

Marshfield Clinic Research Institute

2019 Year in Review



Marshfield Clinic Research Institute

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Mission

We enrich lives through discovery, translation and application of scientific knowledge that improves health and well-being.

Vision

We will innovate and define the future of health care for generations. Our research will be the source of innovation for the future of disease and injury prevention and integrated health care locally and globally.

Values

Discovery – Will be the foundation of the overall activities of the research group.

Translation – A major effort will be made to apply our discoveries in the health care setting.

Dissemination – Results of work done will be distributed broadly on a timely basis.

Teamwork – Will be a hallmark of the research group.

Excellence – Will be the standard for all research and program activities.

Collaboration – Partnerships both internal and external will be sought and encouraged.

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Translating research to care

Marshfield Clinic Health System has most of the key attributes of a Learning Health Care System where we drive the process of discovery as a natural outgrowth of patient care through innovation, quality, safety and value in health care. We have been functioning like this even before the term was coined. This is what caught my attention during my first visit in March 2009 and later influenced my decision to pursue my research career here. The unique type of research that can be realized within the framework of our Health System has always excited me.

In the health research translation process, it takes 17 years on average for an idea to result in research and then translate into health care. The delayed timeframe for the research to move from the research bench to a patient is seen as a waste of the limited resources available for conducting and supporting research. This is also a barrier for people to understand the value of research.

At the Research Institute, we are focusing on not only making sure that we translate the results of the research to our patients, but also in some ways to reduce the time it takes for the translation process. This is why a clear understanding of the bigger picture is important when conveying the value of our research to patients, policy makers, funders, health care professionals and our own Health System leaders.

The Learning Health Care System model allows us to tackle many challenges that are part of translating our research to stakeholders. The solution will involve Health System leaders, clinicians and staff. Integrating the Learning Health Care System model to the Research Institute's planning, dissemination and implementation will further influence the strategic direction we have embarked on.

This direction includes providing clinical trials throughout the Health System, researching the opioid epidemic, working with firefighters to improve farm safety and implementing pharmacogenetic alerts into our electronic health record to improve accurate medication prescriptions. These are just some examples of the translational research we are conducting.

As a result, the Research Institute had a great year and was successful in seeking more than \$31 million in grants/contracts and philanthropic funds to enable the various research activities across the Health System. We are stronger than ever before, and I strongly believe we are uniquely positioned to leverage the many opportunities that lie ahead of us. It is a true honor to be working with a unique group of passionate scientists, clinicians and staff to serve the research mission of our Health System.

"All the research in the world is not worth very much if you don't get it to the patients." - Mr. Melvin R. Laird



Amit Acharya, B.D.S., M.S., Ph.D.
Executive Director
Marshfield Clinic Research Institute



Children enjoyed fun science experiments during the Wisconsin Science Festival event held Oct. 19.

Curiosity unleashed at Wisconsin Science Festival

More than 200 children attended the Wisconsin Science Festival, "MCHS Science for Families," an interactive event held Oct. 19. Research Institute staff demonstrated scientific principles with fun hands-on activities such as dry ice farts, elephant toothpaste and rainbow in a jar. For more information on this statewide celebration of science, go to www.wisconsinsciencefest.org.

Celebrating Research Day

In honor of our 60th anniversary, we celebrated the inaugural "Celebrating Research Day" Oct. 9th. We shared the meaningful research happening here and culminated with the presentation of the 2019 Gwen D. Sebold Fellowship for Outstanding Research.

Clinical Research Unit provides valuable research space

The Unit provides a convenient location for patients to participate in research studies. Located within Marshfield Medical Center in Marshfield, the Unit provides a clinical setting for participants to consent for studies, have samples collected and undergo physical examinations that are required of study participants. This location is home to the All of Us Research Program and many clinical trials.



The Clinical Research Unit provides a clinical setting to conduct research studies.



Dr. Onitilo presents during the annual NCORP conference where clinician researchers and staff received cancer clinical trial accrual awards.

NCI funds Wisconsin clinical trial network

The National Cancer Institute awarded the Wisconsin National Community Oncology Research Program (WiNCORP), a Wisconsin cancer clinical trial network, with \$15.6 million to make the latest treatment options available to people with cancer. WiNCORP is a partnership between Gundersen Health System, Marshfield Clinic Health System and ThedaCare that provides innovative cancer clinical trials to patients in Wisconsin.

