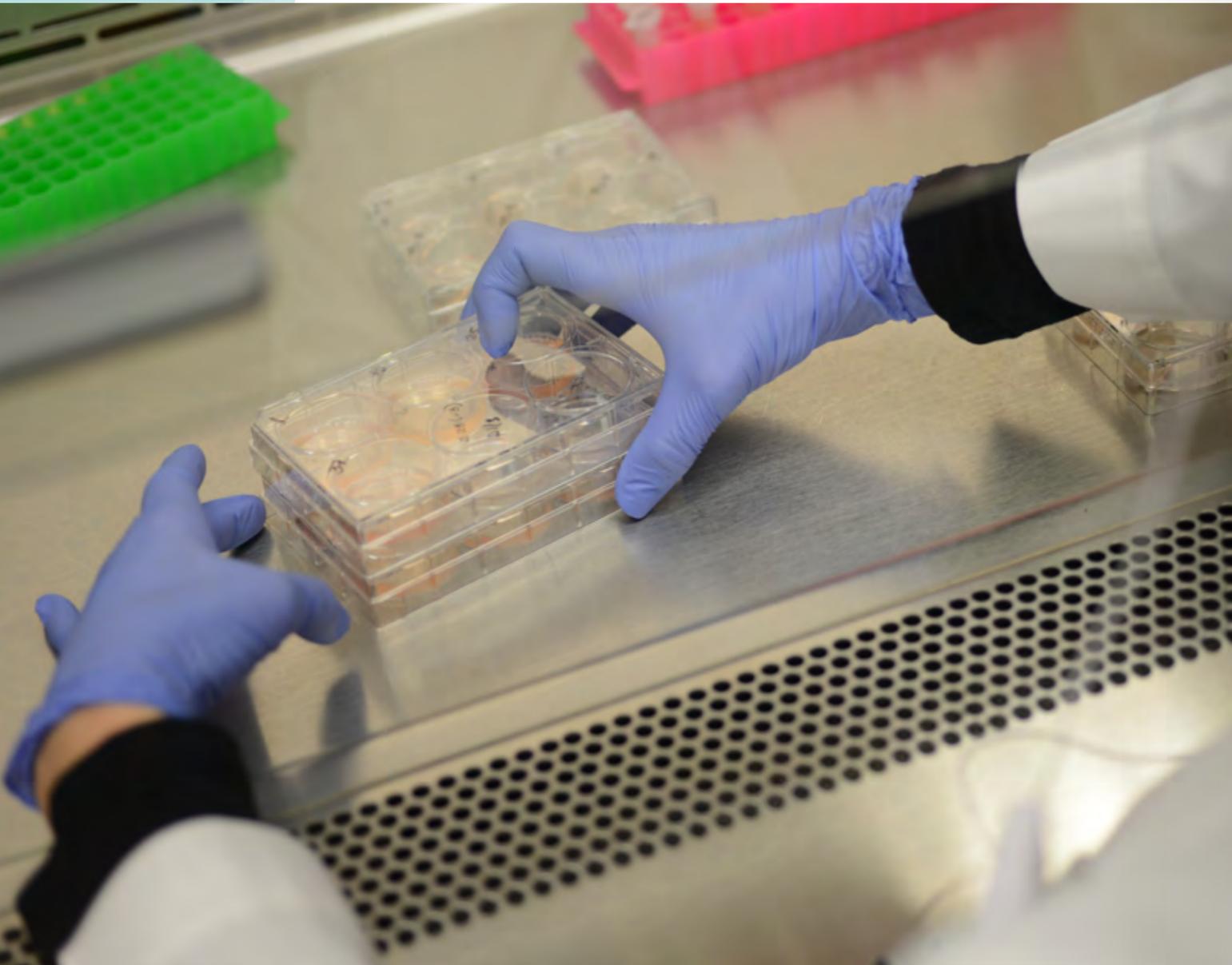
Carolinas HealthCare System has a growing client base with more than 50 master trial agreements.

The Office of Clinical and Translational Research facilitates clinical research and provides programs for direction, guidance, support, education and promotion of regulatory compliance.

Key programs in 2016 included:

- Providing orientation and continuing education for research clinicians and research assistants who assist with all aspects of study coordination
- Adding research monitors to a robust quality control program to ensure study protocol and regulatory compliance
- Facilitating mentorship and preceptorship experiences for college students enrolled in clinical research programs
- Coordinating the Research Summer Scholar Student Intern program

Coordinating all of the systems and processes that underpin our research programs is a significant aspect of Carolinas HealthCare System. Our clinical research associates, research nurses and regulatory professionals are unsung heroes in advancing our research portfolio.



## New Business Development

### *New Infrastructure, Increased Efficiency, More Investigators*

In 2016, Carolinas HealthCare System created a business development function to help expand relationships with biopharmaceutical companies, medical device manufacturers and contract research organizations. Through cross-functional collaborative efforts, we further streamlined the assessment process for new studies and added clinical research staff.

Serving in a matchmaker role, Business Development helps align the pharmaceutical, biotechnology and medical device manufacturer with the investigator within Carolinas HealthCare System who has the expertise, interest and availability to lead their clinical research study. Partners save valuable time working with one business development contact who has insight into and across multiple therapeutic areas, as well as the ability to help expedite their studies through the initial review process. On the flip side, Business Development involvement can provide support and due diligence to Carolinas HealthCare System research teams, allowing them to focus on patient care, manage active studies and initiate new research in a timely manner.

“The approach focuses on efficiency and service for both partners and our clinical research teams, providing our patients with more potential quality-of-life options, aligning quality studies for a world-class program, and promoting service-based collaborations,” said Nancy Zeleniak, director of Business Strategies and Client Engagement at Carolinas HealthCare System.

Carolinas HealthCare System has a range of core research capabilities that have been optimized to meet the needs of biopharmaceutical and device manufacturers, including:

- Access to research teams with a high level of expertise
- A highly diverse subject population of more than 1 million patients
- A state-of-the-art research infrastructure spanning the entire system
- Quality research services across the system
- Considerable experience conducting multi-disciplinary studies

At Carolinas HealthCare System, modern-day biomedical research is unlocking innovative therapies to prevent and treat diseases, reduce treatment side effects, and improve quality of life.

Developed in 2016, the CHS ONE approach is a collaborative, streamlined management process of clinical research teams and support groups working together from the time we hear about a study opportunity to the point we start the trial. This unified, one-point, integrated handoff process includes:

- One business development liaison for point-to-point oversight
- A dedicated budget and contract professional, the Sponsored Programs administration liaison, who interfaces with clinical research teams to enhance document processing turnaround time throughout the study
- Support for master trial agreements, which provides time savings and makes the process of opening new trials easier
- An upfront, transparent fee structure to help speed budget processing
- Rapid review by IRB partner of completed submissions
- One lead research manager, even for multi-disciplinary studies
- One principal investigator and coordinator for single or multiple-site studies, which promotes quality control oversight
- One contract that is applicable across the majority of Carolinas HealthCare System

## Other Important Highlights

**Centralizing IRB Review:** In late 2016, the National Institutes of Health issued new policies requiring all Health and Human Services-sponsored research to utilize a centralized IRB process. In January 2017, the federal Department of Health and Human Services announced significant changes to enhance protection for research participants and modernize IRB oversight. Anticipating these changes, Carolinas HealthCare System decided to partner with a research review company to provide IRB services for its clinical research program.

Through this partnership, a secure, cloud-based technology, can provide real-time review of new research submissions, facilitating patient access to studies as soon as our investigators have received site activation from a trial sponsor. These attributes allow Carolinas HealthCare System to consolidate IRB activity, enhance trial oversight, speed timelines and achieve a higher rigor of review across the entire research enterprise.



Our research team has been able to expedite research, completing a medical device study agreement, from study notification through contract completion, in just 4.5 weeks.

# Levine Cancer Institute Research Endeavors

A nationally recognized program offering early-phase trials closer to home



Four years after its launch, Levine Cancer Institute has made astonishing progress in establishing a robust portfolio of basic, translational and clinical research. The Institute's strong research competency is evident from the overwhelming level of demand from trial sponsors, collaborators and patients to open new studies here – including the types of Phase I and first-in-human trials typically available only at major tertiary institutions.

"I'm proud that we are providing opportunities for our patients in a larger and broader scope than ever before," said Edward Kim, MD, chair of the Department of Solid Tumor Oncology. "It's very gratifying when we can offer opportunities to patients who have been treated and don't have many options. Not every clinical trial is a success, but when you have an option, it offers hope – and that's a great thing."

One unique advantage of Levine Cancer Institute is our ability to support trial participation not only at our main campus, but also at numerous regional centers across the Carolinas. "We are bringing both research and precision medicine closer to home for our patients. We are one of very few sites in the country with Phase I trials open at multiple locations," said Dr. Kim.

*"There is a true interest in advancing research within this healthcare system."*

*– Belinda Avalos, MD  
Vice chair of the Department of Hematologic Oncology and Blood Disorders*

This accessibility is of tremendous value for patients, who may otherwise have had to travel hours for study visits or forgo trial participation. It also allows Carolinas HealthCare System to more rapidly accrue study participants, particularly for studies involving rare cancer subtypes.

The past year has seen continued expansion of our research staff and growth in the number of physicians with subspecialty expertise, enabling Levine Cancer Institute to attract and run clinical trials in new areas. Our physicians have also benefited from training opportunities to extend their expertise in planning and conducting research, thus building the skills to advance innovative therapies and expand the options available to our patients.

"There is a true interest in advancing research and offering patients innovative therapies at Levine Cancer Institute," said Belinda Avalos, MD, vice chair of the Department of Hematologic Oncology and Blood Disorders. "Under (Institute President) Dr. Raghavan's leadership, cutting-edge translational research programs have been established that support investigator-initiated clinical trials utilizing novel drugs and drug combinations. This has enabled us to offer patients at Levine Cancer Institute the same level of care they would get at any major academic cancer center, but closer to home."

## Facts & Figures



More than 50 ongoing Phase I trials



More than 20 ongoing hematology trials



Over 800 tumors genomically tested in 2016



Genomic testing available throughout the Carolinas HealthCare System network



EAPathways program facilitates clinical decision-making including treatment, clinical trials, patient resources



### Early Access to Groundbreaking Therapies

Phase III clinical trials offer patients a valuable opportunity to benefit from emerging therapies before they are available on the market. But whereas Phase III studies often involve dozens to hundreds of institutions, early-phase trials typically involve only a handful. Being home to more than 50 Phase I and first-in-human trials – in addition to numerous Phase II and III studies for a wide range of cancers – means patients have access to emerging treatments at Levine Cancer Institute that they simply can't get elsewhere.

Our ability to attract sponsors and participate in trials at all phases of clinical investigation is a testament to the quality of our research infrastructure and the caliber of our research staff and physicians. "In four short years, we have built a large pool of not only great doctors, but physicians with additional skills in conducting research," said Dr. Kim. "It benefits the entire region. Any place you go, you try to make it better than when you started – and I think we've done that here."

To ensure all patients have the opportunity to benefit from participating in clinical trials, our EAPathways (Electronically Accessible Pathways) initiative embeds up-to-date trial information directly into the treatment pathways. This mechanism guarantees that all physicians are aware of ongoing trials, their current status and pertinent enrollment eligibility criteria.

### Offering Personalized Medicine at All Locations

Genomic analysis and other tools have dramatically expanded our ability to tailor treatments to each individual patient in recent years. Levine Cancer Institute now supports genomic testing at all of our regional sites, in addition to our main campus, ensuring that each patient in our system can take full advantage of available opportunities for personalized therapy. This includes routinely sequencing patients' tumors to identify the optimal course of treatment for each patient's specific cancer. For some treatments, we also use a personalized approach to determine dosing based on indicators of how quickly or slowly a given patient can be expected to metabolize a certain drug.

In addition to contributing to clinical trials, Levine Cancer Institute's researchers conduct basic and translational research in our own on-site laboratories. The Hematologic Oncology Translational (HOT) laboratory, for example, is one of only a few in the world with expertise in isolating leukemia stem cells. Jonathan Gerber, MD, chief, Leukemia Section is collaborating with Institute scientists and physicians to expand this technique to other blood cancers. Using our expertise in molecular biology, growth factor receptors and cell signaling, researchers in the HOT lab are investigating processes that contribute to the development and relapse of blood cancers as well as ways to identify unique properties of blood cancer stem cells that distinguish them from normal blood stem cells. The lab is also studying genetic factors that influence the incidence and aggressiveness of blood cell cancers in different racial and ethnic groups.

"What we've been able to do is not just bench research, but translational research, where we go from the patient to the bench and then translate our findings back to the patient – essentially 'bedside to bench to bedside,'" said Dr. Avalos, who is the director of the HOT lab. "Patients have the opportunity to participate in research trials in which clinical information is gathered, research studies are conducted on a patient's own cancerous blood cells, and the information obtained is then used to determine the best therapy and optimize patient care."

Our hematopoietic stem cell transplant program is the only such program in the Charlotte area. To date, the program has performed more than 240 transplants in the short time since it opened in March 2014. The program has also generated significant new findings and approaches to improve transplant success. A personalized approach is being developed for drug dosing that is based on sequencing targeted genes in individual patients. For patients in need of a stem cell transplant who do not have a fully matched donor, the program offers patients the option of undergoing a transplant using a "half-matched" donor. This approach significantly expands the pool of potential donors since most patients have living children or parents who can serve as half-matched or haploidentical donors.

## The TAPUR Study: Advancing Targeted Therapies for Hard-to-Treat Cancers

It is a tremendous honor for Levine Cancer Institute to be selected as one of just four initial participating institutions in the Targeted Agent and Profiling Utilization Registry, or TAPUR, the first clinical trial sponsored and organized by the American Society of Clinical Oncology.

In an effort to further advance personalized medicine and evaluate the anti-tumor activity and toxicity of commercially available targeted cancer drugs, the goal of this prospective trial is to match patients with cancer drugs that are targeted to the specific genomic variation implicated in their cancer. Eligible patients matching 17 genomic profiles receive free targeted therapy for multiple myeloma, B-cell non-Hodgkin lymphoma or advanced solid tumors that have stopped responding to standard-of-care treatments.

“TAPUR is a consummate reflection of what Levine Cancer Institute does well – open innovative studies, focus on biomarkers and genomic medicine, and engage our regional sites in precision medicine trials,” said Dr. Kim. “We are currently leading the country in patient accrual for this registry, and amazingly, we have just as many patients being enrolled at our regional sites as at our main campus.”

## More Research Highlights

**Immunotherapy Innovations:** Levine Cancer Institute runs a large portfolio of studies involving agents that enlist the patient’s own immune system to fight their cancer. This includes active studies in all clinical phases and agents targeting multiple tumor types.

One noteworthy achievement, for example, was the completion of a Phase III trial of the drug olaratumab, which recently gained FDA approval for treatment of soft-tissue sarcoma. Levine Cancer Institute was pleased to offer our patients the opportunity to participate in this trial for the first drug in several decades that has been proven to increase survival for patients with sarcoma.

Looking forward, Levine Cancer Institute will further expand its cutting-edge immunotherapy work with the launch of a Chimeric Antigen Receptor (CAR) T-cell therapy trial in early 2017 for the treatment of lymphoma, under the direction of Nilanjan Ghosh, MD, PhD, chief, Lymphoma Section.

**Offering New Options for Blood Cancers:** Saad Usmani, MD, chief, Plasma Cell Disorders Section, leads a number of clinical trials aimed at expanding the treatment options available to patients with plasma cell disorders such as multiple myeloma and amyloidosis. Dr. Usmani was the lead investigator for a novel clinical trial using antibody therapy with daratumumab for treatment of myeloma. Through Dr. Usmani, Levine Cancer Institute enrolled the most patients in the United States, which led to FDA breakthrough designation of daratumumab in 2015.

**Building the Biospecimen Repository:** Our system-wide Biospecimen Repository (BSR) coordinates the collection and processing of tissue and blood samples from a large number of patients. This repository is instrumental to our researchers’ ability to identify new drug targets and ask crucial research questions.

## From Dogged Pursuit of Diagnostic Mystery to New Knowledge and a Disease in Remission

One diagnosis made recently at Levine Cancer Institute has had enormous implications for a patient and her family – and also reverberated throughout the oncology community. When a 10-year-old girl came to Carolinas HealthCare System in 2014 with a blood cell disorder that previous care providers had been unable to diagnose, the situation seemed dire. Thankfully, HOT lab physicians and scientists in collaboration with Levine Children’s Hospital physicians were able to trace her disease to a mutation in the CSF3R gene, leading to a diagnosis of chronic neutrophilic leukemia (CNL). In May 2016, she underwent a successful hematopoietic stem cell transplant with her brother as her donor. Today, at age 12, she is doing well and there is no evidence of leukemia.

But her story doesn’t end there. The patient’s diagnosis with CNL at Levine Cancer Institute has actually changed what we know of the natural history of this disease. As we recently reported in the journal *Blood*, our case is the first to demonstrate three previously unknown aspects of CNL: that it can occur in children (previously it had only been reported in older patients, typically

age 65 or older), that it can be congenital, and that it can potentially be cured by a stem cell transplant when the transplant is performed before evidence of disease acceleration.

“Had we not diagnosed this child and performed a transplant when we did, she would have developed a worsening disease, from which she would likely have died within a short period,” said Dr. Avalos. “Typically CNL affects much older patients who go on to die of their disease within two years. Our patient is the first child to undergo a stem cell transplant for this disease, which is the only known therapy with curative potential. I’m proud to know we’ve made a difference for this child, and that we’re making a difference for all patients with CNL through our innovative research studies.”

*Madie (center), stands (left to right) with her mom, brother, Rylan, who donated his bone marrow to help her battle a rare form of leukemia, and her social worker at Levine Children’s Hospital. Her diagnosis with CNL, and the research that went into discovering it, has changed what we know about the natural history of this disease.*



# Levine Children's Hospital Research Endeavors

Enhancing care models and advancing cures for young patients  
with serious conditions



*"As we move ahead, we are looking forward to increasing the number of trials designed and led by our own investigators, while continuing the very important and impactful collaborative efforts we are involved in nationally."*

*– Suzette S. Caudle, MD  
Interim chair of the Department of Pediatrics at  
Carolinas Medical Center and Levine Children's Hospital*

Treating pediatric patients not only means providing the best therapies and optimal care practices – it means bringing hope to seriously ill children and their families. Levine Children's Hospital actively pursues research to find new cures, improve the care experience and give more families reasons for hope.

Participating in drug trials, for example, enables our physicians to offer promising treatment options to children who would not otherwise have access to them. It also gives our medical teams valuable experience with emerging innovations and techniques for treating a variety of conditions, from cancer to infectious disease to congenital disorders.

"We feel very fortunate to be able to bring our patients the latest knowledge and therapies, to make an impact on how they live with these conditions, and to alter the course of these conditions," said Suzette S. Caudle, MD, interim chair of the Department of Pediatrics at Carolinas Medical Center and Levine Children's Hospital. Noting that physicians at Carolinas HealthCare System are not required to participate in research as part of their jobs, Dr. Caudle said she's proud of the fact that so many are motivated to undertake research in order to continually improve and optimize care.

"The primary reason our physicians are here is to take care of patients day to day. But they have the curiosity, insight and wisdom to really go above and beyond by participating in research to try to improve care in the immediate term and in the future," said Dr. Caudle. "I'm extremely proud of our investigators and all of the supporting professionals who make this work possible."

One unique aspect of the Levine Children's Hospital research program is its emphasis on improving how care is delivered, in addition to what therapies are used. "We are especially interested in focusing on studies that we hope will have a direct impact on how we take care of patients, and on how quickly and fully they return to health. We are very excited about working at the intersection of research and quality improvement in order to ensure we are providing the very best treatment options for the individual, in the most effective and efficient way possible," said Dr. Caudle. This focus is at the heart of the Center for Advancing Pediatric Excellence and pervades disease-specific efforts throughout our departments.

