



# 2022

## YEAR IN REVIEW



**Marshfield Clinic<sup>®</sup>**

Research Institute

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## Marshfield Clinic Research Institute Oversight Board

### Marshfield Clinic Health System Physicians, Scientists, and Leaders

**Corey M. Cronrath, D.O., M.P.H.**  
Service Line Medical Director,  
Occupational Health  
Marshfield Clinic Physician  
Class A Member

**Scott J. Hebbring, Ph.D.**  
Research Scientist, Center for Precision  
Medicine Research  
Marshfield Clinic Research Institute  
Marshfield Clinic Health System Leader  
\*Member-at-Large, Executive Committee

**Krista Hoglund, A.S.A., MAAA**  
CEO, Security Health Plan  
Marshfield Clinic Health System Leader

**Matthew J. Jansen, M.D.**  
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**William F. Melms, M.D., M.H.A.**  
Interim Executive Director,  
Marshfield Clinic  
Marshfield Clinic Physician  
Class A Member

**Adedayo Onitilo, M.D., Ph.D., MSCR**  
Medical Oncologist and Hematologist  
Marshfield Clinic Physician  
Class A Member

**Tammy Simon, R.N., M.S.N.**  
Vice President, Institute for Quality,  
Innovation, Patient Safety  
Marshfield Clinic Health System Leader  
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\*Member-at-Large, Executive Committee

**Brent Bergman**  
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\*Vice-Chair, Executive Committee

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**Brian Forrest**  
Owner, Maple Ridge Dairy

**Martin (Marty) Loy, Ph.D.**  
Dean, College of Professional Studies  
University of Wisconsin-Stevens Point

# Improving care through research

We each have our unique story. In this last year, I have spent a lot of time talking to our teams and team members about the meaning of their work: what motivates and inspires them. My favorite conversation to have with colleagues is about the journey that led them to a career in research. For some, the story is a process, following a long and winding road or an unclear path. For others, the story started as a childhood dream: dressing in a white coat for Halloween or asking for a microscope for a birthday. For many, the story is personal: first-hand experiences which manifested in a drive for care innovation.

During these discussions, it intrigues me to learn how each member of our team has found their way to Marshfield Clinic Research Institute (MCRI). Some colleagues grew up in the area or in Wisconsin and stayed to raise families, or stayed because it is their home. Others ended up here by chance, without a strategy for how MCRI would be woven into their intentional plan. Regardless of the path taken, MCRI is a place that holds incredible meaning to each of us.

Serving in the executive director role, I have been incredibly fortunate to meet with many people in our communities, people who support our research mission through words and actions. They too have stories to share about their journey to supporting research as well as why they choose to advocate for the work that we do at MCRI.

Do not be afraid to share your story or ask others to share theirs. Each story helps to assemble the larger tale of research and makes the work conducted at MCRI historical.

We all have a desire to conduct the research that makes a difference.

While every story is different, each is deeply personal and passionately conveyed, and patients are an overarching theme. People are at the core of what we do. The work conducted and supported at MCRI may impact a single patient – or a large population of patients. Our charge is to continue researching, learning and discovering so that the people with whom we share our community have access to the kind of care that is informed by cutting-edge research and discovery.

As we reflect on our 2022 accomplishments, our influences on patients, and our impacts on important policy decisions shaping our collective future, we find much to celebrate. Above all, we find connections to each other, to our patients, and to our communities, which are reminders of why and how we got here.



**Jennifer Meece, Ph.D.**  
Interim Executive Director  
Marshfield Clinic  
Research Institute

## 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.

# Blood testing for ctDNA could be the cancer test of the (near) future

**A** biopsy is a common, yet invasive, process that removes tissue to test for diseases such as cancer. But what if there were another way that were less invasive and could detect cancer sooner?

MCRI's Cancer Care & Research Center is part of two national clinical trials looking at blood tests that detect circulating tumor DNA (ctDNA). As a tumor grows, cancer cells die and release its DNA into the bloodstream.

The first clinical trial, CORRECT-MRD II by Exact Sciences, enrolls patients who have undergone complete surgical resection for Stage II or III colorectal cancer within the last six months. Blood samples drawn every few months for 3-5 years will be analyzed to detect a potential reoccurrence of colon cancer.

The NRG-GI005 (COBRA) study evaluates the use of ctDNA as a predictive biomarker. Finding ctDNA in the blood means small amounts of cancer likely remain after surgery. Cancer detected with this test would be too small to find with other tests. Thus, testing for ctDNA

levels may help distinguish those patients with colon cancer who would benefit from receiving chemotherapy from those who would not.

“Hopefully this is another avenue of doing a blood test rather than an invasive test or a CT scan for recurrence of cancer,” Dr. Demet Gokalp Yasar said. “Many things that were once part of clinical trials, have become standards of care. Research leads to new developments and treatment methods.”

Deana Jansa, an oncology research nurse who works with Dr. Gokalp Yasar, helps coordinate the recruitment for the ctDNA clinical trials. As the Research Institute expands its presence in rural Wisconsin, Jansa said patients appreciate having the opportunity to participate in research.

“Patients in the Northwoods are very open to being part of research and clinical trials, and we need people from all walks in life to participate,” Jansa said. “The trials might not help the patient now, but they want to participate so they can help someone in the future.”

*“The intent of this testing is that we detect cancer at its earliest point possible, even before we see the tumor using traditional methods. When we catch cancer early, we have an increased chance of a better health outcome for the patient.”*



**Demet Gokalp Yasar, M.D., Hematologist/Oncologist**  
Marshfield Medical Center-Minocqua



## Highlights

### **WINCORP recognized for clinical trial accruals**

The National Cancer Institute recognized Cancer Care and Research Center physicians for oncology clinical trial accruals. CCRC partners with Gundersen Health System and ThedaCare to form Wisconsin National Community Oncology Research Program (WiNCORP), which is a NCI-supported network that brings cancer prevention clinical trials and cancer care delivery research to people in their communities.



WiNCORP received the Platinum Award for excellence for exceptional patient enrollments, the highest level of recognition. Individual honors went to Adedayo Onitilo, M.D. (Weston, Stevens Point), Platinum; Isaac Yeboah, M.D. (Marshfield), Gold; Seth Fagbemi, M.D. (Marshfield), Gold; Patcharin Tanawattanacharoen, M.D. (Eau Claire), Silver; and Demet Gokalp Yasar, M.D. (Minocqua), Silver.

### **Health System Cancer Care & Research commitment to research and patient wellbeing**

Adedayo Onitilo, M.D., Ph.D., MSCR, was re-elected to the SWOG Cancer Research Network Board of Governors. This network is a global cancer research community that designs and conducts publicly-funded clinical trials, including those funded by the National Cancer Institute. Dr. Onitilo was selected to represent Marshfield Clinic Health System because of its three-year average annual accrual rate into cancer clinical trials and its commitment to high standards of quality. The honor, Dr. Onitilo said, is truly a team effort: “Congratulations also goes to all oncology physicians and the other service lines that we collaborate with daily. Special thanks to our research staff, as well. We are lucky to have an organization that appreciates research and provides us with a platform to serve our patients and community.”



