RESEARCH *Matters*

FALL 2021

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Association for the Accreditation of Human Research Protection Programs, Inc. — *Full* Accreditation

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RESEARCH AROUND McLAREN

FORMING AN ACADEMIC-PRACTICE PARTNERSHIP BETWEEN MHC AND GVSU

In November 2018, a unique academic-practice partnership (APP) was developed between Grand Valley State University's Kirkhof College of Nursing (KCON) and McLaren Health Care (MHC). Building upon different skillsets, an academic scholar and a clinical informatics leader formed a relationship that was reciprocal and collaborative in nature. Dr. Katherine Moran, Associate Dean of Graduate Nursing Programs and Research at KCON and Dr. Lisa Zajac, Corporate Director of Clinical Informatics at MHC established this partnership based on the underlying trust that developed between a project advisor and mentee years ago during Dr. Zajac's doctoral education.

(Left) Katherine Moran DNP, CDCES, FADCES, FNAP Associate Dean for Graduate Nursing Programs and Research, and Associate Professor, Kirkhof College of Nursing; (Right) Lisa Zajac, DNP, RN, ANP-BC, OCN, Director of Clinical Informatics, Karmanos Cancer Center.

Since November 2018, this academic-practice partnership has resulted in two grants supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) totaling nearly $5 million: Advanced Nursing Workforce Education (ANEW) in 2019 ($2,799,987 with 0% financed with non-governmental sources) and Nursing Workforce Diversity (NWD) in 2021 ($2,219,682 with 0% financed with non-governmental sources). This APP was one of approximately 50 ANEW and 32 NWD award recipients nationwide.

In this short period of time, this academic-practice partnership has resulted in:

- Financial support for 13 MHC nurses to complete the BSN to Doctor of Nursing Practice (DNP) degree program at KCON.
- Funding for 4 MHC nurses as the inaugural cohort for the Interprofessional Healthcare Informatics Certificate Program at KCON.
- Exploration of the potential to gain state funding to support a program to blend informatics and mental health care.
- Exploration of the potential to advance mental health care education for MHC providers
- Financial support for 3 MHC nurses to complete a post-MSN to DNP as Health Systems Leaders
- Financial support for 8 MHC nurses to complete an RN-BSN program

Additional financial support will be provided for nurses for 5 RN-BSN and 4 MSN students beginning in January 2022,

as well as 6 RN-BSN and 6 MSN students in 2023.

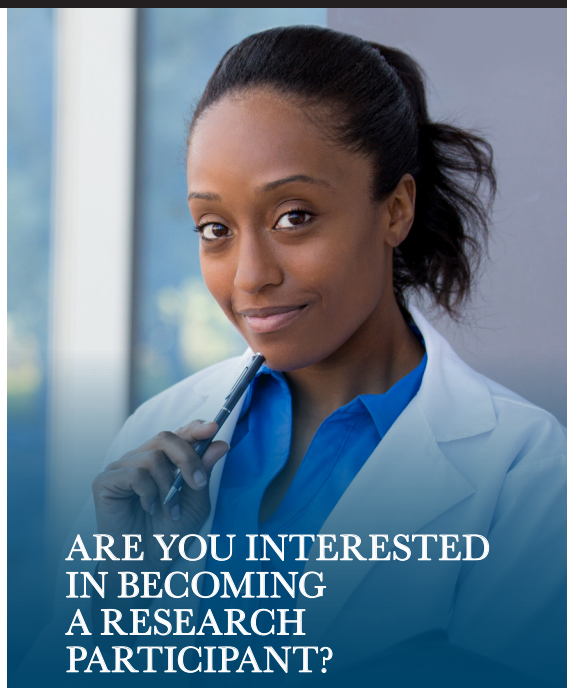
While KCON had academic affiliation agreements with some of the individual MHC subsidiaries and the McLaren Medical Group, there was not a formal APP with the health system as a whole. This partnership has provided MHC clinicians with educational opportunities they did not have in the past and allowed GVSU to broaden their geographic and demographic student reach, as well as expand their practicum sites. This APP has great potential to enhance the healthcare delivery system throughout the state of Michigan and to address the significant access needs present in the state's rural and underserved communities. Both mentor, Dr. Katherine Moran, and mentee, Dr. Lisa Zajac, are grateful to have formed an innovative academic-practice partnership that will improve the lives of Michiganders now and in generations to come.

Building upon different skillsets, an academic scholar and a clinical informatics leader formed a relationship that was reciprocal and collaborative in nature.