Working with other institutions through collaborations, registries and networks amplifies the value of these research efforts. "Since many childhood illnesses are, thankfully, uncommon, working with multiple sites allows investigators to get meaningful information much faster and pool it – and therefore impact patients sooner," said Dr. Caudle. "As we move ahead, we are looking forward to increasing the number of trials designed and led by our own investigators, while continuing the very important and impactful collaborative efforts we are involved in nationally."



## Pursuing Personalized Solutions in Hematology-Oncology

With more than 90 ongoing clinical trials, Levine Children's Hospital has a robust research program for children with cancer and blood disorders. One of our growing areas of emphasis is personalized care; a number of newer trials involve characterizing each patient's tumor and then tailoring the treatment plan accordingly.

"Many of these trials are the only ones of their kind in the Carolinas, and we're often one of only a handful of institutions in the country that are doing this work," said Dr. Caudle. "That really sets us apart and enhances the options we can offer our patients."

Our physicians are active in trials for new cancer drugs and drug delivery mechanisms, as well as pursuing studies of survivors of childhood cancer. In 2016, for example, Javier Oesterheld, MD, reported encouraging outcomes from a novel combination of mitoxantrone and clofarabine for treating relapsed leukemia. Other trials our investigators have brought to Carolinas HealthCare System include a study using gemcitabine and abraxane to treat relapsed solid tumors (through the Sunshine Project, a national consortium for solid tumor research); a novel trial for brain tumor treatment conducted in partnership with Nationwide Children's Hospital; and a study of ambulatory blood pressure in survivors of childhood cancer.

We also have a robust research program for children with blood disorders such as sickle cell anemia. One 2016 care improvement study, for example, was able to shorten hospital stays for children with sickle cell by more than one day on average. That's a remarkable achievement that can make a world of difference for patients who often spend significant amounts of time in the hospital, disrupting school attendance and family life. In addition, a study involving 10 of our sickle cell patients showed minimal toxicity and impressive survival with bone marrow transplant using haploidentical donors – findings that our investigators have been invited to present nationally on several occasions.

Matthew Saxonhouse, MD, director of the Center for Pediatric Research, leads several efforts to improve outcomes for the very youngest patients – newborns with thrombotic events or bleeding problems. This includes participation in the NeoHat study, a multi-site trial aiming to reduce the risks from platelet transfusion and better understand bleeding risks for neonates in the NICU. Looking ahead, Dr. Saxonhouse, along with Dr. Ashley Hinson, plan to develop a neonatal thrombosis center to improve outcomes and treatment modalities for neonates with stroke and other thrombotic events. Levine Children's Hospital will be the only site in the Carolinas offering this type of unique service.

## Building the Evidence Basis for Better Nephrology Care

Although treatment guidelines and protocols are available, there has been a dearth of research to support evidence-based care for children with kidney diseases and there remains a significant need to improve health outcomes for these patients. Emblematic of our dedication in this area is the Levine Children's Hospital Pediatric Nephrology Center of Excellence, launched in October 2016. The center is designed to promote patient- and family-centered care by enhancing patient and clinician engagement, conducting clinical research, and developing best practices to transform the patient experience. With funding from donors and operating under the leadership of Susan Massengill, MD, and Cheryl Courtlandt, MD, the center is well-positioned to build a strong reputation as a regional and ultimately a national leader in clinical trials for children with kidney diseases in the coming years.

The new center builds on a long-standing record of active participation in trials for children with kidney diseases. We currently have 10 ongoing studies in this area, including studies on nephrotic syndrome, hypertension in children with chronic kidney disease, and rare diseases such as atypical hemolytic uremic syndrome. Three ongoing NIH-sponsored studies include the Chronic Kidney Disease in Children (CKiD) study, for which we have longitudinally monitored cardiovascular risks, growth, cognition and disease markers in children with chronic kidney disease for 10 years; the Cure Glomerulonephropathy Network (CureGN) study, for which we have seven enrolled patients; and the Clinical Phenotyping and Resource Biobank Core (C-PROBE) project, for which we have enrolled 97 patients and 33 family members.

Our physicians are also playing leadership roles in the NephCure Accelerating Cures Institute (NACI), a seven-site clinical care network that pools patients and investigators to conduct clinical trials for nephrotic syndrome. In addition to contributing to longitudinal follow-up for nearly 100 patients, Levine Children's Hospital also hosted the first inaugural NephCure walk for North Carolina as part of our participation in NACI. Having been identified as a national leader in glomerular disease research, we were selected as a regional site for a clinical trial of intravenous abatacept for treatment-resistant nephrotic syndrome.

## Facts & Figures



More than 90 ongoing clinical trials in pediatric hematology-oncology



An additional 50 ongoing clinical trials in other areas (enrolling a total of more than 2,000 patients) are being conducted through the Center for Pediatric Research



## More Research Highlights

**Improving Rheumatology Care:** We actively contribute to the Pediatric Rheumatology Care and Outcome and Improvement Network (PR-COIN), an international collaborative that involves representation from the entire medical team to develop best practices and disease management strategies. One project, for example, has shown improvements in process and outcome quality measures in more than 3,700 pediatric juvenile arthritis patients seen at collaborating institutions.

**Opening New Options for Juvenile Arthritis:** Although a wide variety of approved medications are available to adults with arthritis, only a limited number are approved for use in children. We contribute to trials assessing the safety and efficacy of several drugs in the context of juvenile arthritis, including certolizumab, golimumab and tofacitinib. We also are part of the CARRAnet national registry, helping to advance basic research on juvenile arthritis and track outcomes associated with specific medications. Under a collaboration with Cincinnati Children's Hospital, we contribute to an NIH-funded gene expression study seeking new biomarkers for diagnosing and predicting response to medications in juvenile arthritis.

**Examining Key Questions in Pediatric Orthopaedic Trauma:** Several initiatives are underway to enhance care and treatments for pediatric patients with orthopaedic injuries. We are one of six participating sites in the Registry of Orthopaedic Trauma in Children (ROTC), a network established to advance clinical studies on the incidence and severity of injuries and explore treatment strategies. With more than 2,000 enrolled patients, ROTC is already leading to multi-center collaboration on studies. In a separate study, our researchers reported this year that near infrared spectroscopy (NIRS) provides an objective measurement of distal perfusion to aid in monitoring perfusion after supracondylar humerus fracture.

**Innovative Immunotherapies:** For children who are immune compromised, our researchers are pursuing therapies that replace crucial immune agents to boost patients' ability to appropriately respond to infections.

**Improving Outcomes for Traumatic Brain Injury:** Our Division of Pediatric Critical Care has enrolled 24 patients in the Approaches and Decisions in Acute Pediatric TBI Trial (ADAPT), a multi-center, international study seeking to optimize treatment for children experiencing severe traumatic brain injury.

## On the Hunt for Innovative Treatments for Rare Neuromuscular Diseases

At Carolinas HealthCare System, children with neuromuscular diseases such as limb girdle muscular dystrophy, Duchenne muscular dystrophy and congenital myasthenia not only receive outstanding medical care, but also the opportunity to benefit from promising emerging therapies. Our patient care and basic research activities are intricately intertwined both operationally and physically; Levine Children's Hospital is right next to our state-of-the-art basic science laboratories, and physicians and researchers meet regularly to discuss cases and plan research projects. A partnership with the University of North Carolina at Chapel Hill offers further opportunities to advance cutting-edge neuromuscular disease research.

One such clinical trial explores a new treatment, called eteplirsen, which targets the primary genetic defect behind Duchenne muscular dystrophy. Children with this debilitating disease face a high risk for respiratory failure, recurrent infections and heart failure. In a project spearheaded by the McColl Lockwood Muscular Dystrophy Research Laboratory, we are working to develop a genetic treatment for patients with limb girdle muscular dystrophy, another debilitating disease affecting the skeletal muscles.

## Unraveling the Mysteries of Infectious Diseases

Despite incredible achievements in immunization and anti-microbial therapy, infectious diseases remain a serious risk for children. Amina Ahmed, MD, and others in our infectious diseases department, pursue research in several areas to understand and fight both established and emerging infectious disease threats.

In partnership with the University of Alabama at Birmingham, for example, Carolinas HealthCare System in 2016 began a vital new trial aimed at more effectively detecting and treating asymptomatic cytomegalovirus, or CMV. Although it often shows no symptoms, CMV can lead to serious consequences such as deafness and developmental delay. Detection and early intervention can lead to significantly improved outcomes for these infected infants.

Tuberculosis (TB) is another active area of study. Levine Children's Hospital contributes to a large-scale CDC-led epidemiological study seeking to identify pockets of latent TB to further curb the spread of the disease. We also have participated in clinical trials to advance shorter and simpler treatment regimens for latent TB.

*Two brothers, Jordan and Luke, both underwent kidney transplants at Levine Children's Hospital at Carolinas HealthCare System, and have each been followed by Dr. Massengill since birth. Long-term outcomes and complications of transplantation are rich areas for research.*



# Neurosciences Institute Research Endeavors

Blending care, community and a tireless quest for cures



*"We've really fought hard to keep the research in the clinic, and I think that's been key. It's seamless for the patients – when they come in for their research visits, they can very easily meet with their physician and their nurse."*

*– Donna Graves, MD  
Medical director and multiple sclerosis specialist at the Carolinas HealthCare System's Neurosciences Institute*

Being diagnosed with a neurological condition such as Alzheimer's disease or multiple sclerosis is a life-changing event often fraught with fear and confusion for patients and their families. By combining outstanding care with forward-looking science and active engagement of patient communities, Carolinas HealthCare System strives to be a haven for patients facing these daunting diagnoses.

Because many neurological conditions remain incurable, the chance to participate in clinical trials and contribute to basic research is a comfort and a draw for patients. In addition to potentially benefiting from emerging medical advances, patients and their families value the frequent interactions with the expanded care team that comes with study participation.

"We've had patients who seek their clinical care here because they've heard about our research opportunities," said Donna Graves, MD, medical director and multiple sclerosis specialist at Carolinas HealthCare System's Neurosciences Institute. "Our researchers really take ownership of these patients and work in partnership with the physicians as active participants in the care team."

Research opportunities have continued to expand as our patient population and the expertise of our physicians and support staff have grown. "One thing that really makes us unique across the country is our size," said Dr. Graves. "We have 12 neurology clinic locations and a large subspecialty practice, so the volume of patients we care for makes us an interesting site from a sponsor perspective. They know we have a large patient population to pull from and can get a trial going quickly."

A major strength of the Carolinas HealthCare System model is the close integration of clinical and research work. "We've really fought hard to keep the research in the clinic, and I think that's been key. It's seamless for the patients – when they come in for their research visits, they can very easily meet with their physician and their nurse," said Dr. Graves.

That integration is evident in the personalized approach to supporting patients' participation in studies. Dr. Elena Bravver, MD, principal investigator for the Alexion trial studying efficacy of the drug eculizumab for myasthenia gravis, pointed to one study participant who was finding it difficult to make it to appointments because of his role as caregiver for his wife at home. Without someone to care for her during his trips to receive infusions, he feared he'd have to drop out of the study. In response, the research team and the trial sponsor devised a system to allow him to receive infusions at home. If the investigational treatment works, it could improve the patient's quality of life and also support his ability to continue caring for his wife.

This commitment to service extends beyond the walls of our facilities. "We have been very active in the community. Our research teams frequently go out to patient support groups, national consortia and patient educational conferences so that they can share research opportunities and findings," said Dr. Graves.

That type of engagement is crucial to ensuring our work reaches those who can benefit from it the most – and in the process, offers patients and their families a little more clarity, and a little more hope.

## Seeking Ways to Stave Off Alzheimer's Disease

Despite decades of research, drugs that effectively treat Alzheimer's disease remain frustratingly elusive. Our researchers are actively pursuing new avenues for predicting, detecting and interrupting the progression of this devastating disease. This effort has two main prongs: one focused on early identification of high-risk patients and the other on treatments aiming to delay the disease's most severe stages.

A large ongoing international trial with 50 sites that is being led by Robert Mitchell, MD, medical director for neurology at Carolinas HealthCare System, focuses on early identification of Alzheimer's risk. The study, titled The TOMMORROW Study, was initiated after researchers discovered variants of two genes – known as APOE and TOMM40 – that appear to interact in a way that increases the likelihood of developing Alzheimer's disease. The trial, which will track over 3,000 healthy older individuals for five years, aims to uncover whether a biomarker combining age and gene variants can be used to predict a person's disease risk.

One impetus for the study is to help doctors get a jump on treating Alzheimer's in patients before they develop the full-blown disease. "As part of a routine physical you typically have your cholesterol checked, and that gives you a sense of your risk for heart disease. Similarly, the idea here is that if we can identify factors that increase your risk for Alzheimer's, we can use that information to try to prevent or slow the disease in those individuals later on," said Dr. Mitchell.

Another team of researchers, led by Oleg Tcheremissine, MD, is working to advance drugs that could fill in the second part of that plan by helping to stem the progression of the disease. Dr. Tcheremissine has had a laser focus on defeating Alzheimer's since his own mother succumbed to the disease just four years after her diagnosis. He is the principal investigator for several clinical trials examining high-profile novel therapeutics aiming to reduce levels of amyloid-beta protein and amyloid plaques in the central nervous systems of patients with Alzheimer's.

These experimental therapeutics may even help alleviate behavioral and neurological deficits. Currently, no therapeutics that prevent or slow the progression of Alzheimer's disease are approved for clinical use. For this reason, these clinical trials serve not only as a vehicle of innovation, but also provide patients and their caregivers access to advanced diagnostics, rigorous clinical care, and emerging treatment options before they are available on the market.

The opportunity to participate in these trials is also a source of tremendous hope and satisfaction for many patients and their families. One such trial participant is Peter Oosterhuis, a longtime CBS golf broadcaster and seven-time European Tour winner. Oosterhuis and his wife Roothie have been enthusiastic advocates of Alzheimer's research since he received a diagnosis of early onset Alzheimer's in 2014.

"We had to come face to face with Alzheimer's and deal with it," recalled Mrs. Oosterhuis in a video interview. "Our life totally changed. It's a devastating diagnosis and it takes a long time to accept it." When Dr. Tcheremissine offered the chance to participate in a drug trial, she said the couple immediately decided to enroll Peter in the study.

"It's so inspiring to do this for somebody else. We want to help people that get Alzheimer's in the future, to help them have a better chance than we have. That's why we're doing it, and we're very thrilled to be here," said Mrs. Oosterhuis.



*Oosterhuis was referred to Oleg Tcheremissine, MD, director of research at Carolinas HealthCare System, who enrolled Oosterhuis in a clinical trial that uses a drug that could slow the progression of the disease.*

## More Research Highlights

**Enhancing Recovery After Stroke:** Current trials examine post-stroke care and standards of practice. The Stratis registry tracks long-term outcomes in patients treated with neurothrombectomy devices. The MaRISS registry, enrolling now, aims to elucidate outcomes of tPA treatment in patients with mild and rapidly improving stroke.

**Emerging Therapy for Muscular Dystrophy:** In addition to enrolling muscular dystrophy patients in the MDA registry, we have enrolled 24 patients with muscular dystrophy in Marathon DMD, an open label, expanded access program for the investigational drug deflazacort (MP-104), which has been submitted for FDA approval for treating Duchenne muscular dystrophy.

### Welcome News for Multiple Sclerosis

Jill Conway, MD, leads Carolinas HealthCare System's participation in a number of drug trials for the nervous system disease multiple sclerosis (MS). A Phase III trial, called Oratorio OLE, in 2016 reported results showing the new drug ocrelizumab significantly reduced clinical disease progression. A related study, Opera OLE, suggests the drug is also effective in reducing the likelihood of relapses. As of the end of 2016, the drug was being considered for approval by the U.S. Food and Drug Administration (FDA).

"That approval would be huge, because it would be the first drug ever for progressive multiple sclerosis," said Dr. Graves. "I'm very pleased that Carolinas HealthCare System was able to offer this drug for our patients early on through this clinical trial." The system is currently enrolling more patients to receive ocrelizumab through an expanded access program.

Additional studies are underway investigating other therapeutic approaches and treatments for patients in different stages of MS. These include the IVSS trial (alemtuzumab); Optimum-Acetilion (ponesimod); Arpeggio (laquinimod); Expand OLE (siponimod, BAF312); Extend (daclizumab, BIIB019); and Opexa (Tcelna™).

### Offering Options for ALS

Recruiting a sufficient number of patients can pose a significant challenge when conducting clinical trials for rare diseases such as amyotrophic lateral sclerosis (ALS). Our MediciNova trial overcomes this challenge with 70 patients enrolled – a remarkable achievement for such a rare disease. The study is a randomized, double-blind, placebo-controlled trial to evaluate the safety, tolerability and efficacy of ibudilast (MN-166).

In addition, we have enrolled more than 400 total patients in the MDA registry, which collects data on patients with ALS, Duchenne muscular dystrophy and spinal muscular atrophy. We also have 10 enrolled ALS patients in the Phase III Cytokinetics trial to evaluate tirasemtiv and are in the process of enrolling patients for the Neuraltus Phase II study of NP001 for ALS patients with elevated systematic inflammation.



## Facts & Figures



18 active trials and registries including more than 550 patients total



An additional 10 trials in the planning stages



## Ahead of the Curve in Behavioral Health

It is estimated that only 40 percent of Americans with a mental or behavioral health problem actually receive treatment, and a fraction of them receive evidence-based care and show measured improvement. As part of our commitment to offering the very best care for all patients with neurological or behavioral disorders, Carolinas HealthCare System has implemented a number of initiatives to more effectively reach and treat this historically underserved patient population.

According to John Santopietro, MD, chief clinical officer for Carolinas HealthCare System's Behavioral Health, there may be as many as 100,000 people in the Carolinas HealthCare System region with untreated or undertreated mental health problems. Connecting these patients to appropriate care could impact not only their mental health, but also their physical health and overall costs, because untreated mental illness is one of the biggest drivers of unnecessary healthcare costs.

"As healthcare continues its transformation from 'volume' to 'value,' we're trying to do as much clinical research as we can to support system transformation," said Dr. Santopietro. "I believe we're ahead of the curve in understanding the immense value we can provide by addressing untreated mental health issues. We're very committed to having this research feed back into the care at Carolinas HealthCare System and improve it."

One major initiative is the integration of behavioral health into primary care. Primary care teams now use an adapted version of a model called IMPACT to screen for mental health concerns and provide immediate mental health treatment – via a live video connection with a behavioral health care provider – as an integral part of the primary care visit. Two years and over 8,000 patients after its launch, data suggests the model not only helps patients improve from a mental health standpoint, but also results in improved physical health and reduced inpatient utilization.

We also are working to advance quality of care in the inpatient setting. Since Carolinas HealthCare System Behavioral Health-Davidson opened in 2014, this 66-bed hospital has used innovative care models, such as a 7-on, 7-off staffing rotation schedule that has been shown to enhance continuity of care for patients. In addition, each patient's medical team now includes a pharmacist, an internist, and a peer support representative who has personally experienced mental illness, increasing patients' trust and ability to connect with their care providers.

# Sanger Heart & Vascular Institute Research Endeavors

Delivering extraordinary innovations sought after by patients and peers



Dr. Rinaldi performing transcatheter aortic valve replacement in the hybrid operating room.

At Sanger Heart & Vascular Institute, we not only deliver the highest quality care to each and every patient today – we continually push the envelope in order to bring better care tomorrow. Our research program has yielded cutting-edge therapies and techniques that have revolutionized treatment of serious cardiovascular conditions, helping patients around the world to live longer and more enjoyable lives.

“Given our working environment, quality of care and reputation, we are able to attract and retain some of the best physicians in the country,” said Michael J. Rinaldi, MD, interventional cardiologist. “We are truly world class: Other surgeons from around the country, and indeed around the world, travel to Sanger to learn techniques being developed here, and we are frequently invited to present our work internationally.”