### **Clinical Research Unit coming to Marshfield Medical Center-Weston**

Efforts to support research have been a key part of the Health System since the founding of the Marshfield Clinic Research Institute in 1959. These efforts continue and adapt into the future with the addition of a Clinical Research Unit at the Marshfield Medical Center (MMC) in Weston. Team members will use the space to continue already active research projects and clinical trials in the Wausau-Weston region, further integrating staff and resources into MMC-Weston’s working environment. “An expanded physical presence at MMC-Weston will offer the opportunity for more research projects than we’ve traditionally supported,” said Vice President of Medical Affairs Dr. Keshani Bhushan. “We welcome this expansion with open arms, in order to help pioneer the future of health care in our community.”



## Preventing dementia with statin medications

**F**or many years, doctors have looked for treatments to prevent memory loss, dementia, and Alzheimer's disease in their elderly patients. Some recent studies have suggested that drugs called statins, commonly prescribed for lowering blood cholesterol, may help prevent dementia and cognitive decline. About one in three U.S. adults over age 75 without heart disease take statins, but more information is needed to understand the role and benefits of statins.

In partnership with Duke and Wake Forest universities, MCRI is currently participating in a new research study called PREVENTABLE (Pragmatic Evaluation of Events and Benefits of Lipid-Lowering in Older Adults). This study investigates how taking a common statin medication, Atorvastatin (40 mg daily), can help adults aged 75 and over prevent dementia and heart disease.

"PREVENTABLE is a remarkable study for many reasons," said Jeffrey VanWormer, Ph.D., who is leading the local PREVENTABLE study team in Marshfield. "Statins have long been shown to reduce the risk of cardiovascular events, but there is little prior research in elderly populations."

PREVENTABLE is the largest randomized-controlled trial ever conducted exclusively in

older adults. It will eventually include 20,000 participants from over 100 sites across the U.S., including large healthcare and Veterans' Administration systems. Study participants without heart disease or dementia are randomly assigned to receive either Atorvastatin or a placebo, and are then followed over five years to examine key outcomes, including new dementia, cardiovascular disease (e.g., heart attack, stroke), and mild cognitive impairment.

With over 300 study enrollees to date, MCRI is among the top three PREVENTABLE recruitment centers in the U.S. Participants can join the study in person or remotely at home by phone or video. Study follow-ups can also occur online, by phone, and using electronic health records, and participants receive their assigned study drug by mail. The results of the PREVENTABLE trial will not be available for several more years, but this study will fill several evidence gaps regarding the usefulness of statins for healthy aging.

The PREVENTABLE trial is funded by the U.S. National Institute on Aging and is conducted in partnership with the Alzheimer's Association. To learn more about the PREVENTABLE trial and why it is important, visit the study website at [www.preventabletrial.org](http://www.preventabletrial.org).





# Highlights

## Improving future care

Cancer's burden on the patients we serve and their families remains incredibly high. Creating a research platform that can be used by researchers for years to come can help uncover ways to prevent cancer, detect it earlier, and improve the health of cancer survivors. This is the goal of the Connect study, which aims to recruit 7,600 Marshfield Clinic Health System patients. "We need research and we need people that are willing to participate so we can make advances in health care," said Roxy Eibergen, the first participant to sign-up for the study.



## The importance of sharing internationally

Several CCEPH investigators traveled to Northern Ireland to present research findings at the "Options for the Control of Influenza" conference. This is the only global scientific meeting with a dedicated focus on influenza. Kayla Hanson, M.P.H., gave a presentation on the effectiveness of the cell-based influenza vaccine; Jennifer King, M.P.H., presented results from a clinical trial of the immune response to influenza vaccination and a study of COVID-19 vaccine effectiveness; Maria Sundaram, Ph.D., presented results from an influenza B vaccine effectiveness study; and Joshua Petrie, Ph.D., presented results of a study of SARS-CoV-2 antibody levels in the local community.



## Networks to improve care

The Health Care Systems Research Network (HCSRN) aims to improve individual and population health through research that connects the resources and capabilities of learning health care systems. Robert Greenlee, Ph.D., M.P.H., served as the 2021-2022 elected Governing Board Chair and was invited to deliver the State of the Network plenary address at the annual HCSRN conference. Dr. Greenlee also presided over the annual spring board meeting prior to the conference and attended the network award ceremony following his presentation.



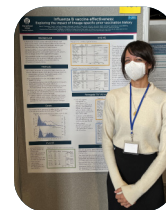
## Trauma research

Data show that low-density population areas have higher rates of trauma fatalities, thus quality rural trauma care and research can be a challenge. With the support of the health system, MCRI leaders across the institute conducted interviews and selected a candidate to help begin to fill this gap in our communities. Heather Rhodes, Ph.D., trauma scientist, joined MCRI in 2022. Rhodes stated that she "was drawn to MCRI to fulfill my passion and purpose in improving the quality of care in trauma and acute care surgery."



## Real-time impact

Throughout the pandemic and beyond, Maria Sundaram, MSPH, Ph.D., an infectious disease epidemiologist and associate research scientist, has been responding to clinician and patient questions regarding COVID-19. In 2022, Dr. Sundaram was featured in interviews with the New York Times and The Atlantic on COVID-19 epidemiology. From March 2020 to March 2022, she was a weekly COVID-19 guest expert for the BBC World Service Radio.



## A dedicated leader

Edward Belongia, M.D., joined the research institute in 1995 after completing an Epidemic Intelligence Service fellowship and working at Minnesota Department of Health. At that time, the center consisted of two M.D./Ph.D. level scientists and a small number of support staff. Since Dr. Belongia's appointment to center director in 2001, he has provided strong scientific leadership for a diverse epidemiology research group. Under Dr. Belongia's leadership, the center's scientific productivity and funding have increased dramatically thanks to the outstanding scientists, administrators and support staff who are committed to our research mission and consequential epidemiology. While Dr. Belongia will step down from the director role after 2022, he will remain with the institute as a senior research scientist and will continue to lead projects that improve overall care in areas of vaccine efficacy/effectiveness, immunogenicity, and vaccine safety.



## Translating research into care

**T**he Center for Precision Medicine Research (CPMR) continues to engage translational research for better understanding the genetic basis of diseases and for improving patient care. It has emphasized the discovery of human disease biomarkers including repurposing such biomarkers for U.S. Food and Drug Administration-approved cancer therapeutics through cancer cell lines. CPMR's achievements towards this goal were highlighted in 20 peer reviewed publications in 2022.