CONGRATULATIONS TO McLAREN MACOMB CARDIOLOGY FELLOWS FOR THEIR RECENT PUBLICATIONS

Dr. Akarsh Parekh, Dr. Vivek Sengupta, Dr. Ryan Malek and Dr. Mark Zainea published a case report in *The Egyptian Heart Journal* (2021) 73:64
"A case report: percutaneous management of high-output heart failure from iatrogenic aortocoronary venous grafting to the coronary sinus."
Doi:10.1186/s43044-021-00186-1

Dr. Akarsh Parekh, Dr. Vivek Sengupta and Dr. Mark Zainea published a case report in the *European Society of Cardiology European Heart Journal*:
"An unusual case report of stress-induced cardiomyopathy presenting as ventricular fibrillation cardiopulmonary arrest and third-degree atrioventricular block."
Doi: 10.109.1093/ehjcr/ytab142



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**
- **Orthopedic Surgery**
- **COVID-19**
- **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

Aniel Majjhoo, MD

Mark Zainea, MD

MCRI SITE SPOTLIGHT:

McLAREN MACOMB

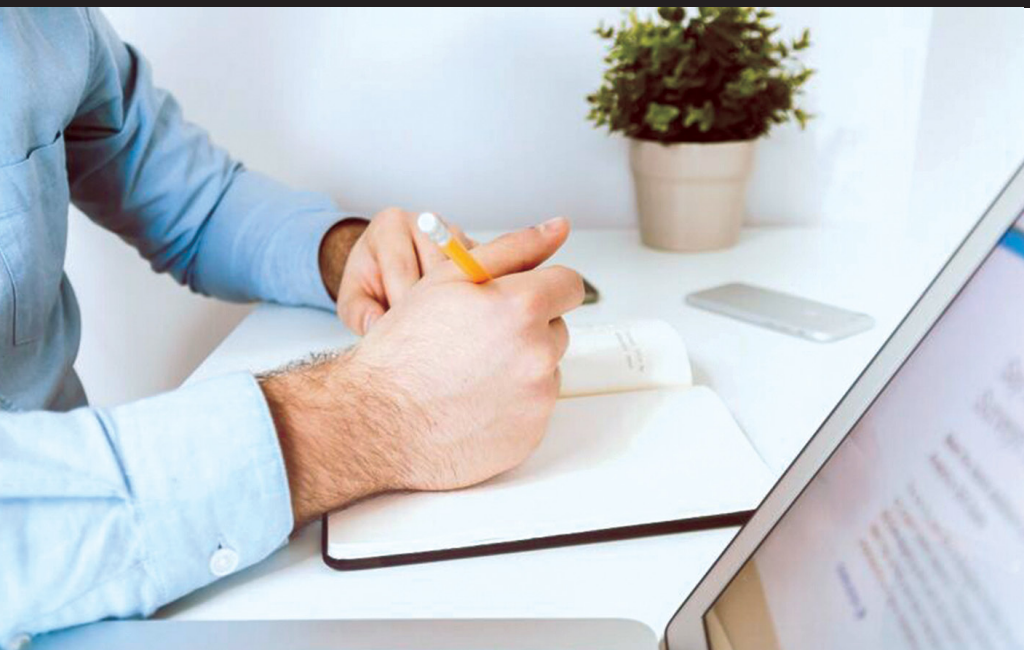
McLaren Center for Research and Innovation at McLaren Macomb has been active in clinical research for over 15 years. Getting their start in cardiology drug and device clinical trials, the site expanded to support the Neuroscience program in 2015, starting with a single device registry. Today, McLaren Macomb has 5 active neuroscience trials, both drug and device, with more in the pipeline. McLaren is a world-wide high enroller in the ASSIST Registry and opened their first acute stroke treatment trial at Macomb in 2021. McLaren Macomb participates in StrokeNet, a National Institute's of Health initiative involving approximately 500 hospitals in the U.S. designed to serve as the infrastructure and pipeline for potential treatments for patients with stroke and those at risk for stroke. "Getting McLaren Macomb involved in StrokeNet trials has increased our visibility with other clinical trial sponsors and absolutely helped grow the research program at McLaren," said Dr. Aniel Majjhoo, Neuro-interventionalist and Principal Investigator, "Clinical trial participation is vital to McLaren Macomb's preparation for their Accreditation as a Comprehensive Stroke Center with the Joint Commission and gives us the ability to offer novel treatment options to our patients."

In 2020 and 2021, McLaren Macomb activated 3 COVID-19 treatment trials and has been a high enroller in the NIH funded ACTIV4C trial with a focus on Post-Hospital Thromboprophylaxis for discharged COVID-19 patients. ACTIV4C Principal Investigator, Dr. Mark Zainea notes, "COVID-19 gave us a unique chance to expand our research program to new providers, new departments and new therapeutic areas. It's been very exciting to be involved in cardiology-related COVID-19 while engaging the whole hospital on these important studies."

The MCRI office at McLaren Macomb is supported by two, full-time Research Coordinators, located on the first floor of the Medical Office Building. Valentyna Onishchuk, PhD is a highly experienced coordinator who came to MCRI from Oncology Research in 2011 and has been a senior member of the MCRI team, helping with new staff training and onboarding across the system, and providing valuable in-depth medical knowledge essential to managing complex clinical trials. Emily Paschall, BS came on board in 2019 as a Research Assistant and within her first year was promoted to Research Coordinator. Her experience as a paramedic and degree in Social Work provided her a solid base to quickly grow and excel in this position.

Augmenting the outstanding MCRI coordinator team at McLaren Macomb, the Cardiology Fellows and Mid-Level providers are highly involved in research at this location, and thanks to the Star of the Month program, are recognized regularly for their contributions to subject enrollment and follow up.

