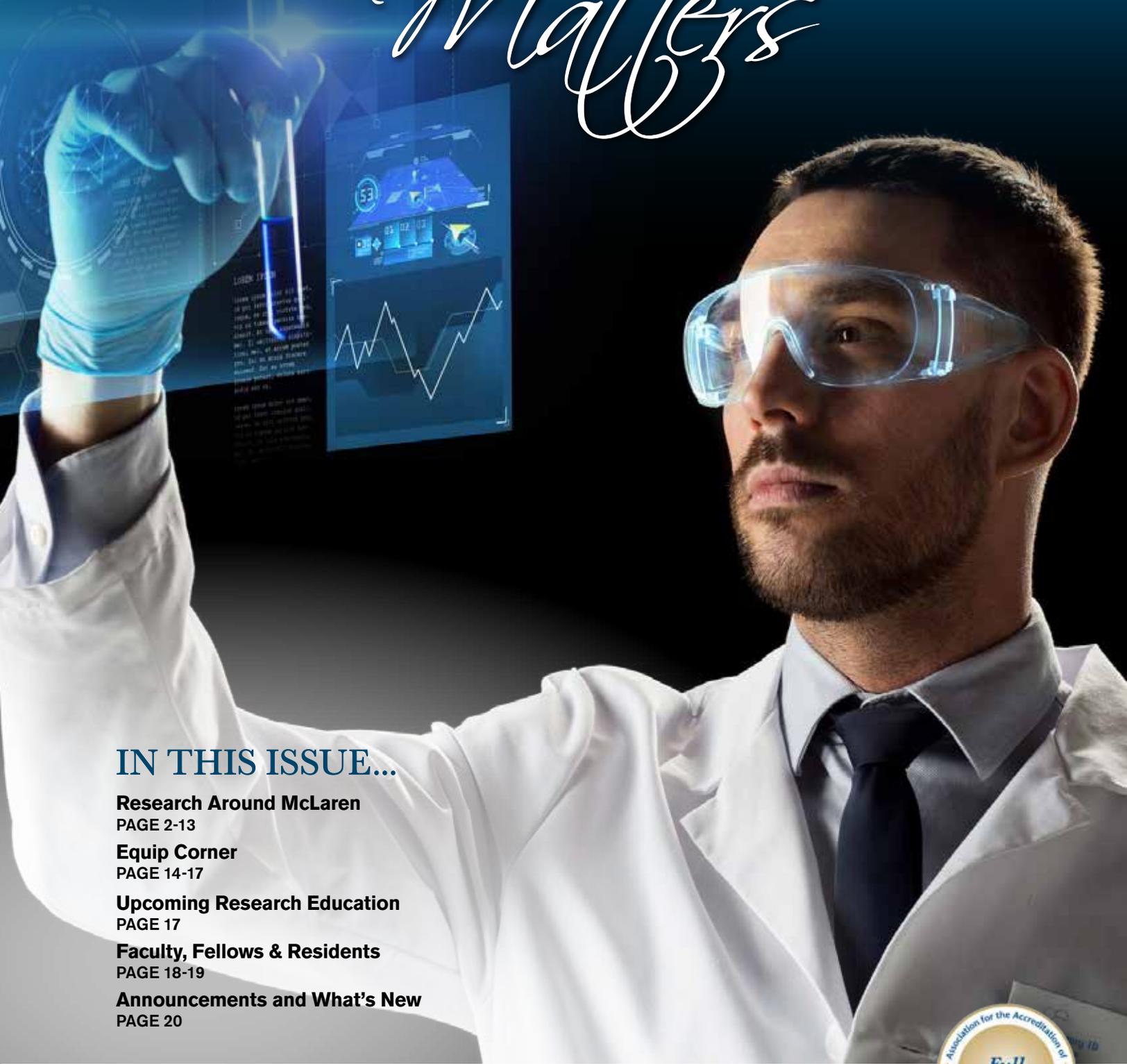


RESEARCH

FALL 2020

Matters



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DOING WHAT'S BEST.®

RESEARCH AROUND McLAREN

McLAREN ENROLLS IN FIRST ACUTE STROKE TREATMENT TRIAL

By Jill George

The McLaren Center for Research and Innovation was started less than 10 years ago, and born out of a desire to grow research opportunities for patients and investigators at McLaren. Before MCRI, each subsidiary had a small research office and conducted a small number of out-patient trials and registries. As MCRI grew over the years, our number of studies increased, the number of patients involved in research at McLaren increased and with that, interest from physician investigators grew as well. It's these physicians and their drive to put McLaren on the map in the research world that has provided us with new opportunities that 10 years ago were just a dream.



Aniel Majjhoo, MD

Dr. Aniel Majjhoo, Neuro-interventionalist and Chair of the Neuroscience Research Council at McLaren, is one of those physician investigators with the drive to make research at McLaren stand out amongst the rest. Dr. Majjhoo initiated a collaboration with University of Michigan and in 2018 McLaren Health Care became a National

Institutes of Health (NIH) StrokeNet research site under University of Michigan as the NIH coordinating center. This alliance provides McLaren with ample research opportunities that we would have otherwise not had access to.

Enrollment in the StrokeNet MOST (Multi-Arm Optimization of Stroke Thrombolysis) Trial has recently begun at McLaren Flint. MOST is an acute interventional trial and is the most complex trial McLaren had participated in to date. "It takes

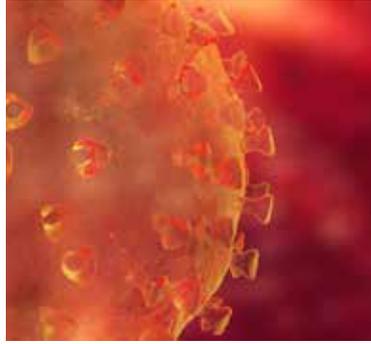
an enormous amount of teamwork and dedication to enroll just one patient," says Principal Investigator, Aniel Majjhoo. "Never before have so many hospital departments come together to take part in an acute stroke treatment trial. It's inspiring to see this kind of work happening at McLaren Flint, and I'm proud to be a part of it." To date 3 patients have been enrolled in the MOST study. Each patient is randomized to receive one of two different blood thinners or a placebo plus their standard tPA treatment for their stroke. "Everything happens so fast, but this team is amazing and it all just comes together," says research coordinator, Marci Roberts, "it's exciting to know we are doing something that's never been done before at McLaren, and I get to be a part of it."