Breast cancer is all too common, but what if there was a minimally invasive diagnostic test to identify early breast cancers? The research of Dr. Srinivas Sathipati, Ph.D., concerns discovering microRNA-based biosignatures for the prediction of cancer diagnosis and survival. "These microRNAs tell us who has cancer and who doesn't, with more than 95% accuracy," Sathipati said. "If the researcher developed minimally or non-invasive methods for the diagnosis, it would be a breakthrough in cancer diagnosis."

CPMR's work in 2022 was diverse and encompassing. Zhi Wen, M.D., Ph.D., a cancer biologist, has employed mouse multiple myeloma cell lines and high-throughput screening of FDA-approved drugs. Together, these cell lines and screenings contribute to

combinatorial therapy with Trametinib and Ponatinib and can ameliorate drug-resistance and relapse of multiple myeloma. Using a cohort of more than 60,000 patients, Scott Hebbing, Ph.D., and Patrick Allaire, Ph.D., report with a high degree of confidence that shortening of the telomere (ends of the chromosome) is closely linked to a wide spectrum of diseases. Such associated diseases, range from multiple forms of cancer, infectious disease, to cardiovascular disease. Using a cohort of Marshfield Clinic Health System multiple sclerosis patients, Sanjay Shukla Ph.D., and colleagues showed a link between patient's genetic susceptibility and gut microbiome dysbiosis in multiple sclerosis. CPMR, meanwhile, showed both the financial and clinical benefits of pharmacogenetics testing in acute coronary syndrome patients.

A wide team of investigators collaborated on the research, including Milind Shah, M.D., Cardiology; Paul Thompson, M.D., Family Medicine; pharmacists Emili Leary, PharmD.; and Noah Budi, PharmD., geneticists and molecular biologists, Hebbing and Shukla. Finally, Tonia Carter, PH.D., is working to identify genetic variants that cause congenital heart defects and how treatments could target underlying genetic mechanisms.

*"If the researcher developed minimally or non-invasive methods for the diagnosis, it would be a breakthrough in cancer diagnosis."*



Srinivas Sathipati, Ph.D.





## Highlights

### Contributing to a national effort

Led by Scott Hebbring, Ph.D., and Sanjay Shukla, Ph.D., the Wisconsin consortium of the prestigious National Institutes of Health-funded *All of Us* Research Program has continued to collect data on Wisconsin participants. This national program aims to gather data from at least 1 million people living in the U.S. to accelerate research and improve individualized health care. The Research Institute and external partners have enrolled 32,000 Wisconsin participants.



### *All of Us* Research Program enrolling in more locations

Marshfield Clinic Health System began enrolling participants for the *All of Us* Research Program at several new locations in 2022. New enrollment sites include Marshfield Medical Center-Eau Claire, Marshfield Medical Center-Weston, and the Mosinee, Rhinelander, and Eagle River centers.



### Pharmacogenomics certificate program

The Certificate in Pharmacogenomics combines the field of pharmacology with the field of genetics to provide pharmacy students with foundational knowledge of how genes affect an individual's response to medications. This certificate program, supported in part by the Clinical and Translational Science Award program through the National Center for Advancing Translational Sciences, has been offered by MCRI since the summer of 2018. To date, 30 students have completed the unique two-week (80 hour) training experience. These students undertake their clinical careers understanding how to use the personalized genetic information of patients for better drug recommendations.



### Pharmacogenomics alerts

In 2019, CPMR and the Office of Research Computing and Analytics collaborated for MCRI to join other large academic health systems in implementing pharmacogenomic alerts aimed at helping patients get the right drug at the right time and at the right dose. "We are trying to implement customized clinical care using genetics," stated Scott Hebbring, Ph.D., research scientist at the Center for Precision Medicine Research, at the project's launch. Over the past four years, the research team has contributed countless hours executing the current 24 alerts existing within the medical record. These alerts allow providers the ability and opportunity to understand more about each patient's individual response to medications.



# Respiratory Syncytial Virus (RSV) trials aim to improve infant care

**E**ach winter RSV causes mild, cold-like symptoms that most people can shake off in a week or two; however RSV can be serious for infants.

But what if there was a vaccination that could reduce the symptoms and reduce RSV's risk for causing serious inflammation or infection in the airways?

Marshfield Clinic Researchers Peter Johnson, M.D., OBGYN; and Keith Pulvermacher, M.D., Pediatrics; are researchers with MCRI's Fritz Wenzel Center for Clinical Research and are local principal investigators for national studies of RSV vaccines.

Dr. Johnson is part of Pfizer's MATISSE (MATernal Immunization Study for Safety and Efficacy), an ongoing randomized, double-blinded, placebo-controlled Phase III clinical study aimed toward evaluating the safety, efficacy, and immunogenicity of its vaccine when administered to pregnant participants to help protect their infants from RSV disease after birth.

Vaccine efficacy of 81.8% for preventing severe lower respiratory tract illness was reported

through the first 90 days of life. The efficacy against severe illness was 69.4% for infants through the first six months. Marshfield Clinic Research Institute enrolled 11 mothers and 11 infants of the more than 7,400 pregnant women in this study.

Dr. Pulvermacher is involved in a study with Merck's MK1654 RSV drug, clesrovimab, a monoclonal antibody. The primary objectives of this phase 2b/3 double-blind, randomized, placebo-controlled study are to evaluate the efficacy and safety of clesrovimab in healthy pre-term and full-term infants. It is hypothesized that clesrovimab will reduce the incidence of RSV-associated medically attended lower respiratory infection in an infant's first 150 days post-dose compared to placebo.

MCRI has enrolled several participants in this nation-wide study of 3,300 participants. Study results are anticipated in 2024.

"If ultimately beneficial, this product will give us a much needed tool to help combat RSV in the most vulnerable age group," Dr. Pulvermacher said.

*Dr. Keith Pulvermacher and Dr. Peter Johnson not only see patients, but also are involved in the RSV research that is behind the care they provide.*



**Keith  
Pulvermacher, M.D.**



**Peter  
Johnson, M.D.**

### **Bardet-Biedl syndrome drug, studied at Marshfield Clinic, approved by FDA**

The U.S. Food and Drug Administration approved a chronic weight management drug for Bardet-Biedl syndrome (BBS) patients. Rhythm Pharmaceuticals' Imcivree (setmelanotide) injection for adult and pediatric patients 6 years of age and older is the first drug approved specifically for chronic weight management in patients with BBS, a rare genetic disease associated with early-onset childhood obesity. MCRI led the way by enrolling the most participants in the Rhythm-sponsored study and enrolling the youngest participant, said Jeremy Pomeroy, Ph.D., associate research scientist at MCRI.



