RESEARCH Matters

Fall 2023

IN THIS ISSUE...

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

McLaren

RESEARCH AROUND McLAREN

THE SYSTEM LEVEL ADVANTAGE

McLAREN CENTER FOR RESEARCH AND INNOVATION

At McLaren Center for Research and Innovation, we strive to do what's best for our research participants, investigators and the research sponsors we collaborate with. One of the ways we do this is by conducting some studies with system level oversight. Having a system level principal investigator allows multiple research sites from across the McLaren system to participate in a study and streamlines the oversight under a single PI who takes responsibility for running the trial. Each participating site may have multiple active investigators and a lead investigator responsible for study activities at their location. System level oversight provides an opportunity for our experienced investigators to act as mentors to those eager to get involved in research and learn how to conduct clinical trials. This is a great way for new investigators to get involved in trials they may not otherwise have access to, and to introduce them to the responsibilities of research gradually. This also allows investigators who may not have time to dedicate to being a PI to take on more limited responsibility that aligns better with their schedule and still be involved in research activity.

System level oversight provides an opportunity for our experienced investigators to act as mentors to those eager to get involved in research and learn how to conduct clinical trials.

System level oversight appeals to many sponsors because it allows us to function as a single site with multiple locations, where in the past, multiple participating locations would be treated as completely independent sites. Functioning as a single site, we can execute a single contract covering activity at all our McLaren locations and negotiate the study budget to apply to the system, rather than individual sites. Administrative burden can be further reduced by having a single IRB application and consent form encompassing all the locations at once.

The FDA typically limits the number of sites an industry sponsor can utilize for a clinical trial, which puts a significant amount of pressure on the sponsor to select the sites most likely to produce strong enrollment and high-quality data. When we are able to utilize a system level approach, the combined enrollment effort from multiple locations provides the sponsor with those high enrollment numbers they need. A site with multiple enrolling locations offers not just more patients, but more demographic diversity. The ability to meet or exceed enrollment goals and simultaneously increase ethnic and racial diversity provides exceptional reporting metrics for the sponsor as well as MCRI.

System level oversight involves regular study team meetings with the PI, site investigators and study coordinators, giving the PI an opportunity to hear about the conduct of the trial at each location, and provide insight and guidance on specific issues that arise. The system level PI is kept up to speed on screening

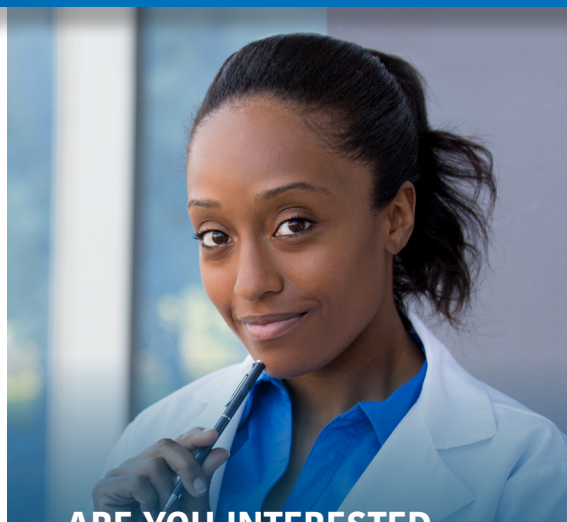
and enrollment efforts and obstacles, questions or issues with the study drug or device, regulatory submissions, patient specific adverse events and any protocol deviations that may have occurred. During these regular meetings, the team presents these issues to the overseeing system level PI for discussion. These meetings are an important way for us to document the system level oversight of a single PI over multiple McLaren locations.

Investigator responsibilities in conducting clinical trials or drugs or biologics and medical devices are outlined in the FDA's Code of Federal Regulations (21 CFR Part 312 and 21 CFR Part 812, respectively). Investigators who commit to serving as a system level principal investigator agree to personally conduct or supervise all research activity, and protect the rights, safety and welfare of each participant, at each participating location. While it is common practice to delegate some of their responsibilities to sub-investigators and research staff, it is ultimately the principal investigator who is accountable. This is a job that requires extra time, effort and responsibility, but the result provides the patients, sponsors and investigators with the clinical excellence in research that McLaren Center for Research and Innovation strives to be known for.

If you have an interest in learning more about being a system level PI or investigator on a clinical trial, please contact the administrative offices of MCRI at **MCRI@mclaren.org** or **(248) 484-4950**.

DO YOU HAVE A RESEARCH PROJECT THAT NEEDS FUNDING?

McLaren Health Care has formed a corporate level Research Funding Committee. This committee has been created to establish a system-wide strategic plan and process for awarding research funding to investigators. One goal of this committee is to support and strengthen 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 October 1st of each year. The application process can be accessed at: **www.mclaren.org/fundingapplication**. Required information for the application includes a detailed description of the research project, as well as a proposed budget.



ARE YOU INTERESTED IN BECOMING A RESEARCH PARTICIPANT?