Our integrated care model, high volume of patients and outstanding in-house expertise make Carolinas HealthCare System uniquely well-positioned for continued growth in research leadership across multiple areas of cardiovascular medicine.

“We are one coordinated system without barriers to collaboration and innovation,” said Dr. Rinaldi. “All subspecialties of adult and pediatric cardiology, cardiac surgery, and vascular surgery are part of the same group, all working in the same environment with the same process and goals. This facilitates an incredible incubator for new ideas and care delivery models, and allows a nimble and coordinated process for implementation.”

“We are one, coordinated system without barriers to collaboration and innovation.”

– Michael J. Rinaldi, MD  
Interventional cardiologist



One particular strength is in pioneering minimally invasive techniques, which allow patients to get back on their feet in days – rather than months – after a cardiovascular procedure. Our physicians are also making valuable research contributions in stem cell therapeutics, cardiac imaging, and treatments for atrial fibrillation and advanced heart failure.

The combination of exceptional patient care and a robust research infrastructure attracts patients, sponsors and collaborators alike. “It’s the entire team – the skill of the doctors, the dedication of the technicians and the expertise of our research team really sets us apart,” said Joseph T. McGinn, MD, chair of the Department of Cardiovascular and Thoracic Surgery within Sanger. “In addition, since our system has such a large volume of patients, we can acquire data very quickly, and many research projects can be published in less than a year’s time. That makes us very attractive as a research collaborator.”

## Advancing Transcatheter Therapies for Valvular Heart Disease

Surgical replacement of the aortic valve is a lifeline for patients with aortic stenosis, who face an extremely poor five-year survival rate without it. But conventional valve replacement requires open-heart surgery, which entails a months-long recovery period and is considered too risky for some patients. Transcatheter aortic valve replacement (TAVR) has emerged as a game-changing option in which the valve replacement is carried out through a catheter inserted in the leg instead of open-heart surgery. This minimally invasive approach allows many patients to leave the hospital within one to two days, followed by a short recovery period at home.

Carolinas HealthCare System has been a leading enroller in TAVR trials. Initially tested in patients considered too ill for open-heart surgery (PARTNER I trial), TAVR is now the standard of

care for high-risk patients. In 2016, the technique gained FDA approval for use in intermediate-risk patients after the PARTNER II trial demonstrated TAVR was superior to surgical aortic valve replacement in this group as well. Sanger Heart & Vascular Institute is now participating in the PARTNER III trial to investigate the potential benefits of TAVR in low-risk patients.

“This work is critical because most patients with severe aortic stenosis are not high-risk, and favorable results from the current study could expand access to this minimally invasive technology to the majority of patients suffering from this condition,” said Dr. Rinaldi, who oversees the system’s participation in TAVR trials. “This could be life-changing for many patients and may have significant implications for care delivery in the United States.”

Carolinas HealthCare System has also played a leading role in testing the MitraClip transcatheter mitral repair system, a catheter-based technique for treating mitral regurgitation, the most common valvular heart disease in adults. As with TAVR, MitraClip is designed to improve outcomes and shorten recovery by using a catheter instead of open-heart surgery to access and repair the faulty valve.

Findings from the EVEREST II trial, published in the *New England Journal of Medicine*, led to FDA approval for MitraClip in patients with symptomatic primary mitral insufficiency who are poor candidates for surgery. Today Carolinas HealthCare System is the highest volume MitraClip repair program in the Carolinas. Moreover, we are currently a top-10 enroller in the COAPT trial investigating MitraClip’s potential benefits for patients with symptomatic secondary mitral regurgitation who fail optimal medical therapy. “This landmark trial will provide crucial guidance to inform treatment for a group of patients with a significant unmet need,” said Dr. Rinaldi.

## Getting Patients Back on Their Feet in Days With Minimally Invasive CABG

Coronary artery bypass grafting (CABG) has long been a mainstay of treatment for coronary heart disease and remains the most common type of open-heart surgery in the United States. But with a standard recovery period of about three months, the lifesaving procedure can be extremely disruptive for patients and their families.

By using specialized surgical devices inserted through the ribs, Dr. McGinn accomplishes CABG without the need for open-heart surgery, dramatically reducing patients' pain and recovery time. It's a welcome improvement for patients eager to get back to work and other daily routines after surgery. One patient, for example, needed surgery for his severe angina but was hesitant to leave his bread truck route for too long. "We used the minimally invasive approach, and he was able to get back to his route within a week or two after discharge – to the great relief of his wife, who had had to drive the truck in the meantime," said Dr. McGinn.

Thanks to Carolinas HealthCare System's high volume of CABG patients, McGinn has been able to apply the minimally invasive approach for many patients over a short period of time, demonstrating its immense advantages. In addition to reducing recovery time for surgery-eligible patients, the approach is also offering new options for patients who are considered poor candidates for open-heart surgery. Such patients show better outcomes with minimally invasive CABG both in the short term and in the long term compared with open-heart bypass surgery. Dr. McGinn recalled one patient who went into cardiac arrest at home and came to Carolinas HealthCare System in grave condition. After receiving minimally invasive bypass surgery, she was able to return home and is "doing fantastic," said Dr. McGinn. "It's really a testimony to the fact that this type of surgery can be applied to just about the sickest patients, and they tolerate it quite well."



Dr. McGinn, assisted by a multidisciplinary surgical team, performs minimally invasive coronary artery bypass grafting.

## Stem Cell Therapy: Using Tomorrow's Medicine, Today

Stem cell therapy is expected to be one of the most transformative cardiovascular treatment advances of the decade. Carolinas HealthCare System is an established center for investigational stem cell therapies. It's also the fourth highest-volume enroller nationally in a major study of the use of stem cells to regenerate left ventricular mass and function in patients with large areas of damaged heart tissue. Sanger Heart & Vascular Institute researchers also contributed to a completed study that demonstrated the benefits of stem cell therapy for refractory angina. We are currently enrolling for a study of the use of stem cells for myocardial regeneration in congestive heart failure patients.

"This is the future – a groundbreaking opportunity to really benefit our patients," said Dr. McGinn. "Stem cell therapy trials are very unique and cutting-edge, and we're honored to play a part in that."

### Facts & Figures



Oversees 50+ clinical trials, involving more than 40 Sanger Heart & Vascular Institute faculty members



436 enrolled research patients (as of December 2016)



18 studies were open to enrollment at some point in 2016; of these, Sanger was among the top 10 enrollers for eight of these trials



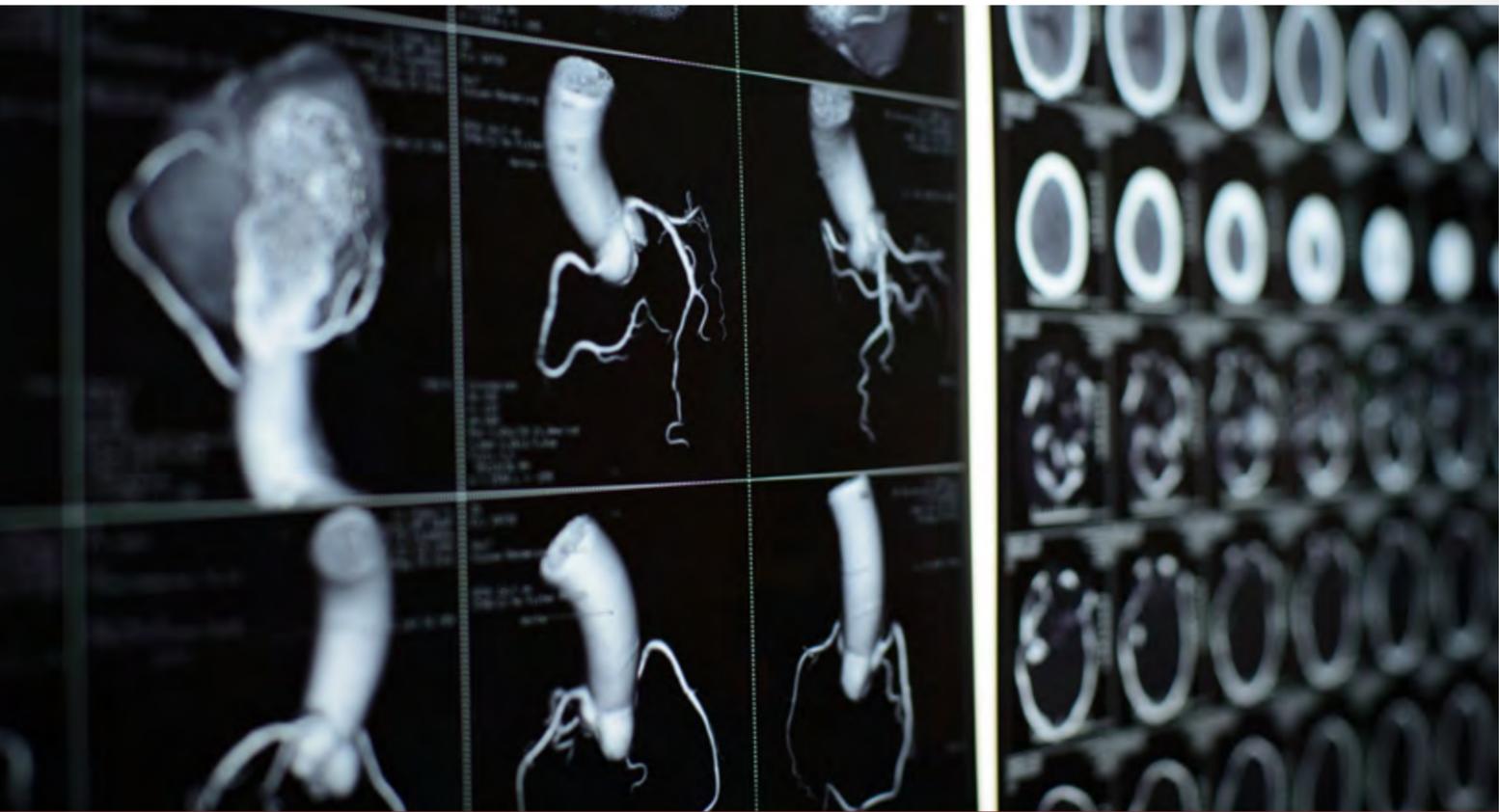
Over 150 publications, abstracts and national presentations



More than 100 cardiac physicians with expertise in every cardiology and surgical specialty, at more than 20 locations throughout the Carolinas



Innovative endovascular solutions for complex vascular diseases, including the world's first implantation of a branched stent graft specially designed to repair thoracic aortic aneurysms



## More Research Highlights

**A Beta Site for FFR-Enhanced Coronary CT Angiography:** As the largest US healthcare system that is actively contributing to the ADVANCE registry, Carolinas HealthCare System is at the nation's leading edge of coronary artery imaging. The new technology, which just became the first-line stress test modality in the United Kingdom, incorporates mathematically derived physiology FFR calculations into CT angiography to offer extremely high-quality imaging with significantly less radiation than a coronary angiogram.

**Next-Generation Ventricular Assist Device (VAD):** Carolinas HealthCare System is the leading enroller for the HEARTMATE III study, investigating enhanced VAD technology for treating advanced heart failure.

**Ablation as First-Line Treatment for Atrial Fibrillation:** The CABANA trial investigates whether ablation should replace medical therapy as the first-line treatment for atrial fibrillation.

## Dr. Frank Arko: A World-Renowned Pioneer in Vascular Surgery

The achievements of Frank R. Arko, MD, are emblematic of the boundary-pushing spirit and remarkable level of skill and expertise seen across Sanger Heart & Vascular Institute. Recognized as one of the top vascular surgeons in the world, Dr. Arko has developed innovative patented technologies, pioneered new forms of endovascular stent graft therapy, and been called upon to teach advanced endovascular techniques worldwide.

Aneurysms occurring in the aorta present significant risks, and their surgical removal can be a complicated endeavor. Traditionally, treatment for aneurysms in the thoracic or abdominal aorta required open surgery, associated with significant morbidity and mortality, and a long recovery. The emergence of endovascular stent graft therapy changed that paradigm dramatically with improved patient outcomes and a faster recovery – but options for patients with aneurysms in hard-to-reach areas, such as along the aortic arch vessels, remained limited.

That changed in 2013, when Dr. Arko became the first surgeon in the world to implant a branched thoracic endograft for complex descending thoracic aortic aneurysm disease involving the aortic arch vessels. The successful implantation of the Valiant Mona LSA system kicked off a groundbreaking clinical trial led by Carolinas HealthCare System and Cleveland Clinic.

Building on the success of that effort, Dr. Arko is now involved in planning a study of new stent graft technology that aims to address aneurysms in the ascending aorta, an area that has remained treatable only through conventional open-heart surgery – making Carolinas HealthCare System, once again, one of only a handful of institutions in the world to bring the promise of endovascular advances to more patients with life-threatening aortic aneurysms.



# Surgery Research Endeavors

Pioneering innovations from the individual patient to the entire care system



*"....We are at the forefront of measuring not only the standard, traditional outcomes of surgery, but we have really pushed hard on measuring and improving the quality-of-life outcomes as well."*

*—Todd Heniford, MD  
Chief of the Division of Gastrointestinal  
and Minimally Invasive Surgery*

The General Surgery Research Laboratory at Carolinas HealthCare System is a nexus of excellence recognized the world over. Surgical techniques, decision-support tools and care improvement processes pioneered on our campuses have earned us a strong reputation for providing outstanding care for even the most complex cases. Our surgeons are devoted to relentlessly pursuing, rigorously testing, and insightfully deploying new methods, tools and procedures to both extend and improve patients' lives.

"Quite honestly, from this institution we've changed the way surgery is done worldwide," said Todd Heniford, MD, chief of the Division of Gastrointestinal and Minimally Invasive Surgery. "A lot of that comes from the complexity of the patients we take care of and our ability to follow them closely. It's also the way we care for patients holistically. We are at the forefront of measuring not only the standard, traditional outcomes of surgery, but we have really pushed hard on measuring and improving the quality-of-life outcomes as well."

One example is the Carolinas Comfort Scale® (CCS), developed and patented by Carolinas HealthCare System surgeons in an effort to better evaluate and track quality-of-life measures for patients undergoing hernia surgery. The scale has been translated into more than 20 languages and is used in more than 30 countries, including by the government health systems in France and the United Kingdom. A recent international study using the CCS for 4,000 patients demonstrates the scale's value for evaluating quality-of-life factors including physical function, pain levels and sensation after hernia repair – the most common operation worldwide.



Clinical excellence is the driving force behind these research endeavors – and a major draw for patients, partners and trainees. "The value of our work is evident in the research we've done, the papers that we've published, the national and international lectures that we've given," said Dr. Heniford. "We've had more than 3,500 surgeons come here to watch us operate. And of course other doctors and surgeons see the outcomes of our work when their patients return home after a complex procedure here."

One common thread throughout our research is a focus on the practical. Many efforts are directed toward systemic quality improvement, while others focus on techniques and approaches that are immediately applicable in the operating room. Our system has also become a leader in the use of technology to propel advances and rapidly disseminate knowledge and tools around the world.

"Our research is patient-centered and can be impactful in a time period that's very tangible," said Brent D. Matthews, MD, professor and chair, Department of Surgery. "Philosophically, the research that we feel has the greatest impact is the research that gets all the way to the bedside where we're actually managing and caring for patients. The most frequent question we ask ourselves is how can clinical care redesign affect the patient experience, quality and cost?"

The value of these efforts is apparent in the improved outcomes among patients and in the positive feedback we receive from patients and their families. But from the day-to-day perspective of our surgeon-scientists, what really sets Carolinas HealthCare System apart is a culture and community that fosters innovation and makes it fun to come to work every day.

"Working with my colleagues makes it all worth it," said Dionisios Vrochides, MD, PhD, vice chair of Quality and Evidence-based Practice and associate professor of surgery, Division of Hepatobiliary and Pancreatic (HPB) Surgery. "Our people work very hard, and they are always smiling and very enthusiastic about what they do. We are happy that we can often be the first place in the United States to offer a new option to patients – we carry the Carolinas HealthCare System badge with pride."

## Achieving Better Outcomes Through a Focus on “Prehabilitation”

One illustration of our holistic, patient-centered approach is a push to advance “prehabilitation,” which centers around methods to get patients in the best possible shape before surgery in order to aid their recovery afterward. This can include anything from nutritional interventions to patient education to sophisticated predictive analytics. By ensuring patients are mentally and physically well-prepared for surgery we can simultaneously improve health outcomes and empower patients for a positive overall experience.

CEDAR (Carolinas Equation for Determining Associated Risks), for example, is a mobile software application we developed to support prehabilitation for patients undergoing hernia surgery. It uses patient-specific medical and lifestyle information to calculate the risk of complications. But the app doesn’t stop there. By changing variables, doctors can illustrate in real time how making changes before surgery can perceptibly reduce a patient’s risk.

“When you have a patient who is overweight, diabetic and/or smokes, it’s challenging for patients to lose weight, get their diabetes under control or stop smoking before surgery,” explained Dr. Heniford, who led the app’s development and regularly uses it in the clinic. “This app adds extra incentive for them by demonstrating how they can decrease complications. People will frequently look at us and say, ‘Nobody ever spoke to me like this before – I get it now.’ It puts objective metrics on how patients can lower their risk.”

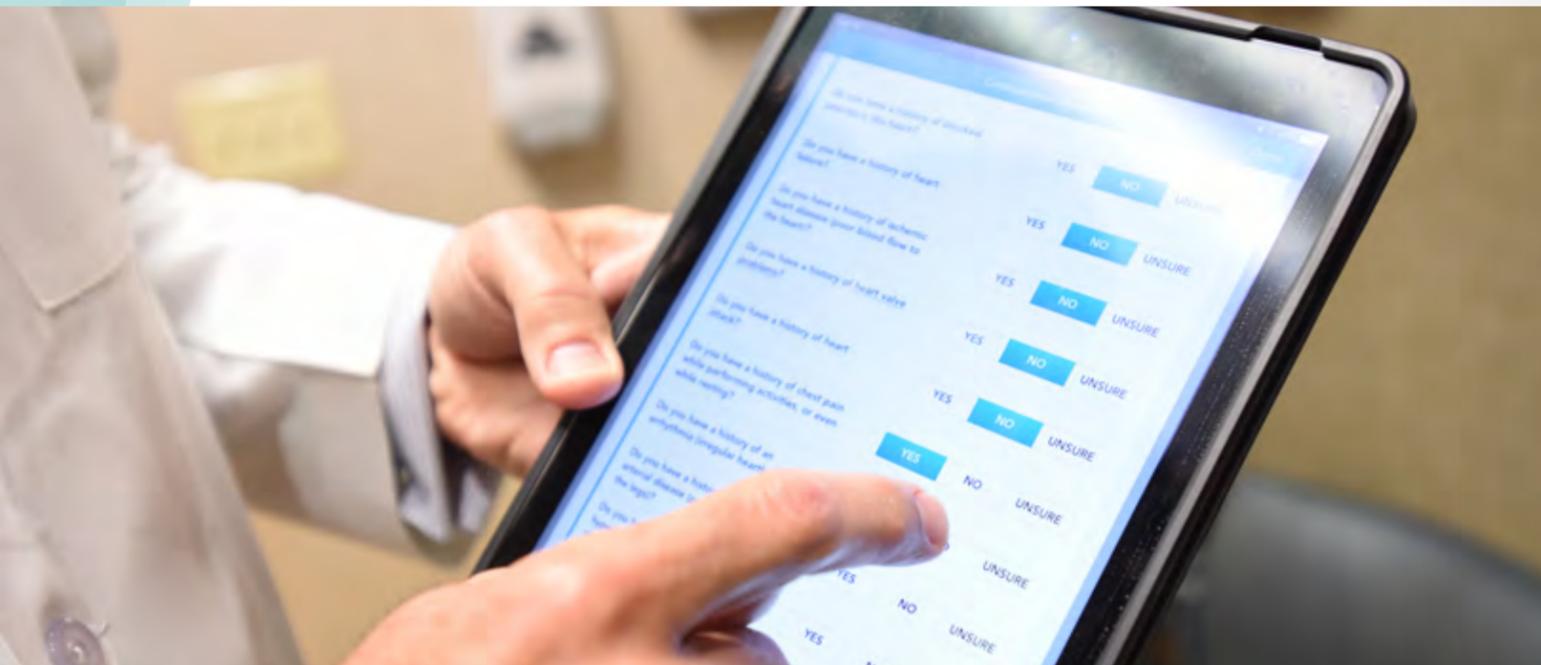
CEDAR was developed based on 1 million data points collected from 500 patients who were tracked for a year after receiving hernia surgery at Carolinas HealthCare System. After initial internal deployment, we validated the app’s predictions with tests at a separate healthcare system. Now freely available through the iTunes app store, the app has been downloaded in 140 countries. Follow-up research shows that using the app not only improves health outcomes but also reduces costs.