McLaren Macomb currently has 8 enrolling clinical trials and is actively pursuing new trial opportunities in cardiology, neuroscience and infectious disease. McLaren is proud to offer their patients in southeastern Michigan these unique treatment options and opportunities to contribute to medical advancement for the benefit of current and future patients.



ATTENTION NEW OR POTENTIAL MCRI INVESTIGATORS

In order to conduct research as an Investigator at McLaren, there are a few basic requirements you will need to complete to get started:

1. Human Subject Protection Training www.CITIprogram.org
   Affiliate with McLaren Health Care and take the required Biomedical Research Human Subjects Protection Training Course, the required Conflict of Interest Course, and a Good Clinical Practice course. (*note, if you have completed CITI training under another institution, your completed modules may apply but additional modules may be required for completion of this institutional requirement.)
2. Have an updated CV with your McLaren affiliation listed and sign and date the first page.
3. Have a current medical or professional license

Once you have met the three requirements above, please email the documents to MCRI@mclaren.org and indicate “New Investigator” in the subject line.

Please provide any available information about the study that you are interested in conducting and if industry sponsored, please provide a contact person from the sponsoring company. If you are interested in conducting your own study or simply interested in future projects, please explain what research opportunities you are looking for. Include your preferred method of contact and your best email address, so we will be able to reach you easily.

You will be contacted shortly after receipt of your email request to discuss how McLaren Center for Research and Innovation can best support your research interests.

TECHNICAL SUPPORT FOR IRIS USERS

McLaren Research Informatics now has a dedicated email address to technical issues related to iRIS. Research.Informatics@mclaren.org. Please use this email for assistance with technical issues only. Questions regarding the system that are not of a technical matter can continue to be sent to hrpp@mclaren.org.

RESEARCH AROUND McLAREN

RESEARCH FUNDS AWARDED

Tolutope Oyasiji, MD

The McLaren Health Care Corporate Research Funding Committee has made a funding decision for the initial July 1st application deadline. Please help us to congratulate Dr. Tolutope Oyasiji, surgical oncologist, on being the first funding recipient! Dr. Oyasiji will be using the funds to conduct two studies at multiple Karmanos network sites. He intends to study perception of cancer spread with surgical intervention, as well as survival outcomes in early-onset pancreatic cancer.

The committee continues to accept applications in support of investigator-initiated research within the corporation. Awards of up to $5,000 will be awarded to individuals involved in Graduate Medical Education Research (Residents and Fellows). Awards of up to $20,000 will be awarded to non-GME individuals interested in pursuing Investigator-Initiated research. Non-GME awards are open to all McLaren employees or affiliated providers. These funds are to be used for the conduct of the observational or interventional research study and will be awarded on a quarterly basis. Due dates for application submissions are January 1st, April 1st, July 1st, and November 1st of each year. The application is available at **www.McLaren.org/FundingApplication**.

Lauren M. Hamel, PhD

ACCC INNOVATOR AWARD GIVEN TO LAUREN HAMEL FOR THE DISCO (DISCUSSIONS OF COST) APP

Congratulations to Lauren M. Hamel, PhD, Assistant Professor, Department of Oncology, Karmanos Cancer Institute and Wayne State University School of Medicine and her team for being recognized with an Association of Community Cancer Centers (ACCC) Innovator Award. This recognition was given for The DISCO App: A Patient-Focused Tool to Reduce Financial Toxicity.

The ACCC Innovator Award recognizes projects and initiatives that advance the goals of improving access, quality and value in cancer care delivery.

The DISCO (DIScussions of COst) app educates patients with cancer about potential treatment-related costs and generates tailored questions to prompt cost-related conversations with providers. In a pilot study, the app significantly improved patients' self-efficacy for managing treatment costs and interacting with providers while decreasing cost-related distress. Most importantly, 100% of these video-recorded clinic visits included a cost discussion on topics ranging from patient co-pays to transportation.

Dr. Hamel will be recognized at the ACCC 38th National Oncology Conference on Thursday, October 21, 2021 in Austin Texas.

To learn more, and view a video about the project, visit **www.accc-cancer.org**.

McLAREN HEALTH CARE AND KARMANOS CANCER INSTITUTE CEOS LISTED ON dBUSINESS' "DETROIT 500"

Every year, dBusiness Magazine highlights the 500 most influential business leaders in metro Detroit on their list of "Detroit 500." We are pleased to announce that in 2021, Phil Incarnati, President and CEO of McLaren Health Care and Gerold Bepler, MD, PhD, President and CEO of Karmanos Cancer Institute, have been included on the list.

The Detroit 500 list is a highly selective biographical database of business leaders in our region and state. Individuals are selected based on several factors, including the size of a given company or organization, growth rate, geographical reach and extensive personal contacts. A presence on this list serves as a reinforcement of something we see every day: our leaders are outstanding.

View the complete list of leaders at **dbusiness.com**.