Clinical trial accruals

Our clinician researchers and research staff received recognition for NCI-sponsored oncology clinical trial accruals. WiNCORP received the Platinum Award for excellence in enrollments - the highest recognition possible. Dr. Onitilo and his research staff also received an award as the top enrolling physician in the U.S. Additional recipients of accrual awards included Demet Gokalp Yasar, M.D., and Sueyi Lai, M.D.

Cancer Care and Research Center

Conducting clinical trials and research to improve prevention, early detection, care delivery and patient outcomes for cancer patients.

Researching mammography to catch breast cancer sooner

A new study will provide valuable insight into the effectiveness of two different types of mammography – directly impacting the recommended screening methods for breast cancer in the future.

We worked with the National Community Oncology Research Program through the National Cancer Institute on the Tomosynthesis Mammographic Imaging Screening Trial (TMIST). Along with our Wisconsin NCORP partners, we are leading the way on TMIST and received the Silver Certificate of Excellence for outstanding achievement in patient enrollments for the study.

TMIST is the first randomized, controlled clinical trial that seeks to identify in which populations digital breast tomosynthesis (3-D) will outperform traditional 2-D digital mammography. TMIST will enroll 165,000 healthy women between the ages of 45 and 74 - resulting in the world's largest curated data set of breast cancer screening data, images and bio-specimens.

TMIST is extremely important because breast cancer is the most prevalent cancer in our region. It will provide important answers about how we should be screening and preventing breast cancer for our patients.

We are grateful to be involved in TMIST to help answer an extremely important question regarding how often to screen patients for breast cancer and whether 2-D or 3-D mammography should be performed. It is anticipated the results of TMIST will help shape the future of personalized mammography.

We partnered with Gundersen Health System and ThedaCare to form WiNCORP, which is a NCI-supported network that brings cancer prevention clinical trials and cancer care delivery research to people in their communities. All WiNCORP partners opened TMIST to their patients.

As a member of WiNCORP, our Center and its partners provide access to NCI-sponsored clinical trials to more than 680,000 community members within its collective, largely rural, service area spanning most of Wisconsin, upper Michigan and adjacent counties in northern Iowa and southeastern Minnesota.



**Adedayo
Onitilo, M.D.,
Ph.D.**
Director
Cancer Care and
Research Center



**Kristie
Guite, M.D.**
Radiologist
Marshfield
Clinic Health
System

Center for Clinical Epidemiology and Population Health

Research on disease occurrence, risk factors, prevention and treatment. Major focus on vaccine and cancer research.

Tapering opioids safely

In the past 20 years across the U.S., there has been more than 200,000 deaths from opioid pain reliever overdoses according to the National Center for Health Statistics. In response to this opioid epidemic, the Centers for Disease Control and Prevention released a guideline that has encouraged physicians to consider reducing or discontinuing (i.e., tapering) high-dose opioid therapy among patients with chronic pain. However, research from the CDC and Oregon Health and Science University shows that misapplication of the tapering guideline could lead to increased pain and withdrawal symptoms, prompting some patients to seek illicit opioids such as heroin or illegally made fentanyl.

Investigators at the Center for Clinical Epidemiology and Population Health and the Center for Precision Medicine Research at the Research Institute have begun to study the effectiveness and safety of tapering doses of opioid prescription drugs among patients with chronic pain.

This observational study will examine the relationship of opioid tapering patterns and outcomes of increased pain and withdrawal, substance use disorder and overdose. The study team will apply machine-learning procedures to identify patients at risk of heroin and other substance use disorder outcomes for prevention or treatment interventions. The results will help improve guidelines on opioid management for patients with chronic pain.

The study is funded for four years by a grant from the National Institutes of Health to Kaiser Permanente Institute for Health Research in Colorado. Marshfield Clinic Research Institute will participate as a collaborating site.



David McClure, Ph.D.

Senior Epidemiologist
Center for Clinical Epidemiology and Population Health



Epidemiologist Robert Greenlee, Ph.D., hosted a site visit by the National Cancer Institute to discuss a long-term community cancer study.

Long-term cancer research

The National Cancer Institute funded planning for a large national cohort of cancer occurrence and outcomes in adults. Participants will be followed over a decade or more to learn about cancer causes and strategies to improve survival and quality of life.

Donahue presents flu vaccine safety study to CDC advisory committee

Epidemiologist James Donahue, Ph.D., M.P.H., presented results of a Marshfield-led vaccine safety study at the CDC Advisory Committee on Immunization Practices (ACIP) meeting in Atlanta, Georgia February 27, 2019. The study found that miscarriage was not associated with flu vaccination in any season or across all seasons. The study results were reported by CNN.