"IT'S INSPIRING TO SEE THIS KIND OF WORK HAPPENING AT McLAREN FLINT, AND I'M PROUD TO BE A PART OF IT."

– Aniel Majjhoo, MD

McLaren Center for Research and Innovation is extremely proud to be involved with cutting edge research at all our locations, and we look forward to seeing what the future holds. What was just a dream less than 10 years ago has finally become a reality and we have our dedicated research staff and investigators to thank. We also thank each and every department and hospital staff member who went above and beyond their usual duties to support research and help bring this treatment option to our patients. "McLaren Neurosciences program strives to exceed standard of care with cutting edge technology, and research options through MCRI make it possible," said Dr. Majjhoo.

COVID-19 AND EVIDENCE-BASED MEDICINE



Residents, as well as their attendings and every other clinician, need to read the medical literature to keep up-to-date with the most recent advances in their respective specialties. However, not all medical literature is created equal. This means that there is very good quality literature but also very poor quality literature; fortunately, very few of the latter. To evaluate the quality of the constantly evolving medical literature most residency training programs require residents to understand and apply EBM principles. These principles have been usually summarized in five steps (5 A's). 1. Ask (formulate the clinical question); 2. Acquire (search the relevant evidence); 3. Appraise (critically evaluate the evidence for internal validity and generalizability); 4. Apply (incorporate evidence into the clinical decision-making process); and 5. Assess (evaluate the process and seek ways to improve next time).

The COVID-19 pandemic presented a major and unusual challenge to the application of most of the EBM principles. To treat patients infected with COVID-19 it was necessary to ask, for example, what current treatments are available? Acquiring/gathering information about the available treatments was the next step. However, the novel nature of this virus made it almost impossible to find any available treatment supported by rigorous research. In addition, the medical community became desperate and frustrated by the lack of a proven treatment and the need to somehow treat patients that were dying because of this disease. The combination of these two factors might have had an impact on the decision to start using anecdotal evidence and poorly designed studies to identify possible pharmacological treatments for patients infected with COVID-19. EBM principles became an after thought during the early stages of the pandemic. This could have partially explained how hydroxychloroquine became a commonly prescribed treatment for COVID-19.

It is said that hindsight is 20-20, but if at least Step 3 of EBM would have been implemented to evaluate the first published study (1) on hydroxychloroquine many of the design flaws could have been identified. The identification of these flaws would have challenged the internal validity and generalizability of this study. Thereafter, it would have been concluded that the findings from this study did not support hydroxychloroquine as an adequate treatment choice for COVID-19 because of the study major flaws and limitations. Currently, at least three well-designed studies (2-4) have documented the lack of benefit of hydroxychloroquine on treating patients infected by COVID-19. The COVID-19 pandemic has taught us, among many other things, the critical importance of following EBM principles even in the presence of great need and human suffering. It has also demonstrated one the reasons why EBM is an integral component of any residency training program.

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ARE YOU INTERESTED IN BECOMING A RESEARCH PARTICIPANT?

For information on enrolling in a clinical trial please visit our website at <https://www.mclaren.org/main/research-trials1.aspx> . Here you will find a list of open enrolling studies at McLaren, including which hospital the research is being done at and contact information for each study.

We have enrolling studies for the following conditions (not a complete list):

- Diabetes
- High Blood Pressure (Hypertension)
- Stroke
- Heart Attacks / Heart Failure / Heart Disease
- Kidney Diseases
- Lung Diseases
- Peripheral Artery Disease
- Carotid Artery Disease
- Mastectomy
- Various Cancers
 - Breast
 - Lung
 - Prostate
 - Multiple Myeloma
- Patients who underwent intracranial aneurysm coiling
- Drug study for patients with recent acute coronary syndrome

For a complete list of conditions, please visit our website listed above.

RESEARCH AROUND McLAREN



PRESENTATION AWARDS

Online Symptom Checkers for Obstetrical Triage: Computer Versus OBGYN Resident: Who has Better Diagnostic Accuracy

Dr. Chadwick Densley, OB/GYN McLaren Greater Lansing, won first place in the oral presentation.

MSU SCS OB/GYN Research George W. Russian Resident Research Day, December 19, 2019

Epidural Anesthesia Use after the Introduction of Nitrous Oxide During Labor at a Community Hospital

Dr. Amy Houser, OB/GYN McLaren Greater Lansing, won third place in the oral presentation.

MSU SCS OB/GYN Research George W. Russian Resident Research Day, December 19, 2019

Association of Clinical Symptoms of Chorioamnionitis and Positive Findings on Placental Pathology

Dr. Audrey Hemmings, OB/GYN McLaren Greater Lansing, won second place in the poster presentation.

MSU SCS OB/GYN Research George W. Russian Resident Research Day, December 19, 2019

We sincerely regret if we left out any fellow or resident, due to our publication deadline. Nevertheless, our congratulations to all of you that received any recognition for your scholarly activity work. We also would like to recognize faculty, program directors, and all medical education staff for their support and assistance. Without you, none of this would have been possible.

MANUSCRIPTS ACCEPTED FOR PUBLICATION

A case report of absolute thrombocytopenia with ticagrelor

Khan MR, Adhikari G, Khan H, Changezi HU. European Heart Journal, 2020. <https://doi.org/10.1093/ehjcr/yttaa169>

Anomalous takeoff of left internal mammary artery from thyrocervical trunk arising off the aortic arch

Malek R, Lala V, Bykowski A, Yamasaki H. Journal of Cardiovascular Imaging, 2020. <https://doi.org/10.4250/jcvi.2020.0057>

DR. KAMIAR MOIN SECURES PRESTIGIOUS R50 GRANT

Kamiar Moin, PhD, director of the Microscopy, Imaging & Cytometry Resources (MICR) Core at the Barbara Ann Karmanos Cancer Institute and professor in the Department of Pharmacology at Wayne State University School of Medicine (WSU SOM), has secured a five-year, \$1.5 million R50 grant by the National Cancer Institute (NCI). The grant number is CA251068-01.

R50 grants, also known as NCI Research Specialist Awards, encourage the development of stable research career opportunities for exceptional scientists who want to pursue research within the context of an existing cancer research program, but not necessarily serve as independent investigators, according to the NCI website.

Karmanos' MICR is the largest facility core of the Institute and is funded in part by the Cancer Center Support Grant (CCSG). Dr. Moin serves as a co-investigator on the CCSG grant.