PHILIP A. INCARNATI
President and CEO
McLaren Health Care, Grand Blanc

Incarnati began his health care career in 1977, and has held executive positions at the Wayne State University School of Medicine, Detroit Receiving Hospital and University Health Center, and Horizon Health System prior to joining McLaren Health Care. Today, the hospital system includes 15 hospitals, ambulatory surgery centers, imaging centers, a 490-member employed primary and specialty care physician network, and commercial and Medicaid HMOs.

EDUCATION: Eastern Michigan University (B, M)
BOARD MEMBER: Premier Inc., Charlotte, N.C.
MCLAREN SERVICES: Home health, infusion and hospice providers, pharmacy services, a clinical laboratory network, and a wholly owned medical malpractice insurance company.
EMPLOYEES: 26,000
NETWORK PROVIDERS: 85,200
OPERATIONS: More than 350 inpatient and ambulatory facilities
HIGHLIGHT: McLaren operates Michigan's largest network of cancer centers and providers, anchored by the Barbara Ann Karmanos Cancer Institute in Detroit.

DR. GEROLD BEPLER
President and CEO
Karmanos Cancer Institute, Detroit

Bepler is a thoracic oncologist who has spent his career researching risks, progression, treatments, and outcomes related to lung cancer, with a special focus on non-small cell lung cancer. He began his tenure at the Barbara Ann Karmanos Cancer Institute in 2010. Previously, Bepler was director of the comprehensive lung cancer research center, department chair of thoracic oncology, and program leader of the lung cancer program at the Moffitt Cancer Center in Tampa, Fla.

EDUCATION: College of Music and Performing Arts (B), Philipps University (MD, Ph.D.)
FIRST JOB: Choir director and organist in a Lutheran church near Frankfurt, Germany.
INSPIRATIONAL QUOTE: "You can't make a silk purse out of a sow's ear."
TOUGHEST CHALLENGE: Immigrating to the United States.
BEST ADVICE FOR A YOUNG PERSON: Live with passion
HOBBY: Handiwork around the house.
WHO SHOULD PLAY ME IN A BIOGRAPHICAL MOVIE: Robert Redford
PUBLISHED: More than 200 peer-reviewed articles..

RESEARCH AROUND McLAREN

Michael Simon, MD, MPH

KARMANOS RESEARCHERS PUBLISH REVIEW COVERING 30 YEARS OF RESEARCH INTO DISPARITIES IN THE CARE OF BLACK AND WHITE PATIENTS WITH CANCER IN DETROIT

As the only National Cancer Institute-designated comprehensive cancer center in Metro Detroit, Karmanos Cancer Institute is at the forefront of research and innovation. While our laboratory and clinical studies may be the first to come to mind, a great deal of extraordinary population-based research is being conducted here every day. We may visualize the bench when discussing research, but examining patient experience at the bedside is equally important. This is especially true when we consider disparities in care and inequity among those with cancer.

In July 2021, Michael Simon, MD, MPH, co-leader of the Breast Cancer Multidisciplinary Team at Karmanos and a group of researchers from Karmanos Cancer Institute and Wayne State University published "A Review of Research Disparities in the Care of Black and White Patients with Cancer in Detroit" in Frontiers in Oncology. This detailed study compiles the work of Karmanos researchers in the Population Studies and Disparities Research Program. The group, along with collaborators, has spent the past three decades investigating racial disparities in cancer incidence, treatment and outcomes among Black and white patients in Southeast Michigan, with a specific focus on the Detroit area, a city with a majority Black population.

Using an organizational framework of three generations of studies on racial disparities, the review describes racial disparities by primary cancer site, disparities associated with the presence or absence of comorbid medical conditions, disparities in treatment and disparities in physician-patient communication, all of which contribute to poorer outcomes for Black cancer patients. The review also highlights evidence-based strategies that can help mitigate disparities, improve care for vulnerable populations and build an equitable health care system. Lessons learned can also inform a more equitable response to other health conditions and crises. The findings suggest that to reduce or eliminate racial disparities in cancer outcomes, it is also of utmost importance to address larger questions of inequality inherent in the legacy of

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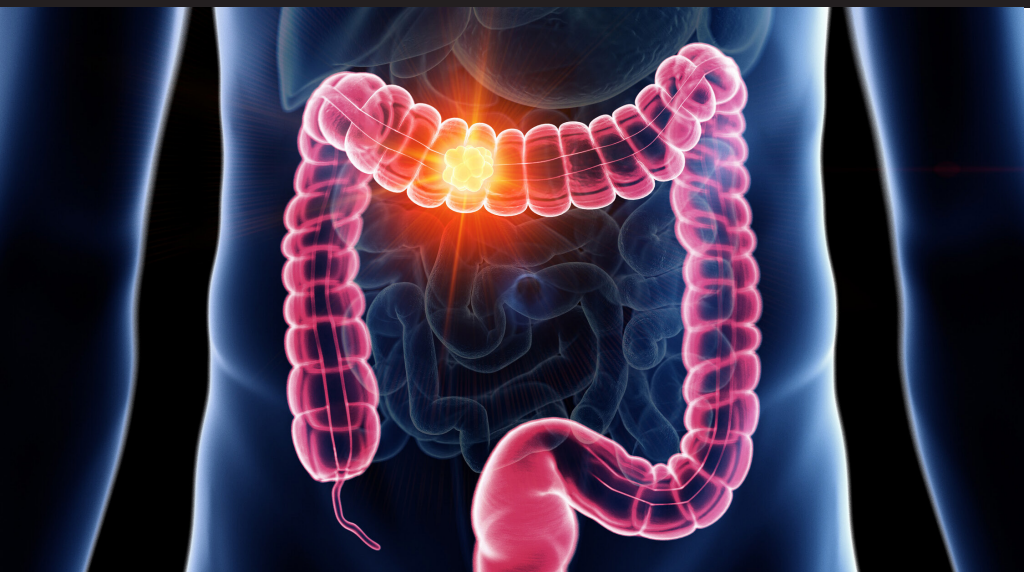