McLean receives Sebold Fellowship

The Gwen D. Sebold Fellowship for Outstanding Research was presented to Huong McLean, Ph.D., M.P.H., a lead investigator with the Center. Dr. McLean has led research on influenza and vaccines at the Research Institute since 2012. The Sebold Fellowship has been given by D. David "Dewey" Sebold since 1988 to recognize an outstanding medical researcher and support continued research in his or her field.



Dr. McLean receiving the Gwen D. Sebold Fellowship for Outstanding Research from Sebold.



New director selected

Radha Nagarajan, Ph.D., has joined the Center as its new director. He will lead the scientific efforts and implement strategic initiatives for the further growth and expansion of the Center. Dr. Nagarajan has extensive research experience in biomedical informatics.

Impact of oral health on pneumonia

Researchers are studying oral health's impact on pneumonia by using the integrated medical-dental electronic health record at Marshfield Clinic Health System. Researchers were awarded a National Institute for Dental and Craniofacial Institute funded grant to conduct this research.

Researchers contribute to textbook

Amit Acharya, B.D.S., M.S., Ph.D., co-edited Integration of Medical and Dental Care and Patient Data (Springer, 2nd edition). The textbook highlights progress made in the integration of dental and medical care. Sixteen individuals from the Health System contributed as authors to nine of the 18 book chapters.



Center for Oral and Systemic Health

Researching the interactions between oral and overall health, with the goal of translating actionable findings to patient care.

Statewide dental sealant registry tracks childhood tooth decay

Tooth decay is the single most common childhood disease. School-based sealant programs target schools that serve children from low-income families and focus on sealing newly-erupted permanent molars, thereby reducing caries in children.

Most school-based sealant programs collect examination, service and follow-up data using a paper form, which can vary slightly from state to state. This data is then entered into an Excel-based application. At the end of the school year, annual reports are created.

In late 2013, we were tasked to design a state-of-the-art software application that could overcome some of the limitations of the excel-based application and move away from collecting data on paper forms. Delta Dental of Wisconsin supported this project.

DentaSeal is a secure, web-based dental sealant registry software program we designed and developed. It has provided an important platform to help users find information about a child's oral health and dental sealant information so it can be monitored across multiple years.

Since its inception in 2014, DentaSeal has been used within Wisconsin's 48 Seal-A-Smile programs and has supported approximately 180,000 children's dental sealant records. Wisconsin's Seal-A-Smile sealant program, with support from Delta Dental of Wisconsin, is a nationally recognized model for school-based sealant program implementation and success. Children's Health Alliance leads and manages the Seal-A-Smile program in collaboration with the Wisconsin Department of Health Services' Oral Health Program.

DentaSeal is able to capture, evaluate and track the effectiveness and efficiency of school-based sealant programs across multiple schools and years. It is an intuitive data capture tool that provides users the ability to accurately collect and look up a child's oral health and dental sealant information – providing improved care for these children. This real-time reporting tool queries useful information during the school year and for end-of-year reports.

Delta Dental of Wisconsin awarded an additional \$125,000 to the Center in 2019 for a total of \$438,000 for the research and development of DentaSeal.



Amit Acharya, B.D.S., M.S., Ph.D.

Research Scientist
Center for Oral and Systemic Health
Chief Dental Informatics Officer
Family Health Center of Marshfield, Inc.

Center for Precision Medicine Research

Combining research on the human genome with biomedical informatics and applies that knowledge to health care.

Understanding disease through genetic causes

Researchers have been studying the genetic principles of inheritance since 1866 when Gregor Mendel published his work on Mendelian inheritance.

Researchers in the Center not only discover genes that contribute to diseases, but also how genes metabolize medications to effectively treat a disease; develop novel genetic screening methods; and the nexus between gut microbiome and risk for chronic and neurological diseases.

We use a multidisciplinary research approach to advance the understanding of genetic causes of the diseases to help our patients. Our researchers exemplify the cutting edge of precision medicine research.

Steve Schrödi, Ph.D., Shicheng Guo, Ph.D., and Mehdi Maadooliat, Ph.D., developed and used a novel genetic screening method to discover a new mechanism producing hemochromatosis, enabling potentially new pharmaceutical treatments for both iron overload and anemia.