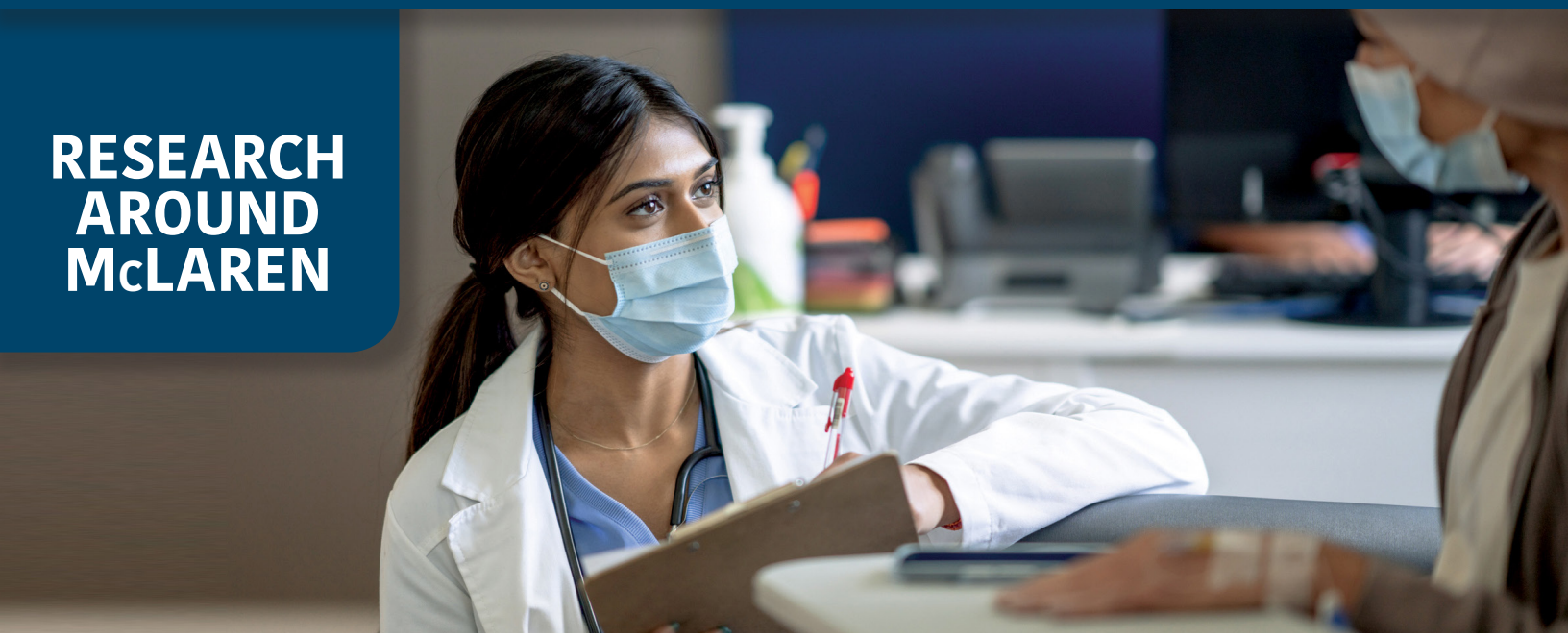
For information on enrolling in a clinical trial please visit our website at www.mclaren.org/main/clinical-research-trials. Here you will find a list of open enrolling studies at McLaren, including which hospital the research is being done at and contact information for each study.

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



INVESTIGATOR INITIATED TRIALS

Also referred to as an Investigator Initiated Study (IIS), Investigator Initiated Trials (IITs) are clinical research trials in which the Principal Investigator conceives of the research question, develops the study protocol and serves as the "sponsor-investigator". The FDA defines a "sponsor-investigator" as an investigator who both initiates and conducts an investigation, and under whose immediate direction the investigational drug or device is administered or dispensed. In such trials, the sponsor-investigator assumes the responsibilities of, and must comply with, FDA regulations applicable to both a sponsor and an investigator. The sponsor-investigator takes on the responsibility of initiating the clinical trial and acting as the coordinating center, and often times takes on a dual role of an investigator conducting the trial as well.

In many aspects, IITs are the same as an industry sponsored trial and need to follow the same pathways for study feasibility, start-up and regulatory approvals as a sponsored clinical trial. As a sponsor, an IIT investigator's responsibilities include:

- Selection and training of qualified investigators
- Obtaining executed FDA Form 1572 and financial disclosures from each PI
- Assuring the protection and safety of human subjects at all study locations
- Providing the investigators and their study staff with information to conduct the study properly
- Monitoring the progress of the investigation
- Controlling and documenting disposition of the investigational agent

An investigator invited to participate in an IIT, or planning on conducting their own IIT, has the same responsibilities as they would conducting a sponsored clinical trial. Those responsibilities include:

- Ensuring the investigation is conducted according to the investigational plan (protocol)
- Maintaining case histories on each patient
- Providing reports to various vested entities including regulatory entities like the FDA or IRB and the sponsor or funding agency
- Submitting progress reports, safety reports, final reports, and other regulatory documents like financial disclosures and FDA Form 1572
- Protecting the rights and safety of subjects under the investigator's care
- Obtaining and properly documenting informed

If you want to increase your knowledge base and take your research education to the next level, consider becoming a member of one of the accredited Clinical Research Associations, SOCRA (Society of Clinical Research Associates) or ACRP (Association of Clinical Research Professionals).

consent from each patient
- Assuring review by a responsible IRB and complying with its requirements
- Permit FDA inspections of the study records and site

A common question amongst investigators interested in conducting their own IIT is what regulations apply and which rules need to be followed? This is dictated by the funding agency as well as the products employed in the trial. For FDA-regulated products, drugs (FDA 21 CFR 312) or devices (FDA 21 CFR 812) the Code of Federal Regulations (CFR) apply and dictate the conduct of the study. If another federal agency funds the research, Health and Human Services rules may apply (FDA 45 CFR 46). If a study is federally funded by an agency other than HHS, but involves an FDA-regulated product, both sets of rules may apply. There are many FDA guidance documents and HHS guidance documents available online for review prior to initiating an IIT, so an investigator can be aware of what rules might apply give the particular drug or device they wish to study.

Some protocols may require the sponsor-investigator to submit an Investigational New Drug (IND) or Investigational Device Exemption (IDE) application to the FDA. Criteria for this requirement are outlined in the FDA regulations at 21 CFR 312.2(b) or 21 CFR 812. If a sponsor-investigator is unsure what applies to their particular protocol, they should seek counsel from the FDA to be sure they are following all applicable rules and regulations, as well as submitting the proper applications, if required.