### **Clinical Trials Day raises awareness**

The Association of Clinical Research Professionals leads Clinical Trials Day, a celebration that raises awareness of clinical trials and of clinical research as a career option among the greater public. It's no exaggeration to say that clinical trials save the lives of Marshfield Clinic Health System patients every day. MCRI undertakes more than 100 clinical trials across Marshfield Clinic Health System at any given time. "Clinical trials performed at Marshfield Clinic have given patients and their families hope, extended the quality of their life, and helped bridge the gap between research and care delivery," said Bobbi Bradley, M.P.H., M.B.A., Institute Research Administrator. "Every advance we make helps make a difference in the health of the communities we serve."



*To find a clinical trial offered at MCRI, visit [www.marshfieldresearch.org/clinicaltrials](http://www.marshfieldresearch.org/clinicaltrials).*

### **Acclaimed pediatric nephrologist retires**

In 2022, MCRI wished a fond farewell to Bob Haws, M.D., Center for Clinical Research director. Dr. Haws practiced clinically as a dedicated pediatric nephrologist with a deep passion for the BBS community. In 2014, he established the Clinical Registry Investigating Bardet-Biedl syndrome (CRIBBS), an international registry that examines the health of individuals with BBS. Dr. Haws also served as the Director for the Treatment Center for Bardet-Biedl syndrome from inception in 2013. Under his leadership, the Center was officially recognized as the Center of Excellence for Bardet-Biedl syndrome in 2019. Dr. Haws is continuing his support of patients through humanitarian efforts abroad.



### **Global Day encourages people to take action to raise awareness**

The second annual Bardet-Biedl syndrome Global Day is recognized across the world on September 24. At Marshfield, the day holds a special significance as members of the BBS Center for Excellence provide care to patients with BBS on a daily basis. "Families travel to Marshfield from around the world due to the camaraderie and expertise they know they will receive. The Health System is a home away from home for those affected by BBS," said Dr. Kelsie-Marie Offenwanger, child and adolescent psychologist.



*If you are a provider interested in participating in clinical research, contact **Steve Theis**, research navigator with the MCRI Office of Research and Sponsored Programs, at ext. 9-4496.*





# Training prepares current and future generations of firefighters, EMS

**T**ravis Serocki has trained extensively to prepare for his role as Owen-Withee-Curtiss Fire & EMS District Chief. When responding to a call for a tractor that overturned in September 2022, the practice and training he and his department underwent at National Farm Medicine Center's Agricultural Rescue Training possibly saved the tractor operator's life. Techniques learned at the training allowed rescuers to quickly and safely lift the tractor off the farmer, who was discharged from the hospital later that day with no more than bumps and bruises.

"Rescue operations on farms require specialized training," Serocki said. "The farm environment contains machinery, chemicals, toxic gases and other hazards that firefighters don't normally encounter. The classroom and hands-on sessions at Agricultural Rescue Training help us keep both our farm patients and ourselves safe."

The National Farm Medicine Center first offered farm rescue training in 1981, helping more than 1,400 firefighters and emergency responders learn the latest rescue techniques while navigating agricultural hazards. With that generation of local first responders retiring, a greater need to train the next generation emerged. Farm Medicine reintroduced the training in 2021 through philanthropic support from the Auction of Champions. In October 2022, more than 70 people from 31 fire and EMS agencies participated in the training.

Perhaps most importantly, 18 people were specifically trained to teach rescue techniques to other emergency responders, further spreading Farm Medicine's training to fire and EMS departments across rural Wisconsin.

The training includes a classroom session on another Farm Medicine program, Rural Firefighters Delivering Agricultural Safety and Health (RF-DASH). This program equips responders with safety consultation capabilities and farm hazard mapping strategies that they can share with farmers. Both Agricultural Rescue Training and RF-DASH are being adopted by fire departments across North America.

"Historically, many rural fire departments had members who grew up on farms, but that has changed," said Casper Bendixsen, Ph.D., director, Farm Medicine. "These trainings can help emergency responders feel more confident, not only on the rescue side, but on the injury prevention side as well."

Serocki says word is getting out.

"Interestingly, the patient under the tractor last September had watched the tractor rollover rescue demonstration at Wisconsin Farm Technology Days (a demo hosted by Farm Medicine), so he understood what we were doing while we were doing it."



## Highlights

### National Children's Center director testifies before Congress

Barbara Lee, Ph.D., director of the National Children's Center for Rural and Agricultural Health and Safety, testified Sept. 7 before the Workforce Protections Subcommittee of the House Committee on Education and Labor. The hearing, "Children at Risk: Examining Workplace Protections for Child Farmworkers," covered the current state of federal child labor laws and protections and policy proposals to improve them. The sub-committee invited Dr. Lee to provide perspective as an expert on health and safety issues facing child agricultural workers.



### 25th anniversary of National Children's Center

The National Children's Center for Rural and Agricultural Health and Safety celebrated 25 years of preventing injuries associated with the agricultural worksite, one of the nation's most hazardous worksites and the only one where children of any age may be present. Early accomplishments include the development of guidelines for parents to match chores with their child's developmental and physical capabilities. Follow-up data demonstrated a 56% decline in youth farm injury rates from 1998 to 2009. The center was established in 1997 with funding from the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.



### Sebold Award

Farm Medicine Director Casper Bendixsen, Ph.D., was selected as recipient of the 2022 Gwen D. Sebold Fellowship for Outstanding Research. The fellowship has been given by D. David "Dewey" Sebold since 1988 to recognize an outstanding researcher and support continued research in his or her field. "The Sebold Fellowship is a wonderful reminder that we're making meaningful contributions to the community," said Bendixsen. "I'm very appreciative of the Sebold family and Marshfield Clinic Health System Foundation. This award represents the positive energy produced when donors engage with our research teams. I'm humbled, to be sure."



### National Farm Medicine Center serves key data and reports

Public roadways remain a persistent site for fatalities related to farmwork-related fatalities, according to the Wisconsin Farm Related Fatalities report published this year. The report and others like it have been facilitated through a partnership that includes NFMC, MCRI, the University of Wisconsin (UW) Madison Division of Extension, and UW's College of Agricultural and Life Sciences. One important database compiled by NFMC for the creation of the reports has been AgInjuryNews.org, an interactive online tool built from publicly-available news reports and containing more than 4,000 cases. Today, researchers across the country use AgInjurynews.org for research, and it has been featured in numerous peer-reviewed articles.



### Research makes child care a Farm Bill priority

The nation's two largest farmer advocacy groups, American Farm Bureau Federation and National Farmers Union, have voted to include child care/early childhood education in their Farm Bill policy priorities. That's gratifying news for Florence Becot, Ph.D., and her colleagues, whose research is being used to develop solutions to support the health, safety and economic viability of the farm population. Congress will debate the Farm Bill in 2023. The Farm Bill is the primary agricultural and food policy instrument of the federal government. "As rural researchers, our conversations with policymakers suggest that there may be bipartisan support to help increase access to affordable quality rural child care as lawmakers hear from families," said Becot, an investigator with the National Children's Center.