Tonia Carter, Ph.D., is investigating genes and biological pathways to help understand the causes of birth defects and develop new strategies for potential interventions.

Scott Hebring, Ph.D., has identified more than 60 individuals that have clinically significant genetic findings that may put them at high risk for devastating diseases including cancer and cardiovascular disease.

Through the Marshfield Microbiome Initiative, I am working with Paula Aston, M.D., to identify microbial triggers from the gut for the Multiple Sclerosis Gut Microbiome Dysbiosis study. We have also identified promising metabolic markers linking oral health to Type 2 diabetes and periodontal disease.

Working with colleagues from National Farm Medicine Center and Center for Clinical Epidemiology and Population Health, we are investigating what effect exposure to the environmental microbiome in dairy workers modulates their risk/benefit for flu-like and gastrointestinal illnesses.

In a look towards the future, Narayana Murali, M.D., Dr. Hebring and their collaborative partners are actively recruiting subjects for the NIH-funded *All of Us* Research Program. I want to also thank Murray Brilliant, Ph.D., for leading this initiative for the last two years.



Sanjay K. Shukla, Ph.D.

Director

Center for Precision Medicine Research

Patents awarded for early prediction

Steve Schrödi, Ph.D., recently discovered a new method to predict rheumatoid arthritis and psoriasis in patients that are genetically tested. He was recently awarded two U.S. patents for this new method.

The right drug at the right time

Scott Hebring, Ph.D., is working to reduce the risk for bad outcomes related to drugs influenced by genes. The Health System's prescription software sends an alert to the doctor when they have prescribed a medicine that doesn't work based on genetic information for specific patients.

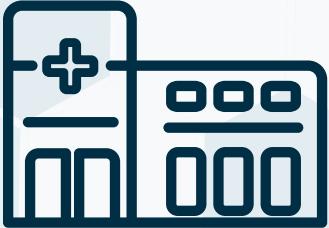
New director announced

Sanjay K. Shukla, Ph.D., is the new director of the Center for Precision Medicine Research. The central theme of his research has been to gain insights into human-pathogen interactions that aided in biomarker discovery, and clinical treatment of infectious and complex diseases. He is the primary investigator of an ongoing investigator-initiated \$2.4 million R01 grant from CDC/NIOSH to study the nasal and gut microbiome of dairy farm workers and how it affects their health.

All of Us Wisconsin adds Gundersen

Gundersen Health System has now partnered with the Research Institute in the *All of Us* Research Program, a nationwide effort to gather data from one million or more people living in the U.S. to accelerate research and improve health. *All of Us* enrollment sites in Wisconsin are currently located in Marshfield, Wausau, Chippewa Falls, Madison and Milwaukee. The Research Institute has started part-time enrollment in Stevens Point, Minocqua and Wisconsin Rapids. Go to www.marshfieldresearch.org/allofus for more information.





Translating research to care at

Marshfield Clinic Research Institute

Our discoveries today affect health care tomorrow. Some discoveries may prevent disease, while others treat serious health conditions. Every function of the Research Institute works on translating our research to the care provided at Marshfield Clinic Health System and around the world.

- More than **30** scientists, **200** staff and **150** clinician researchers engaged in research.
- More than **\$31** million in externally-funded projects in 2019.
- More than **800** research projects conducted in 2019.

Use the below key to find how we are translating research to care.

- Working with partners to improve health care at Marshfield Clinic Health System.
- Working with partners to improve health care around the world.
- Sharing research knowledge with the world.
- Supporting the research conducted at the Research Institute.



Office of Research Support Services

research support | community outreach | administration

- **142** funding awards processed and 166 funding proposals submitted
- Clinical Medicine & Research journal had **1,715** citations and **68,863** downloads
- **435** new and continuing reviews completed by Institutional Review Board



Cancer Care and Research Center

prevention | early detection
care delivery | patient outcomes

- Over **700** patients enrolled in cancer clinical trials
- **\$15.6 million** in funding awarded for 6 additional years
- WINCORP is enrolling patients in **44 of 72** Wisconsin counties
- Over **120** active clinical trials



Center for Clinical Epidemiology and Population Health

disease occurrence | risk factors
prevention | major focus on vaccine and cancer research

- **28** original research publications during 2019
- Over **\$5 million** in external grant funding in 2019
- **1,877** patients enrolled in influenza vaccine effectiveness study during 2018-2019 season



Office of Research Computing and Analytics

technology | data support

- 514 REDCap projects consisting of **321,277** total records.
- Over 1,800 hours annually supporting **300** research/research feasibility data requests.
- Over **130** solutions developed to support more than **50** research studies.