Dr. Moin established the MICR in 1994 as the Confocal Imaging Core and provided what was then the most current expertise and innovative technology in fluorescent microscopy, confocal microscopy and related techniques used to study normal and cancerous cells.

Since its establishment, Dr. Moin has expanded and significantly upgraded the MICR numerous times, culminating in the current multimodal imaging and flow cytometry service center (which detects and measures the physical and chemical characteristics of cancer cells), with more than 4,000 square feet of space and 22 capital instruments.

Dr. Moin's mission through MICR is to support and enhance peer-reviewed funded research activities of Karmanos and WSU's scientific community whose members' research requires advanced cytometry, as well as cellular, tissue and animal imaging and analysis. To fulfill this mission, Dr. Moin and his colleagues provide expertise in analytical methods development, technology development and validation, and imaging and cytometry study design.

This MICR core also provides collaboration and consultation for grant proposals and publications; provides and maintains state-of-the-art advanced instrumentation in flow cytometry, microscopy and imaging; promotes opportunities for intra- and inter-programmatic interaction among scientific members; minimizes costs and effort for Karmanos investigators while increasing efficiency; and provides educational and training opportunities in microscopy, imaging and flow cytometry.

Dr. Moin is a nationally- and internationally-recognized expert and leader in imaging and cytometry. He has served on 18 National Institutes of Health study sections and has conducted numerous presentations and workshops. He has more than 30 years of experience and over two decades of facility core management and administrative skills. We congratulate Dr. Moin on securing this prestigious grant!



RESEARCH AROUND McLAREN



This article describes the work presented in a clinical trial operations completed project authored by J. Ventimiglia, E. Doppel, B. Olsen, Barbara Ann Karmanos Cancer Institute, Wayne State University.

Metropolitan Management of Mitten-wide Clinical Trials:

COORDINATION FROM OUR OWN BACKYARD

When Karmanos Cancer Institute (KCI) became part of McLaren Health Care Corporation to become Michigan's largest cancer care and research network, one goal was to increase access to transformative cancer care in communities throughout the state. The KCI Clinical Trials Office (CTO), based in Detroit, was tasked with developing and standardizing policies and procedures for conducting research across all subsidiaries. Policies covered patient enrollment, study coordination and data management. To streamline training and operations, we developed a central data management (CDM) plan. The goals were to:

- Increase the feasibility of clinical trial operations across the state
- Implement the research nurse role at each subsidiary to improve protocol compliance and data quality, based on the KCI-Detroit model
- Centralize study coordination and data management to ensure data integrity across all sites and studies
- Expand the reach and responsibilities of CTO staff to ensure efficient utilization of current resources
- Facilitate the increase in industry, cooperative group and investigator-initiated trial accruals

To reach these goals, the team constructed a comprehensive, step-by-step guide to CDM tasks (e.g., consenting process, patient eligibility, protocol deviations, serious adverse events, etc.) and developed a process document to differentiate between the responsibilities of the research nurse at each network site and study coordinator at KCI-Detroit. We dedicated a shared drive to CDM studies to securely and expeditiously transmit study-related documents. This CDM module was added to the CTO New Employee Orientation program, a mandatory onboarding program for KCI research staff. Finally, we established a collaborative focus group consisting of KCI-Detroit study coordinators and network staff to regularly review CDM processes and procedures and revise accordingly.

Since the integration, the CTO has seen an increase of approximately 500% in network accruals while utilizing the SCs at KCI-Detroit to manage network data collection and entry. This is the foundation of CDM, which has reduced discrepancies and errors in data entry, retention and management. With the implementation of CDM, KCI-Detroit has seen a positive outcome in same-day communication of patient consents and study visits at network sites, instantaneous record-sharing through the shared drive and electronic health records (EHR) and a new role for network research nurses to facilitate the onboarding of patients to clinical trials. The CDM focus group meets monthly to discuss workflows and challenges in real time. These meetings provide a forum to identify problems and collaboratively work on solutions, as well as foster open discussions to prevent barriers.

One of the biggest hurdles in implementing the CDM process was navigating multiple EHRs throughout the network. This is a common problem in healthcare in general. KCI is working toward utilizing one standardized EHR software, which is accessible by all staff at all sites. This will improve the continuum of care for our patients as they seek to remain within the KCI network for their care, while simultaneously expediting the efficiency of CDM by storing true source in one internally universal, safe electronic location. As the landscape of oncology research evolves, we will continue to ensure our practices provide outstanding support to clinical trials to improve cancer therapy and patient quality of life through research.

KARMANOS TEAM CREATES PROCESS TO ENHANCE DOCUMENTATION AND COMMUNICATION OF DRUG ACCOUNTABILITY FOR OUR RESEARCH PATIENTS

Karmanos Cancer Institute is an NCI designated Comprehensive Cancer Center and a Quality Oncology Practice Initiative (QOPI) certified site. In preparation for our QOPI re-certification, we recognized that we could apply those standards to enhance documentation and communication of drug accountability for our research patients. There was a need for more robust, real-time documentation of drug compliance that could be standard for all clinical trial patients. We created and implemented the Management of Oral Investigational Drug (OID) policy, workflow and nursing documentation aid that met the needs of the hospital requirements and research standards. This included compliance, patient education, return visit instructions, clinic contact and specific dosing instructions.

The goals were to:

- Monitor patient adherence to OID administered outside of the health care setting at clinically meaningful intervals
- Ensure documentation of dosing, education, and compliance is available in the electronic health record (EHR)
- Standardize OID accountability across all Multidisciplinary Team (MDT) services
- Address and limit discrepancies between OID dispensed and OID returned to improve data accuracy

First, we developed a working group consisting of Research Nurses (RN) and Study Coordinators (SC) to ensure the process met all needs. Institutional standards, QOPI and research requirements were utilized to design process and workflow. The team created standardized pill diary templates when not provided by the sponsor. This process was piloted for one month (approximately 100 patient visits) to identify potential issues and amended based on pilot experience then finalized and formally implemented across all Multidisciplinary Teams.

Standardizing this process among patients receiving OID has created a notable positive effect on the patient experience, compliance, data quality and documentation. This policy and workflow guide the RN in a conversation with the patient and clinician to review compliance and enhance patient safety, enable clarification of discrepancies between the diary and pill count and identify patient dosing errors contemporaneously. OID dosing is documented more frequently and enables timely data entry and query resolution. The development of the OID policy, workflow and nursing documentation aid ensure consistency across all MDTs and among clinical and research staff.