## Innovative Tools to Eliminate Waste

When the Institute of Medicine reported in 2012 on the alarming level of unnecessary medical expenditures in the United States, the institute identified unnecessary medical services as a significant contributor to the problem. Carolinas HealthCare System has made a concerted, multipronged effort to save our patients money by eliminating unnecessary costs. One example is CESP (Carolinas Established Surgical Preoperative Algorithm), a decision-support application that identifies which tests are truly necessary before a patient undergoes surgery – and, importantly, which ones can be skipped.

The app integrates algorithms from all relevant medical guidelines with patient-specific information – input by patients via a tablet-based 10-minute questionnaire and verified by the provider – to produce a list of recommended pre-op tests. The app, currently in beta, has been deployed at Carolinas Medical Center in Charlotte, NC, and will soon be expanded throughout Carolinas HealthCare System before being released nationally. An analysis of CESP use in the first 346 patients revealed potential savings of more than \$500 per patient by eliminating unnecessary pre-op tests.

“The problem is that the algorithms put out by the medical associations are just too difficult to use, so many providers just order all of the labs anyway,” said Dr. Heniford, who oversaw the app’s development. “With this tool we anticipate saving \$7 million to \$10 million at the Carolinas Medical Center location alone, by eliminating things that simply aren’t needed. That’s an incredibly dramatic impact.”



## Facts & Figures



84 clinical, translational and basic science research projects in 2015 and 2016



Home to a prospective study of more than 8,000 patients undergoing hernia repair



One of just 15 ERAS® Centers of Excellence worldwide and the first such designee in the United States

- 4 ongoing ERAS-related randomized controlled trials
- 6 ERAS-related grants
- 10 ERAS-related cohort or quality improvement studies

## An Enhanced Recovery After Surgery (ERAS®) Center of Excellence

After an intensive, multi-year process we were thrilled to have Carolinas Medical Center designated a Center of Excellence by the ERAS Society in 2016, becoming one of just 15 such centers worldwide and the first in the United States. This distinction recognizes our dedication to applying evidence-based practices to improve surgical care quality and patient outcomes. It also identifies our center as an exemplar to teach ERAS practices to other institutions. Currently more than 100 institutions are ERAS-accredited and more are in the process of earning accreditation.

Initiated in the Division of Hepatopancreatobiliary (HPB) Surgery, already the ERAS practices are being implemented in surgical departments throughout Carolinas HealthCare System. ERAS encompasses best practices for all aspects of a patient's surgery experience, as well as systems for tracking compliance and outcomes.

"There are 23 components of this multi-modal program, and you monitor compliance to the protocols in order to target areas that have barriers to implementation," explained Dr. Matthews. "It's a very comprehensive way of managing each patient and also using data to drive and manage improvement."

Program audits 30 days, 90 days and one year after implementation showed an increase in best-practice compliance, decreased average length of stay and a decreased readmission rate.

One implementation of ERAS is the Pre-Operative Learning and Readiness in Surgery (POLARIS) patient-education course. The program allows patients undergoing open or robotic/laparoscopic pancreaticoduodenectomy (Whipple procedure), distal pancreatectomy and hepatectomy – as well as their families – to visit the hospital before their operation to receive a tour of the care unit, learn about the surgery itself and prepare for post-operative management. Patient questionnaires show the program has a significant impact on the patient experience and on patient's understanding of their surgery.

"Patients really like this program," said Dr. Vrochides. "They report feeling more actively involved in their post-operative care, understanding what to expect, and having their family more involved in their pre-operative education."



## More Research Highlights

**Emerging Techniques for Minimally Invasive Surgery:** Several ongoing trials investigate innovative, minimally invasive methods for ablating tumors in the pancreas and liver. These techniques allow surgeons to ablate tumors with less damage to nearby blood vessels. Microwave ablation, for example, helps surgeons navigate through the liver to identify and destroy tumor tissue – akin to a “medical GPS.”

**Notable Firsts in Intrauterine Surgery:** Dr. Courtney Stephenson, DO, in collaboration with HPB Surgery, has pioneered specialized procedures for fetal surgery in the womb. For example, she is one of only a few surgeons in the country to use ablation to address twin-twin transfusion syndrome, a rare condition that results in unequal distribution of blood among twins in utero.

**Exploring Artificial Intelligence:** Our in-house software development teams are partnering with physicians and researchers to develop artificial intelligence-based interfaces to aid in diagnoses and patient follow-up. One application, for example, is designed to track healing after surgery by analyzing patient-provided images of the incision using machine learning methods.

**Advancing Colorectal and HPB Surgery:** A number of ongoing clinical trials address quality improvement methods for abdominal surgery. We also are home to several trials investigating new medical devices such as mesh implants and abdominal wall reconstruction techniques.



# Other Division and Department Research Highlights

|   |    |
|---|----|
| Division of Hepatology .....                                    | 44 |
| Liver Pathobiology Research Laboratory .....                    | 45 |
| McColl-Lockwood Laboratory for Muscular Dystrophy Research..... | 46 |
| Physical Medicine & Rehabilitation Research .....               | 47 |
| Department of Obstetrics and Gynecology .....                   | 48 |
| Department of Orthopaedics .....                                | 49 |
| Department of Oral Medicine .....                               | 50 |
| Division of Pediatric Nephrology & Hypertension .....           | 52 |
| Department of Emergency Medicine .....                          | 53 |
| Department of Family Medicine .....                             | 54 |
| Carolinas Simulation Center .....                               | 55 |
| Center for Outcomes Research and Evaluation .....               | 56 |

# Division of Hepatology

**Fast Facts: 6 publications; 1 book chapter; 4 presentations**

The Division of Hepatology and the Center for Liver Disease and Transplant conduct state-of-the-art research aimed at improving the lives of patients with a wide range of liver diseases. Our faculty have presented and published the findings of their research at national meetings and in leading medical journals. We currently have 261 patients enrolled in nine different clinical studies.

## Research Highlights:

- Philippe Zamor, MD, is conducting a clinical trial of a novel oral therapy for hepatitis C, a serious disease that can lead to cirrhosis, liver cancer and liver transplantation. Thus far, cure rates seen in these trials exceed 95 percent, and the regimens are well tolerated.
- Andrew deLemos, MD, is taking part in several clinical trials investigating the potential benefit of new medications for the treatment of nonalcoholic steatohepatitis, a form of nonalcoholic fatty liver disease (NAFLD). NAFLD is one of the most common causes of liver disease worldwide and a condition for which there is currently no FDA-approved drug. These new therapies are targeted at stopping the progression of liver fibrosis to prevent the development of cirrhosis, reduce the risk of liver cancer and reduce the risk of needing a liver transplant.
- Paul Schmeltzer, MD, is planning a clinical trial for the treatment of hepatocellular carcinoma (HCC, also known as liver cancer), which occurs predominantly in patients with chronic underlying liver disease and cirrhosis. In addition, Dr. deLemos is collaborating with four other academic liver transplant centers in a retrospective study to identify risk factors for HCC development in patients with NAFLD. Laura Schrum, PhD, director of the Liver Pathobiology Laboratory at Cannon Research Center, is collaborating with the Division of Hepatology to identify promising biomarkers for HCC and liver fibrosis progression.
- Mark Russo, MD, medical director for Liver Transplantation and chief of Hepatology at Carolinas HealthCare System, leads a study evaluating kidney function in liver transplant recipients. He also serves as mentor for projects focused on evaluating the efficiency of liver transplant evaluation and readmissions after liver transplant.

## Advancing Patient Care and Improving Outcomes

Patients tell us that the opportunity to participate in clinical trials is a valued benefit of coming to Carolinas HealthCare System for treatment of liver disease. Knowing that they are among the first patients to access experimental therapies offers hope and comfort for patients facing serious diseases that have limited available treatment options, such as NAFLD. Our researchers are passionate about developing innovative therapeutic approaches to slow disease progression and help patients avoid the need for higher-risk treatments.

# Liver Pathobiology Research Laboratory

**Fast Facts: 8 publications; 1 presentation; 2 grants**

With the combined efforts of bench scientists and clinicians, the Liver Pathobiology Research Lab, under direction of Laura W. Schrum, PhD, is uniquely positioned to investigate the intricate cellular and molecular mechanisms behind liver pathologies and cancer. With an overarching goal of discovering better diagnostic techniques and therapies, our researchers focus on genes and biochemical pathways involved in hepatic fibrosis/cirrhosis with further advancement to hepatocellular carcinoma (HCC).

## Research Highlights:

- Our team is investigating the role of microRNAs during development of fibrosis/cirrhosis, which show great potential for new diagnostic and therapeutic strategies in managing liver disease. For example, our preclinical studies demonstrated that re-introduction of miR19b via an adeno-associated virus inhibits development of hepatic fibrosis. We also observed similarities in miR19b expression in cardiac fibrosis, suggesting miR19b as a global regulator of fibrotic injury. This work has resulted in a patent application.
- Our group is also examining Rev-erb, a transcriptional repressor, as a key regulator in hepatic stellate cell activation. We have shown the therapeutic potential of targeting Rev-erb, using a biologically active agonist, to impede the development of hepatic fibrosis in a CCl4-induced fibrotic mouse model.
- We were able to identify extracellular matrix protein, tenascin-C (TnC), as a potential non-invasive biomarker for cirrhosis and liver cancer as well as an important signaling molecule in liver cancer development. Further, patients successfully treated for HCC demonstrate decreased TnC compared to patients without treatment. Recently, we have initiated studies to directly target TnC expression in order to impede the development and progression of HCC.
- Our group is focused on comparative-effectiveness and outcomes research projects that aim to improve delivery, and value, of healthcare to patients with chronic liver diseases. One example of this work is a retrospective study to determine the safety of prescribing aspirin to patients with liver disease.

## Advancing Patient Care and Improving Outcomes

The Liver Pathobiology Research Laboratory is focused on performing outcomes and translational research in close collaboration with clinicians with the goal of developing novel therapies and identifying biomarkers to optimize healthcare for patients with liver diseases. Our liver research program is making significant strides in improving the health of patients with chronic liver diseases by transforming the way we deliver care and diagnose and treat liver diseases.

# McColl-Lockwood Laboratory for Muscular Dystrophy Research

**Fast Facts: 8 publications; 6 presentations; 6 grants**

The McColl-Lockwood Laboratory focuses on translational research for muscular dystrophy, specifically limb-girdle muscular dystrophy (LGMD) 2I caused by genetic defects in the gene FKRP. This disease causes disruption of normal muscle structure and weakening of skeletal, cardiac and respiratory muscle functions, often resulting in premature death. There is currently no cure or effective treatment for LGMD2I.

## Research Highlights:

- Our laboratory established the fact that an AAV-FKRP gene therapy approach prevents disease progression for LGMD2I. The lab is now moving forward to pursue a clinic trial of this gene therapy. With sponsorship from our pharmaceutical partner, this effort includes pre-IND preparation, dose escalating systematic efficacy and toxicity tests of the AAV gene therapy in LGMD2I models.
- Currently steroids are the only option drugs prescribed for LGMD2I, but their effectiveness in modifying the disease is unknown. Our researchers are conducting a comprehensive evaluation of steroid and bisphosphonate treatment in mouse models for muscular dystrophy, providing valuable guidance for the clinical applications of these drugs and helping to identify new compounds with higher efficacy and less side effects.
- Studies in our mouse models have also led to the discovery that, despite the obvious defect in functions of the mutant FKRP gene, diseased muscles and some other types of tissues are able to maintain their normal patterns of protein expression and sugar modifications. Defects in specific sugar modification of critical cell membrane proteins are associated with the characteristic of patients and diseased animals. These findings have led us to explore novel experimental therapies involving modulation of gene expression and gene editing.

# Physical Medicine & Rehabilitation Research

**Fast Facts: 30+ papers and abstracts in peer-reviewed journals, 40+ presentations and posters and 4 new federal or consortium grants**

Our nationally and internationally known Physical Medicine & Rehabilitation researchers focus on advancing the field and providing treatment and recovery enhancement for patients with traumatic and acquired brain injury, spinal cord injury, stroke, neuromuscular and degenerative disorders, and other disorders resulting in disability. Our researchers are funded to conduct rigorous trials of treatments and devices, pursue translational investigations, and advance cutting-edge technology and interventions. We foster productive partnerships with peer institutions and have led our community, region and state in providing supportive services and opportunities for people with disabilities.

## Research Highlights:

- With an NIH K-Award, Jesse Lieberman, MD, is investigating the effect of nutrition education after spinal cord injury for improving body composition, cardiovascular risk factors and overall health.
- Janet Niemeier, PhD, is studying biomarkers and outcomes for traumatic brain injury along with collaborators in Carolinas Medical Center Acute Care, Orthopaedic Surgery, Emergency Medicine, OB/GYN Fertility and Cannon Research Labs.
- Mark Hirsch, PhD, is working with investigators in both the US and Holland to expand his Parkinson's research.
- Our investigators are also working on studies with Duke, Ohio State, University of Pittsburgh and Indiana University with funding from NIH and the National Institute on Disability and Rehabilitation Research. For example, Mark Newman, PhD, worked with the University of Pittsburgh to merge the two sites' traumatic brain injury (TBI) model systems and data on early post-TBI recovery.
- Our researchers are involved with nine TBI Model Systems sites to explore gender differences in outcomes for people aging with TBI; differences between adolescents, young adults and older adults with TBI; pediatric TBI needs; and effect of comorbidities. In our role as an active data collection and follow-up site, we have achieved 97 percent completeness for data collection and a 92 percent follow-up rate.

## Advancing Patient Care and Improving Outcomes

A series of focus groups conducted in 2016 revealed great enthusiasm for collaborating in research among our former patients and their family members. Their desire to make the recovery journey better for those who follow them dovetails perfectly with the sentiments and dedication of the physical medicine and rehabilitation providers and researchers. Improving recovery and quality of life for people who have disabilities is a primary goal for us, and it is gratifying that our research reaches far beyond the walls of our facility and into patient and family communities.

We also are pleased to play a leading role in bringing new therapies and devices to patients. For example, after more than 15 years of clinical trials in the area of neuromodulation for post-stroke shoulder pain, Carolinas Rehabilitation was proud to learn that it will be the first US site to implant the newly FDA-approved device developed by SPR-Therapeutics for this indication, and will be the first training center for other providers.

# Department of Obstetrics and Gynecology

**Fast Facts: 29 presentations; 14 book chapters; 23 presentations**

The Department of Obstetrics and Gynecology pursues basic science, translational research and multi-center clinical trials to address a wide range of women's health issues. Our Division of Reproductive Endocrinology and Infertility is involved in numerous studies designed to discover new methods to enhance fertility and improve pregnancy outcomes for infertile couples, and our Division of Gynecologic Oncology at Levine Cancer Institute focuses on improving cancer diagnosis and treatment. The department also has a robust resident research program to equip our medical residents with the skills and knowledge to pursue independent research.

## Research Highlights:

- Under the supervision of Rebecca Usadi, MD, Carolinas HealthCare System is actively enrolling patients in the NIH-funded Males, Antioxidants and Infertility (MOXI) trial. This randomized, placebo-controlled, multi-center trial investigates an antioxidant formulation for the male partner. If effective, this treatment would reduce the treatment burden on the female partner, lower costs and provide an alternative for couples with religious or ethical objections to assisted reproductive technology. Because some specialists currently prescribe antioxidants to men based on the limited data supporting their use, a negative finding (lack of benefit) from this trial would also alter current treatment of infertile males.
- Dr. Usadi is also supervising enrollment for the ACTorNOT trial, which examines optimal management to resolve the nonviable pregnancy.
- Several investigator-initiated studies are exploring methods to simplify monitoring for ovulation induction and intrauterine insemination using an ovulation monitor and a novel slow-release insemination system; assessing optimal aspiration pressure for oocyte retrieval in women undergoing IVF; and evaluating two methods of endometrial activation to enhance implantation for women undergoing embryo transfer.
- In collaboration with researchers from the Cancer Pharmacology/Translational Research group at Levine Cancer Institute, David Tait, MD, has helped develop an ovarian cancer translational research program with a primary focus on genetic profiling of high grade serous ovarian/fallopian tube cancers. The group presented research at the 2016 Society of Gynecology Oncology meeting and published an article in Gynecologic Oncology highlighting the analysis of HOX genes in ovarian cancer.

# Department of Orthopaedics

**Fast Facts: 4 publications; 5 presentations; 5 grants**

The Orthopaedic Biology Research Laboratory offers orthopaedic surgery faculty and residents the opportunity to participate in clinically focused basic science research in disc degeneration, osteoarthritis, bone fracture healing and bone physiology.

## Research Highlights:

- Critical research funded by the North American Spine Society in 2014 and 2016 has expanded our understanding of how cells within the disc can communicate with nerve cells and thereby potentially directly influence nerve ingrowth into the disc. This research has direct clinical relevance related to nerve ingrowth and pain, especially in regions where nerves penetrate into the disc via annual tears.
- The disc laboratory and its faculty are nationally and internationally recognized. Edward J. Hanley, Jr., MD, received the 2013 lifetime achievement award from the International Society for the Study of Lumbar Spine. Helen Gruber, PhD, received the 2012 Henry Farfan Award from the North American Spine Society for outstanding contributions to spine-related research.

## Advancing Patient Care and Improving Outcomes

Disc degeneration and its associated low back pain are a major health concern with high patient suffering and a substantial economic impact on healthcare costs. Approximately 26 million Americans (seven out of 10 people) suffer from back pain and patient care for this condition costs more than \$100 billion in health services each year. Unfortunately, there are limited effective therapy options for degeneration-related back pain, and surgical procedures often do not reduce pain or restore function. In a unique effort to help this patient population, Dr. Hanley has established the Carolinas Back Pain Research Endowment at Carolinas Medical Center to support research focused on augmenting discs with adult stem cells. The endowment was launched with a \$1 million donation from one of Dr. Hanley's Charlotte-area patients.

# Department of Oral Medicine

**Fast Facts: 18 publications; 6 presentations; 8 grants**

The scope of the research program in the Department of Oral Medicine ranges from clinical research to translational bench-top research. Our department has obtained \$12.5 million in National Institutes of Health funding through six grants and supplements in the past four years; current studies address important patient management issues at the interface of dentistry and medicine, ranging from oral manifestations of systemic disease and its management to systemic implications for oral disease. Our translational bench-top research is conducted within the Oral Medicine Microbiome and Translational Genomics Laboratory. This research combines microbial metagenomics, genomics and computational systems biology approaches to determine biomarkers of disease or complications of therapy.