All investigators taking part in a sponsored clinical trial or considering an IIT should ensure their knowledge of ethical and scientific standards as well as human subject protection is up to date and documented. Getting started with the basic training requirements is an essential first step. Biomedical Research Training, Conflict of Interest training and Good Clinical Practice training are all made available to McLaren investigators and research staff at www.citiprogram.org . You will need to affiliate with McLaren Health Care to access the required courses. To participate in clinical trials or initiate an IIT, these training courses are an institutional requirement.

If you want to increase your knowledge base and take your research education to the next level, consider becoming a member of one of the accredited Clinical Research Associations, SOCRA (Society of Clinical Research Associates) or ACRP (Association of Clinical Research Professionals). Both associations have a wealth of educational opportunities, articles, webinars and courses available to members and non-members. For those who want to certify their knowledge, ACRP offers a Certified Principal Investigator exam to earn the “CPI” credentials. Experienced investigators may also wish to consider attending or speaking at one of the national conferences held yearly by ACRP or SOCRA.

As an investigator at McLaren, if you wish to discuss your ideas for an IIT or becoming an investigator on a clinical trial, your first step is to contact the administrative offices of the McLaren Center for Research and Innovation.

CONTINUED ON PAGE 7

INVESTIGATOR RESOURCES

McLaren Research Administration and Research Integrity
www.mclaren.org/main/research

CITI Training, Biomedical, GCP
www.citiprogram.org

SOCRA
www.socra.org

ACRP
www.acrp.org

Health and Human Services
www.hhs.gov/programs/research

FDA Guidance for Industry: Investigator Responsibilities
www.fda.gov/media/77765/download

FDA Guidance for Sponsor-Investigators
www.fda.gov/media/92604/download

GCP Regulations
www.fda.gov/science-research/clinical-trials-and-human-subject-protection/regulations-good-clinical-practice-and-clinical-trials

Code of Federal Regulations
www.ecfr.gov/current/title-21

- **21 CFR 312 – Investigational New Drug Application**
- **21 CFR 812 – Investigational Device Exemptions**
- **45 CFR 46 – Protection of Human Subjects**

Clinical Trials.gov
www.clinicaltrials.gov

RESEARCH AROUND McLAREN

THE ADVANTAGES OF KARMANOS AND THE GROUNDBREAKING DISCOVERIES TO COME

By Boris C. Pasche, MD, PhD, FACP, President & CEO, Barbara Ann Karmanos Cancer Institute

It's a pleasure to join such an esteemed healthcare system and institution. Joining McLaren Health Care to be the Barbara Ann Karmanos Cancer Institute's president and CEO and the principal investigator of the National Cancer Institute's Comprehensive Cancer Center Core Grant is an honor. Thank you for such a warm welcome. In the very little time I've been here, I've seen such commitment from staff, physicians, researchers, and scientists to provide transformative cancer care at the bedside and through research and education. I look forward to the breakthrough discoveries we will accomplish together in cancer treatment.

Boris C. Pasche, MD, PhD, FACP

What attracted me to Karmanos is the organization's National Cancer Institute comprehensive cancer center designation, its dedication to serving multiple Michigan communities, and its offering of over 250 promising new treatments to patients. The fact that Karmanos is the largest cancer care network in Michigan and serves cancer patients in over 96 counties in the state and Northwest Ohio through 16 locations was another reason why I wanted to be part of this organization. I am excited to continue this movement of bringing high-quality care and clinical trial opportunities to communities so that many can benefit from novel treatments.

As a physician-scientist and experienced hematologist and medical oncologist, I have not only spent decades

treating my patients facing gastrointestinal malignancies and hereditary cancers with promising drugs, but I have been at the forefront of research and discovering new drug therapies and plans that have improved my patients' lives. Finding ways to beat cancer is not only a professional goal of mine, but this disease has impacted me and my family personally, as well, so this work is significant to me.

My research focuses on cancer susceptibility and new therapies. I developed a medical device for treating hepatocellular carcinoma, which received regulatory approval in Europe in 2018, FDA breakthrough designation in 2019, and FDA Humanitarian Use Designation in 2022. I look forward to sharing more news about the research and development I am doing, the groundbreaking research that our scientists are conducting here in Detroit, and their collaborative work with many physicians and researchers across the network.

Before my arrival, Team Karmanos had accomplished many groundbreaking discoveries in cancer and has been on track to finding improved treatments that offer patients a better quality of life. I look forward to continuing down this road with this incredible organization.

INVESTIGATOR INITIATED TRIALS

CONTINUED FROM PAGE 7

The MCRI administrative team can meet with you to discuss the resources available to you for protocol writing assistance or statistical analysis, how to create a budget and apply for funding for your project, data collection tools, coordinator and regulatory support options, and work with you to create a project plan and timeline for initiation of your trial. MCRI can also be your resource for listing your trial on www.ClinicalTrials.gov , a federal requirement for qualifying clinical trials.

Investigator initiated trials are important to medical science because they drive translational research, taking data and applying it to day to day, real world practices. IITs demonstrate the commitment of a health care institution to growth and learning, as well as the dedication of a physician to their patients by initiating change in standard practices and innovation in treatment options. They are an important piece of any institution's research portfolio and McLaren strives to support their investigators in such endeavors. Developing and conducting an IIT as a sponsor-investigator is a significant investment of your time and a great deal of effort, but well worth the outcome for you and your patients.

For more information or to start a discussion about your research interests, please contact the administrative offices of MCRI at **MCRI@mclaren.org** or **(248) 484-4960**.

RESEARCH AROUND McLAREN

REVOLUTIONIZING HOW IBD IS DIAGNOSED

KARMANOS RESEARCHERS CONTRIBUTE TO NEW USE OF PET IMAGING

Investigators want to look further into whether this technique can help detect certain gastrointestinal cancers. Researchers have discovered they can image inflammatory bowel disease (IBD) using positron emission tomography (PET) imaging. Their findings, titled "Detection of IL12/23p40 via PET visualizes inflammatory bowels disease," were published in the Journal of Nuclear Medicine in July 2023.