We have observed an improvement in patient compliance and expectation when patients are mindful that their dosing will be reviewed at every study visit. In turn, patients are empowered to become active participants in their own care. This frequent interaction has strengthened the rapport between patient and staff.



This article describes the work presented in a clinical trial operations completed project authored by C. Galasso, B. Dickow, C. Houde, J. Ventimiglia, M. Ventimiglia, C. Zack, C. Zuccaro, Barbara Ann Karmanos Cancer Institute, Wayne State University.

RESEARCH AROUND McLAREN

Karmanos researchers and providers recorded segments for the Partnering Around Cancer Clinical Trials (PACCT) informational video.



EDUCATIONAL VIDEO ON CLINICAL TRIALS WINS PRETIGIOUS TELLY AWARDS

Congratulations to Susan Eggly, Ph.D., professor and a member of the Population Studies and Disparities Research Program at Karmanos Cancer Institute and Wayne State University School of Medicine and her research team for being recognized with gold and silver 2020 Telly Awards. These accolades were given for the Partnering Around Cancer Clinical Trials (PACCT) informational video. The gold was won in the category of Non-Broadcast: Employee Communications and the silver for Non-Broadcast: General Recruitment.

The Telly Awards honor excellence in local, regional and cable television commercials as well as non-broadcast video and television programming. Annually, the awards showcase the best work created across video for all screens, selected from over 12,000 entries from all 50 states and five continents. Telly Award winners represent work from some of the most respected advertising agencies, television stations, production companies and publishers from around the world.

The winning video was created as part of a training module designed to improve the way health care providers communicate with patients and their family members about clinical trials. It is part of the larger PACCT research initiative, a National Cancer Institute-funded award, which aims to increase clinical trial rates in a diverse patient population. The overall goal of the study is to test two communication interventions, one for patients and another for physicians, as a way to increase rates at which African-American and White men with prostate cancer make informed decisions to participate in a clinical trial. Designed to encourage physicians to offer trials to all eligible patients using high-quality, patient-centered communication, an earlier version of the PACCT provider



Susan Eggly, PhD

“WE ARE HONORED AND PRIVILEGED TO HAVE THE COOPERATION AND PARTICIPATION OF SO MANY CLINICIANS, PATIENTS, AND FAMILY MEMBERS. THEIR PARTICIPATION HELPS US TO ANALYZE AND IMPROVE COMMUNICATION, WHICH WILL IMPROVE CANCER CARE.”

– Susan Eggly, PhD

training module was delivered throughout the 16 Karmanos network locations in Michigan, with positive results. The latest training modules will soon be nationally available.

The use of video is central to PACCT research. With permission from patients, family members and providers, clinical interactions are recorded and reviewed as a way to better understand and improve patient-physician communication. In addition, videos from these actual interactions are re-enacted and used to provide evidence-based instruction to both providers and patients.

Filming clinical interactions requires a great deal of time and organization from the research team. Dr. Eggly, Principal Investigator for PACCT explained, “We are honored and privileged to have the cooperation and participation of so many clinicians, patients, and family members. Their participation helps us to analyze and improve communication, which will improve cancer care.”



PACCT is funded by a grant from the National Cancer Institute. Johns Hopkins School of Medicine/Sidney Kimmel Comprehensive Cancer also serves as a research site and oversaw the production of the video, with the script and planning from Wayne State University School of Medicine and Karmanos Cancer Institute.

The team from Wayne State University School of Medicine and Karmanos Cancer Institute includes Susan Eggly, Ph.D., Lauren M. Hamel, Ph.D., Elisabeth Heath, M.D., Mark A.

Manning, Ph.D., Terrance L. Albrecht, Ph.D., Ellen Barton, Ph.D., Mark Wojda, Tanina Foster, Ph.D., Seongho Kim, Ph.D., Nicole Senft, Ph.D. and Louis A. Penner, Ph.D., as well as several researchers from Johns Hopkins School of Medicine/Sidney Kimmel Comprehensive Cancer.

RESEARCH AROUND McLAREN



KARMANOS' DR. PODGORSKI RECEIVES RO1 GRANT TO CONTINUE RESEARCH ON METASTATIC PROSTATE CANCER

Izabela Podgorski, PhD, co-leader of the Prostate Cancer Research Team at the Barbara Ann Karmanos Cancer Institute and associate professor of Pharmacology at Wayne State University (WSU) School of Medicine, was the first researcher to suggest a link between bone marrow fat cells (adipocytes) and metastatic prostate cancer back in 2010.

She has recently obtained a new five-year, \$2,028,733 million RO1 grant from the National Institutes of Health/National Cancer Institute to continue her studies into how prostate cancer cells are affected by bone marrow fat and how they adapt and survive in bone in an effort to identify new ways of treating metastatic prostate cancer. The grant number is CA251394-01.

Her new study hypothesizes that tumor cell and bone marrow adipocyte interactions enhance prostate cancer metastatic progression, while simultaneously reducing the tumor cells' response to current treatments.

"Bone by itself is a very harsh microenvironment that is a difficult to treat," she said. "For a long time, people thought bone marrow fat cells were just energy storage units. We knew they were abundant in adult bones and that their numbers prematurely increased with obesity and metabolic diseases. But we had no idea what role(s), if any, they played in metastatic prostate cancer. In the past few years our studies, and others, began to reveal that when you have tumor cells in the bone marrow, they trigger some changes in the metabolism of adipocytes, and those changes ultimately help the tumor cells to survive and escape therapy."



Izabela Podgorski, PhD

Adipocytes are cells specialized for the storage of fat. Those cells expel lipids, which are fatty acids.

“Cancer cells take up those fatty acids and use them as energy,” Dr. Podgorski said. “Tumor cells push the adipocytes to expel more lipids. They have this interactive relationship that supports (tumor) growth and promotes resistance to standard chemotherapy treatments, which includes docetaxel and cabazitaxel.”

Men who are diagnosed with prostate cancer typically have a five-year survival rate of close to 100 percent if the cancer is contained in the original site, according to Dr. Podgorski. But if it metastasizes, the cancer cells will often migrate to a portion of the axial skeleton such as the hip, pelvis or ribs. Metastatic prostate cancer cells could also target a visceral organ such as the liver or travel to the lymph nodes.