COLON CANCER PATIENTS FIND NEW HOPE WITH IMMUNOTHERAPY, WITH POTENTIAL FUTURE ADVANCES

Colon cancer was the fourth most common cancer in 2020, with almost 150,000 new cases diagnosed and a little more than 53,000 deaths related to this cancer. It was just behind breast, lung and prostate cancers in the number of cancer cases diagnosed in this country, according to Surveillance, Epidemiology and End Results Survey (SEER) data from the federal government.

While these statistics may be considered 'grey clouds,' the silver lining is that colon cancer patients now have new treatment options with immunotherapy, a type of therapy that uses the human immune system to fight tumor cells.

The immunotherapy agent Keytruda, also known by its scientific name Pembrolizumab, was approved by the FDA to treat colon/colorectal cancers on June 29, 2020, making it a first-line treatment for metastatic and resectable colon cancer (i.e., cancer that can be removed surgically).

"Immunotherapy had no part in colon cancer treatment before Keytruda's FDA approval," said Mohammed Najeeb Al Hallak, MD, MS, member of the Gastrointestinal and Neuroendocrine Multidisciplinary Team at Karmanos Cancer Institute and assistant professor at Wayne State University School of Medicine. "This is a revolutionary approval."

Keytruda is approved for subsets of patients with advanced colorectal cancer that has high microsatellite instability (MSI-High), a DNA mismatch repair deficiency, or high tumor mutational burden. In lay terms, MSI-High means that the tumor's DNA cannot repair its own damage, causing the tumor to be surrounded by immune cells.

In clinical studies, the use of Keytruda, as opposed to chemotherapy, increased the median progression-free survival (surviving without cancer progression) of participants to 16.5 months compared to 8.2 months with chemotherapy alone.

Dr. Al Hallak is very excited about these results. "With all the previous treatments used, none improved progression-free survival," he said. "I had not seen a cure for Stage 4 colon cancer before immunotherapy. This is a doubling of the median progression-free survival as a first-line treatment."

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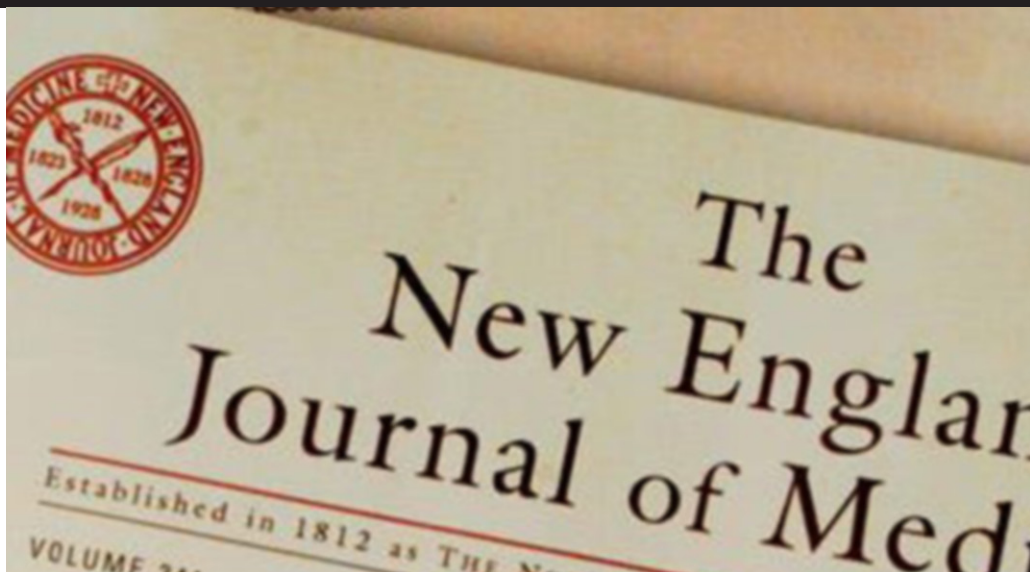
Mohammed Najeeb Al Hallak, MD, MS

RESEARCH AROUND McLAREN



RESEARCHERS FROM KARMANOS CANCER INSTITUTE PUBLISH IN *THE NEW ENGLAND JOURNAL OF MEDICINE*

Jeffrey Zonder, MD

Congratulations to **Jeffrey Zonder, MD**, leader of the Multiple Myeloma and Amyloidosis Multidisciplinary Team at Karmanos Cancer Institute. Dr. Zonder co-authored a paper that was recently published by *The New England Journal of Medicine*. Titled "Daratumumab-Based Treatment for Immunoglobulin Light-Chain Amyloidosis," the paper includes the results of a randomized trial, which led to the first FDA approval of any therapy for AL amyloidosis: Daratumumab-FasPro + CyBorD. Three former Karmanos fellows are also co-authors.