Nerissa Viola, PhD

IBD includes Crohn's disease and ulcerative colitis. Both conditions increase a patient's risk of developing colorectal cancer. The current standard of detecting IBD is endoscopy, however, molecular changes occur that are not captured when conducting this procedure. So, investigators at the Barbara Ann Karmanos Cancer Institute, Wayne State University (WSU), and Corewell Health Beaumont Hospital, Royal Oak, set out to develop a new diagnostic agent using positron emission tomography imaging to track inflammation within the gastrointestinal tract.

"Endoscopy with biopsy is limited only to segments of the bowel. It cannot probe through the whole gastrointestinal tract, which is a main limitation of this procedure," explained Nerissa Viola, PhD, leader of the Molecular Imaging Research Program at Karmanos and associate professor at WSU School of Medicine. "By administering a PET agent like this, inflammation is visualized throughout the whole alimentary tract, essentially generating an abdominal map. Moreover, PET imaging eliminates the need for extensive bowel cleansing preparations that most patients, especially children, do not tolerate well."

When PET scans are performed, a small amount of radioactive material is injected into the body's bloodstream and circulates until it finds its target that is housed within the disease site. According to Dr. Viola, this new way of detecting IBD can potentially revolutionize how we diagnose these diseases. The abdominal map she refers to can show where the inflammation is in the gastrointestinal tract without having a patient prepare for an invasive diagnostic procedure.

The team is now looking into the possibility of using this diagnostic agent to further track chronic inflammation and monitor the development of IBD into colorectal cancer.

"We still are a long way from using PET as a tool for diagnosis in the case of IBD, but these studies bring us one step closer toward translation and lay down the roadmap toward potentially transforming the standard of care," Dr. Viola concluded.

CONTINUED ON PAGE 11

STUDY FINDS MUSIC REDUCES STRESS, IMPROVES MOOD DURING CHEMOTHERAPY

A study conducted by the Barbara Ann Karmanos Cancer Institute and Wayne State University (WSU) researchers and physicians has found that patients who listened to music while undergoing chemotherapy experienced significant benefit to their mood and level of distress during treatment.

The study, "Using Music as a Tool for Distress Reduction During Cancer Chemotherapy Treatment," is published in the journal JCO Oncology Practice.

"Music medicine is a low-touch, low-risk and cost-effective way to manage patients' psychological wellbeing in the often-stressful context of a cancer infusion clinic," said Felicity Harper, PhD, clinical psychologist, member of the Supportive Oncology Multidisciplinary Team (MDT), associate center director of Population Sciences, member of the Population Studies and Disparities Research (PSDR) Program at Karmanos, associate professor of Oncology at WSU School of Medicine, and lead author of the study. "There were significant differences in change in positive and negative mood and distress (although not pain) from pre- to post-intervention between the music and control groups. Participants who were married or widowed and those receiving disability income reported greater benefit outcomes after listening to music."

Felicity Harper, PhD

Future research should be directed to understanding other factors that may mitigate negative mood states and pain for certain groups during treatment, Dr. Harper said.

The study involved 750 adult patients receiving outpatient chemotherapy infusion. Patients were randomly assigned to listen to no music, or, up to 60 minutes of music during treatment. Patients listening to music were allowed to self-select an iPod programmed with up to 500 minutes of music from a single genre (Motown, '60s, '70s, '80s, classical and country). Outcomes were self-reported changes in pain, positive and negative mood, and distress.

After the listening period, music participants completed a post-survey assessing pain, positive and negative mood, and distress levels. They also recorded the amount of time spent listening to music.

The average study participant was 60.39 years old and female (65%). Twenty-eight percent of the sample identified as African American; the remainder were White (68%) or other ethnicities (1% Asian, 1% American Indian or Native Alaskan, and 2% multiracial). The majority were married or in a committed relationship (56%). Forty-one percent had a

CONTINUED ON PAGE 11

RESEARCH AROUND McLAREN

GRANT SUPPORTS CONTINUING STUDY AT KARMANOS

OBESITY AND ENDOMETRIAL CANCER

Michael Wilson, PhD

Research at the Barbara Ann Karmanos Cancer Institute into how obesity affects endometrial cancer is underway with new funding. The DMC Foundation has awarded Michael Wilson, PhD, a $75,000 grant for the study "Obesity impacts the endometrial cancer tumor microenvironment." His team's research focuses on immune cell populations associated with endometrial tumors and how obesity impacts both the abundance and the characteristics of these cell types.

"Obesity is a risk factor for many types of cancer, but endometrial cancer is unique in that the majority of patients are obese, so we want to understand the reasons for this," said Dr. Wilson, a member of the Molecular Therapeutics (MT) Research Program at Karmanos and an assistant professor in the Department of Oncology at Wayne State University (WSU) School of Medicine.

Dr. Wilson's team's research focuses on immune cell populations associated with endometrial tumors and how obesity impacts both the abundance and the characteristics of these cell types.

"This grant allows our research team to test endometrial cancer tumors further to identify unique factors within the tumors of endometrial cancer patients with obesity. Our long-term goal is to identify preventative treatments for obesity-driven endometrial cancer and reduce the incidence of this disease."

The project is a collaboration between Dr. Wilson's Lab, Katherine Gurdziel, PhD, director of the WSU Genome Sciences Core, and Julie Boerner, PhD, director of the Biobanking and Correlative Sciences Core and member of the MT Research Program at Karmanos. Sanjeev Ganesh, a WSU Cancer Biology Program master's candidate, and Jessica Long, a second-year MD and PhD student in WSU's Biomedical Graduate Program, will also assist with the project.

The study began on July 1, 2023, and is expected to run for a year, ending on June 30, 2024.

The DMC Foundation is a supporting organization of the Community Foundation for Southeast Michigan. The foundation awards health-related research, education, and community benefit activities that promote the well-being of metro Detroiters.