According to Dr. Podgorski, 85 to 90 percent of men with metastatic prostate cancer have bone metastases. That lowers a man’s five-year survival rate to below 30 percent. If the tumor cells migrate to bone and a visceral organ, it creates the most lethal scenario.

In Dr. Podgorski’s research, she and the researchers in her lab have discovered that marrow fat cells can modify normal functions of metabolic enzymes (such as PKM2) or inflammatory molecules (such as interleukin 1B). This helps tumor cells grow more robust and resist therapeutic agents. With the latest RO1 grant, she and her colleagues are striving to demonstrate that inhibiting lipid release by adipocytes will improve therapy response and uncover new molecular targets for therapy.

They are utilizing a variety of different techniques to identify these new molecules. These methods include 3D culture techniques, patient samples, mouse models, models that mix both human and mouse samples, proteomics (the study of cellular proteins) and RNA sequencing approaches. They will use these approaches to study previously unexplored mechanisms that link bone marrow adipocytes with the survival of cancer cells that also resist standard therapy.

Given the research they have already established about bone marrow adiposity, Dr. Podgorski is confident that this will provide progress in the development of new prostate cancer therapies.

“I think we have a lot of tools to answer the questions we’ve asked,” she said. “We already identified potential molecules to target, including PKM2 or interleukin 1B. Fat cells change the activity of these targets in the tumor to help it live. They also affect other processes, such as iron metabolism. The design of this study promises to show that lipids supplied by fat cells in the bone marrow are key contributors to chemoresistance. The study is also likely to identify new mechanistic targets for therapy.”

We congratulate Dr. Podgorski and her Karmanos and WSU collaborators on the prestigious R01 grant, including James Granneman, PhD, Maik Hüttemann, PhD, Paul Stemmer, PhD, Elisabeth Heath, MD and Dr. Seongho Kim, PhD.

RESEARCH AROUND McLAREN

“WHEN WE THINK ABOUT HOW COVID-19 HAS AFFECTED MINORITY POPULATIONS, THE FACTORS THAT CONTRIBUTED TO THE UNEQUAL BURDEN OF CANCER ON THE AFRICAN-AMERICAN COMMUNITY ARE THE SAME FACTORS THAT CONTRIBUTED TO THE BURDEN OF THE CORONAVIRUS ON AFRICAN AMERICANS.”

– Hayley Thompson, PhD

KARMANOS RESEARCHERS LOOK TO CANCER STUDIES TO UNDERSTAND RACIAL DISPARITIES IN HEALTH CARE

Cancer and COVID-19 vary vastly in their classification, treatment and symptoms but the two have something in common: they are disproportionately affecting the African-American community, not only in Detroit, but also in other parts of the nation.



Hayley Thompson, PhD

At the Barbara Ann Karmanos Cancer Institute, clinical and scientific researchers focus on developing treatments for cancer. In doing so, they are also examining factors that have led to the African-American population shouldering the heavy burden of cancer. Now, the global COVID-19 pandemic is providing a new lens through which researchers can examine disparities in care. Through dedicated departments, programs and staff whose sole function is to understand the socioeconomic and systemic factors that explain these common health disparities, Karmanos is able to work towards solutions that create equity.

Hayley Thompson, PhD, serves as the associate center director for Community Outreach and Engagement, which oversees the Office of Cancer Health Equity and Community Engagement. “When we think about how COVID-19 has affected minority populations, the factors that contributed to the unequal burden of cancer on the African-American community are the same factors that contributed to the burden of the coronavirus on African Americans.”

Research shows that these factors include racial bias on the part of health care providers, breakdowns in patient-provider communications, mistrust of the medical community from minority groups and issues of health literacy. Underserved groups also face a lack of access to financial resources, insurance coverage and quality health care overall.

“I tell a lot of my colleagues, we’re all COVID-19 researchers to some extent,” Dr. Thompson said. “The way people manage their health care is affected by COVID-19. The virus has made it more difficult for people to maintain their health. We know people haven’t been able to get their mammograms or colonoscopies. What does this mean for people who already have a mistrust of the medical community?”

As a National Cancer Institute-designated comprehensive cancer center based in Detroit, Karmanos is responsible for serving everyone in the community through education, diagnostic and treatment services. The Institute recently received a five-year, \$3 million grant from the National Institutes of Health (NIH) to identify targets of change and ways to address causes of poorer health-related quality of life experienced by African-American cancer survivors.

Thompson and her colleagues have also developed a survey about COVID-19 and social distancing to determine their effect on cancer care across the continuum, including cancer screening, treatment and prevention. They hope to reach 2,000 people.

Karmanos also has a Populations Studies and Disparities Research (PSDR) program, in collaboration with Wayne State University School of Medicine (WSU SOM). The staff at PSDR secured the \$3 million NIH grant. PSDR's goals are to identify risk factors underlying disease onset and progression and develop and test intervention strategies to reduce risk and improve diagnosis, treatment and outcomes of cancer. The primary intended outcome is to decrease race- and ethnicity-related disparities and overall disease burden.

PSDR's other areas of study include investigating the distribution and determinants of cancer and cancer risk, survivorship and outcomes, with attention to racial and ethnic disparities. Program members examine patient, family member, physician and community interactions and behavior in order to understand and conduct interventions. These interventions address cancer risk, treatment and outcomes.

PSDR members collaborate with Karmanos oncology physicians and researchers from 14 multidisciplinary teams (MDT). Each team consists of specialists who are focused on a particular cancer and work closely with the patient to offer the best treatment options.

Michael Simon, MD, co-leader of the Breast Oncology Multidisciplinary Team, is partnering with members of PSDR to conduct a literature review of approximately 90 articles that Karmanos and WSU SOM have published over the last 30 years regarding health disparities and the African-American population in Detroit and the state of Michigan.



Michael Simon, MD

Dr. Simon said he was inspired to conduct this literature review after hearing WSU President M. Roy Wilson in an interview about COVID-19 disproportionately affecting African Americans.

"We've known this about cancer for more than 30 years," Dr. Simon said. "I was motivated to email him (and suggest that) maybe an oncologist working in Detroit can help to understand why the coronavirus is affecting

more African Americans. We've learned a lot of lessons in cancer and could take all the work that we've done and create a review article that could provide commentary on coronavirus and underserved populations." Dr. Simon and his colleagues hope to have the article published in the next couple of months.

While the epidemiology of coronavirus infection is different from cancer, Dr. Simon said the same living conditions that place African Americans at greater risk of coronavirus also contribute to a lack of timely screenings for cancer among this population. African Americans have the lowest survival

rate of any racial or ethnic group in the United States for most cancer, according to Karmanos research.