Nitin Vaishampayan, MD

Additional congratulations go to **Nitin Vaishampayan, MD**, radiation oncologist at Karmanos Cancer Institute. Dr. Vaishampayan also co-authored a paper that was recently published by *The New England Journal of Medicine* titled "Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer."

KARMANOS RESEARCHERS PUBLISH REVIEW COVERING 30 YEARS OF RESEARCH

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structural racism in the US, along with disparities across the spectrum of chronic comorbid and medical conditions, which have a disproportionately negative impact on Black people.

The review is organized into three generations of cancer disparities research. First-generation studies are those that both identify and document the existence of health disparities. Second-generation studies are analytic or evaluative and attempt to assess variables that could potentially explain the noted disparities. Third-generation studies have the goal of testing interventions that could serve as solutions to mitigate disparate outcomes. A fourth-generation is also included, the purpose of which is to take action that may help in eliminating disparities.

The comprehensive and complete study is available at www.frontiersin.org. This review captures the valuable work that has been done at Karmanos Cancer Institute to identify and understand disparities in cancer care. The critical task now is to put this information to use so we may create a more equitable system of care for patients.

COLON CANCER PATIENTS FIND NEW HOPE

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Keytruda, which was initially approved by the FDA in 2014, was initially used for advanced melanoma. It then gained approval for non-small cell lung cancer as a follow-up treatment after chemotherapy. Later, it received approval for use in metastatic head and neck squamous cell carcinoma. Since 2016, it has been approved for use in Hodgkin's lymphoma, bladder cancer, cervical cancer, esophageal cancer, gastric and gastroesophageal cancers and advanced renal cell carcinoma.

Finally, Keytruda is having its day as a treatment for some types of colon cancer.

Keytruda, which is administered intravenously, is a type of immunotherapy known as an immune checkpoint inhibitor. Immune checkpoints are a normal part of the human immune system. Their role is to prevent an immune response from being so strong that it destroys healthy cells. The immune checkpoints engage when proteins on the surface of immune cells called T-cells recognize and bind to partner proteins on other cells, such as some tumor cells. These proteins are called immune checkpoint proteins.

"Pembrolizumab (Keytruda) inhibits PD1 and blocks the interaction between PD-1 and PD-L1 checkpoint proteins, which, if left to interact, would create a shield around the tumor cell, making it immune to T-cells," Dr. Al Hallak said. When Keytruda intercepts that interaction, it removes the tumor cell's shield, allowing T-cells to attack and kill the tumor cells.

Dr. Al Hallak is now hoping to move forward to utilize immunotherapy on most colorectal cancer patients for whom immunotherapy alone does not work.

"I hope that Keytruda, in combination with chemotherapy, will be approved for all colon cancer patients," he said. "I think we're going to see clinical study results soon. If those are positive, then this will bring more hope for most colon cancer patients to use Keytruda early in their treatment."

EQuIP CORNER

Andrea Klaver, MBA, CHRC

FDA POLICY FOR DEVICE SOFTWARE FUNCTIONS AND MOBILE MEDICAL APPLICATIONS

By Andrea Klaver, MBA, CHRC

As we are acutely aware, the COVID-19 pandemic has altered our way of life dramatically, both personally and professionally. And the clinical research field is, of course, not immune to these changes. In some cases, the pandemic did not initiate these types of changes as much as it hastened them. That is, things were changing well before the pandemic became standard nightly news fodder. One such area of change related to clinical research is the explosive growth and use of mobile medical applications.

The Proliferation of Mobile Medical Apps

Since the beginning of the COVID-19 pandemic, more users than ever have downloaded and used personal mobile applications, or apps, to connect with their medical providers, manage their prescriptions, or streamline much of the healthcare activity traditionally done in hospitals and clinics. Included as part of a smart phone's digital wallet, a "vaccine passport" may soon be the norm to verify one's vaccination status for things like international travel or attending large events, like concerts. What once was innovative is now ordinary as digital health technology has exploded across the U.S. and the world.

Which types of mobile medical apps do you use? With the record growth of mobile medical apps on the market, one would be hard-pressed to find someone who has not used an app to count their steps, track their sleep, manage their diet, or improve their general health and wellness. Technology growth has enabled apps to be capable of more and more every year.

With these types of apps becoming more and more closely linked to one's personal health and wellbeing, at what point does an app cross the line and become "more than an app?" Can a mobile medical app perform the same way as a traditional medical device? If the app were to malfunction and put the user at risk, who, if anyone, is responsible? Thus, it is critical at this point for app developers and manufacturers to assess if the apps they market are (1) merely an unregulated software function, or (2) a regulated medical device – and mobile medical apps may certainly be classified as such, according to the U.S. Food and Drug Administration (FDA).