KARMANOS RESEARCHERS CONTRIBUTE TO NEW USE OF PET IMAGING

CONTINUED FROM PAGE 8

Co-authors of this study include Najeeb Al-Hallak, MD, MS, medical oncologist, member of the Gastrointestinal and Neuroendocrine Oncology Multidisciplinary Team (MDT) and the Molecular Therapeutics Research Program at Karmanos; Bashar Mohamad, MD, gastroenterologist and member of the Gastrointestinal and Neuroendocrine Oncology MDT; Kang Chen, PhD, member of the Tumor Biology and Microenvironment Research Program; Farzaneh Rezazadeh, PhD, former Karmanos research fellow; and Nicholas Ramos and Allen-Dexter Saliganan, both research assistants. Wendy Wiesend, MD, Beaumont Royal Oak, also contributed to the study.

STUDY FINDS MUSIC REDUCES STRESS, IMPROVES MOOD DURING CHEMOTHERAPY

CONTINUED FROM PAGE 9

high school education or less with 24% having attended some college. Many participants had advanced (stage III or IV) cancer (58%).

The most frequently selected music genre was Motown (28%) followed by hits from the ’80s (20%). The majority of intervention participants (90%) indicated they were very satisfied or quite satisfied with their music selection and listened to music for an average of 56.68 minutes out of the possible 60-minute listening period.

Study patients who listened to music reported more positive and less negative moods, less distress, and lower pain post-procedure than the control participants. There was no significant difference in change for pain between the two groups.

Other members of the research team included Allison Heath, BS, of the WSU Department of Oncology; Tanina Foster Moore, PhD, of the WSU Department of Oncology and the Karmanos PSDR Program; Seongho Kim, PhD, professor of Oncology for the School of Medicine and member of the Molecular Therapeutics Research Program at Karmanos, and Elisabeth Heath, MD, FACP, medical oncologist, leader of the Genitourinary Oncology Multidisciplinary Team at Karmanos and professor of Oncology for the School of Medicine.

The study was supported by funding from the Barbara Ann Karmanos Cancer Institute.

Originally published at Today@Wayne, an online publication of Wayne State University.

RESEARCH AROUND McLAREN

INTERNATIONAL SMOKING ABSTINENCE STUDY

PROVING THE BEST TIME TO QUIT SMOKING IS NOW, IMPROVING LUNG CANCER SURVIVAL OUTCOMES

The Barbara Ann Karmanos Cancer Institute and Wayne State University (WSU) School of Medicine researchers were part of an international study that looked into the survival rate of patients who quit smoking prior to being diagnosed with non-small-cell lung cancer (NSCLC). "Association between duration of smoking abstinence before non-small-cell lung cancer diagnosis and survival: A retrospective, pooled analysis of cohort studies" was published in Lancet Public Health in September 2023. In the study, survival rates of patients who quit smoking at least one year before being diagnosed were significantly better than those who were considered current smokers (who had smoked within one year of their diagnosis).

Ann Schwartz, PhD

The data used in this study was compiled from 26 studies that are part of the Clinical Outcomes Studies of the International Lung Cancer Consortium (COS-ILCCO). These studies took place at 23 hospitals around the world, with 16 of those hospitals in North America.

"The COS-ILCCO represents a large number of partners in North America, Europe, Asia and South America who have contributed data from their lung cancer studies to generate robust evaluations of predictors of survival after a lung cancer diagnosis. We contributed data from three population-based studies of lung cancer in metro Detroit where I served as principal investigator," explained Ann Schwartz, PhD, MPH, deputy center director and executive vice president for Research and Academic Affairs at Karmanos.

"The study results demonstrate that any duration of smoking cessation affects health outcomes, including survival after a lung cancer diagnosis, suggesting that smoking cessation strategies should be applied across the lifespan," concluded Dr. Schwartz, who is also a professor and associate chair of Oncology at WSU School of Medicine and a member of the Population Studies and Disparities Research Program at Karmanos.

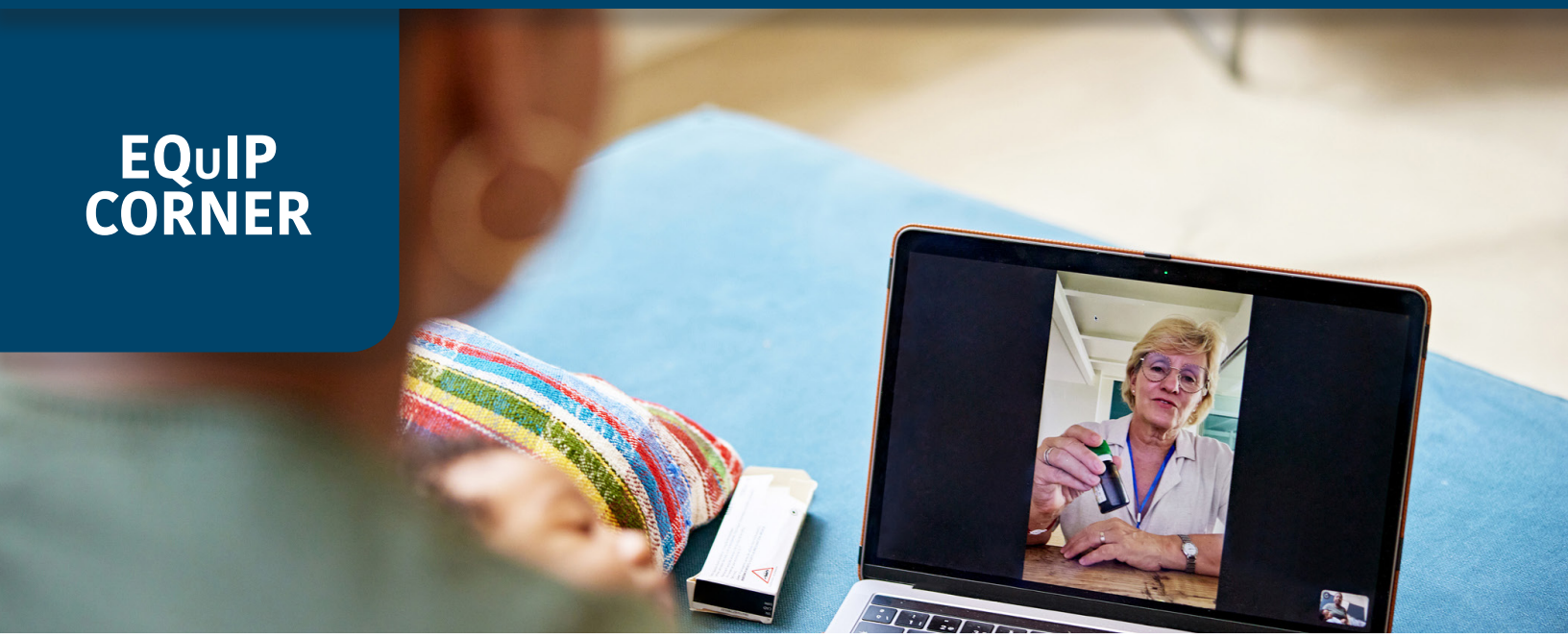
COE LEADERS EXPRESS CONCERNS FOR PROPOSED LEGISLATIVE CHANGES THAT COULD IMPACT THEIR WORK IN CANCER HEALTH EQUITY