Beyond addressing issues of health disparities and comorbidities that contribute to cancer diagnoses and higher risks of coronavirus infections, Dr. Simon believes communication between doctor and patients can help close the health disparities gap.

Susan Eggly, PhD, professor and a member of the PSDR program, agrees and focuses her research on the ways that patients and providers communicate, particularly around clinical trials. She leads the Partnering Around Cancer Clinical Trials (PACCT) study which is designed to encourage physicians to offer trials to all eligible patients using high-quality, patient-centered communication. The overall goal of the study is to test two communication interventions, one for patients and another for physicians, as a way to increase the rates at which African-American and White men with prostate cancer participate in clinical trials based on informed decisions.

With permission from patients, family members and providers, clinical interactions are recorded and reviewed as a way to better understand and improve patient-physician communication. In addition, videos from these interactions are re-enacted and used to provide evidence-based instruction to both providers and patients. These videos are utilized in training modules, which include techniques and instruction for better care. Thus far, 16 Karmanos network locations in Michigan have benefited from using these videos and reported positive results. These latest training modules will soon be available nation-wide.

"Nationally, we see that African-American patients are less likely to ask questions and state concerns and that doctors provide less information to African-American patients. Our work encourages patients to participate actively during clinic visits by asking questions and stating concerns, and doctors to elicit patients' questions and then answer them fully," said Dr. Eggly.

Through many initiatives, Karmanos Cancer Institute is dedicated to comprehensive work aimed at ending racial disparities in health care. While the work is data-driven and rigorous, it also requires adaptation at a more human level.

As Dr. Simon puts it, "I'm thinking about how we can become better health providers for all people. I think it has to do with getting to know people on a personal level. We really have to mix it up and have dialogue as real people."

EQUIP CORNER



RECRUITMENT: REVIEW OF HIPAA, FDA, AND IRB GUIDANCE

By Andrea Klaver

The inability to recruit enough patients for clinical trials might be one of the biggest factors keeping many studies from getting off the ground. A streamlined patient recruitment process that is targeted and effective has long been the holy grail of clinical trials. With many barriers to participation, ranging from financial, logistical, or a lack of resources to support enrollment and retention, it's important that we understand the recruitment process so we can find ways to improve it.

Despite efforts over the years to address the issue with limited success, recruitment and retention remains a key bottleneck in the study timeline. Can a solid understanding of the regulatory and ethical landscape help us overcome these barriers?

Recruitment Regulations and Ethical Concerns

Let's go back to the basics with a review of the ethical principles of The Belmont Report, created as a result of the National Research Act of 1974.

1. **Respect for Persons.** This clause is two-pronged; that is, prospective study patients should be treated as autonomous agents, and should that autonomy be diminished, they are entitled to protection. We give weight to each patient's choices and opinions, while ensuring they are participating in the study voluntarily after being supplied adequate information (i.e. informed consent).
2. **Beneficence.** Not two-pronged but complementary, beneficence is understood to mean "do no harm," while at the same time maximizing potential benefits and minimizing potential risks.
3. **Justice.** Who receives the benefits of research and who will bear its burdens? This principle stresses the fair selection of subjects and sharing the risks and benefits of the study considered in the beneficence discussion equitably.

Consider the respect for privacy – does the recruitment method take this into consideration? The first point of contact for a research subject may be someone to whom personal information will be offered. Scripts and procedures should be in place to protect the patient privacy.

Studies should be introduced to prospective subjects in a way that allows them ample time to consider their decision, with no undue pressure. Pressure could arise from the timing of the request, who makes the request, or how the request is made.

Unbiased presentation and “therapeutic misconception” should also be thoughtfully considered during the recruitment process. Any information presented to prospective subjects should be accurate, balanced, and complete, with no information left out intentionally to make the study sound better than it really is. The best recruitment plans actively work to counteract this misconception.

Generally Accepted Recruitment Methods

At McLaren Health Care (MHC) and many other institutions, recruitment materials must be approved by the institutional review board (IRB) prior to use. Some examples include personal contact, advertisements (newspaper, website), media (video, audio), hard copies (letters, scripts, flyers, brochures), and referrals.

With referrals, remember that offering payment to or accepting payment from medical or research staff for referring patients to research studies (so-called “finders fees”) is not allowed by the MHC IRB.

While developing your recruitment strategy, it is best to avoid initial contact by unknown individuals. Prospective research subjects should be contacted by people directly involved in their care. Further, individuals initiating contact with potential subjects must have basic knowledge about the study so they can answer questions and training in the voluntary nature of trial participation.

HIPAA and the Preparatory Research Provision

Medical record access, protected health information (PHI), and personally identifiable information (PII) should be restricted except to those directly involved in a patient's care. No HIPAA-regulated PHI should be used in an ethical recruitment strategy. If it contains any of the following identifiers or parts of the identifier, all must be removed from the data set.

The 18 Identifiers that Make Health Information PHI

Names	Health plan beneficiary numbers
Dates including birthdates (except year)*	Certificate/license numbers
Telephone numbers	Vehicle identifiers and serial numbers including license plates
Geographic data smaller than state	Web URLs
Fax numbers	Device identifiers and serial numbers
Social Security numbers	Internet protocol (IP) addresses
Email addresses	Full face photos and comparable images
Medical record numbers	Biometric identifiers (i.e. retinal scan, fingerprints)
Account numbers	Any unique identifying number or code

**All ages over 89 years should be aggregated into a single category of age 90 or older.*

The HIPAA preparatory research provision allows covered entities to use or disclose PHI for purposes preparatory to research without authorization – like supporting recruitment. To do this, the entity must obtain some form of attestation

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EQUIP CORNER

RECRUITMENT: REVIEW OF HIPAA, FDA, AND IRB GUIDANCE

CONTINUED FROM PAGE 15

from the researchers that the PHI will be used solely to prepare a protocol or for a similar purpose, it will not be removed from the covered entity, and it is necessary for research.

Researchers who are employees or a member of an entity’s workforce may also use PHI to contact prospective research subjects. The provision allows researchers to identify prospective research subjects to seek their authorization to use or disclose their PHI for a study. Removing PHI from the entity’s site is still prohibited.

The FDA

The FDA expects IRBs to review all the research documents and activities that directly impact the rights and welfare of the subjects of proposed research, like the protocol, the consent document, and recruitment materials. They consider direct advertising for study subjects to be the start of the informed consent and subject selection process.