Center for Oral and Systemic Health

oral and overall health | improve patient care

- Received Quality Innovator's Spotlight for dental quality analytics dashboard
- Graduated the Center's **26th** research intern
- **5,000** oral exams for diabetic patients in pilot program



Integrated Research and Development Laboratory

lab services | infectious disease research

- **102** studies supported in 2019
- **393** years of experience among our staff
- Received specimens from **13** countries in 2019



Clinical Research Center

specialty clinical trials

- Currently participating in **45** active clinical trials
- Enrolled more than **250** subjects in **18** different studies
- Conducted more than **2,070** study visits



Center for Precision Medicine Research

precision medicine | human genome | biomedical research

- **1,389** patients learned about their genetic risks through research in 2019
- More than **3,000** participants enrolled in the *All of Us* Research Program
- **3,000** participants enrolled in pharmacogenetic research



National Farm Medicine Center

human health and safety | rural and ag life

- National Children's Center is **23** years old
- Journal of Agromedicine published papers from **10** countries
- Farm Medicine hosted **3** Mental Health First Aid workshops in Wisconsin



A camper at the first-ever BBS Lions Camp in Rosholt, Wisconsin takes aim during archery. The event was led in-part by staff at the Research Institute.

Phase 3 BBS obesity trial

We were the first site to begin enrollment in a phase 3 clinical trial for a drug expected to reduce obesity in patients with Bardet-Biedl syndrome (BBS). BBS is a rare genetic disorder that affects almost every organ system in less than 3,000 individuals in the U.S.

Cardiovascular inflammation reduction trial

We were an integral part in research that showed taking low-dose methotrexate does not reduce additional cardiovascular events in patients with either diabetes or metabolic syndrome. The Cardiovascular Inflammation Reduction Trial was a 5-year study conducted by the National Institutes of Health.

Clinical Research Center

Conducting clinical trials in many specialty areas.

Our role in the FDA approval of Botox for spasticity in children

The U.S. Food and Drug Administration (FDA) approved onabotulinumtoxinA (Botox, Allergan) in 2019 for treatment of upper limb spasticity in children and adolescents aged 2 to 17 years. With the help of Sandra Freeman, clinical research coordinator, I was the primary investigator for the clinical trials here at the Research Institute.

Common causes of spasticity in children include cerebral palsy, traumatic brain injury, spinal cord injury and stroke.

Botox is now approved in the U.S. to treat upper limb spasticity in pediatric patients. Most pediatric rehabilitation physicians have used it as standard of care for spasticity treatment. The Health System has actually been using Botox injections for more than 20 years on pediatric patients.

Botox had previously been FDA-approved beginning in the 1970s for use on adults for various conditions such as blepharospasm, cervical dystonia, upper limb spasticity after stroke, chronic migraines and others.

There have been many studies over the last two decades documenting these benefits, but a systematic, double-blinded placebo-controlled study assessing the safety of Botox in pediatric patients with upper and lower limb spasticity was not formally conducted. This study verified that Botox is a safe and useful tool in the treatment of pediatric limb spasticity.

I am glad a study specifically on children was completed because it gives my patients and I more scientific knowledge on best techniques, dosing and safety. For example, it was exciting to scientifically confirm that Botox had few side effects in this pediatric population with cerebral palsy. The clinical trial showed that the incidence of side effects was similar in the placebo group compared to the Botox group.

During this process, I co-authored a paper on the findings that is currently in review for publication. I also gave a presentation about the research at the annual meeting of the American Academy of Cerebral Palsy and Developmental Medicine in September 2019.



**Jill
Meilahn, D.O.**
Physical
Medicine and
Rehabilitation
Marshfield Clinic
Health System



**Sandy
Freeman**
Research
Coordinator,
Clinical
Research
Center

National Farm Medicine Center

Conducting research on human health and safety associated with rural and agricultural life.

Rural firefighters promote farm safety through national program

Firefighters and farmers, two groups that often work in hazardous environments, are teaming up in a program aimed at improving agricultural safety and health nationwide.

The Rural Firefighters Delivering Agricultural Safety and Health (RF-DASH) project trains emergency responders to provide resources and consultation to farmers.

Our research indicates that firefighters can be influential and can motivate farmers to make changes to improve health and safety on their farms. Rural firefighters and first responders are highly esteemed in their communities. With the new tools and knowledge we're giving them, they can impact farmers' health and safety decisions.