### Remembering Dr. Gunderson

Paul Gunderson, Ph.D., former director of the National Farm Medicine Center (1992-96) and MCRI (1994-2000), died on Dec. 17 while clearing snow at his farm in Harvey, N.D. He was 82. During his years in Marshfield, Paul led Farm Medicine to national prominence, beginning with its establishment as one of the first National Institute for Occupational Safety and Health (NIOSH) agricultural research centers. He helped broaden the scope of Farm Medicine's research to include not only farm-related injury and exposure, but also medical illnesses related to farm exposures, particularly in the area of cancer.





# Tick-borne diseases: Improving care through translational and clinical research

**T**ranslational and clinical research advance patient care. Where the former implements advances made in basic research to clinical care, the latter documents safety and efficacy of such advances through clinical trials. MCRI researchers and Health System providers have advanced both aspects of research to improve patient diagnosis and care for those experiencing tick-borne illness.

We live in the Midwest's epicenter for Lyme disease, anaplasmosis, ehrlichiosis, babesiosis, and Powassan virus. These diseases spread through the bite of the *Ixodes scapularis* tick, colloquially known as the deer- or black-legged tick. Ticks carry both acute and chronic diseases, with more serious outcomes in certain populations. While most tick-borne diseases are readily treatable when recognized early, misdiagnosis of certain infections may result in serious outcomes. Accurate diagnosis is based upon patient history, clinical findings, and laboratory diagnostic tests.

"Unfortunately, in the case of Lyme disease, laboratory tests based upon detection of blood-stream antibodies may not be positive early in the infection when clinical symptoms first appear," said Thomas Fritsche M.D., Ph.D., Emeritus Researcher. "Reliance upon such tests may give the false impression that the patient is negative, requiring additional testing at a later date should a strong suspicion of infection exist."

Improving laboratory test accuracy when patients first present to their provider has been an important goal for researchers and the diagnostics industry. The Research Institute is recognized internationally for its development of improved diagnostics through participation in studies sponsored by the Centers for Disease Control and Prevention, and the Bay Area Lyme Foundation, and through partnerships sought by diagnostics and pharmaceutical industries for clinical trial participation.

Recently, the Integrated Research and Developmental Laboratory (IRDL) and Marshfield Labs participated in a national clinical trial sponsored by Zeus Scientific. This trial led to the first FDA approval of a novel diagnostic algorithm that enhances assay sensitivity early in infection. The algorithm also improves test specificity; participation in similar studies with other companies have followed suit. Other novel industry-supported research being conducted by IRDL and Marshfield Labs includes the detection of cellular immune responses prior to appearance of bloodstream antibodies.

MCRI scientists are recognized for their breadth in publications examining tick and disease organism ecology, immune responsiveness, clinical disease presentation, clinical diagnostics, and disease epidemiology. The Health System also participates in a phase III clinical trial assessing the safety and efficacy of a novel Lyme vaccine candidate with promise in earlier phase studies.





## Highlights

### Giving back to our community

In continued partnership with Soup or Socks and the Marshfield Area Community Foundation, Inc., Krystal Boese, assistant manager-research for IRDL, coordinated, encouraged, and collected donations from MCRI staff. Donations were collected in efforts to keeping area children warm this winter, having the best snow day, and ensuring that children had their best first day of school. The total collected for these three events included 488 items and a total of \$490.



### Giving back to our system

Over the summer, IRDL staff sold vegetables from their gardens to raise \$1000 for the Marshfield Clinic Health System Palliative Patient Care fund. They also collected over 100 blankets for the Marshfield Child Advocacy Center. These are given to comfort children who've endured trauma or abuse. The total collected for these two events included 116 blankets and a total of \$1,000.



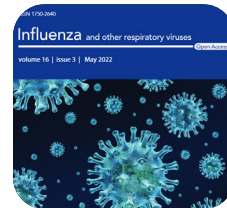
### Surprise visit

For more than a year, IRDL staff ran over 6,000 tests a week to support multiple COVID-19 vaccine and epidemiological studies for the Centers for Disease Control and Prevention (CDC). These efforts resulted in a surprise visit from Dr. Mark Thompson, the deputy chief of science for the Epidemiology and Prevention Branch of the CDC Influenza Division. During the visit Dr. Thompson noted that “the results from the laboratory work you all have done has given us the first estimate of the vaccine’s effectiveness now for the first wave post-vaccine, for the Delta wave and chances are you will be one of the first to do it for the Omicron wave.”



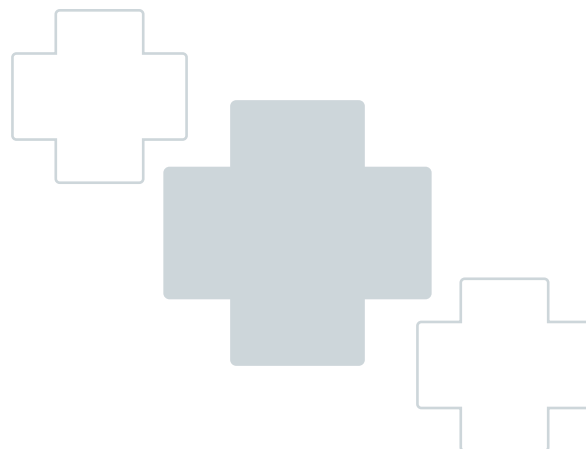
### Broad impacts

The tests and results not only affect clinical care at MCRI, but also have an impact on care provided across the country. The COVID-19 tests for adult populations conducted by IRDL and the corresponding results have been in use by the CDC since January 2021. On January 13, 2022, the CDC published an article that depicted the changes in vaccine effectiveness among COVID-19 vaccinated and unvaccinated individuals from January-September 2021.



### Clinical trial begins

Dr. Matt Hall, M.D., infectious disease physician and clinician researcher is leading the Pfizer Phase 3 clinical trial at MCRI. Vaccine Against Lyme for Outdoor Recreationists (VALOR) trial investigates the efficacy, safety and immunogenicity of their investigational Lyme disease vaccine. While the trial is worldwide, MCRI is the only research site in the Midwest. The trial has already enrolled more than 4,000 adults and 300 children.



## A peek behind the curtain

**R**esearch administration means more than filing paperwork, and the Office of Research and Sponsored Programs (ORSP) touches nearly everything the Research Institute does. From grants and support before research begins to helping publish articles raising standard of care for patients everywhere, ORSP is the bridge between our scientists and study teams to funding agencies and sponsors.

Of the countless proposals that pass through ORSP on a yearly basis, few reach the stunning sums of the \$20 million infrastructure project awarded to MMC Park Falls. Grants and contracts specialists in ORSP worked diligently to process and accept the award, which was announced by Gov. Tony Evers in March 2022.