Hayley S. Thompson, PhD, associate center director of Community Outreach and Engagement (COE), faculty supervisor of the Office of Cancer Health Equity and Community Engagement at Karmanos, and professor in the Department of Oncology at Wayne State University School of Medicine, is one of seven members of the Alliance of Black COE Scientific Directors who penned a guest editorial titled, "Threats to the NCI COE agenda impede our ability to meet the needs of our cancer center catchment area communities." The leaders explain their concerns about recent legislative actions they feel threaten the COE mission of the nation's cancer centers, which include achieving equity in cancer prevention, control and care, and reducing disparities, including those related to race, ethnicity, gender identity and sexual orientation.

Hayley S. Thompson, PhD

Each of the COE leaders represents seven of the National Cancer Institute (NCI)-Designated Comprehensive Cancer Centers across the country. As COE leaders, their teams concentrate on advancing impactful community outreach and engagement in cancer research across their cancer center's catchment areas, a required component of the NCI Cancer Center Support Grant. The COE leaders express that the proposed legislation stops progress in eliminating disparities in cancer outcomes. Their editorial was published in the July 7 issue of *The Cancer Letter* (Vol. 49, No. 27).

EQuIP CORNER



CHALLENGES AND ETHICAL CONSIDERATION WITH THE USE OF DEVICES AND TECHNOLOGIES IN DECENTRALIZED CLINICAL TRIALS

Introduction

During the COVID-19 pandemic, changes in public health measures impacted clinical research structure. New and ongoing clinical trials were adapted by decentralizing essential elements, such as enrollment, administration of study interventions, data collection and safety monitoring. This involved a wide range of digital and remote approaches, including remote consenting, remote monitoring, study drug dispensing and management, as well as home visits to ensure subject safety and study continuation throughout the trial. This later became known as decentralized clinical trials (DCT).

DCTs are conducted either in whole or in part remotely, through telemedicine, mobile technologies, local sites, and mobile healthcare providers. Study activities like enrollment, participants' completion of required tasks and scheduled activities, notification schedules and responses to those notifications, sensor data, e-Patient Reported Outcomes, safety signals, endpoints, outcome measures and overall compliance can be monitored in real time with the use of devices and technologies. E-consent, the use of digital reporting platforms, digitally acquired endpoints, and wearable technologies are already proven to be effective elements of traditional clinical trials.

A decentralized trial approach can promote greater inclusivity, diversity, ease recruitment, decrease delays, enhance participant retention, and be less costly. However, the use of the devices and new technologies can create distinct ethical challenges.

Challenges in remote data collection and monitoring

Implementing innovative technologies comes with challenges. This is especially true when it comes to complex technology which involves computers and artificial intelligence when it is still being developed and optimized. This article discusses some of those challenges and key points that need to be considered while reviewing clinical trials with remote data collection and monitoring.

Inequality

- Internet access, connectivity, and comfort with the use of digital technologies varies among different demographics and geographic populations. This may disproportionately affect people of color, people with disabilities, older adults, low-income households, and people who live in rural areas.
- Software may not be available in multiple languages, limiting participation for individuals whose preferred language is other than English.

Safety

- Remote study visits and data collection offers fewer opportunities for direct interaction between

participants and study personnel than in conventional trials which may affect the robustness of safety monitoring.

Privacy and Confidentiality

- With the Health Insurance Portability and Accountability Act (HIPAA), patients have the right to privacy and control over their personal health information (PHI), including how their PHI is disclosed and used. Researchers and healthcare organizations must comply with HIPAA regulations and as well as other applicable privacy laws to ensure patients' PHI is protected.
- Managing data collected from mobile technologies necessitates IT specialists and other technology vendors outside of the research team, which invites unintentional disclosure of PHI to third parties.
- Some individuals may not have isolated areas in their homes to host a telemedicine visit or may be unable to disable digital monitoring systems such as Alexa.

Security

- Maintaining security of collected data, transfer, storage, and retrieval is still a challenge.
- Trials using wearables, apps, and web-based interactions might increase system vulnerabilities and cybersecurity risks.

Scientific Validity

- Drug development and device engineering are historically separate scientific fields. Biopharmaceutical R&D scientists and device engineers may not always be familiar with each other's processes, which can create a barrier for adoption of technologies in drug development and clinical trials.
- How does one assure that the technology will produce usable scientifically valid data? How data will be validated must be addressed before implementing remote technologies.