From November 2017 through October 2019, RF-DASH trained 68 individuals from 10 states who have, in turn, trained dozens more. A final training for the year was scheduled as part of the Wisconsin EMS Association (WEMSA) conference at Wisconsin Dells, Wisconsin.

From here on out, we will be revolving the program around supporting our existing trainers and expanding their networks of influence. Participants have included agricultural health and safety specialists, fire/EMS, health care providers and National Fire Protection Association committee members.

Farmers who volunteer as emergency responders are likely to become the ideal trainees in the program. I myself am a former rancher and volunteer firefighter, so I know these individuals can help bridge the farming community and the local departments.

RF-DASH structures its curriculum towards National Fire Protection Association standards, specifically the 1300 standard, which addresses community risk assessment. This "stamp of approval" helps assure participants that the program is reducing risks and improving overall health and safety in rural communities.

Funding is provided through the Upper Midwest Agricultural Safety and Health Center, with a grant from the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.

Find more information online at www.umash.umn.edu.



Casper Bendixsen, Ph.D.

Director

National Farm Medicine Center

Childhood Agricultural Injury Prevention Workshops

Interactive 1.5-day workshops took place in four locations throughout the U.S. The combined attendance of more than 100 included representatives of insurance companies, health care systems, Extension, government agencies, media, farm organizations and agribusinesses.

Auction raises funds for farm safety, research

Supporters of agricultural safety and health pledged nearly \$230,000 towards the work of the National Farm Medicine Center during the annual Auction of Champions gala, Sept. 19, 2019, at RiverEdge Golf Course near Marshfield, including \$53,500 for farm rescue training to be implemented with area fire departments.

ROPS Rebate Program

Since 2013, the Wisconsin Rollover Protection Structure (ROPS) Rebate Program installed rollbars on more than 280 farm tractors in more than 30 counties. A ROPS with a seatbelt is 99 percent effective in preventing injury or death in the event of an overturn, the No. 1 cause of farm deaths.

Assembly suicide task force public hearing

We hosted a public hearing of the Speaker's Task Force on Farmer Suicide Prevention July 29, 2019. The 15-person Assembly task force heard from Casper Bendixsen, Ph.D., director, National Farm Medicine. He reported that a long-term, multi-pronged strategy is needed to support farmers' mental health needs.



The scene during the Speaker's Task Force Public Hearing on Farmer Suicide Prevention July 29.



Meece selected for infectious disease endowment

Jennifer Meece, Ph.D., research scientist and director of the Laboratory, was selected for the Infectious Disease

Distinguished Physician/Scientist Endowment. The endowment supports research in infectious diseases such as tick-borne, fungal, bacterial or viral conditions. Dr. Meece plans to use the endowment to advance understanding of important infectious diseases.

Antibiotic utilization after tick bite

We are studying provider utilization of a dose of antibiotic doxycycline following a tick bite to prevent Lyme disease. The Infectious Disease Society of America recommended the practice in Lyme hotspots such as Wisconsin in 2006, but there are no data on the frequency of prescriptions. We hope to follow with a study of the outcomes of this practice.

Federal tick-borne working group

Anna Schotthoefer, Ph.D., was selected to serve on the Babesiosis and Tick-borne Pathogens subcommittee of the federal Tick-borne Disease Working Group. It was established by Congress in 2016 as part of the 21st Century Cures Act to provide subject matter expertise and to review federal efforts related to all tick-borne diseases.



Integrated Research and Development Laboratory

Offering a unique research portfolio and diverse lab services dedicated to insuring the success of Research Institute scientific endeavors.

Finding ways to catch Lyme disease earlier

Lyme disease is the most common illness transmitted by ticks in the U.S., including in Wisconsin where at least 3,000 people are infected each year. Although most people fully recover when diagnosed and treated, the disease can be difficult to diagnose.

The symptoms can be non-specific, similar to the flu, or may look like other diseases. For instance, even though Lyme disease patients often present with a characteristic rash that looks like a bull's-eye, many times the rash lacks central clearing, such that it may look more generally like cellulitis.

Further complicating a diagnosis are limitations with the currently available laboratory test for the disease. Many patients will test negative in the initial stage of Lyme disease. Failure to diagnose and treat early then has the unfavorable consequences of leading to more serious manifestations of the disease that may involve the joints, nerves and heart, and also may require more treatment to resolve.