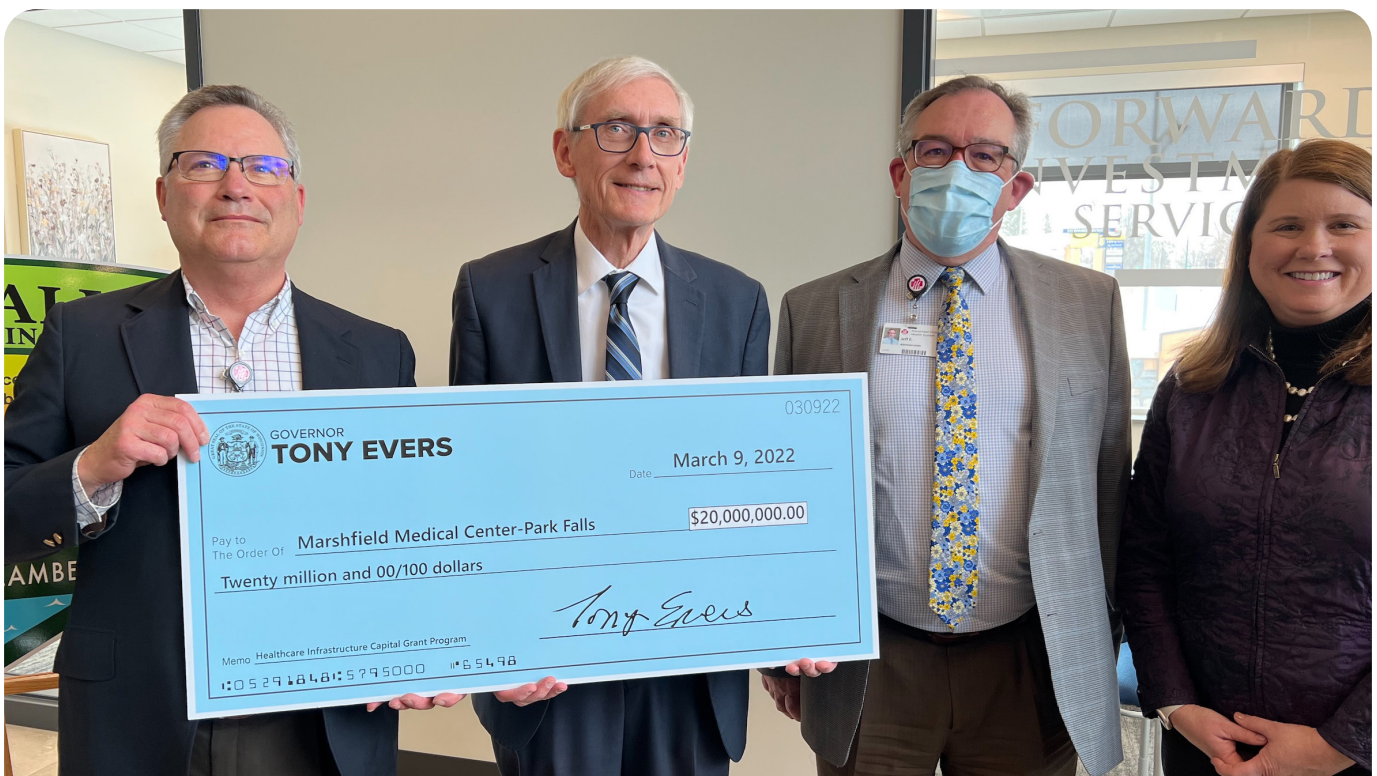
Brian Nikolai continued working with Integrated Research and Development Laboratory (IRDL) to secure additional COVID-19 research funding as a subrecipient. “Our IRDL lab was THE lab that processed specimens” for sponsors, he recalled, work that drew national attention.

Supporting research also means supporting publications. Marie Fleisner, editorial specialist, helped with several papers that saw print in 2022, including one on kidney failure and diabetes related to Bardet-Biedl syndrome,

“The One-and-a-Half syndrome with Trigeminal Cephalalgia,” and a chapter entitled “Rural and Agricultural Environments.” Publication venues included Clinical Genetics, Current Opinion in Endocrinology, Journal of Neuro-Ophthalmology, and the book Children’s Environmental Health. She also assisted with a paper on cancer care during the COVID pandemic in Nigeria.

David Puthoff, scientific writer, helped with publication of “The gut microbiome molecular mimicry piece in the multiple sclerosis puzzle” in *Frontiers in Immunology* and an article, “Childcare for farm families: A key strategy to keep children safe yet largely absent from farm programming,” for *Frontiers in Public Health*.

The ORSP team implemented new tracking, filing, and grant application tools and systems in 2022 and Project Manager Madalyn Palmquist helped the Research Institute more efficiently manage its data. The COVID-19 pandemic altered workflow as many staff worked remotely and ORSP transitioned from paper circulation and hand-off to remote and hybrid productivity. “The pandemic taught us the importance of adjusting our workflow to meet our business needs and we can smoothly move forward in our electronic world,” Palmquist said.



# Highlights

## An incredible accreditation effort

Every five years, the Food and Drug Administration conducts routine inspections of Institutional Review Boards. Marshfield Clinic's IRB was inspected in 2022, a massive undertaking that involved nearly all of the 15 ORSP staff, the IRB Chair, and colleagues from the Office of Research Computing and Analytics, aiding as FDA inspectors combed through years of records and procedures. The inspection was a success, with no findings.

Re-accreditation from the Association for the Accreditation of Human Research Protection Programs (AAHRPP) helps ensure organizations conducting human research maintain the highest ethical standards. After a multi-year process of record and document review, the Health System and MCRI's Human Research Protection Program welcomed AAHRPP site visitors to meet with members across the Research Institute. Their glowing review commended MCRI's research culture, especially our commitment to research and trials in rural areas. They also complimented our data integration, research protections, security review, and IS expertise in IRB review.



## Journal marks 20 years of publishing research

Clinical Medicine & Research (CM&R), a peer-reviewed publication released quarterly, reached its 20th year in 2022. Publications in CM&R are indexed in major U.S. and international databases of scientific information, which allows the potential for research outcomes to impact patient care at home and across the world. The 30 published 2022 articles were from authors around the world, including seven from Marshfield Clinic Health System authors. More than a thousand articles based on original scientific medical research on topics such as clinical research, preventive medicine, epidemiology, rural medicine and translational medicine have been published since 2003.



## Ethics Committee supports tough situations

The Marshfield Clinic Health System Clinical Ethics Committee serves as an interdisciplinary group of professionals from Health System hospitals, clinics and administrative offices who are responsible for developing and updating policies surrounding common medical ethical issues, case reviews, and consultations. "We offer educational sessions on such topics as principles of biomedical ethics, ethics and pediatrics, spirituality and ethics, ethical considerations in gerontology, end of life decisions, medical futility, and advance directives and power of attorney for health care," said Elizabeth Buchanan, Ph.D., director of ORSP and committee coordinator.