Accessibility and Affordability

- New technologies come with financial costs. Moreover, the technology may not be accessible to all medical institutions at the initial phase of development. Depending on where the technology is produced and marketed, it may only be available to a limited group of organizations.

Study Oversight

- Providing adequate PI oversight is always a challenge in remote trials.

Technology

- Technologies continue to update and improve as new data is collected. Good performance at the time of deployment does not guarantee that the model will continue to perform well. This introduces the need to regulate and validate throughout the lifetime of the device and the need to continually demonstrate safe and effective practices.
- Technology support and training may be required for clinical staff to be familiar with the technology distributed to patients and to be

CONTINUED ON PAGE 16

RESOURCES

https://www.fda.gov/media/77832/download

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-public-health-emergency

https://www.fda.gov/media/88572/download

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9084261/

EQuIP CORNER

CHALLENGES AND ETHICAL CONSIDERATION

CONTINUED FROM PAGE 15

able to address patient concerns regarding these technologies.

Regulatory challenges

- There could be ethical concerns built into the tools themselves. A database or application could include built-in hidden biases, it could have been developed using data resources that were not appropriately collected, or it could put subjects' privacy at risk. Researchers and IRB members may not fully understand bias and privacy risks associated with the device or application they are using. IRBs may need ad-hoc additional expertise in this area.
- There are significant ethical concerns surrounding data ownership and control, especially when commercial devices are used. Do all the parties clearly understand who owns the data collected and how they can exercise control over its use?

Regulatory overview

During the COVID-19 pandemic, the FDA supported DCT technology adoption and encouraged the research community to keep clinical investigations running during the public health emergency.

Since then, regulatory bodies continue to innovate to keep pace with the rapid changes and evolution of research conduct and have consequently issued various guidance statements on how to implement such adaptations.

IRBs must become familiar with this technology to appropriately consider how such innovations impact the review requirements and a given study's risk to benefit assessment.

The IRB is responsible for reviewing the content of materials presented to participants, including advertisements, consent forms, questionnaires, diaries, and patient-reported outcomes. They must ensure everything is consistent with the protocol and nothing unduly influences a participant to enroll or stay enrolled in the trial.

Key points to consider for IRBs, Sponsors, and Investigators

- IRBs need to consider whether third-party vendors are engaged in the research and whether the training, and qualifications of the personnel involved must be verified. Additionally, they should determine if reliance agreements or other contractual agreements are needed to define responsibilities and liabilities.
- Reviewing the plan and any changes to the plan for reporting and replacing a device lost, damaged or stolen.
- What back-up systems are in place should devices, technologies, data transfer, or data storage process fail? Are back-up systems proportionally secure?
- IRBs need to consider other aspects of safety of those devices such as any physical discomforts or possibilities of harms (e.g., skin rash, irritation, shocks, burns, chemical exposure, or movement restriction).
- What approaches or mitigation strategies are in place to assure adequate participant compliance for completing questionnaires throughout the study? Participants may attenuate to and tire of completing questionnaires, increasing the potential for missing information and will impact on data quality.
- Can participants request withdrawal of their data? If the wearable device is providing data the participant can see, how valid are is the data? Will access to data or results impact trial integrity or blinding?
- PIs should establish an understanding with the participant about intended uses and potential risks of the device, its ownership, and access in advance.
- Sponsors and/or investigators should ensure PHI and clinical trial data are encrypted at rest and in transit. If a device is lost or stolen, it should be remotely accessed and wiped to remove all information.
- Any possibility of disclosure of PHI through lost or stolen data should be reported to the IRB and to any covered entities as a potential HIPAA violation, as applicable.
- Informed consent should include the information such as costs or penalties associated with the device, if a device is lost, damaged, or stolen. Instructions on disposition or return of the device at the end of the study and contact information should also be provided in the informed consent process.

Conclusion

Technology is not meant to replace clinical trial professionals, but rather to supplement the work that is being done to support the development of groundbreaking medical products, which will positively impact countless lives. Although technology brings with it a new set of challenges, research communities can differentiate themselves by adopting technology, taking ownership of their systems, and leveraging their own data.

IRB CONSULTATIONS

New to MHC? First time submitter to the MHC IRB via iRIS? Have a question? The Research Integrity/Office of Research Protections offers consultations with researchers. Consultations provide an opportunity for researchers to meet on Microsoft Teams with an experienced IRB staff reviewer. The purpose is to provide education and guidance to research teams prior to submission of IRB applications, or before making major changes to IRB-approved studies. Getting help pre-submission may shorten review time and spare you unnecessary confusion. Consultations are available upon request for any type of study, but we especially recommend them for:

- Researchers new to the IRB review process who would like additional guidance before submitting their first IRB application.
- Study teams planning multi-site or complex projects.
- Study teams considering making major changes to IRB-approved studies.

Submit a consultation request form by clicking here:
https://www.mclaren.org/main/irb-consultations

FACULTY, FELLOWS & RESIDENTS

SCHOLARLY ACTIVITY NEWS

FIRST McLAREN SCHOLARLY ACTIVITY FORUM

By Carlos F. Rios-Bedoya, ScD, MPH

Carlos F. Rios-Bedoya, ScD

I would like to take this opportunity to share an important McLaren milestone in the area of scholarly inquiry. The first McLaren Scholarly Activity Forum will be held on May 1, 2024, at the Gateway Hotel & Convention Center located at 5353 Gateway Centre Boulevard in Flint. After many years of logistical and implementation challenges, we have reached a point where we have the ability to organize an event of this scale. This will be an event where all residents at all McLaren subsidiaries will have the opportunity to showcase their scholarly activity projects. It is also an occasion for residents, fellows and faculty to interact, share ideas, and encourage collaboration across subsidiaries for multi-site scholarly activity projects. This will also be an opportunity to become acquainted with nursing research and high value care projects at McLaren, as these areas will participate and display their projects.