We are contributing to efforts to develop diagnostic tests that would be better at detecting Lyme disease infections early in the disease, as well as more rapidly, while patients are waiting in the doctor's office. Of note, in 2019 we participated in three industry-sponsored studies, one of which has resulted in the first FDA-cleared, improved alternative to the current testing process.

Additionally, a study funded by donors to the Research Institute is exploring the application of novel methods that are capable of detecting very small amounts of pathogen DNA in a sample to diagnose Lyme disease. Such efforts are expected to eventually result in fewer patients suffering from an extended illness caused by the disease.

For more information about ticks, please download our tick cards at marshfieldresearch.org/nfmc/lyme-disease. A Lyme disease medical conference for medical and allied health providers is also being planned for April 30 and May 1, 2020 in Minocqua.



Anna Schotthoefer, PhD.

Project Scientist

Intrgrated Research and Development Laboratory

Office of Research Support Services

Providing essential resources to support research and community outreach through a dynamic administrative environment.

Advancing translational science

The Office of Research Support Services provides essential resources to support research and community outreach within Marshfield Clinic Health System. Our mission is to enrich research and health outcomes by creating a dynamic administrative environment open to helping those engaged in medical sciences and community outreach.

One of the ways we accomplish this is by connecting researchers to opportunities available through our partnerships with external collaborators. UW-ICTR is one such partnership with the University of Wisconsin-Madison. UW-ICTR is supported through a Clinical and Translational Science Award funded by NIH's National Center for Advancing Translational Sciences.

In late 2018, UW-ICTR announced it was reviving its Collaborative Research Award. This pilot funding mechanism awards \$75,000 for a 12-month project that pairs co-principal investigators from UW-Madison and the Research Institute. The funding was awarded in 2019 to Thomas Fritzsche, M.D., Ph.D. (Research Institute) and Laurel Legenza, PharmD, M.S. (Madison).

Their project entitled "Geo-mapping antimicrobial resistance in E. coli from humans and animals" will utilize genetic characterization of E. coli samples from humans, canines and bovines to determine the relationship of genetic patterns associated with antimicrobial resistance and geographic location in northcentral Wisconsin. The study has the potential to be the basis for a tool that will aid providers in antibiotic prescribing practices.

In addition to administrating organizational collaborations, we support:

- Research navigation
- Extramural funding proposals and awards
- Research Integrity and protections/human subjects in research
- Scientific writing
- Publication and editorial assistance
- Administrative oversight for Research Institute program initiatives
 - Scientific Review Committee
 - Summer Interns
 - Post-Doctoral Program
- Publication of our peer-reviewed medical journal, and communications.

The Office works as a team with researchers, project directors and Health System staff towards achieving their research and project goals. We strive to keep research alive and well and are ready to take on the next challenge on a continual basis.



Jordon Ott
Director
Office of Research Support Services



The Boldt Company is the primary donor for the Summer Research Internship Program. Here, Tom Boldt, CEO of The Boldt Company, stands with this year's interns.

Summer Research Internship Program

In its 45th year, seven interns presented their research during the Research Symposium held August 7. The program enables students to put their education into practice as they work side-by-side during the summer with scientists and clinician-researchers who are experts in their fields.

Community outreach

Our staff prides itself on giving back to local communities. More than 400 clothing items, 3,000 food items and \$3,300 in monetary donations were provided to community organizations including Best First Day, Keep Kids Warm, United Way and many others.

Research navigator

Successful research projects involve advanced planning, preparation, knowledgeable staff and adequate funding. Our newly-launched Research Navigation Program will identify collaborative opportunities and orient the Health System to the resources, tools and staff that are here to help our research succeed.



Steve Theis
Research Navigator

Deering and Kadolph recognized nationally for survey tool work

Members of the Office received national recognition for their work with the research survey tool REDCap at REDCapCon Sept. 16-19 in Vancouver. REDCap is the premier online survey and database tool for the research community. It uses a secure web application for building and managing online surveys and databases.

Leila Deering, senior applications analyst, and Chris Kadolph, software development team lead, are both REDCap experts. As members of the REDCap Consortium, they belong to a vast network of collaborators who use and support REDCap for thousands of institutional partners in more than 100 countries. Deering and Kadolph both presented four trainings during REDCapCon, and Deering received first place for a training material she created.



Deering and Kadolph at 2019 REDCapCon.

Office of Research Computing and Analytics

Providing full service technology and data support for the research being conducted at the Research Institute.