## Research Highlights:

- Several studies are focused on addressing antibiotic resistance. For example, Peter Lockhart, DDS, received \$625,000 from NIH via the Dental Practice Based Research Network to survey 2,500 dentists nationwide regarding their preventative use of antibiotics prior to invasive dental procedures. Given the increasing concern about antibiotic overuse, the project aims to address a pressing problem in both dentistry and general medicine. In another study, from a translational research standpoint, Jean-Luc Mougeot, PhD, is studying ways to manipulate the oral microbiome without antibiotics as a way of reducing the emergence of antibiotics resistance or related complications.
- We have enrolled 431 patients in OraRad U01, a study run by the National Institute of Dental and Craniofacial Research (NIDCR) focused on dental and oral medicine outcomes of patients who have received high-dose radiation therapy to the head and neck region. This study will guide decision-making and standard of care protocols for dental management of patients in the pre- and post-radiation period. In 2016, the department was awarded a diversity supplement award to support research training related to this study. In addition, our researchers are applying Human Oral Microbe Identification using Next Generation Sequencing (HOMINGS) in the OraRad U01 dataset to identify microbial signatures predictive of oral complications of cancer therapy. We have identified significant microbiome profile changes following radiation therapy, including increases in the relative abundance of oral bacteria associated with caries and periodontal disease along with changes in clinical surrogate outcomes measures for caries and periodontal disease. This research has been presented at several conferences and the potential use of oral microbial profiles as biomarkers for oral complications following cancer therapy has been filed as a provisional patent application.
- Our researchers are known for work investigating the connections between oral bacterial species and conditions affecting the rest of the body, in particular the devastating cardiac infection known as infective endocarditis. In 2016 our team received the prestigious Millard Award from The American Academy of Oral Medicine for a publication that concluded infective endocarditis may come from bacteria in the oral cavity, but that using antibiotics prior to dental procedures does not prevent it. To build on this research we are now enrolling patients for a five-year NIH/NIDCR study aimed at determining whether oral bacterial species associated with poor oral hygiene, gingivitis or periodontitis may contribute to infective endocarditis. In related work, our researchers are using a metagenomics approach to investigate the role of the oral microbiome in atherosclerosis; we recently determined, for example, that the oral pathogen *Porphyromonas gingivalis* is the most abundant species detected in clinically healthy coronary and femoral arteries of atherosclerotic patients.

- To determine oral microbiome profiles associated with the incidence and severity of oral mucositis, we are investigating a cohort of adult and pediatric patients with leukemia undergoing conditioning therapy for hematopoietic stem cell transplant. This work is presented in a monograph of the Journal of the National Cancer Institute.
- By combining text mining and molecular pathway analysis tools, we have established a knowledge-based gene expression database for Sjögren's syndrome and related rheumatic diseases. This work has generated several published abstracts and a provisional patent application.
- In collaboration with Carolinas Physical Medicine and Rehabilitation, our researchers are investigating salivary biomarkers in Parkinson's patients during exercise. Preliminary findings from this study have been published in the Oral Diseases Journal.

## Advancing Patient Care and Improving Outcomes

A recent case illustrates our comprehensive, coordinated approach to care and the ways our research program helps to improve outcomes. A 42-year-old male was diagnosed with squamous cell carcinoma of the right tonsil. The patient had no tobacco or alcohol-related risk factors, and it was determined that his cancer was related to human papilloma virus. The cancer treatment plan for this patient was to receive combined chemotherapy and radiation therapy (chemoRT) for his head and neck cancer. Before the start of his chemoRT, dental clinicians at Carolinas Medical Center evaluated the patient to eliminate potential sources of dental infection and minimize the risk of osteoradionecrosis (ORN) post-chemoRT, which presents as necrotic jaw bone and has the highest morbidity of any long-term complication post-chemoRT. The patient was approached and enrolled in the NIH-funded OraRad surveillance study and at his 18-month follow-up visit, the patient was found to have early signs of ORN. The patient was quickly referred for management of ORN by his clinicians and the impact of this condition was efficiently minimized by our research staff. The patient completed his final follow-up visit at 24 months with resolution of his ORN.

# Division of Pediatric Nephrology & Hypertension

**Fast Facts: 26 publications; 10 book chapters**

The Division of Pediatric Nephrology & Hypertension, under the leadership of Susan Massengill, MD, is involved in 10 active studies with a focus on children with chronic kidney disease, hypertension and rare diseases such as nephrotic syndrome, atypical hemolytic uremic syndrome and bone disorders. We view research as integral to advancing quality improvement strategies, improving the efficiency and quality of care, and better educating our families, our medical teams and our community.

## Research Highlights:

- Our division is an active participant in the NephCure Accelerating Cures Institute, a clinical care network directed toward facilitating clinical trials in nephrotic syndrome. Through this collaborative, we have enrolled nearly 100 patients for longitudinal monitoring, and Levine Children's Hospital has been designated as a clinical site for a phase 2, randomized, placebo-controlled study to evaluate Abatacept for treatment-resistant nephrotic syndrome.
- We continue to actively enroll patients in other NIH-sponsored studies, including Clinical Phenotyping and Resource Biobank Core (C-PROBE) and Cure Glomerular Nephritis (CureGN). We are in our 10th year contributing to the Chronic Kidney Disease In Children (CKiD) study monitoring longitudinally cardiovascular risks, growth, cognition and disease markers in progression in children with chronic kidney disease.
- The Center of Excellence for Pediatric Nephrology, launched in October 2016 with \$1.8 million in donations, provides a platform to grow Carolinas HealthCare System into a local, regional and ultimately a national leader in novel clinical trial development and implementation for pediatric patients with kidney diseases. The Center of Excellence promotes family-centered care for children impacted by kidney disease by leveraging patient and clinician engagement, clinical research, improvement science and best practices to transform the overall patient experience and quality of life.

## Advancing Patient Care and Improving Outcomes

Currently, health outcomes for children with kidney diseases are suboptimal. These diseases are disruptive to daily life, and if unresponsive to therapies may result in kidney failure. Treatment guidelines and protocols are available, but often based on anecdotal opinion rather than medical evidence. We aim to advance the quality of care delivery by identifying and sharing best practices and improving health outcomes for children with kidney disease.

# Department of Emergency Medicine

**Fast Facts: 61 publications; 18 book chapters; 48 presentations; 8 grants**

The Department of Emergency Medicine conducts clinical research focused on a broad spectrum of acute illness and diagnostic methodology to improve care delivery and in turn provide the best care to the patients we serve. We conduct research in acute cardiac and neurologic emergencies, trauma, concussion, pre-hospital care, sepsis, pediatrics, toxicology, ultrasound, injury prevention and international medicine.

## Research Highlights:

- We recently completed a multidisciplinary, double-blind, randomized, controlled, comparative effectiveness trial of intranasal ketamine compared with intranasal fentanyl for analgesia in children with suspected, isolated extremity fractures. This complex trial involved coordination with nursing, pharmacy, orthopaedics and emergency department physicians to identify eligible patients, obtain informed consent and administer pain-relieving study medication without delays in care. Many clinicians prefer ketamine and believe it to be safer, but there is limited data on its use for pain management in children. The results of this study will be used to design a larger study that will provide data on the safety and efficacy of ketamine in the pediatric population.
- Through our international partnerships, we are conducting a qualitative study to begin to address the disproportionate prevalence of undertreated pain in children in sub-Saharan Africa, where limited resources and cultural views of pain amplify the disparity. The Faces Pain Scale-Revised (FPS-R) has been validated in many countries, although not in Cameroon. Given that appropriate pain management can improve outcomes and the patient experience, this study aims to improve methods of identifying pain by evaluating whether the FPS-R may be culturally acceptable and appropriate for pediatric use across cultural groups in Cameroon.

## Advancing Patient Care and Improving Outcomes

A healthy 36-year-old female presented to the Carolinas Medical Center Emergency Department following an episode of acute shortness of breath. She was found to have a fast heart rate and low oxygen saturations. Given her symptoms and physical findings, the clinical team suspected a pulmonary embolus (PE). An immediate point-of-care ultrasound was performed, which revealed a dilated right ventricle, a finding suggestive of this diagnosis. A large pulmonary embolus was confirmed following a CT scan of the chest and a "CODE PE" was rapidly activated. She was then given thrombolytic therapy (clot busting medicine) at the bedside. Within the ensuing eight hours the patient's symptoms resolved completely. She was contacted by phone 10 days after being discharged, and is doing well.

This case illustrates two areas of ongoing research in our Department of Emergency Medicine. The first is the use of point-of-care ultrasound to aid rapid diagnosis of pulmonary embolism. Our researchers have published two papers in high-impact journals attesting to the value of this practice, and it is an area of active research at Carolinas HealthCare System. The second is the CODE PE program, which was developed at Carolinas Medical Center and is now deployed across all Carolinas HealthCare System emergency departments. This program provides clinical guidance on the management of pulmonary embolus and collects data to help clinicians understand optimal management strategies. Additionally, there is active ongoing research evaluating the use of point-of-care ultrasound in the rapid diagnosis of pulmonary embolus, with two publications in high-impact journals.

# Department of Family Medicine

## Fast Facts: 7 publications; 1 book chapter

The Department of Family Medicine's Division of Research pursues applied research that expands access to care, improves patient outcomes and ultimately drives positive change in the broader healthcare system. This includes community research and engagement, implementation of innovative primary care interventions that improve patient outcomes and participation in clinical trials that are relevant to primary care.

### Research Highlights:

- Two recent publications from the Asthma Comparative Effectiveness study (ACE) describe the successful pilot of a communication system between inpatient care providers, outpatient care providers and school nurses through linked electronic medical record systems and demonstrate how shared decision-making for asthma care can improve outcomes.
- Our researchers presented preliminary results of the ADAPT-NC PCORI study, a state-wide intervention to improve outcomes for patients with asthma through shared decision-making, at the 2016 Practice-based Research Network Conference, where they received the 2016 David Lanier Top Poster Presentation Award.
- Through our Transdisciplinary Approach to the Understanding Social Determinants of Health project, we have worked with community partners to understand the social determinants of health at the neighborhood level and develop sustainable interventions. One intervention, a community-based group called "Hispanos Unidos," officially launched this year. Another effort, a partnership between our Department of Family Medicine, the Stratford Richardson YMCA and the Charlotte Action Research Project of the University of North Carolina at Charlotte, is engaging youth along the West Boulevard corridor to develop a youth task force to address neighborhood social determinants of health.
- Hazel Tapp, PhD, was awarded a FOCUS Investigator Initiated Program Award from Gilead Pharmaceuticals to support Carolinas HealthCare System's efforts to increase HIV and HCV screening in primary care. The program, a collaboration between our Family Medicine Research Division and the Department of Infectious Disease, includes the development of an HIV/HCV screening initiative being rolled out to multiple primary care practices within our system along with protocols for patients found to be positive for HIV/HCV.

### Advancing Patient Care and Improving Outcomes

A 65-year-old college educated patient, who had recently been divorced from a substance-abusing partner, came to Carolinas HealthCare System for primary care and was screened for hepatitis C based on her baby boomer age and was found to be positive. After several therapies failed, she received Harvoni therapy, resulting in an undetectable viral load (cure). The patient recently became certified as an addiction specialist, and works to help clients struggling with addiction.

This story demonstrates how our research and practice improvements, such as efforts to increase screening for hepatitis C and HIV, can help patients receive successful treatment and dramatically improve disease outcomes.

# Carolinas Simulation Center

## Fast Facts: 10 publications

Carolinas Simulation Center works to improve patient care by conducting high-quality, multidisciplinary research, simulation and education. We combine theory with applied research and incorporate expertise from fields including healthcare, education, health communication, human factors and ergonomics to design and implement innovative research to understand methods to advance patient care.

### Research Highlights:

- One recent project funded by the Center for Medicare and Medicaid Services Partnership for Patients assessed whether a coaching program for practicing surgeons could improve surgeons' technical and nontechnical skills to improve patient outcomes. Thirty-two practicing surgeons (18 general, 14 gynecologic) participated, with seven receiving a four-hour group coaching session and an additional two receiving coaching sessions on technical skills. By helping to identify areas for improvement with regard to surgeons' technical and nontechnical skills, the project helped to guide the implementation of coaching programs for surgeons on an ongoing basis to improve outcomes in operating rooms across Carolinas HealthCare System.
- The Mental Skills Curriculum project, funded by the Agency for Healthcare Research and Quality, is an ongoing effort focused on equipping surgical residents with the mental skills to perform effectively in stressful operating environments. After completing the Mental Skills Curriculum as part of the simulation-based Fundamentals of Laparoscopic Surgery Curriculum, residents undertook operations in a porcine lab, where their results indicated the Mental Skills Curriculum helped prevent performance deterioration. Our research teams are now observing the residents in patient operating rooms to assess their use of mental skills before and during surgeries.
- In a collaboration with the Pediatric Emergency Department, our researchers helped develop a pediatric airway checklist to decrease complications that can occur during intubation of pediatric patients. The checklist, which contains specific items that need to be performed by physicians, nurses, respiratory therapists and healthcare technicians, is currently being evaluated for compliance and impact on patient outcomes in our children's emergency department.

### Advancing Patient Care and Improving Outcomes

Simulation based education and research provides a vital service by providing clinicians with the opportunity to learn in a safe environment where they can learn from their mistakes. Engaging with simulations allows clinicians to practice technical and nontechnical skills and receive feedback before they ever interact with patients. Honing physicians' skills in this way ultimately has a significant positive impact on patient care and outcomes.

# Center for Outcomes Research and Evaluation

## Fast Facts: 28 publications; 1 book chapter

The Center for Outcomes Research and Evaluation (CORE) was launched in 2016 to catalyze and support rigorous research and disciplined evaluation of Carolinas HealthCare System initiatives to enhance our capacity as a learning healthcare system. Building upon its predecessor organization, known as DA2 Applied Outcomes Research, CORE's mission is to transform healthcare quality and improve patient outcomes through research, evaluation and education.

## Research Highlights:

- With a \$286,000 grant funded by Merck and Co., Inc., CORE researchers collaborated with pharmacy and primary care clinicians to complete the Clinical Inertia in Type 2 Diabetes Mellitus Study. This important study found that nearly half of patients experienced clinical inertia in their metformin treatment and that timely treatment intensification was associated with a higher probability of achieving glycemic control after metformin failure. The results showed that higher baseline A1c values, renal disease, liver disease and younger provider age were associated with a lower likelihood of clinical inertia. These results, which were presented at the American Diabetes Association 76th Scientific Sessions and the 2016 Academy of Managed Care Pharmacy Nexus, can help to inform interventions for improving diabetes outcomes.
- A new integrated practice unit designed by Carolinas HealthCare System aims to improve transitions of care for the highest risk, most complex patients. To test the unit's impact on 30-day readmission rates for high-risk patients, CORE is leading a randomized quality improvement trial known as Aiming to Improve Readmissions Through InteGrated Hospital Transitions (AIRTIGHT). AIRTIGHT is a non-blinded, pragmatic, controlled trial with two parallel groups evaluating the effect of referral to the integrated practice unit inclusive of comprehensive multidisciplinary care and virtual visits. AIRTIGHT provides a template for how future Carolinas HealthCare System initiatives will be evaluated in the context of a learning healthcare system.
- CORE established a Data Coordinating Center to support a five-year study funded by the National Institute of Dental and Craniofacial Research and overseen by Peter Lockhart, DDS. The goal of this research is to determine whether oral bacterial species associated with poor oral hygiene, gingivitis or periodontitis may contribute to infective endocarditis. To support this project, CORE is responsible for creating the Case Report Form, creating and managing the database and data management plan, query management, statistical analysis, site database training and data safety monitoring. This study has built CORE's expertise in data coordination, providing Carolinas HealthCare System investigators with additional research support capacity and helping to generate NIH referrals for additional opportunities.

## Advancing Patient Care and Improving Outcomes

CORE regularly collaborates with clinicians, administrators, patients and families to identify issues and guide research directions. For example, interactions with patients have underscored the importance of effective communication between the patient and the provider in effective diabetes management. In another example, we learned through one patient that the complexity of the process for self-administering injections may be an important barrier to successful outpatient parenteral antibiotic therapy. Our researchers are investigating this issue in greater detail in order to offer solutions that reduce barriers and improve outcomes.

# Selected Publication Listing

Abzug, J.M., Ho, C.A., Ritzman, T.F., Brighton, B.K. Transphyseal Fracture of the Distal Humerus. *Journal of the American Academy of Orthopaedic Surgeons*. 2016;24(2):e39-e44. [doi: 10.5435/JAAOS-D-15-00297]

Anderson-Montoya BL, Scerbo MW, Ramirez DE, Hubbard T. Running memory for clinical handoffs: a look at active and passive processing. *Hum Factors*. 2016. PMID 27793979.

Anton NE, Howley LD, Pimentel M, Davis CK, Brown C, Stefanidis D. Effectiveness of a mental skills curriculum to reduce novices' stress. *J Surg Res*. 2016;206(1):199-205. PMID 27916362.

Baker EH, Drummond J, Stefanidis D, Iannitti DA, Naumann RW. Use of a Novel, Cordless Ultrasonic Dissector for Gynecologic Minimally Invasive Surgical Procedures. *J Minim Invasive Gynecol*. 2015 Nov-Dec;22(6S):S43-S44. doi: 10.1016/j.jmig.2015.08.119. Epub 2015 Oct 15. PMID: 27679240.

Bemenderfer, T.B., Rozario, N.L., Moore, C.G., Karunakar, M.A. Morbidity and Mortality in Elective Total Knee Arthroplasty Following Surgical Care Improvement Project Guidelines. *Journal of Arthroplasty*. 2016 Sep;31(9 suppl):202-206.

Bemenderfer T, Rozario N, Moore CG, Karunakar M. (2016) Decreased morbidity and mortality in higher risk patient populations undergoing total knee arthroplasty procedures following surgical care improvement project core measures *Journal of Arthroplasty* 2016 Sep;31(9Suppl):202-6. PMID 27067761.

Benbow JH, Thompson KJ, Cope HL, Brandon-Warner E, Culberson CR, Bossi KL, et al. Diet-Induced Obesity Enhances Progression of Hepatocellular Carcinoma through Tenascin-C/Toll-Like Receptor 4 Signaling. *Am J Pathol* 2016; 186:145-158.

Bickett A, Peterman AH, Warren-Findlow J, Tapp, H. Anxiety and Diabetes: Innovative Approaches to Management in Primary Care. *Experimental Biology and Medicine*. 2016; vol. 241 (15) pp. 1724-1731. PMID 27390262.

Bilgic E, Watanabe Y, Stefanidis D, Anton ND, Vassiliou MC. Multicenter proficiency benchmarks for advanced laparoscopic suturing tasks. *Am J Surg*. 2016 Oct. 8. PMID 27776755.

Blaeser A, Awano H, Wu B, Lu QL. Progressive dystrophic pathology in diaphragm and impairment of cardiac function in FKRP P448L mutant mice. 2016 Oct 6;11(10). PMID 27711214.

Blair, J.A., Eisenstein, E.D., Pierrie, S.N., Gordon, W., Owens, J.G., Hsu, J.R. Lower Extremity Limb Salvage: Lessons Learned from 14 Years at War. *Journal of Orthopaedic Trauma*. 2016 Oct;30 Suppl 3:S11-S15.

Bobby G. Ng, Sergey A. Shiryayev, Daisy Rymen, Hudson H. Freeze et al. ALG1-CDG: Clinical and molecular characterization of 39 unreported patients. *Hum Mutat*. 2016 Mar 2. doi: 10.1002/humu.22983.

Bogdan, Y., Tornetta, P., Einhorn, T. A., G. Pierre, Leveille, L., Robinson, J., Bosse, M.J., Haines, N., Horwitz, D., Jones, C., Schemitsch, E., Sagi, C., Thomas, B., Stahl, D., Ricci, W., Brady, M., Sanders, D., Kain, M., Higgins, T.F., Collinge, C., Kottmeier, S., Friess, D. Healing Time and Complications in Operatively Treated Atypical Femur Fractures Associated with Bisphosphonate Use: A Multicenter Retrospective Cohort. *Journal of Orthopaedic Trauma*. 2016;30(4):177-181.  
Bouton, D., Ho, C.A., Abzug, J., Brighton, B., Ritzman, T.F. The Difficult Supracondylar Humerus Fracture: Flexion-Type Injuries. *Instructional Course Lectures*. 2016;65:371-378.