We hope that promoting this event months in advance will allow subsidiary programs to plan ahead, allowing as many residents and fellows as possible to participate or attend. This is a unique opportunity for residents and fellows to not only present their work but also to know what their peers are doing at other hospitals. This interaction should promote networking and the synergy of ideas that could lead to collaborations and high-impact scholarly activity projects. High-impact scholarly activity projects are not only good for the residents and fellows, the program, and McLaren but they can and should also turn into high-impact publications. These publications bring prestige and recognition to the institution. This in turn brings prestige and recognition to our GME program. Events like this have the potential to generate this kind of domino effect. In addition, it provides an opportunity for residents and fellows to present at a regional conference and meet one of their ACGME requirements for scholarly activity. Furthermore, CME credits will also be offered to those attending the event.

We are in the process of planning the agenda which will be distributed as soon as it becomes available. However, we can announce that there will be a keynote speaker (TBD), oral presentations, poster viewing, and an award ceremony with cash prizes (amount TBD) for the best oral and poster presentations. We plan to engage volunteers to serve as judges for this event. Judges will be responsible for reviewing abstracts, providing feedback on submissions, and determining winners of the oral and poster competitions. More information about how volunteer as a judge will be available soon. The Division of Scholarly Inquiry is committed to supporting and facilitating scholarly activity for McLaren residents, fellows, and faculty. If you would like additional information, contact Dr. Carlos F. Ríos-Bedoya at **carlos.rios@mclaren.org**.

UPCOMING RESEARCH EDUCATION

MHC Research Integrity Brown Bag
Including Vulnerable Subjects with Cognitive Impairment in Research

November 9, 2023
12:00 pm - 1:00 pm

Speaker:
Laura Holtz, MS, PMP, CCRP
Clinical Research Associate
Yale School of Medicine Center for Clinical Investigation
President-Elect SOCRA

To register, contact:
susmita.jain@mclaren.org

ACRP Webinar
Broadening Your Approach to Trial Diversity on a Global Scale

November 8, 2023
12:00 pm - 1:00 pm EST

To register, follow the link:
https://acrpnet.org/event/broadening-your-approach-to-trial-diversity-on-a-global-scale/

PRIM&R Events
Considering the Ethical, Legal, and Social Implications of Digital Health Research

October 31, 2023
1:00 pm EDT

To register, follow the link:
https://www.pathlms.com/primr/webinars/35484

Exploring FDA Regulations
3-Part Session:
November 3, 10, and 17
1:00 pm - 3:00 pm ET

For Registration follow the link:
https://www.pathlms.com/primr/courses/53573

Community Engagement in Research: Ethical Considerations for HRPPs
November 14, 2023
1:00 pm EST

For Registration follow the link:
https://www.pathlms.com/primr/webinars/35494

2023 PRIM&R Annual Conference
December 4-6, 2023
Walter E. Washington Convention Center
Washington, DC

Available to attend virtually.

To register, follow the link:
https://primr23-sber23.eventscribe.net/aaStatic.asp?SFP=WE1BREZXR05AMTQ3MjM

ANNOUNCEMENTS AND WHAT'S NEW

Tenia Martin

MCRI is happy to welcome **Tenia Martin** to the team! Tenia is our new Research Financial Analyst. She has a Bachelor's Degree in Accounting from the University of Detroit – Mercy and six years of experience in accounting and finance. Tenia joins us from Karmanos where she worked as an Accountant II.

Marci Roberts

MCRI is happy to announce the promotion of **Marci Roberts** to Lead Clinical Research Coordinator. In her new role, Marci will support all MCRI research sites. She is a long-time research coordinator with extensive organizational skills. Marci transitioned to this role from her position as an MCRI Research Coordinator at McLaren Flint.

Office of Clinical Excellence

VICE PRESIDENT
Chandan Gupte
chandan.gupte@mclaren.org

ADMINISTRATIVE ASSISTANT
Tamara Leo
tamara.leo@mclaren.org

McLaren Corporate Research
2701 Cambridge Court, Ste. 110
Auburn Hills, MI 48326

CORPORATE DIRECTOR, RESEARCH ADMINISTRATION AND THE HUMAN RESEARCH PROTECTIONS PROGRAM
Pam Wills-Mertz
pamela.wills-mertz@mclaren.org

McLaren Center for Research and Innovation
mclaren.org/Main/Research.aspx
(248) 484-4960

CORPORATE RESEARCH MANAGER
Jill George
jill.george@mclaren.org

REGULATORY SPECIALISTS
Tanya Gardner-Mosley
tanya.gardner-mosley@mclaren.org

Vidya Yarlagadda
srividya.yarlagadda@mclaren.org

FINANCIAL ANALYST
Tenia Martin
tenia.martin@mclaren.org

DIRECTOR OF RESEARCH FUNDING
Barb Rauschendorfer
barb.rauschendorfer@mclaren.org

CLINICAL RESEARCH INFORMATICS MANAGER
Donna Mott
donna.mott@mclaren.org

Research Integrity
hrpp@mclaren.org
(248) 484-4950

CORPORATE RESEARCH INTEGRITY MANAGER
Patricia Ivery
patricia.ivery@mclaren.org

IRB ANALYSTS
Michael Flores
michael.flores@mclaren.org

Jacki Wilson
jacki.wilson@mclaren.org

RESEARCH QI COMPLIANCE AND EDUCATION SPECIALIST
Susmita Jain
Susmita.jain@mclaren.org

RESEARCH INTEGRITY ASSISTANT
Lauren Thomas
lauren.thomas@mclaren.org

Karmanos Cancer Institute Clinical Trials Office

DIRECTOR
Sarah Bigelow
bigelows@karmanos.org

MANAGERS
Elizabeth Bowie
bowiee@karmanos.org

Jaclyn Ventimiglia
ventimij@karmanos.org

Kasha Donahue
krulk@karmanos.org

Elizabeth Cunningham
cunninge@karmanos.org

Paige Dykema
dykemap@karmanos.org