## Oral Health research spotlight

The American Medical Association Journal of Ethics published a MCRI-authored article that detailed improvements in diabetes care at the Health System after integrating medical and dental electronic health records. The article was authored by Neel Shimpi, B.D.S., Ph.D., associate research scientist at the Center for Oral and Systemic Health and Elizabeth Buchanan, Ph.D., director of the ORSP and staff senior research scientist. Their paper demonstrated and validated that integrating medical and dental care, supported by use of informatics, can deliver high-quality care at reduced cost.





# Revealing personalized care recommendations through data integration

**W**hat if changes in your DNA could make you more susceptible to serious side effects of a commonly prescribed medication? Precision Medicine, an emerging area of healthcare, helps clinicians understand so-called “drug-gene interactions” with enormous implications for use of certain medications. These insights can be communicated to your healthcare provider as “pharmacogenetic alerts” and have been available in our homegrown, electronic medical record (CattailsMD) for years for specific research populations and across specific medications.

When the Health System implemented Cerner, an integrated medical record, across our ambulatory and acute care settings, the Office of Research Computing and Analytics (ORCA) had an opportunity and an obligation to bring forward those historical alerts. In addition to bringing the historical information into the new medical record integration, ORCA began expanding the scope of alerts with new genetic testing vendors. The new partnership ensures ongoing personalized care and safety of our patients.

This work entails a defined orchestration of data movement via an HL7, or Health Level 7, integration. This integration allows for transfer of electronic data across disparate systems that follow a standard definition and format. Determining the appropriate steps for the alert to trigger and inform the care team has required the expertise and close partnership of many staff within the Center for Precision Medicine Research, Health System Lab Operations, Information Services-Interoperability and Integration Services, Provider and Pharmacy Solutions, Ancillary Solutions, and the ORCA team. Placing an order transforms the information flow into structured data that triggers the alert and makes associated documents available, ultimately informing the care team. Testing this process from end-to-end is a complex chain of events requiring inputs from each of these areas. Implementation is anticipated to occur in February 2023.

*“We are working hard behind the scenes to facilitate communication of these pharmacogenetic alerts to clinicians to help improve patient safety and plan to further improve upon and expand these alerts over time.”*



Lynda Kubacki-Meyer,  
ORCA director

## Highlights

### Biospecimen tracking in REDCap

ORCA's REDCap team is paving the way in REDCap to allow tracking of biospecimens. Their Biospecimen Tracking External Module makes specimen tracking possible in REDCap and has caught the eyes of many in the REDCap community. Medical studies contain thousands of samples, and the REDCap module employs efficient coding that allows staff to enter and track these samples quickly. The most challenging part has been setting up validation, which provides accuracy when entering samples. The module is expected to be complete in early 2023 with a release to the REDCap community for global utilization.



### Research Analytics and OneSystem

ORCA collaborates with other MCRI Centers, internal and external scientists, quality and care delivery staff, and clinicians. Together, they identify and incorporate appropriate data sources, develop data models or tools, and deliver analyses that accelerate scientific discovery analysis from bench to bedside, thus improving the delivery, quality, and safety of care. In 2022, the team continued to assist clinicians and researchers in determining the feasibility of their research projects and supporting the data and analytical needs for their approved research studies. 2022 was a year of incorporating and understanding new data sources. With all acute and ambulatory sites converted over to Cerner by early 2023, it was a journey to investigate and understand where new workflows were introduced, the impact to downstream data sources, and the process for identifying where these new sources reside in our data repositories. Through collaboration with MCHS IS and the Analytics Center of Excellence, ORCA was able to confidently apply these new sources to feasibility requests, research studies, and data models.



### Oral health support tools improve clinical decision

A study team developed a key tool for integrating its medical and dental electronic health records. By alerting primary care providers to conduct a visual oral examination of patients with diabetes, the tool supports clinical decisions in oral health. It has resulted in additional referrals from the providers for dental care. In addition, a similar tool was created for dentists using informatics techniques. The study team screened patients for risk of developing diabetes using their medical and dental records. This enabled dentists to refer patients at high risk of developing diabetes to physicians. "The establishment of medical-dental interoperability, via EHR integration, supported development of informatics tools and integrated service delivery which facilitated patients' access to prevention and management interventions for chronic diseases such as diabetes," said Dr. Neel Shimpi, associate research scientist at the Center for Oral and Systemic Health.



# \$1 million donation recognizes the Fritz Wenzel Center for Clinical Research

**T**he name Frederick J. “Fritz” Wenzel is legendary at Marshfield Clinic Health System. Fritz Wenzel has helped shape the organization both through his professional career and as a philanthropist. His legacy has culminated with a \$1 million donation from his son, Tom Wenzel, to name the Fritz Wenzel Center for Clinical Research in honor of his father.

Fritz Wenzel served as executive director of the Health System from 1976-93 and was instrumental in its growth and success. He also served as the interim director of the Research Institute and continues to serve on the Health System Board of Directors.

“Having worked with Fritz when he served as the interim director of the Research Institute, his commitment to more full integration of research into the Health System’s mission was evident every day,” said Jennifer Meece, Ph.D., current Research Institute interim director. “He continually advocated with leadership the importance of the Research Institute in making our system of care different and better. This opportunity to honor Fritz and support medical research is a demonstrable testimony to his passion for making a difference in health care and research.”

The Wenzel family has a long history of supporting the Health System, including establishing the Fritz Wenzel Science Conference.

This milestone \$1 million gift to research from Tom Wenzel will be used to create an endowment that expands MCRI’s applied and translational research programs, expanding access to research for patients across the Health System and improving health in our rural communities. When the gift was announced, Fritz also announced a \$250,000 donation to add to his son’s support.

“Each of his gifts has been extremely thoughtful, but the \$1 million gift announcement to honor his dad was a day I’ll always remember,” said Teri Wilczek, chief philanthropy officer at Marshfield Clinic Health System Foundation. “For Fritz to show his gratitude and continued support with another \$250,000 donation of his own made it even more special. The Wenzels are a remarkable family and their dedication to our mission is inspiring.”





## Highlights

### Golden Autumn Moon

The Auction of Champions, presented by Miron Construction, raised nearly \$250,000 to support the work of the National Farm Medicine Center. “Auction of Champions continues to mean an incredible amount to our rural community,” said Tiffany Halan, Foundation director of operations. Themed as The Golden Auction and held Sept. 15 at RiverEdge Golf Course in Marshfield, the annual gala generated proceeds to support trauma research and other programs dedicated to keeping farmers healthy, happy, and safe.