Regulators Playing Catch-Up?

As often happens despite best efforts, while technology growth proliferates, laws and regulations struggle to catch up. Rather than creating entirely new regulatory schemes, the FDA has previously tried to fit software functions, including mobile medical apps, into their existing regulatory structures regarding technology and medical devices. Unsurprisingly, this has caused much confusion, given the agency's broad definition of medical devices.

The FDA defines a medical device as an instrument intended for the diagnosis, treatment, or prevention of disease that does not achieve its primary purpose through chemical action. Many, if not all, mobile medical apps could fall into this definition, no matter how harmless!

However, it is not the intention of the FDA to regulate every mobile medical app in existence. After passage of the 21st Century Cures Act, the U.S. exempted many software functions from the "medical device" definition, including those intended to maintain or encourage a healthy lifestyle that are unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition. An app that "treats," "diagnoses," or "cures" a disease or condition will be regulated differently than one that "improves" or "tracks" general health and wellness.

Therefore, many software functions are not medical devices (meaning such software functions do not meet the definition of a device under section 201(h) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)), and the FDA does not regulate them as devices.

To address industry and consumer confusion, the FDA issued guidance in 2019 outlining their approach to regulatory interpretation of "device software functions," including:

- Software as a medical device,
- Software in a medical device, and
- Mobile medical apps.

The Streamlined Regulatory Approach of the FDA

The FDA has categorized software functions into three distinct groups:

1. Not a medical device;
2. A medical device, but not subject to FDA enforcement; and
3. A medical device subject to FDA enforcement.

Further, the FDA only intends to apply regulatory oversight to software functions that are medical devices and whose functionality may pose a risk to a patient's safety if the device were to malfunction. So, as described above in number two, it is possible that an app is a medical device, but the FDA has elected to exercise enforcement discretion in not regulating it as such.

For software functions that are considered medical devices (category three above), the FDA's specific regulatory focus is on software functions that:

- Are an extension of one or more medical devices by connecting to such devices for the purpose of controlling the device or analyzing the device data (mobile apps that control delivery of insulin or software that controls inflation and deflation of a blood pressure cuff through a mobile platform);
- Transform the mobile platform into a regulated medical device by using attachments, display screens, or sensors, or by including functionalities like those regulated medical devices (a software function that uses the built-in accelerometer on a mobile platform to collect motion information for monitoring sleep apnea or a glucose meter attachment on a mobile phone); and

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EQuIP CORNER

UPCOMING RESEARCH EDUCATION

SOCRA

Please visit the SOCRA Events Calendar at https://www.socra.org/conferences-and-education/events-calendar/ for virtual continuing education and training opportunities.

ACRP 2022

Annual Conference
Tentative: Orlando, Florida
April 22 – 25, 2022

Please visit https://acrpnet.org/ for updates

BROWN BAG SERIES

Our next Brown Bag Session is tentatively scheduled for December 2021. Please watch your email for more details as the time approaches. The Research Integrity team hopes you can attend.

For more information, contact Andrea Klaver at (248) 484-4987 or andrea.klaver@mclaren.org.

FDA POLICY FOR DEVICE SOFTWARE FUNCTIONS AND MOBILE MEDICAL APPLICATIONS

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- Become a regulated medical device by performing or providing patient-specific analysis, diagnosis, or treatment recommendations (a device that calculates or creates a dosage plan for radiation therapy; a resource for radiation oncology professionals designed to be useful at the point-of-care and to promote evidence-based practice).

You can find a list of examples of device software functions that the FDA intends to regulate as medical devices at https://www.fda.gov/medical-devices/device-software-functions-including-mobile-medical-applications/examples-device-software-functions-fda-regulates.

Conversely, the FDA does not intend to enforce device requirements on software functions that help manage diseases or conditions without providing specific treatment suggestions, or those that automate routine tasks for providers. In cases like these, the FDA intends to exercise enforcement discretion. For example, mobile apps that perform simple calculations, such as BMI trackers, nutrition coaching, or medication prompts would not be subject to regulation.

You can find a similar list of examples of device software functions on which the FDA intends to exercise enforcement discretion at https://www.fda.gov/medical-devices/device-software-functions-including-mobile-medical-applications/examples-software-functions-which-fda-will-exercise-enforcement-discretion.

If the FDA does choose to regulate a company's app as a medical device, the company will need to obtain the appropriate agency approval, licensure, or clearance prior to marketing the device. They may also need to satisfy specific registration and marketing requirements, and any other regulatory requirements applicable to a device's manufacturer or distributor.

Not all app manufacturers have to submit a premarket submission (i.e., a 510(k) or PMA) prior to marketing their device software function. This determination depends on the classification of the device. However, failure to follow these steps could pose a significant risk to consumers and result in enforcement activity by the FDA.