Advertisements should be reviewed and approved by the IRB as part of the initial study review, and if the investigator decides later to advertise for subjects, it may be considered an amendment to the ongoing study. Generally, the FDA believes that any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest.

Ads, Flyers, and Media Guidelines

Do’s	Don’ts
Name and address (PI or Institution)	Benefits beyond what is in the consent
Condition under study	Claims that procedures are safe/effective
Purpose of the research	Claims that procedures are equivalent or superior to others
Summary of eligibility criteria	Terms like “new treatment,” or “new medication,” without explaining that the research is investigational
Brief list of participation benefits, if any	Promises of “free treatment”
Time or other commitment required	Payment emphasized with larger or bold type
Location, person, or office to contact	Language that the PI cannot be held liable for any research related event

Recruitment Policy at MHC

The recruitment and screening guidelines set forth in McLaren policy closely follow HIPAA and FDA guidance. The disclosure of a subject’s PHI to another party (including another covered entity or health care provider) for recruitment in a research study requires either (1) the patient’s specific Authorization or (2) an IRB waiver of Authorization.

A clinician may discuss opportunities to enroll in research studies with his/her own patients without an Authorization if no PHI will be disclosed to another party. If the patient agrees to participate in a study in which the clinician is taking part, then the clinician must obtain a signed Authorization from the patient to use and disclose PHI.

Approved research staff may also perform screening to identify potential subjects. An Investigator who is not employed by MHC may not screen any patient records to identify possible study participants unless the Investigator has received a Waiver to do so from the IRB. Investigators who are employed by MHC may screen their own patient records to identify possible study subjects, but they must obtain a Waiver from the IRB to screen the records of patients not in their care.



Improving the Recruitment Process in the COVID-19 Era – and Beyond

Recruiting during the COVID-19 pandemic is not easy, but it can be done. To maximize safety, study teams may need to modify protocols, launch remote procedures, or implement risk mitigation measures for sites to continue running studies. Some issues impacting recruitment include more cancelled visits due to fear of COVID-19 exposure, or difficulty conducting study visits remotely.

Each issue alone may be manageable for sites trying to meet enrollment goals. Together, they have the potential to slow or stop recruitment and force sites to drop out of studies they planned to conduct. So, what can we do?

- Empower patients. Patients may be less likely to consider a clinical trial if they don't feel they will get something in return. By recruiting them as research partners rather than test subjects, study teams might be able to interest more prospective patients.
- Incorporate virtual elements. Designing trials with more virtual elements (e.g. remote monitoring and consults) could encourage a more diverse set of patients to join clinical research. Advances in telemedicine and connected medical devices can mean more data can be collected from patients while they are home.
- Build a strong patient database through pre-screening prior to obtaining informed consent or enrollment. Clinical trials and their role in finding vaccines and treatments are being discussed now more than ever, due to COVID-19. This can be beneficial to recruitment and awareness of the need for and importance of clinical trials. By determining if individuals meet inclusion/exclusion criteria, sites will have a resource available to them to quickly contact pre-screened patients once enrollment is initiated or reinstated.

UPCOMING RESEARCH EDUCATION

2020

SOCRA
2020 Annual Conference
ONLINE

September 23 – 26, 2020

MAGI's Clinical Research
Conference 2020
ONLINE

November 2 – 5, 2020
and November 9 – 12, 2020

2021

ACRP 2021 Annual Conference
May 14 – May 17, 2021
Toronto, Canada

MAGI's Clinical Research
Conference – 2021 East
May 23 – 26, 2021
Arlington, Virginia

BROWN BAG SERIES

Research Jeopardy
December 15, 2020
12:00 – 12:45
LIVE WEBINAR

To register contact *Andrea Klaver*
at (248) 484-4987 or
andrea.klaver@mclaren.org.

FACULTY, FELLOWS & RESIDENTS SCHOLARLY ACTIVITY NEWS



Carlos F. Rios-Bedoya, ScD

CLARIFICATION: By the time this issue of Research Matters goes to press the IRB would still be transitioning to a new online application submission system called iRIS. As with almost everything, the COVID-19 pandemic has delayed the transitioning and implementation of the new IRB online application submission system. Once the transition takes place, I would be updating the sections of the diagram/flowchart to include iRIS instead of eProtocol.

SCHOLARLY PROJECT STAGES EXPLAINED, PART 4

BY CARLOS F. RIOS-BEDOYA, ScD

McLaren's Division of Scholarly Inquiry in its efforts to encourage, promote, and support scholarly activity among residents/fellows and teaching physicians developed a scholarly project stages diagram/flowchart (Figure 1) over two years ago. Over these past two years, it has been modified in response to suggestions and recommendations from residents/fellows and teaching physicians. The updated diagram/flowchart should serve as the roadmap for scholarly activity from its conception to its IRB/SARC approval. Even when residents/fellows, teaching physicians, and PhDs are aware of this diagram/flowchart, some misunderstanding seems to exist. Part 4 of this series will describe and explain the aim and purpose of the diagram/flowchart depending on the IRB/SARC decision (*Figure 1 blowout section*).

Non-Approved Decision (All Protocols). The IRB/SARC sends a decision letter informing the Principal Investigator (PI) that after reviewing the proposed study protocol it has not been approved. The letter will include the specific reasons for the non-approval decision and the comments made by reviewers that will include major and minor flaws in the study as well as comments on how to address them. If this is the decision, the PI has at least two options. First, together with the PhD, make major changes to the protocol addressing ALL flaws identified by the reviewers and resubmit the protocol as a new and different one. Second, rethink the project and together with the PhD come up with another research question and develop it as a new protocol. Both options require the PI to go through all the scholarly project stages again.