### Golf Fore Research

On August 16, 144 golfers teed off at Lake Arrowhead Golf Club in Nekoosa to support the 23rd Golf Fore Research, presented by The Boldt Company and Solarus. This year’s event raised nearly \$65,000 to support pediatric cancer and cancer research at the Research Institute. The funds will help provide essential resources to researchers as they continue to find better ways to screen, diagnose and treat cancer. Through this support MCRI can “continue to make a difference in the lives of the patients we serve by offering access to clinical trials and care they might otherwise be able to obtain or may have to travel great distances to obtain” said Jennifer Meece, Ph.D., Research Institute interim executive director.



### Cruise for a Cause

Dan and Linda Neve continued to support cancer research right here in Wisconsin by cruising for the cause of research and healthcare. Dan travels across the state and country year-round, raising funds at car shows. He ends each year in Wisconsin Dells during the first weekend of October with a golf tournament and a car show of his own. In 2022, Cruise for a Cause made a donation of \$160,267 to Marshfield Clinic Health System, bringing their total donations over the last 12 years to nearly \$1 million!



### Security Health Plan supports aid for those affected by Huntington’s disease

Security Health Plan’s Employee-Driven Corporate Giving Program is helping achieve the goal of creating local awareness and support for people living with Huntington’s and their families one step closer to reality. The Security Health Plan donation will go toward community resources and clinical research. “Researchers are actively investigating the genetic mutation that causes Huntington’s and finding ways to lessen the severity of Huntington’s symptoms,” said Debbie Zwickey, social worker with the Huntington’s Disease Society of America (HDSA).



Marshfield Clinic  
Health System  
Foundation

**Interested in supporting the work at Marshfield Clinic Research Institute, visit [marshfieldclinic.org/giving](https://marshfieldclinic.org/giving) or contact Rikki Harry, Director Philanthropic Programs, Marshfield Clinic Health System Foundation, [harry.rikki@marshfieldclinic.org](mailto:harry.rikki@marshfieldclinic.org) or 715-387-9247.**

# BY THE NUMBERS



## Rural Roots

**65** clinical locations in  
**45** communities

**713,947** people in the  
**33** counties we serve

**45%** of the population  
are our patients



## Investigators and Staff

**304** active  
Researchers

**45** Ph.D. and M.D.  
Scientists

**124** Clinician  
Researchers

**222** Research and  
Support Staff



## Projects

**292** new and  
continuing reviews  
completed by the  
Institutional Review  
Board

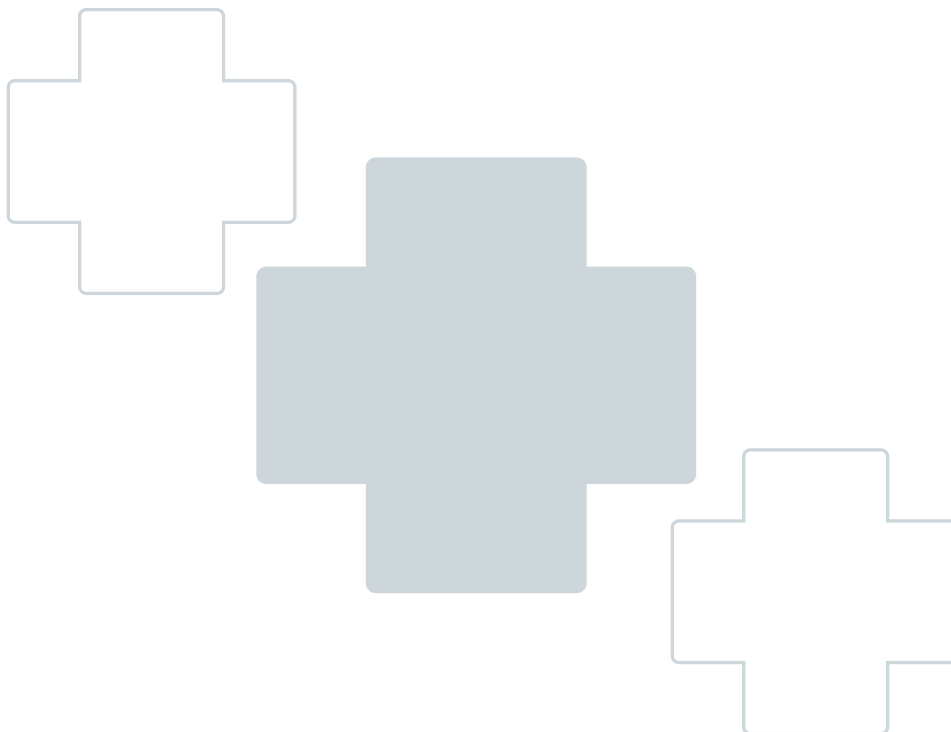
**20** Resident research  
projects supported

**51** active clinical trials

**25** active clinician-  
lead clinical trials

**26** active MCRI-lead  
clinical trials

**20** active donor-  
funded projects





## Awards

- 118** external grants and contracts received
- 41** new and continuing Marshfield Clinic Health System grants and contracts
- 77** new and continuing Research Institute grants and contracts
- 15** new donor-supported projects awarded
- 59** new and continuing clinical trial contracts received



## Publications and Media

- 39** authors cited on Research Institute publications
- 131** unique Research Institute publications
- 2** Opinion Letters to Editor
- 101** Original Research
- 1** Original Research Letter to Editor
- 26** Published Abstracts
- 1** Review
- 963** digital mentions of “Marshfield Clinic Research Institute” on news media, health care, research and blog websites.
- 10** media releases distributed that focused on research



## Research Environment

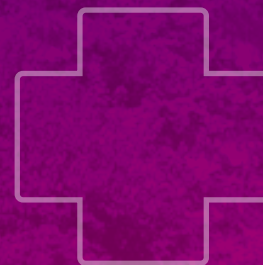
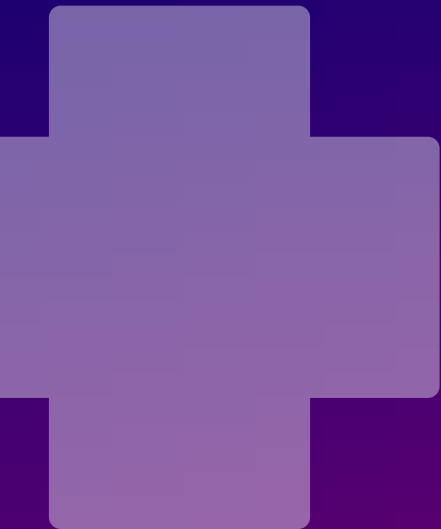
- 11** Hospitals
- 65** Clinical Locations
- 10** Dental Clinics
- 1,600+** Providers
- 13,000+** Employees
- 350,000+** Unique Patients



## Financial Overview

- \$36,197,512.70** in external grants and contracts awarded (includes state, private and federal)
- \$9,540,624.46** awarded to support Marshfield Clinic Health System projects
- \$26,656,888.24** awarded to support Research Institute projects
- \$2,407,559.80** in support utilized from our donors
- \$8,221,619** awarded to support clinical trials





# Marshfield Clinic Health System

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