Bosse MJ, Hsu JR, Karunakar MA, Sims SH, Seymour RB, Churchill C and the Major Extremity Trauma Research Consortium. Building a Clinical Research Network in Trauma Orthopaedics: The Major Extremity Trauma Research Consortium (METRC). *Journal of Orthopaedic Trauma*. 2016;30(7):353-361.

Bowdin S, Gilbert A, Bedoukian E, Ian D. Krantz et al. Recommendations for the Integration of Genomics into Clinical Practice. *Genet Med*, 2016 Nov;18(11). PMID 27171546.

Brennan MT, Mougeot JL. Alu retroelement-associated autoimmunity in Sjögren's syndrome. *Oral Dis*. 2016 Jul;22(5):345-7. PMID 26866712.

Brannan, P., Gaston, R.G., Lewis, D., Loeffler, B. Complications with the Use of BMP-2 in Scaphoid Nonunion Surgery. *Journal of Hand Surgery Am*. 2016;41(5):602-608. (OCRI)

Brandon-Warner E, Feilen A, Culberson CR, Field CO, deLemos AS, Russo, MW, Schrum LW. Processing of miR17-92 cluster in hepatic stellate cells promotes hepatic fibrogenesis during alcohol induced injury. *Alcohol Clin Exp Res* 2016 June 40:1430-1442. PMID:27291156.

Brandon-Warner E, Feilen NA, Culberson CR, Katz M, deLemos AS, Bridges C, Russo MW, Schrum LW. AAV2-mediated reintroduction of microRNA-19b attenuates experimental hepatic fibrosis. *J Pathol*. Under review.

Brenner AT, Hoffman, R, McWilliams A, Pignon, MP, Rhyne RL, Tapp H., Weaver MA, Callan D, de Hernandez BU, Harbi K, Reuland DS, 2016. Colorectal Cancer Screening in Vulnerable Patients: Promoting Informed and Shared Decisions. *American Journal of Preventive Medicine*. PMID27242081.

Breuckmann F, Olligs J, Hinrichs L, Koopmann M, Lichtenberg M, Böse D, Fischer D, Eckardt L, Waltenberger J, Garvey JL. Coronary Artery Calcium as an Independent Surrogate Marker in the Risk Assessment of Patients with Atrial Fibrillation and an Intermediate Pretest Likelihood for Coronary Artery Disease Admitted to a German Chest Pain Unit. *Clin Cardiol*. 2016 Mar;39(3):157-64. doi: 10.1002/clc.22506. PMID: 27001202.

Brighton, B., Abzug, J., Ho, C.A., Ritzman, T.F. Current Strategies for the Management of Pediatric Supracondylar Humerus Fractures: Tips and Techniques for Successful Closed Treatment. *Instructional Course Lectures*. 2016;65:353-360.

Brown J, Naumann RW, Seckl M, Schink J. 15 Years of Progress in Gestational Trophoblastic Disease: Scoring, Standardization, and Salvage. *Gynecol Oncol* 2016 (in press).

Brown J. Perspective, on Intraperitoneal chemotherapy improved ovarian cancer survival. *HemOnc Today*, July 2016.

Burzawa J, Schmeler K, Soliman P, Lacour R, Meyer L, Bevers M, Frumovitz M, Pustilnik T, Anderson M, Ramondetta L, Tortolero-Luna G, Urbauer D, Broaddus R, Chang S, Gershenson D, Brown J, Gershenson D. Insulin Resistance in Endometrial Cancer. *J Clin Oncol*. In Press.

Callaway DW. Don't Let the Word "Myopic" Blind You. *J Spec Oper Med*. 2016 Fall;16(3):120-122. PMID: 27734454.

Callaway D, Bobko J, Smith ER, Shapiro G, McKay S, Anderson K, Sarani B. Building community resilience to dynamic mass casualty incidents: A multiagency white paper in support of the first care provider. *J Trauma Acute Care Surg*. 2016 Apr;80(4):665-9.

Caprio, AJ. Palliative care: renaming as supportive care and integration into comprehensive cancer care. *Canadian Medical Association Journal* 2016 vol 188(10). PMID 27091796.

Carsons SE, Vivino FB, Parke A, Carteron N, Sankar V, Brasington R, Brennan MT, Ehlers W, Fox R, Scofield H, Hammitt KM, Birnbaum J, Kassin S, Mandel S. Treatment Guidelines for Rheumatologic Manifestations of Sjögren's: Use of Biologics, Management of Fatigue and Inflammatory Musculoskeletal Pain. *Arthritis Care Res (Hoboken)*. 2016 Jul 7. doi: 10.1002/acr.22968. PMID 27390247.

Croft KM, Bosse PM, Naumann RW. Total Laparoscopic Hysterectomy (TLH): Where Does the Money Go? *J Minim Invasive Gynecol*. 2015 Nov-Dec;22(6S):S96. doi: 10.1016/j.jmig.2015.08.256. Epub 2015 Oct 15. PMID: 27679389.

Corey KE, Gawrieh S, deLemos AS, Zheng H, Scanga AE, Haglund JW MD, Sanchez J, Danford CJ, Comerford M, Bossi K, Munir S, Chalasani N, Wattacheril J. Risk factors for hepatocellular carcinoma in cirrhosis due to nonalcoholic fatty liver disease: A multicenter, case-control study. *World Journal of Hepatology: Under Review*.

Chan JK, Deng W, Higgins RV, Tewari KS, Bonebrake AJ, Hicks M, Gaillard S, Ramirez PT, Chafe W, Monk BJ, Aghajanian C. A phase II Evaluation of Brivanib (BMS582664, IND# 108417) in the Treatment of Persistent or Recurrent Carcinoma of the Cervix: an NRG Oncology/Gynecologic Oncology Group study. Accepted for Publication to *Gynecologic Oncology*.

Chan J, Brown J, et al. Sunitinib in Phase II Clear Cell Carcinoma of Ovary:A GOG/NRG Study. *Gynecol Oncol*. In Press.

Chapman Jr., T.M. Baseline Patient Outcomes Correlate Weakly with Radiographic Parameters: A Multicenter, Prospective NIH Adult Symptomatic Lumbar Scoliosis Study of 286 Patients. *Spine*. 2016; April 5. [Epub ahead of print] (OCRI).

Chapman Jr., T.M., Blizzard, D.J., Brown, C.R., CT Accuracy of Percutaneous vs. Open Pedicle Screw Techniques: A Series of 1609 Screws. *European Spine Journal*, 2016;25(6):1781-1786. (OCRI).

Cho, E.H., Garcia, R.M., Blau, J., Levinson, H., Erdmann, D., Levin, L.S., Hollenbeck, S.T. Microvascular Anastomoses using End-to-End versus End-to-Side Technique in Lower Extremity Free Tissue Transfer. *Journal of Reconstructive Microsurgery*. 2016;32(2):114-120. (OCRI).

deLemos AS, Ghabril M, Rockey DC, Gu J, Barnhart HX, Fontana RJ, Kleiner DE, Bonkovsky HL; Drug-Induced Liver Injury Network (DILIN). Amoxicillin-Clavulanate-Induced Liver Injury. *Dig Dis Sci*. 2016 Aug;61(8):2406-16.

Dranove J, Tipnis N. High resolution manometry with multiple rapid swallows confirms the diagnosis of type III achalasia in an adolescent. 2016. *J Pediatr Gastroenterol Nutr*. In Press

Drawz P, Pajewski N, Bates J, Bello N, Cushman W, Dwyer J, Fine L, Goff, Jr D, Haley W, Krousel-Wood M, McWilliams A, Rifkin D, Slinin Y, Taylor A, Townsend R, Wall B, Wright J, Rahman M. Effect of intensive versus standard clinic-based hypertension management on ambulatory blood pressure - results from the SPRIN. *Hypertension*. 2017;69:00-00. DOI: 10.1161

Edens MH, Khaled Y, Napeñas JJ. Intraoral Pain Disorders. *Oral Maxillofac Surg Clin North Am*. 2016 Aug;28(3):275-88.

Eskew AM, Crane EK. Levonorgestrel Intrauterine Device Placement in a Premenopausal Breast Cancer Patient with a Bicornuate Uterus. *J Minim Invasive Gynecol*. 2016 Jan;23(1):133-5. doi: 10.1016/j.jmig.2015.08.888. Epub 2015 Sep 3. PMID: 26342448.

Fegelman E, Knippenberg S, Schwiens M, Stefanidis D, Gersin KS, Scott JD, Fernandez AZ. Evaluation of a powered stapler system with gripping surface technology on surgical interventions required during laparoscopic sleeve gastrectomy. *J Laparoendosc Adv Surg Tech A*. 2016 Dec 19. PMID 27991838.

Finneran MM, Pickens R, Templin M, Stephenson CD. Impact of recipient twin preoperative myocardial performance index in twin-twin transfusion syndrome treated with laser. *J Matern Fetal Neonatal Med*. 2016 May 26:1-5. [Epub ahead of print] PMID: 27150066.

Finneran M, Temming L, Stephenson C. Medical termination of pregnancy after endometrial ablation resulting in uterine rupture. *J Obstet Gynaecol*. 2016 Jul;36(5):681-2. doi: 3109/01443615.2015.1133581. Epub 2016 Mar 25. PMID: 27012735.

Finneran M, Temming L, Templin M, Stephenson C. Effect of Cervical Length Recovery after Laser Surgery for Twin-Twin Transfusion Syndrome. *AJP Rep*. 2016 Mar;6(1):e137-41. doi: 10.1055/s-0036-1579654. PMID: 26989569.

Ford SE, Patt JC, Scannell BP. A Comprehensive, High-Quality Orthopedic Intern Surgical Skills Program. *Journal of Surgical Education*. 2016;73(4):553-558.

Franklin M, Wailoo A, Dayer MJ, Jones S, Prendergast B, Baddour LM, Lockhart PB, Thornhill MH. The Cost-Effectiveness of Antibiotic Prophylaxis for Patients at Risk of Infective Endocarditis. *Circulation*. 2016 Nov 13. pii: CIRCULATIONAHA.116.022047. PMID 27840334.

Frumovitz M, Burzawa JK, Byers LA, Lyons YA, Ramalingam P, Coleman RC, Brown J. Sequencing of mutational hotspots in cancer-related genes in small cell neuroendocrine cervical cancer. *Gynecol Oncol* 141(3):588-91, 2016. PMID: 27079212.

Garg M, Pearson DA, Bond MC, Runyon M, Pillow MT, Hopson L, Cooney RR, Khadpe J, Nomura JT, Inboriboon PC. Survey of Individual and Institutional Risk Associated with the Use of Social Media. *West J Emerg Med*. 2016 May;17(3):344-9.

Garvey JL, Zegre-Hemsey J, Gregg R, Studnek JR. Electrocardiographic diagnosis of ST segment elevation myocardial infarction: An evaluation of three automated interpretation algorithms. *J Electrocardiol*. 2016 Sep-Oct;49(5):728-32. doi: 0.1016/j.jelectrocard.2016.04.010. PMID: 27181187.

Gaspari R, Weekes A, Adhikari S, Noble VE, Nomura JT, Theodoro D, Woo M, Atkinson P, Blehar D, Brown SM, Caffery T, Douglass E, Fraser J, Haines C, Lam S, Lanspa M, Lewis M, Leibmann O, Limkakeng A, Lopez F, Platz

E, Mendoza M, Minnigan H, Moore C, Novik J, Rang L, Scruggs W, Raio C. Emergency Department Point of Care Ultrasound in Out of Hospital and in ED Cardiac Arrest. *Resuscitation*. 2016; PMID 27693280.

Gomez-Hidalgo NR, Darin MC, Dalton H, Jhingran A, Fleming N, Brown J, Ramirez PT. Ovarian torsion after laparoscopic ovarian transposition in patients with gynecologic cancer. *J Minim Invasive Gynecol* 22(4): 687-90, 2015. PMID: 25772021.

Gong K, Bruegl A, Ramondetta LM, Gershenson DM, Brown J. Salvage chemotherapy for gestational trophoblastic neoplasia: utility or futility? *Gynecol Oncol* 2016, in press.

Griffin M, Kosmisky DE, Templin MA, Huynh T, McCurdy III LH, Pasquale TR, Martin KE. Antifungal Use in Immunocompetent, Critically Ill Patients with Pneumonia Does Not Improve Clinical Outcomes. *Heart & Lung: The Journal of Acute and Critical Care*. 2016 nov-Dec;45(9):538-543. PMID 27601213.

Gruber, HE, Hoelscher, GL, Bullock L, Ingram JA, Norton HJ, Hanley EN. Human Annulus Signaling Cues for Nerve Outgrowth: In Vitro Studies. *Journal of Orthopaedic Research*. 2016;34(8):1456-1465. PMID 27155444.

Gruber, HE, Riley FE, Hoelscher, GL, Ingram JA, Bullock L, Hanley EN. Human Annulus Progenitor Cells: Analyses of this Viable Endogenous Cell Population. *J of Orthop Res*. 2016 Aug 34(8):1351-1360. PMID 27249627.

Gruber HE, Ode G, Hoelscher G, Ingram J, Bethea S, Bosse MJ. Osteogenic, Stem Cell and Molecular Characterization of the Human Induced Membrane from Extremity Bone Defects. *Bone & Joint Research*. 2016;5:106-115.

Gruber HE, Marrero E, Ingram JA, Hoelscher G, Hanley EN. The Chemokine CXCL16 and its Receptor CXCR6 are Constitutively Expressed in the Human Annulus Fibrosus, and Expression of CXCL16 is Upregulated by Exposure to IL-1 $\beta$  In Vitro. *Biochem & Biophys Res Commun*. 2016 Nov 21:1-8. PMID 27869573.

Haines NM, Lack WD, Seymour RB, Bosse MJ. Defining the Lower Limit of a "Critical Bone Defect" in Open Diaphyseal Tibial Fractures. *Journal of Orthopaedic Trauma*. 2016;30(5):e158-e163.

Hanley EN, Ode G, Jackson J, Seymour R. Coccygectomy for Patients with Chronic Coccydynia: A Prospective, Observational Study of 98 Patients. *The Bone & Joint Journal*. 2016;98-B:526-533.

Hansen C, Kragholm K, Pearson D, Tyson C, Monk L, Corbett C, Nelson D, et al. The Role of Bystanders, First Responders and Emergency Medical Service Providers in Timely Defibrillation and Related Outcomes After Out-of-hospital Cardiac Arrest: Results from a Statewide Registry. *Resuscitation*. 2015 Nov;96:303-9.

Hansen CM, Kristian Kragholm K, Pearson DA, Tyson C, Corbett C, Darrell Nelson RD, Dupre ME, Fosbøl EL, Granger CB, Strauss B, Fordyce CB, McNally B, Jollis JG. The Role of Bystanders, First Responders and Emergency Medical Service Providers in Timely Defibrillation and Related Outcomes After Out-of-hospital Cardiac Arrest: Results from a Statewide Registry. *JAMA* 2015;314(3):255-264.

Hardy LA, Chang CH, Myers EM, Kennelly MJ, Fried NM. Computer simulations of thermal tissue remodeling during transvaginal and transurethral laser treatment of female stress urinary incontinence. *Lasers Surg Med*. 2016 Feb 22 [Epub ahead of print]. PMID 26900038.

Harmer, L.S., Phelps, K.D., Crickard, C.V., Sample, K.M., Andrews, E.B., Hamid, N., Hsu, J.R. A Comparison of Exposure Between the Classic and Modified Judet Approaches to the Scapula. *Journal of Orthopaedic Trauma*. 2016;30(5):235-239.

Harris VM, Sharma R, Cavett J, Kurien BT, Liu K, Koelsch KA, Rasmussen A, Radfar L, Lewis D, Stone DU, Kaufman CE, Li S, Segal B, Wallace DJ, Weisman MH, Venuturupalli S, Kelly JA, Alarcon-Riquelme ME, Pons-Estel B, Jonsson R, Lu X, Gottenberg JE, Anaya JM, Cunninghame-Graham DS, Huang AJ, Brennan MT, Hughes P, Alevizos I, Miceli-Richard C, Keystone EC, Bykerk VP, Hirschfield G, Xie G, Ng WF, Nordmark G, Bucher SM, Eriksson P, Omdal R, Rhodus NL, Rischmueller M, Rohrer M, Wahren-Herlenius M, Witte T, Mariette X, Lessard CJ, Harley JB, Sivils KL, Scofield RH. Klinefelter's syndrome (47,XXY) is in excess among men with Sjögren's syndrome. *Clin Immunol*. 2016 Jul;168:25-9 PMID 27109640.

Hart GP, Kneisl JS, Springe, BD, Pat, JC, Karunakar MA. Open Reduction vs. Distal Femoral Replacement Arthroplasty for Comminuted Distal Femur Fractures in Patients 70 Years and Older. *Journal of Arthroplasty*. 2016;Jun 23. [Epub ahead of print]

Hartigan DE, Carrol, KW, Kosare, FJ, Piasecki DP, Fleischli JF, D'Alessandro, D.F. Visibility of Anterolateral Ligament Tears in Anterior Cruciate Ligament-deficient Knees with Standard 1.5-Tesla Magnetic Resonance Imaging. *Arthroscopy*. 2016;32(10):2061-2065. (OCRI).

Hayes MG, Urbanek M, Ehrmann DA, Armstrong LL, Lee JY, Sisk R, Karaderi T, Barber TM, McCarthy MI, Franks S, Lindgren CM, Welt CK, Diamanti-Kandarakis E, Panidis D, Goodarzi MO, Azziz R, Zhang Y, James RG, Olivier M, Kissebah AH; Reproductive Medicine Network, Stener-Victorin E, Legro RS, Dunaif A. Corrigendum: Genome-wide association of polycystic ovary syndrome implicates alterations in gonadotropin secretion in European ancestry populations. *Nat Commun*. 2016 Feb 12;7:10762. doi: 10.1038/ncomms10762. No abstract available. PMID: 26867975.

Herzog TJ, Kutarska E, Bidziński M, Symanowski J, Nguyen B, Rangwala RA, Naumann RW. Adverse Event Profile by Folate Receptor Status for Vintafolide and Pegylated Liposomal Doxorubicin in Combination, Versus Pegylated Liposomal Doxorubicin Alone, in Platinum-Resistant Ovarian Cancer: Exploratory Analysis of the Phase II PRECEDENT Trial. *Int J Gynecol Cancer*. 2016 Sep 19. [Epub ahead of print]

Heyer CM, Sundsbak JL, Abebe KZ, Chapman AB, Torres VE, Grantham JJ, Bae KT, Schrier RW, Perrone RD, Braun WE, Steinman TI, Mrug M, Yu AS, Brosnahan G, Hopp K, Irazabal MV, Bennett WM, Flessner MF, Moore CG, Landsittel D, Harris PC; HALT PKD and CRISP Investigators. Predicted Mutation Strength of Nontruncating PKD1 Mutations Aids Genotype-Phenotype Correlations in Autosomal Dominant Polycystic Kidney Disease. *J Am Soc Nephrol*. 2016 Sep;27(9):2872-84. PMID 26823553.

Hicks-Little, C.A., Peindl, R.D., Hubbard-Turner, T.J., Cordova, ML. The Relationship Between Early-Stage Knee Osteoarthritis and Lower-Extremity Alignment, Joint Laxity, and Subjective Scores of Pain, Stiffness and Function. *Journal of Sport Rehabilitation*. 2016 Aug;25(3):213-218.