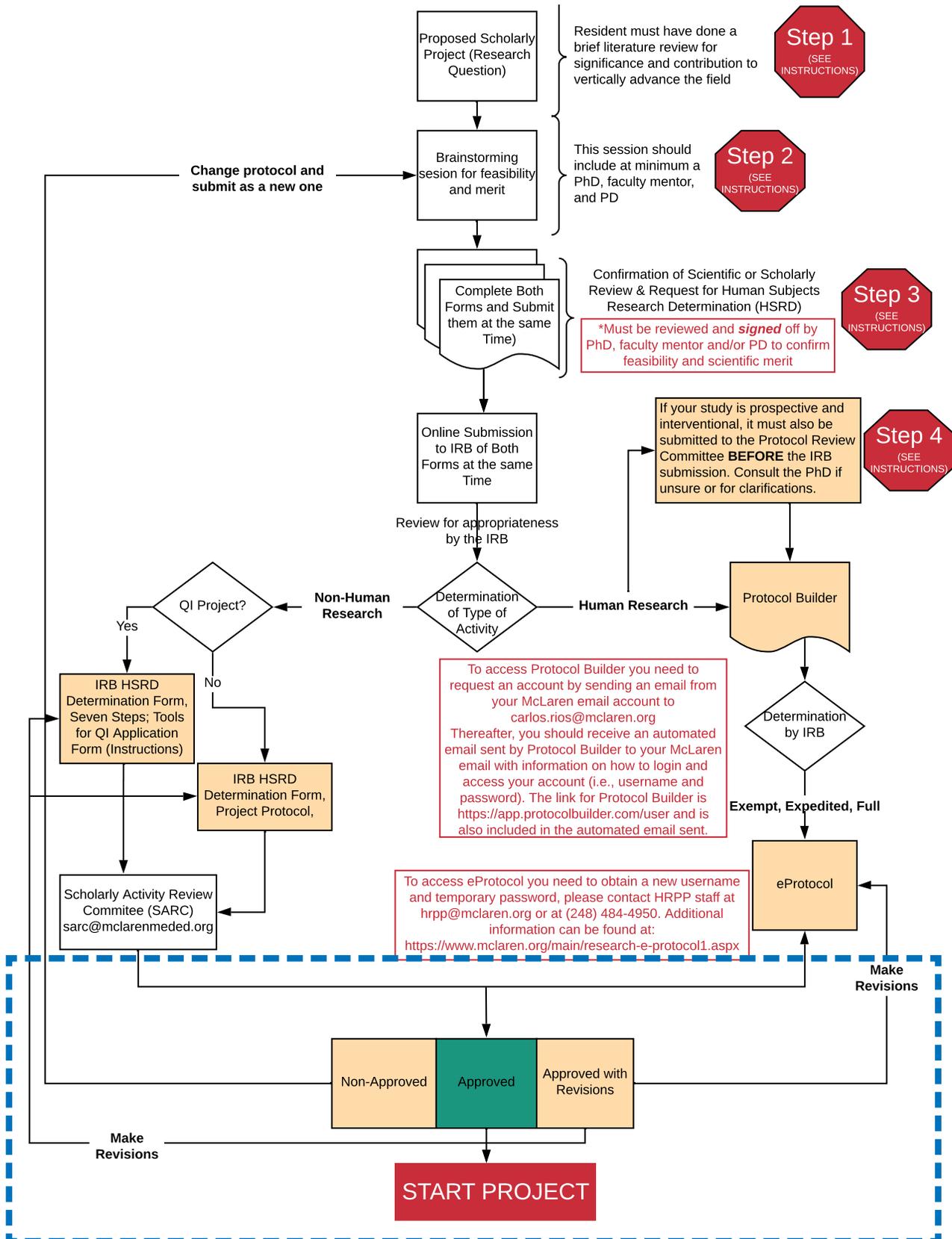
Approved with Revisions Decision (All Protocols). The IRB/SARC sends a decision letter informing the Principal Investigator (PI) that after reviewing the proposed study protocol it has been approved but with revisions. The letter will include the comments made by reviewers that will include the minor flaws in the study that need to be addressed before the project receives approval. If this is the decision, the PI together with the PhD, should address ALL those flaws identified by the reviewers and resubmit the protocol as a revised project. The project should NOT begin until these flaws have been addressed, the revised protocol has been reviewed, and an IRB/SARC letter of approval has been received.

Approved Decision (All Protocols). The IRB/SARC sends a decision letter informing the Principal Investigator (PI) that after reviewing the proposed study protocol it has been approved without stipulations. The letter might include comments made by reviewers. These will include suggestions on how to improve the project or details that might negatively impact the proper implementation and execution of the project to alert the PI of these potential barriers. Once the IRB/SARC approval letter has been received by the PI, the project can start.

The diagram/flowchart presented and discussed in this article is available upon request to a PhD. In the Division of Scholarly Inquiry, we have a commitment and responsibility to promote, expedite, facilitate, and support scholarly activity productivity among McLaren residents, fellows, and teaching physicians.

For additional information or questions contact Dr. Carlos F. Rios-Bedoya at carlos.rios@mclaren.org.

Figure 1 Scholarly Project Stages



ANNOUNCEMENTS AND WHAT'S NEW



Emily Thompson

Employee Promotion – MCRI's Emily Thompson started her career at McLaren as a part-time Clinical Research Assistant in June 2019 and was recently promoted to Clinical Research Coordinator. Emily has worked hard at learning the in's and out's of research and successfully consented/ enrolled her first patient after six months

on the job. Emily embraced the challenges of her new position and quickly grew them into a career path. MCRI looks forward to all the amazing accomplishments that she will achieve in the years to come.



Kelley McCall

New Employee – Kelley McCall joined the McLaren Research Integrity department in July 2020 as the new Research Integrity Administrative Assistant. She obtained her Bachelor of Health Science from Saginaw Valley State University. After 3 years of working in Real Estate, Kelley has returned to her health science background.

Kelley brings a wealth of administrative assistant experience and is eager to learn the ins and outs of the Research Integrity department..

RESEARCH COMMUNITY NEWS

IMPORTANT UPDATE ON IRIS IMPLEMENTATION

We had previously announced a tentative September 14th launch of the new IRB software, iRIS. This date was contingent on the steady progression of data migration from eProtocol to iRIS. Unfortunately, IT is experiencing problems with the migration. Until this issue is resolved, the IRB office is again faced with the decision to pause opening iRIS to the research community.

All of the Following Submissions can be Submitted to the IRB and eProtocol Until Further Notice:

- Requests for External IRB
- Requests for Human Subject Research Determinations
- New Submission Applications
- Continuing Review Applications and Annual Status Reports
- Modifications and Final Reports
- UPIRSO Reports and Violations
- Emergency Use Test Articles

Live training classes dates/times and instructions for setting up user access will be communicated as soon as they are available. If you are not able to attend a scheduled training, a recording of the course will be made available.

Please visit <https://www.mclaren.org/main/iris-research> for up-to-date information.

The Research Integrity Department regrets this delay and we apologize for any frustration this may have created. Thank you for your patience.

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