Conclusion and Key Takeaways

As companies and products evolve, the regulatory landscape will too. No matter what the future holds, mobile medical apps are here to stay. The FDA's interest in the regulation of mobile medical apps has increased significantly. For companies with devices that fall into a regulatory gray area of enforcement, it is crucial that they:

- Are an extension of one or more medical devices by connecting to such devices for the purpose of controlling the device or analyzing the device

For the entire policy, see FDA Policy for Device Software Functions and Mobile Medical Applications (September 27, 2019), available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-device-software-functions-and-mobile-medical-applications.

FACULTY, FELLOWS & RESIDENTS
SCHOLARLY ACTIVITY NEWS

RESEARCH, QUALITY IMPROVEMENT, AND HUMAN SUBJECTS RESEARCH DETERMINATION

By Carlos F. Rios-Bedoya, ScD

The Division of Scholarly Inquiry receives quite a few emails requesting clarification or explanation about the difference between research and quality improvement (QI) scholarly activity projects and its impact on the human subjects research determination. This is understandable given that most clinical research involves human subjects with some exceptions. Similarly, QI is considered most of the time a non-human subjects research scholarly activity but also with some exceptions. Therefore, it is possible to have clinical research determined non-human subjects research as well as QI classified as human subjects research. I intend to, hopefully, provide a simple explanation on the federal criteria use to make a human subjects research determination regardless of the type of scholarly activity (i.e., clinical research or QI).

I like to start by providing some definitions used by the federal regulations (45 CFR 46), also known as the Common Rule, in making the human subjects research determination. The first term I would like to provide the definition provided by the federal regulations is research. "Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge". The second term is human subject. According to the federal regulations, "human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains:

1. Data(i) Obtains information or biospecimens through intervention or interaction with the individual, or
2. Identifiable and, uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens."

These definitions are the framework used to determine whether research or QI projects are determined as human subjects research. Let us take a look at how these definitions are implemented when making a human subjects research determination. The Office of Human Research Protections provides a decisions chart to assist in making this determination (https://www.hhs.gov/ohrp/regulations-and-policy/decision-charts-2018/index.html). This decision chart begins by answering the question on whether the activity meets the definition of research. If the answer is No then the activity is determined as non-human subjects research. If the answer is Yes then the next step in the decision chart is to determine if the proposed project fits the criteria for excluded research. If it fits any of the exclusions, then the project is also not considered research. However, if the criteria are not met then the next step is to check if the proposed project involves human subjects. If the research involves human subjects, then is determined as human subjects research.

Based on these regulations, there are some research projects that do not meet the criteria for human subjects research. Examples of these projects include (1) Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction; (2) Secondary research for which consent is not required; (3) Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording).

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ANNOUNCEMENTS AND WHAT'S NEW

Lisa Winters

The McLaren Center for Research and Innovation is pleased to introduce our newest staff member, **Lisa Winters**. She is a Clinical Research Nurse at our McLaren Bay Region location. Prior to her nursing career, Lisa worked as a phlebotomist and a histology technician in a leadership role. She joins us from Ascension Tawas and brings a love of patient-focused care with her to McLaren. Lisa will be working with Cardiology, Vascular Surgery and COVID-19 clinical trials. We look forward to working with her and watching her grow in her new role. She has already shown great energy and teamwork. Welcome, Lisa!

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These are some of the categories that are exempt and each category includes some additional criteria to be met that I am not including because of space limitations. In contrast there are some QI projects that do meet the criteria for human subjects research. Examples of these QI project might include (1) the activity seeks to develop new knowledge or validate new treatments rather than to assess the implementation of existing knowledge; (2) the QI methodology employs a standard research design, such as randomization; (3) the protocol is fixed with a rigid goal, methodology, population, time period, etc.; (4) the funding for the QI project comes from outside organizations such as the NIH or those with a commercial interest in the results; (4) when the risks from the QI intervention to participants are greater than minimal. Below I am attaching a table and a figure that compare QI and human subjects research that provide additional information on when a QI project is not human subjects research.

Veronica Gorden

Karmanos Cancer Institute (KCI) Clinical Trials Office (CTO) is pleased to announce **Veronica Gorden**'s promotion to Manager, CTO Regulatory. Veronica has served in the role of Interim Manager since May and will now retain this role on a permanent basis alongside Kasha Donahue. Together they will oversee the KCI CTO regulatory staff. Veronica approaches problems with calmness, creativity and an open mind. She is always looking for ways to improve efficiency and reduce redundant work. She has been a supervisor of CTO Regulatory at Karmanos for the last three years. During that time, she provided excellent support to her staff and was a valued member of the leadership team. Prior to serving in this role, she accumulated 13 years of clinical research experience in the areas of internal medicine, neurology, psychiatry and pediatrics. Research has been her passion since 2001. Congratulations Veronica!

I like to finish by clarifying that the information presented is a simplified description of the federal regulations guiding the human subjects research determination and does not represent the process or methods McLaren's IRB follows to implement those federal regulations regarding the human subjects research determination. In the Division of Scholarly Inquiry, we have a commitment and responsibility to expedite and facilitate scholarly activity productivity for McLaren residents, fellows, and faculty.

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