Jackson JB, Crimaldi AJ, Peindl R, Anderson W, Norton J, Patt JC. The effect of polyether ether ketone on therapeutic radiation to the spine – a pilot study. *Spine*. 2016 May 18. PMID 27196026.

Jackson, J.B., Frick, S.L., Brighton, B.K., Broadwell, S.R., Wang, E.A., Casey, V.F. Restoration of Blood Flow to the Proximal Femoral Epiphysis in Unstable Slipped Capital Femoral Epiphysis by Modified Dunn Procedure: A Preliminary Angiographic and Intracranial Pressure Monitoring Study. *Journal of Pediatric Orthopaedics*. 2016;May 12. [Epub ahead of print]

Jobson MA, Hogan SL, Maxwell CS, Hu Y, Hladik GA, Falk RJ, Beuhler MC, Pendergraft WF. Clinical Features of Reported Ethylene Glycol Exposures in the United States. *PLoS One*. 2015 Nov 13;10(11):e0143044. doi: 10.1371/journal.pone.0143044. PMID: 26566024.

Jollis JG, Al-Khalidi HR, Roettig ML, Berger PB, Corbett CC, Dauerman HL, Fordyce CB, Fox K, Garvey JL, Gregory T, Henry TD, Rokos IC, Sherwood MW, Suter RE, Wilson BH, Granger CB; Mission: Lifeline STEMI Systems Accelerator Project. Regional Systems of Care Demonstration Project: American Heart Association Mission: Lifeline STEMI Systems Accelerator. *Circulation*. 2016 Aug 2;134(5):365-74. doi: 10.1161/CIRCULATIONAHA.115.019474. PMID: 27482000.

Katz MG, Brandon-Warner E, Fagnoli AS, Williams RD, Kendle AP, Kaplan RL, Hajjar RJ, Schrum LW, Bridges CR. 2016. Mitigation of myocardial fibrosis by molecular cardiac surgery mediated gene overexpression. *J Thorac Cardiovasc Surg*. 151:1191-1200.

Kennedy RA, Scerbo MW, Anderson-Montoya BL, Belfore II LA, Abuhamad AZ, Davis SS. The influence of a crosshair visual aid on observer detection of simulated fetal heart rate signals. *Am J Perinat Rep*, 2016;6:e115-120.

Karunakar, M.A. Posterior Column Tibial Plateau Fractures. *Journal of Knee Surgery*. 2016 Jan; 29(1):1.

Keramaris E, Lu PJ, Tucker J, Lu QL. Expression of glycosylated  $\alpha$ -dystroglycan in newborn skeletal and cardiac muscles of Fukutin related protein mutant mice. *Muscle Nerve*. 2016 Aug 12. doi: 10.1002/mus.25378. PMID 27515093.

Kiefer D, Keller SM, Weekes AJ. Prospective Evaluation of Ultrasound Guided Short Catheter Placement in Internal Jugular Veins of Difficult Access Patients. *Am J Emerg Med*. 2016 Mar 34(3): 578-81. PMID: 26776533.

Konda, S.R., Seymour, R., Manoli, A., Gales, J., Karunakar, M.A., Carolinas Trauma Network Research Group. Development of a Middle-Age and Geriatric Trauma Mortality Risk Score: A Tool to Guide Palliative Care Consultations. *Bulletin of the Hospital for Joint Diseases*. 2016 Nov;74(4):298-305.

Krueger CA, Hsu JR, Belmont PJ. What to Read and How to Read It: A Guide for Orthopaedic Surgeons (The Orthopaedic Forum). *Journal of Bone and Joint Surgery*. 2016;98A(3):243-249. [Review]

Lack W, Elkins J, Lujan T, Peindl RD, Kellam JF, Anderson DD, Marsh JL. Motion Predicts Clinical Callus: Construct-Specific Finite Element Analysis of Supracondylar Femur Fractures. *Journal of Bone and Joint Surgery*. 2016;98A(4):276-284.

Legro RS, Dodson WC, Kunselman AR, Stetter CM, Kris-Etherton PM, Williams NI, Gnatuk CL, Estes SJ, Allison KC, Sarwer DB, Diamond MP, Schlaff WD, Casson PR, Christman GM, Barnhart KT, Bates GW, Usadi R, Lucidi S, Baker V, Zhang H, Eisenberg E, Coutifaris C, Dokras A. Benefit of Delayed Fertility Therapy With Preconception Weight Loss Over Immediate Therapy in Obese Women With PCOS. *J Clin Endocrinol Metab*. 2016 Jul;101(7):2658-66. doi: 10.1210/jc.2016-1659. Epub 2016 May 12. PMID: 27172435

Limeres Posse J, Álvarez Fernández M, Fernández Feijoo J, Medina Henríquez J, Lockhart PB, Chu VH, Diz Dios P. Intravenous amoxicillin/clavulanate for the prevention of bacteraemia following dental procedures: a randomized clinical trial. *J Antimicrob Chemother*. 2016 Jul;71(7):2022-30.

Liu K, Kurien BT, Zimmerman SL, Kaufman KM, Taft DH, Kottyan LC, Lazaro S, Weaver CA, Ice JA, Adler AJ, Chodosh J, Radfar L, Rasmussen A, Stone DU, Lewis DM, Li S, Koelsch KA, Igoe A, Talsania M, Kumar J, Maier-Moore JS, Harris VM, Gopalakrishnan R, Jonsson R, Lessard JA, Lu X, Gottenberg JE, Anaya JM, Cunninghame-Graham DS, Huang AJ, Brennan MT, Hughes P, Illei GG, Miceli-Richard C, Keystone EC, Bykerk VP, Hirschfield G, Xie G, Ng WF, Nordmark G, Eriksson P, Omdal R, Rhodus NL, Rischmueller M, Rohrer M, Segal BM, Vyse TJ, Wahren-Herlenius M, Witte T, Pons-Estel B, Alarcon-Riquelme ME, Guthridge JM, James JA, Lessard CJ, Kelly JA, Thompson SD, Gaffney PM, Montgomery CG, Edberg JC, Kimberly RP, Alarcón GS, Langefeld CL, Gilkeson GS, Kamen DL, Tsao BP, McCune WJ, Salmon JE, Merrill JT, Weisman MH, Wallace DJ, Utset TO, Bottinger EP, Amos CI, Siminovitch KA, Mariette X, Sivils KL, Harley JB, Scofield RH. X Chromosome Dose and Sex Bias in Autoimmune Diseases: Increased 47,XXX in Systemic Lupus Erythematosus and Sjögren's Syndrome. *Arthritis Rheumatol*. 2016 May;68(5):1290-300.

Liu TL, Trogdon JG, Weinberger M, Barritt AS, Fried B. Diabetes is Associated with Clinical Decompensation Events in Patients with Cirrhosis. *Dig Dis Sci* 2016 Nov;61(11):3335-3345. PMID 27480088.

Liu TL, Barritt AS, Weinberger M, Paul JE, Fried B, Trogdon JG. Who Treats Patients with Diabetes and Compensated Cirrhosis. *PLoS One* 2016;11(10):e0165574. PMID 27783702.

Lookabill S, Alwasiyah D, Stripp M, Kerns W. Articles You May Have Missed. *J Med Toxicol*. 2016. doi:10.1007/s13181-016-0585-1.

Loumeau TP, Darden BV, Laxer EB, Kesman TJ, Odum SM, Murrey DB. A RCT Comparing 7-year Clinical Outcomes of One Level Symptomatic Cervical Disc Disease (SCDD) Following ProDisc-C Total Disc Arthroplasty (TDA) Versus Anterior Cervical Discectomy and Fusion (ACDF). *European Spine Journal*. 2016;25(7):2263-2270. (OCRI).

Long EB, Patel N, Sautter RL, Antosyk J, Dollar J, and Rupar D. A nine year-old girl with eye swelling. Accepted for publication, *J Clin Micro* 5/11/2016.

Marable DR, Bowers LM, Stout T, Stewart CM, Berg KM, Sankar VS, DeRossi SS, Thoppay JR, Brennan MT. Oral candidiasis following steroid therapy for oral lichen planus. *Oral Dis*. 2016 Mar;22(2):140-7.

MacNeill EC, Cabey W, Kluge R, Norton J, Mitchell AM. Emergency Department Utilization in Children <36 Months Is Not an Independent Risk Factor for Maltreatment. *Acad Emerg Med*. 2016 Nov;23(11):1228-1234. doi: 10.1111/acem.13100. PMID: 27717129.

Mahabaleshwarkar R, Taylor YJ, Spencer MD, Mohanan S. Prevalence of Metabolic Syndrome in a Large Integrated Healthcare System in North Carolina. *NC Medical Journal*. May 2016 77:168-174; doi:10.18043/nmc.77.3.168. PMID 27154881.

Mahabaleshwarkar, R, Taylor, YJ, Tapp, H and Dulin, MF. Psychometric Properties of the Mini Pediatric Asthma Quality of Life Questionnaire in a US Sample. *Pediatric Allergy, Immunology and Pulmonology*. 2016 vol29 (3).

Manasco AT, Griggs C, Leeds R, Langlois BK, Breaud AH, Mitchell PM, Weiner SG. Characteristics of state prescription drug monitoring programs: a state-by-state survey. *Pharmacoepidemiology and drug safety*. 2016 Jul;25(7):847-51. doi: 10.1002/pds.4003. Epub 2016 Apr 8.

Maricelli JW, Lu QL, Lin DC, Rodgers BD.. Trendelenburg-like Gait, Instability and Altered Step Patterns in a Mouse Model for Limb Girdle Muscular Dystrophy 2i. *PLoS One* 2016 Sep 14;11(9). PMID 27627455

Mauerhan DR, Cook KD, Botts TD, Williams ST. Patient-Directed Valgus Stress Radiograph of the Knee: A New and Novel Technique (Tips of the Trade). *The American Journal of Orthopedics*. 2016;45(1):44-46.

Mauffre, C, Giannoudis PV. Conway, J.D., Hsu, J.R., Masquelet, A.C. Masquelet Technique for the Treatment of Segmental Bone Loss Have We Made Any Progress? *Injury*. 2016 Oct;47(10):2051-2052. doi: 10.1016/j.injury.2016.09.018.

Merrill M, Runyon M, Heffner A, Wares, Pearson, D. Early neurologic exam is not reliable for prognostication in post-cardiac arrest patients who undergo therapeutic hypothermia. *Am J Emerg Med*. 2016 Jun;34(6):975-9.

Merrill MS, Wares CM, Heffner AC, Shauger KL, Norton HJ, Runyon MS, Pearson DA. Early neurologic examination is not reliable for prognostication in post-cardiac arrest patients who undergo therapeutic hypothermia. *Am J Emerg Med*. 2016 Jun;34(6):975-9. doi: 10.1016/j.ajem.2016.02.002. PMID: 26994681.

Miller KR, Patel JN, Ganapathi MK, Tait DL, Ganapathi RN. Biological role and clinical implications of homeobox genes in serous epithelial ovarian cancer. *Gynecol Oncol*. 2016 Jun;141(3):608-15. doi: 10.1016/j.ygyno.2016.03.004. Epub 2016 Mar 21. PMID: 26957480

Modisett K, Walsh S, Pearson D, Heffner A, Kerns R. Outcomes in Cardiac Arrest Patients due to Toxic Exposure Treated with Therapeutic Hypothermia. *Journal of Medical Toxicology*, 2016 Sep; 12(3):263-9. *J Med Toxicol*. 2016 Sep;12(3):263-9. PMID:26856349.

Morone NE, Greco CM, Moore CG, Rollman BL, Lane B, Morrow LA, Glynn NW, Weiner DK. (2016) Mind-body program for older adults with chronic low back pain: A randomized controlled trial. *JAMA Internal Medicine* 2016 2016 Mar 1;176(3):329-37.

Mougeot JL, Hirsch MA, Stevens CB, Mougeot F. Oral biomarkers in exercise-induced neuroplasticity in Parkinson's disease. *Oral Dis*. 2016 Nov;22(8):745-753. PMID 26878123.

Mougeot JL, Stevens CB, Morton DS, Brennan MT, Mougeot FB. Oral Microbiome and Cancer Therapy-induced Oral Mucositis. *Journal of NCI Monograph - Oral Toxicities of Cancer Therapies*. 2016

Mougeot JL, Stevens CB, Cotton SL, Morton DS, Krishnan K, Brennan MT, Lockhart PB, Paster BJ, Mougeot FB. Concordance of HOMIM and HOMINGS technologies in the microbiome analysis of clinical samples. *J Oral Microbiol* 2016 Apr 8;8:30379. PMID 27065347.

Murphy CM, Williams C, Quinn ME, Nicholson T, Shoe T, Beuhler MC, Kerns WP. Pilot trial of intravenous lipid emulsion treatment for severe nifedipine-induced shock. *J Med Toxicol*. DOI 10.1007/s13181-016-0572-6 PMID:27501853.

Murphy CM, Williams C, Quinn ME, Nicholson B, Shoe T, Beuhler MC, Kerns WP. Pilot Trial of Intravenous Lipid Emulsion Treatment for Severe Nifedipine-Induced Shock. *J Med Toxicol*. 2016 Aug 8. PMID: 27501853.

Naumann RW, Brown J. Complications of Electromechanical Morcellation Reported in the Manufacturer and User Facility (MAUDE) Database. *J Minim Invasive Gynecol* 22(6);1018-21, 2015. PMID:25987522.

Norton HJ, Anderson WE, Divine G. Flawed forensic analysis of microscopic hair: statistical and legal issues. *Significance*. 2016 April;13(2):26-29.

Ode, G.E., Piasecki, D.P., Habet, N.A., Peindl, R. Cortical Button Fixation: A Better Patellar Tendon Repair? *American Journal of Sports Medicine*. 2016 Sept 30;44:2622.

Page, A.E., Kim, L., Patt, J. The Importance of the 21st Century Cures Act: Legislation May have Significant Impact of orthopaedists. *AAOS Now*. 2015;Jul:22-23.

Patt, J.C., Haines, N. Soft Tissue Sarcomas in Skin: Presentations and Management. *Seminars in Oncology*. 2016 Jun;43(3):413-418. [doi: 10.1053/j.seminoncol.2016.02.026]

Patterson PD, Higgins JS, Lang ES, Runyon MS, Barger LK, Studnek JR, Moore CG, Robinson K, Gainor D, Infinger A, Weiss PM, Sequeira DJ, Martin-Gill C. Evidence-Based Guidelines for Fatigue Risk Management in EMS: Formulating Research Questions and Selecting Outcomes. *Prehosp Emerg Care*. 2016 Nov 18:1-8. PMID: 27858581.

Pearson DA, Nelson RD, Monk L., et al. Comparison of Team-Focused CPR vs Standard CPR in Resuscitation from Out-of-Hospital Cardiac Arrest: Results from a Statewide Quality Improvement Initiative. *Resuscitation*. 2016 Aug;105:165-72.

Pearson DA. Review of Clinical Guidelines for Cardiopulmonary Resuscitation. *N C Med J*. 2015 Sep-Oct;76(4):257-9.

Pearson DA, Nelson RD, Monk L., Tyson C., Jollis JG., Granger CB., Corbett c., Garvey L., Runyon MS. Comparison of Team-Focused CPR vs Standard CPR in Resuscitation from Out-of-Hospital Cardiac Arrest: Results from a Statewide Quality Improvement Initiative. *Resuscitation*. 2016 Aug;105:165-72.

Pearson DA, Darrell Nelson R, Monk L, Tyson C, Jollis JG, Granger CB, Corbett C, Garvey L, Runyon MS. Comparison of team-focused CPR vs standard CPR in resuscitation from out-of-hospital cardiac arrest: Results from a statewide quality improvement initiative. *Resuscitation*. 2016 Aug;105:165-72. doi: 10.1016/j.resuscitation.2016.04.008. PMID: 27131844.

Pearson DA, Wares CM, Mayer KA, Runyon MS, Studnek JR, Ward SL, Kraft KM, Heffner AC. Troponin Marker for Acute Coronary Occlusion and Patient Outcome Following Cardiac Arrest. *West J Emerg Med*. 2015 Dec;16(7):1007-13. doi: 10.5811/westjem.2015.10.28346. PMID: 26759645.

Perkins, C., Scannell, B., Brighton, B., Seymour, R., VanderHave K. Orthopaedic Firearm Injuries in Children and Adolescents: An Eight-Year Experience at a Major Urban Trauma Center. *Injury*. 2016;74(1):173-177.

Petfield JL, Hayeck GT, Kopperdahl DL, Nest, LJ, Keaveny TM, Hsu JR. Skeletal Trauma Research Consortium (STReC). Virtual Stress Testing of Fracture Stability in Soldiers with Severely Comminuted Tibial Fractures. *Journal of Orthopaedic Research*. 2016 Jun 15. [Epub ahead of print]

Phelp, KD, Ming BW, Fox WE, Bellamy N, Sims SH, Karunakar MA, Hsu J.R. A Quantitative Exposure Planning Tool for Surgical Approaches to the Sacroiliac Joint. *Journal of Orthopaedic Trauma*. 2016;30(6):319-324.

Pierrie SN, Harmer LS, Karunakar MA, Angerame MR, Andrews EB, Sampl, KM, Hsu JR. Limited Added Value of the Posterolateral Approach. *Journal of Knee Surgery*. 2016 Jan;29(1):21-27.

Peery AF, Crockett SD, Barritt AS, Dellon ES, Eluri S., Gangarosa LM., Jensen, ET, Lund JT, Pasricha S, Runge T, Schmidt M., Shaheen NJ, Sandler RS. Burden of Gastrointestinal, Liver, and Pancreatic Diseases in the United States. *Gastroenterology* 2015;149:1731-1741 e3.

Rao MP, Dupre ME, Pokorney SD, Hansen CM, Tyson C, Monk L, Pearson DA, Nelson RD, Myers B, Jollis JG, Granger CB. Therapeutic Hypothermia for Patients with Out-of-Hospital Cardiac Arrest in North Carolina. *Prehosp Emerg Care*. 2016 Mar 17:1-7.

Rainville J, Laxer EB, Kee, JC, Carkner EP, Milam RA, Kim DH. Exploration of Sensory Impairments Associated with C6 and C7 Radiculopathies. *The Spine Journal*. 2016;16: 49-54. (OCRI)

Rajakumar K, Moore CG, Yabes J, Olabopo F, Haralam MA, Comer D, Holick M, Greenspan S (2016) Estimations of dietary vitamin D requirements in black and white children. *Pediatric Research* 2016 Mar 9. doi: 10.1038/pr.2016.46. [Epub ahead of print].

Reeves KW, Taylor Y, Tapp H, Ludden T, Shade LE, Burton B, Courtlandt C, Dulin M. Evaluation of a Pilot Asthma Care Program for Electronic Communication between School Health and a Healthcare System's Electronic Medical Record. *Applied Clinical Informatics*. September 10, 2016. PMID 27757472.

Reynolds SL, Studnek JR, Mrayant K, Moore CG, Young J, Hogg M, Runyon M. Study Protocol of a Randomized Controlled Trial of Intranasal Ketamine Compared to Intranasal Fentanyl for Analgesia in Children with Suspected, Isolated Extremity Fractures in the Pediatric Emergency Department. *British Medical Journal Open* 2016 Sep 8;6(9):e012190. doi: 10.1136/bmjopen-2016-012190. PMID 27609854.

Richards JE, Matuszewski PE, Griffin SM, Koehler DM, Guillaumondegui OD, O Toole RV, Bosse M., Obremsky WT, Evans JM. The Role of Elevated Lactate as a Risk Factor for Pulmonary Morbidity After Early Fixation of Femoral Shaft Fractures. *Journal of Orthopaedic Trauma*. 2016;30(6):312-318.

Rubin RA, Russo MW, Brown KA, Fontana RJ, Levistky J, Vargas H, Yoshida EM, Brown Jr RS. Twice-daily telaprevir for posttransplant genotype 1 hepatitis c virus: A prospective safety, efficacy, and pharmacokinetics study. *Experimental and Clinical Transplantation* 2016, in press.