Resources developed for Precision Medicine Initiative

As a Marshfield Clinic Health System support service, we constantly seek to provide resources to improve research. The Precision Medicine Initiative showcases a variety of ways we can support studies: population identification, recruitment tools/enrollment monitoring, data capture/acquisition and compiling, study outcome analysis, and translational implementation. This project is also an excellent example of interdepartmental collaboration and commitment to data-driven translational science.

This project integrated final results into participants' electronic health record through medication alerts and uploaded the genetic report; making it possible for practitioners to utilize results as part of care. Patients received a copy of their genetic results and, through partnership with Medical Genetics, were offered the opportunity to talk through results with licensed geneticists. In the end, we impacted not only patients, but entire families.

To do this, electronic health record data was combined with predicted family mapping data (produced in partnership with UW-Madison) to algorithmically identify eligible families/family members for recruitment based on relationships to targeted phenotypes. Through partnerships with research coordinators in the Center for Precision Medicine Research and the mail room at the Health System, we created and sent recruitment mailings.

We developed and implemented an application called RecruitTracker to help track patients and events from identification to final results. This resource was also supported by and used in other studies like many of our tools. We collaborated with the Integrated Research and Development Laboratory staff to send biospecimens to an external collaborator for genotyping and utilized a REDCap project to electronically collect survey data from recruited individuals.

Throughout the study we compiled data and reported (both in real-time and intermittently) on enrollment, attributes of recruited persons (group identity, deceased status, map location) and results (both survey collected and genetic variants). We analyzed in-process data and used it to steer future recruitment, track sub-groups and provide preliminary insights.



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Research Programmer/Analyst

Office of Research Computing and Analytics

Marshfield Clinic Health System Foundation

Partnering with individuals and organizations to enrich lives in our communities by supporting advancements in research

The moment a scientist or clinician begins their latest study investigating a new approach to cancer treatment...

The moment parents in the heart of Wisconsin find hope because their sick child qualifies for a clinical trial...

The moment a student presents their research after spending the summer in Marshfield with a scientist or physician mentor, launching their career in medical research...

These are the moments you help make possible when you give to research at Marshfield Clinic Research Institute. 100% of funds donated to research through the Foundation support the Research Institute's initiatives.

Though many of the studies are funded through national grants, donations from people like you are vital to ensuring that research continues right here in Wisconsin. Your gifts help initiate and sustain studies that impact people in our communities and beyond. Most of all, your support creates moments of hope and innovation that enriches lives.

Generous people like you donated more than \$2.2 million to research in 2019. The support came in many forms, including support from loyal donors who have been supporting research at the Research Institute for as many as 40 years, legacy gifts from the estates of grateful patients and others who want to advance research at the Research Institute, memorial gifts given with hope to find new cures and treatments for diseases such as those that impacted the life of a loved one, and funds raised at events throughout the year.



The Krause family of Marshfield, Dave, wife Becky and sons Will and Ben, shared their story during a \$100,000 check presentation from the MACC (Midwest Athletes Against Childhood Cancer) Fund to Marshfield Clinic Research Institute in June 2019. The Krauses spoke about how donations to pediatric cancer research and cancer care at Marshfield Clinic Health System have helped support their son Will through three rounds of cancer treatments at Marshfield Children's Hospital.

Your impact on research

• **Cancer research:** The Cancer Care and Research Center gives all cancer patients treated at Marshfield Clinic Health System access to innovative care through research. Your support increases access to clinical trials and funds cancer research studies at the Health System.

• **Rural health:** Thanks to you, the Research Institute can continue investing in research that impacts communities throughout central and northern Wisconsin. Studies on Lyme disease, blastomycosis, and agricultural health and safety are vital to support patients close to home.

• **Pioneering support for a rare disease:** The Health System is home to the only center in North America dedicated to research and care for the rare disease Bardet-Biedl syndrome. This condition affects less than 3,000 individuals in the U.S. The internationally-recognized Clinical Registry Investigating BBS at the Research Institute is the largest in the world with more than 500 BBS patients from six continents and more than 30 countries. This groundbreaking research can only continue with donor support.

• **Support where it's needed most:** General research gifts supports the Research Institute's emerging needs. These gifts support studies investigating life-threatening diseases, community health, precision medicine, integrated medicine and more.

To support Marshfield Clinic Research Institute, please contact Karen Piel at
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or **715-389-3868**.



**Marshfield Clinic
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