Russo MW, Koteish A, Fuchs M, Reddy G, Fix O. Workforce in Hepatology: Update and a critical need for more information. *Hepatology* 2016, Sept 16 PMID 2768621.

Russo MW, Levi DM, Pierce R, Casingal V, Eskin L, deLemos A, Schmeltzer PA, Zamor PJ. A prospective study of a protocol that reduces readmission after liver transplantation. *Liver Transpl* 2016;22:765-72. PMID 26919494.

Samuelso, EM, Odum SM, Fleischli JE. The cost-effectiveness of Using Platelet-rich Plasma During Rotator Cuff Repair: A Markov Model Analysis. *Arthroscopy*. 2016;32(7):1237-1244. (OCRI).

Sanjak M, Hirsch, MA, Habet NA, Peindl RD, Zheng N, Holsten S, Morgan BS, Mash T, Englert, D, Iyer S, Lucas N, Russo P, Bravver E, Bockenek B. Electronically-Augmented Timed-Up-and-Go Test (EATUG) Differentiates Sit-to-Stand (STS) Mobility and Balance in Ambulatory Individuals with Amyotrophic Lateral Sclerosis (ambALS) and Parkinson Disease (ambPD). *Neurology*. April 5, 2016 vol. 86 no. 16 Supplement P3.290.

Sawe HR, Mfinanga JA, Ringo FH, Mwafongo V, Reynolds TA, Runyon MS. HIV counselling and testing practices for children seen in an urban emergency department of a tertiary referral hospital in Dar es Salaam, Tanzania: a retrospective cross-sectional study. *BMJ Open*. 2016 Feb 15;6(2):e010298. doi: 10.1136/bmjopen-2015-010298. PMID: 26880672

Sawe HR, Mfinanga JA, Mwafongo V, Reynolds TA, Runyon MS. The test characteristics of physician clinical gestalt for determining the presence and severity of anaemia in patients seen at the emergency department of a tertiary referral hospital in Tanzania. *Emerg Med J*. 2016 May;33(5):338-44. doi: 10.1136/emered-2015-204908. PMID: 26612857

Saxena V, Korashy FM, Sise ME, Lim JK, Schmidt ML, Chung RT, Liapakis A, Nelson DA, Fried MW, Terrault NA and HCV-TARGET. Safety and Efficacy of Sofosbuvir-Containing Regimens in Hepatitis C Infected Patients with Impaired Renal Function. *Liver International* 2016.

Scannell, B. Yaszay, B., Bartley, C., Newton, P., Mubarak, S. Surgical Correction of Scoliosis in Patients with Duchenne Muscular Dystrophy: 30 Year Experience. *J Ped Orthop*. 2016;Jan 11. PMID 26756984.

Schatz K, Maccia, M, Templin M, Rector K, Guffey J. Pharmacists' impact on opportunistic infection prophylaxis in patients with HIV/AIDS. *Journal of Hospital Infection*. PMID 27810222.

Scerbo MW, Britt RC, Montano M, Kennedy RA, Prytz E, Stefanidis D. Effects of a retention interval and refresher session on intracorporeal suturing and knot tying skill and mental workload. *Surgery*. 2016 Dec 20. PMID 28011014.

Scerbo MW, Britt RC, Stefanidis D. Differences in mental workload between traditional and single-incision laparoscopic procedures measured with a secondary task. *Am J Surgery*. 2016 Oct 8. PMID 27760704.

Schultz KA, Brown J. Ovarian sex cord-stromal tumors, *Journal of Oncology Practice* 2016 (in press).

Seymour RB, Leas D, Wally MK, Hsu JR. PRIMUM Group. Prescription Reporting with Immediate Medication Utilization Mapping (PRIMUM): Development of an Alert to Improve Narcotic Prescribing. *BMC Medical Information and Decision Making*. 2016 Aug 22;16:111.

Shapiro G, Smith R, Callaway DW. Committee for Tactical Emergency Casualty Care. Spring Update. *J Spec Oper Med*. 2016 Spring;16(1):137-9. PubMed PMID: 27265918.

Sheean AJ, Tennent DJ, Hsu JR, Burn, TC. Elbow Arthrodesis as a Salvage Procedure for Combat-Related Upper Extremity Trauma. *Military Medicine*. 2016;181(8):773-776.

Sheean AJ, Tennent DJ, Owens JG, Wilken JM, Hsu JR, Stinner DJ. Skeletal Trauma Research Consortium (STReC). Effect of Custom Orthosis and Rehabilitation Program on Outcomes Following Ankle and Subtalar Fusions. *Foot & Ankle International*. 2016;37(11):1205-1210.

Slomovitz B, Brown J, Gershenson DM, Coleman RC. A phase II study of everolimus and letrozole in patients with recurrent endometrial carcinoma. *J Clin Oncol*. In Press.

Smith J, Fox SM. Pediatric Abdominal Pain: An Emergency Medicine Perspective. *Emerg Med Clin North Am*. 2016 May;34(2):341-61. doi: 10.1016/j.emc.2015.12.010. PMID: 27133248.

Stefanidis D, Anderson-Montoya B, Higgins RV, Pimentel ME, Rowland P, Scarborough MO, Higgins D. Developing a coaching mechanism for practicing surgeons. *Surgery*. 2016 Sep;160(3):536-45. PMID: 27302107

Stefanidis D, Anton NE, McRary G, Howley LD, Pimentel M, Davis C, Yurco AM, Sevdalis N, Brown C. Implementation results of a novel comprehensive mental skills curriculum during simulator training. *Am J Surg*. 2016 Nov 22. PMID 27908500.

Stefanidis D, Chintalapudi N, Anderson-Montoya B, Oommen B, Pimentel M. How often do surgeons obtain the critical view of safety during laparoscopic cholecystectomy? *Surg Endosc*. 2016;1-5.

Stolz L, Stolz I, Fields J, Saul, T, Secko M, Flannigan M, Sheele J, Rifenburg R, Weekes A, Josephson E, Bedolla J, Resop DM, Dela Cruz J, Boysen-Osborn M, Caffery T, Derr C, Bengiamin R, Chiricolo G, Backlund B, Heer J, Hyde RJ, Adhikari S. Emergency Medicine Resident Assessment of the Emergency Ultrasound Milestones and Current Training Recommendations. *Acad Emerg Med*. 2016; PMID: 27739636.

St-Onge M, Anseeuw K, Cantrell L, Gilchrist IC, Hantson P, Bailey B, Lavergne, V, Gosselin S, Kerns W, Laliberté M, Jang D, Lavonas EJ, Juurlink DN, Muscedere J, Yang CC, Sinuff T, Rieder MJ, Mégarbane B. Recommendations for the treatment of calcium channel blocker poisoning. *Crit Care Med*. 2016 Oct 3. [Epub ahead of print] PMID: 27749343.

Stopyra JP, Bozeman WP, Callaway DW, Winslow J 3rd, McGinnis HD, Sempsrott J, Evans-Taylor L, Alson RL. Medical Provider Ballistic Protection at Active Shooter Events. *J Spec Oper Med*. 2016 Fall;16(3):36-40. PMID: 27734440.

Tan CA, Rabideau M, Blevins A, Westbrook MJ, Ekstein T, Nykamp K, Deucher A, Harper A, Demmer L. Autosomal Recessive MFN2-Related Charcot-Marie-Tooth Disease with Diaphragmatic Weakness: Case Report and Literature Review *Am J Med Genet A*. 2016 Mar 8. doi: 10.1002/ajmg.a.37611.

Tang N, Shapiro G, Smith ER, Kamin R, Callaway DW. Proceedings of the 2016 Spring/Summer Meeting of the Committee for Tactical Emergency Casualty Care. *J Spec Oper Med*. 2016 Summer;16(2):148-150. PMID: 27689384.

Tapp H, Kuhn L, Mahabaleshwarkar R, Taylor YJ, Ludden T, Dulin MF. Results from a Prospective Cohort Study: Shared Decision Making Improves Outcomes for Children with Asthma. *Journal of Asthma*. Accepted August 18, 2016. PMID 27813670.

Tapp H, Derkowski D, Calvert M, Welch M, Spencer S. Patient Perspectives on Engagement in Shared Decision Making for Asthma Care. *Family Practice* 2016. PMID 28034918.

Taylor K, Frumovitz M, Irwin J, Cone M, Brown J. Laparoscopic supracervical hysterectomy: Factors influencing the risk of malignancy. *J Min Inv Gynecol*. In Press.

Taylor YJ, Laditka SB, Laditka JN, Brunner Huber LR, Racine EF. Associations of Government Health Expenditures, the Supply of Health Care Professionals, and Country Literacy with Prenatal Care Use in Ten West African Countries. *Health Care for Women International*. PMID 27797654.

Taylor YJ, Laditka SB, Laditka JN, Brunner Huber LR, Racine EF. Associations of household wealth and individual literacy with prenatal care in ten West African countries. *Maternal and Child Health Journal*. 2016 Jul 12. doi: 10.1007/s10995-016-2068-z.

Tewari K, Brown J. Prospective Validation of Pooled Prognostic Factors in Women with Advanced Cervical Cancer Treated with Chemotherapy with/without Bevacizumab; NRG Oncology/GOG Study. *Clinical Cancer Research*, 21(24):5480-7, 2015. PMID: 26672085.

Thomes PG, Brandon-Warner E, Li T, Donohue TM, Schrum LW. 2016. Rev-erb agonist and TGF- $\beta$  similarly affect autophagy but differentially regulate hepatic stellate cell fibrogenic phenotype. *Int J Biochem Cell Biol*. 81:137-147. PMID27840152

Thomes PG, Benbow JH, Brandon-Warner E, Thompson KJ, Jacobs C, Donohue TM, Schrum LW. Dietary fructose supplementation augments ethanol-induced liver pathology. *J Nutr Biochem*. Under review.

Thomes PG, Brandon-Warner E, Li T, Donohue TM, Schrum LW. Data on the effect of pro-fibrotic cytokine TGF- $\beta$  on hepatic stellate cell autophagy. *Data Brief*. 2016 Dec 8;10:312-314. PMID 27995168.

Thornhill MH, Dayer M, Lockhart PB, McGurk M, Shanson D, Prendergast B, Chambers JB. Guidelines on prophylaxis to prevent infective endocarditis. *Br Dent J*. 2016 Jan 22;220(2):51-6.

Thornhill MH, Dayer M, Lockhart PB, McGurk M, Shanson D, Prendergast B, Chambers JB. A change in the NICE guidelines on antibiotic prophylaxis. *Br Dent J*. 2016 Aug 12;221(3):112-4.

Thornhill MH, Dayer M, Lockhart PB, McGurk M, Shanson D, Prendergast B, Chambers JB, Jones S, Baddour LM. Prophylaxis guidelines: Plea to NICE. *Br Dent J*. 2016 Jul 8;221(1):2-3.

Thornhill MH, Dayer MJ, Jones S, Prendergast B, Baddour LM, Lockhart PB. The Effect of Antibiotic Prophylaxis Guidelines on Incidence of Infective Endocarditis. *Can J Cardiol*. 2016 Mar 4. pii: S0828-282X(16)00219-1. doi: 10.1016/j.cjca.2016.02.074. [Epub ahead of print]

Torres V, Abebe K, Schrier R, Perrone R, Chapman A, Yu A, Braun W, Steinman T, Fick-Brosnahan G, Hogan M, Oskoui F, Grantham J, Bae K, Moore C, Flessner M. (0000) Effect of dietary salt on the progression of Autosomal Dominant Polycystic Kidney Disease in the HALT PKD clinical trials. *Kidney International*. PMID 27993381.

Vannoy CH, Zhou H, Qiao C, Xiao X, Bang AG, Lu QL. AAV-Mediated Mini-Agrin Delivery is Unable to Rescue Disease Phenotype in a Mouse Model of Limb Girdle Muscular Dystrophy Type 2I. *Am J Pathol*. Accepted for publication.

Vissers RJ, Gibbs MA. Respiratory Emergencies. *Emerg Med Clin North Am*. 2016 Feb;34(1):xiii-xiv. doi: 10.1016/j.emc.2015.10.002. PMID: 26614248

Vila MC, Klimek MB, Novak JS, Rayavarapu S, Uaesoontrachoon K, Boehler JF, Fiorillo AA, Hogarth MW, Zhang A, Shaughnessy C, Gordish-Dressman H, Burki U, Straub V. Lu QL, Partridge TA, Brown KJ, Hathout Y, van den Anker J, Hoffman EP, Nagaraju K. Elusive sources of variability of dystrophin rescue by exon skipping. *Skelet Muscle*. 2016 Dec 1;5:44. doi: 10.1186/s13395-015-0070-6. PMID 26634117.

Vivino FB, Carsons SE, Foulks G, Daniels TE, Parke A, Brennan MT, Forstot SL, Scofield RH, Hammitt KM. New Treatment Guidelines for Sjögren's Disease. *Rheum Dis Clin North Am*. 2016 Aug;42(3):531-51.

Vivino FB, Hammitt KM; Sjögren's Syndrome Foundation Clinical Practice Guidelines Committee. Clinical practice guidelines for oral management of Sjögren disease: Dental caries prevention. *J Am Dent Assoc*. 2016 Apr;147(4):295-305.

Von Gruenigen VE, Huang HQ, Beumer JH, Lankes HA, Tew W, Herzog T, Hurria A, Mannel RS, Rizack T, Landrum LM, Rose PG, Salani R, Bradley WH, Rutherford TJ, Higgins RV, Alvarez Secord A, Fleming G. Chemotherapy Completion in Elderly Women with Ovarian, Primary Peritoneal or Fallopian Tube Cancer – An NRG Oncology/Gynecologic Oncology Group Study. Accepted for Publication to *Gynecologic Oncology*

Wang M, Wu B, Tucker JD, Bollinger LE, Lu P, Lu Q. Poly(ester amine) Composed of Polyethylenimine and Pluronic Enhance Delivery of Antisense Oligonucleotides In Vitro and in Dystrophic mdx Mice. *Mol Ther Nucleic Acids*. 2016 Aug 2;5(8):e341. doi: 10.1038/mtna.2016.51. PMID 27483024.

Wang M, Wu B, Tucker JD, Lu P, Lu Q. Poly(ester amine) constructed from polyethylenimine and pluronic for gene delivery in vitro and in vivo. *Drug Deliv*. 2016 Mar 29:1-10. PMID 26960992.

Weaver DJ, Jr., Mitsnefes MM. 2016. Cardiovascular effects of systemic hypertension. *Prog Ped Cardiol*. <http://dx.doi.org/10.1016/j.ppedcard.2015.11.005>. In press.

Weekes A, Oh, L, Thacker G, Johnson A, Rose G, Johnson T, Runyon M, Templin M, Norton, H. Interobserver and Intraobserver Agreement on Qualitative Assessments of Right Ventricular Dysfunction With Echocardiography in Patients With Pulmonary Embolism. *Journal of Ultrasound in Medicine* 15.11007; Published Online First August 8, 2016, doi:10.7863/ultra.15.11007.

Weekes A, Johnson AK, Troha D, Thacker G, Chanler-Berat J, Runyon M. Prognostic Value of Right Ventricular Dysfunction Markers for Serious Adverse Events in Acute Normotensive Pulmonary Embolism. *J Emerg Med*. 2016; PMID 27751702

Weekes AJ, Oh L, Thacker G, Johnson AK, Runyon M, Rose G, Johnson T, Templin M, Norton HJ. Observer Agreement in Qualitative Echocardiographic Right Ventricle Dysfunction Detection in Patients with Submassive Pulmonary Embolism. *J Ultrasound Med*. 2016 Aug 8; PMID 27503757

Weekes AJ, Thacker G, Troha D, Johnson AK, Chanler-Berat J, Norton JH, Runyon M. Diagnostic Accuracy of Right Ventricular Dysfunction Markers In Normotensive Emergency Department Patients With Acute Pulmonary Embolism. *Annals of Emerg Med*. 2016; PMID: 26973178

Weekes AJ, Keller SM, Efun B, Ghali S, Runyon M. Prospective Comparison of Ultrasound and CXR for Confirmation of Central vascular Catheter Placement. *Emerg Med J*. 2016 Mar; 33(3): 176-80. PMID: 264463.

Welch J, Sawtelle S, Cheng D, Perkins T, Ownbey M, MacNeill E, Hockberger R, Rusyniak D. Faculty Mentoring Practices in Academic Emergency Medicine. *Acad Emerg Med*. 2016 Nov 17. doi: 10.1111/acem.13136. [Epub ahead of print] PMID: 27860044.

Wertman GV, Gaston RG, Heisel WD. Upper Extremity Injuries in NASCAR Drivers and Pit Crew: An Epidemiological Study. *The Orthopaedic Journal of Sports Medicine*. 2016 Feb 12;4(2):2325967116629427. [doi: 10.1177/2325967116629427. eCollection 2016] (OCRI)

Wilson MS, Konda S, Seymour R, Karunakar M. Carolinas Trauma Network Research Group. Early Predictors of Mortality in Geriatric Trauma Patients. *Journal of Orthopaedic Trauma*. 2016 Jul;30(7):353-361.

Wilson WR, Bower TC, Creager MA, Amin-Hanjani S, O'Gara PT, Lockhart PB, Darouiche RO, Ramlawi B, Derdeyn CP, Bolger AF, Levison ME, Taubert KA, Baltimore RS, Baddour LM; American Heart Association Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Surgery and Anesthesia; Council on Peripheral Vascular Disease; and Stroke Council. Vascular Graft Infections, Mycotic Aneurysms, and Endovascular Infections: A Scientific Statement From the American Heart Association. *Circulation*. 2016 Nov 15;134(20):e412-e460. PMID 27737955.

Wingfield JJ, Ho CA, Abzug J, Ritzman TF, Brighton B. Open Reduction Techniques for Supracondylar Humerus Fractures in Children. *Instructional Course Lectures*. 2016;65:361-370.

Winter JD, Taylor Y, Mowrer L, Winter KM, Dulin MF. BMI at birth and overweight at age four. *Obesity Research and Clinical Practice*. 2016 Apr 7. doi: 10.1016/j.orcp.2016.03.010.

Wu B, Shah SN, Lu P, Richardson SM, Bollinger LE, Blaeser A, Madden KL, Sun Y, Luckie, TM, Cox MD, Spark, S, Harper AD, Lu QL. Glucocorticoid Steroid and Alendronate Treatment Alleviates Dystrophic Phenotype with Enhanced Functional Glycosylation of  $\alpha$ -Dystroglycan in Mouse Model of Limb-Girdle Muscular Dystrophy with FKRPP448L Mutation. *Am J Path*. 2016;186(6):1635-1648. PMID 27109313.

Wyman AJ, Mayes BN, Hernandez-Nino J, Rozario N, Beverly SK, Asimos AW (2016) First-time seizure Emergency Department electroencephalogram study. *Annals of Emergency Medicine* 2016: Oct 10. PMID 27745763.

Yun HC, Murray CK, Nelson KJ, Bosse MJ. Infection after Orthopaedic Trauma: Prevention and Treatment. *Journal of Orthopaedic Trauma*. 2016 Oct;30 Suppl 3:S21-S26.

Zègre-Hemsey JK, Garvey JL, Carey MG. Cardiac Monitoring in the Emergency Department. *Crit Care Nurs Clin North Am*. 2016 Sep;28(3):331-45. doi: 10.1016/j.cnc.2016.04.009. Review. PMID: 27484661.

Zero DT, Brennan MT, Daniels TE, Papas A, Stewart C, Pinto A, Al-Hashimi I, Navazesh M, Rhodus N, Sciubba J, Singh M, Wu AJ, Frantsve-Hawley J, Tracy S, Fox PC, Ford TL, Cohen S,

## Research Highlights

---

# 2016



Carolinian HealthCare System