Marshfield Clinic
Research Institute

Research Matters **June 2017**

Research Matters is a monthly newsletter published by Marshfield Clinic Research Institute.

Director's Report

Frederick Wenzel, Interim Executive Director

June has been a busy month with activities encompensing the planning of future research and securing funding for MCRI projects.

The Family Health Center Board of Directors will be providing funding for the re-creation of the dental model within MCIS Clinicals which was a part of the MCIS dental software found in Cattails. Under the leadership of Amit Acharya BDS, PhD, Director of the Center for Oral and Systemic Health, the project will begin in September of this year. The model will enable dental records to become part of the patient's medical record as is currently found in Cattails.

Dr. Barbara Lee and the National Children's Center for Rural and Agricultural Health and Safety received notice of its $1.2 million renewal funding from the National Institute for Occupational Safety and Health (NIOSH) at the CDC. Established in 1997 as part of MCRI's National Farm Medicine Center, the National Children's Center is the leader in setting voluntary guidelines to protect children who live, visit and work on farms.

Two research projects submitted for the internally-funded Clinician Scientist Collaborative Research Award were reviewed and scored by the Research Committee earlier this month. Drs. Paula Aston and Sanjay Shukla submitted a project entitled "The Role of Gut Microbiome in Multiple Sclerosis" while Drs. David Kim and Scott Hebbring proposed "Exploration of Telomere Biology in Seborrheic Keratosis and Cancer, Utilizing Genome-Wide/Phenome-Wide Association Studies and Tissue-Based Techniques". Based on scoring, both projects were recommended for funding and have been forwarded to the MCRI Board of Trustees for final approval.

Work on the MCRI strategic plan continues with Center Administrators operationalizing the plan strategies. Several strategies have already been completed and a number are underway. The Center Directors have been assigned the task of establishing priorities within a research growth plan for the future. This aspect of the plan will involve facilitated sessions and a report that will be completed in an August /September timeframe.

Work on the reestablishment of the Precision Medicine biobank continues with internal funding from donors and the potential for external funding as well. We are seeing an increasing interest among MCHS donors in genetic studies and the philanthropy foundation has adopted this project as one of its priorities.

In the next several weeks discussions between the staff of the Trauma Center and Institute scientists will be held to develop a plan for establishing a trauma research program as part of

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Director's Report

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the qualification for the movement from a Level II Trauma to a Level I Trauma Center in Marshfield. The discussions will center around the research necessary to fulfill the requirements as laid out by the American College of Surgeons.

Conversations have begun with the Institute for Quality, Innovation & Patient Safety (IQIPS). Of special interest is work in the area of health services research. MCRI representatives including Robert Greenlee, PhD, Jeff VanWormer, PhD and Fritz Wenzel met with Kori Krueger, MD and IQIPS staff to discuss potential joint projects and relationships.

Associate Director's Report

Steve Ziemba,
Associate Director

Hope everyone is enjoying the warmer weather…at least on the days when we have warmer weather! It has been cool and rainy, and my garden has not been taking well to it. Regardless, be sure to take advantage of getting outside and having some downtime as you can. The stress and pressures at work can affect individuals negatively and is something we all experience. Getting away from the office, desk or lab (what have you) is needed, and helps greatly in terms of refreshing oneself. I hear people say that the work will just be that much greater when they get back or that they can't leave because of certain projects. These are certainly true and realistically part of our environment and not just at Marshfield Clinic either. They are also factors that can be handled, though exactly how depends on the situation. The point is to get away for some period of time, regain your perspective, and come back to continue the great work MCRI is engaged in.

Recent Publications and Grants

Each month, MCRI researchers and MC clinical investigators are active publishing journal articles and seeking research funding. Please select the hyperlink to view recent publications. There were no new grants for May.

If you have recently published an article or received a grant or an award and want it included in the next issue of *Research Matters*, please contact Patti Baer at baer.patricia@mcrf.mfldclin.edu

MCRI On The Move

The **Research Compliance** department has moved from ML7 to the first floor of the Lawton Building. **Linda Jaros, Molly Dowden,** and **Julie Graves** are now located at **1R5**.

BIRC currently has a **Project Scientist I, PhD** position open. This position is eligible for an ERP bonus if your referred candidate is selected. Applicants should visit HR's Career Opportunities webpage to apply.

MCRI Welcomes New Staff

Brooke Delgoffe joined the **Research Analytics team** in **BIRC** on May 15. Brooke obtained a Bachelor of Science degree in Psychology (Applied Statistics minor) from Grand Valley State University (GVSU) in Grand Rapids, Michigan. More recently she completed a Master of Science in Biostatistics from the same institution. Brooke has nearly five years of experience working with SAS, including work with preclinical trial pharmaceutical data at MPI Research. She coauthored a paper on hospital readmission rates, which will be presented at an upcoming conference. Brooke is originally from Menominee, Michigan and enjoys outdoor activities, reading, dancing, and listening to music.

Judith Hase joined **CCEPH** on May 15 as a **Project Manager**. Hase has over 16 years of experience as a project manager with the Defense Advanced Research Projects Agency (DARPA) located in Arlington, VA. Hase is also pursuing a master degree in project management. Hase will be working closely with Jeff VanWormer, PhD to manage the Rural Engagement in Primary Care for Optimizing Weight Reduction (RE-POWER) pragmatic trial. This trial is currently managed by Tenisha Hill, MPH, who will be leaving MCRI in July to attend medical school.

Jake Howey joined **CCEPH** on May 15 as an **Assistant Manager**. Howey comes from FHC Marshfield Clinic Dental Center, where he also held an assistant manager position. Prior to Marshfield Clinic he worked at Roehl Transport as a Fleet Manager for 6 years. He earned his undergrad in business administration at UW-Stout, with a minor in Speech and Military Leadership. Howey has almost served 15 years in the Wisconsin National Guard. He currently serves as the Company Commander at the Forward Support Company, 724th Engineer Battalion.

Please welcome **Outreach Specialist Melissa Ploeckelman** to **NFMC**. Ploeckelman graduated in 2010 from the University of Wisconsin-River Falls with a BS in agricultural education. While attending college she served as the 2006-2007 State FFA Parliamentarian, was named 2008 Marathon County Fairest of the Fair, and selected the 2009 State Fairest of the Fairs, attending 47 county, district and state fairs in one summer. She joined the Colby School District in 2011 where she was the Ag instructor, FFA advisor and Youth Apprenticeship coordinator. Ploeckelman, who grew up on a dairy farm in Stetsonville, is experienced in outreach, presentations and media interviews, as well as event, activity and project planning. Her first tasks at the Farm Center include assessment of the center's outreach efforts and taking the lead on the center's website and social media strategy.

CCEPH Researcher to Serve on Advisory Board

CCEPH Senior Research Scientist Robert Greenlee, PhD, MPH has recently accepted an invitation to serve on the Research Advisory Board for the Medica Research Institute (MRI). Medica is a non-profit health insurance company based in Minneapolis, MN with about 1.2 million members. MRI formed in 2010 as the research arm of Medica, and has a mission focused on population health, health policy, and informatics research. The Board includes 8 scientists involved in health policy at the national level or in health delivery research in academic or other health system settings. Dr. Greenlee attended his first annual in-person Research Advisory Board meeting in June, and will continue to provide input on the Institute's research agenda through regular discussions with MRI executive director, Kristina Bloomquist.

Dr. Greenlee had previous interaction with MRI and their director through the Governing Board of the Health Care Systems Research Network (HCSRN), where he served as the on-boarding mentor for MRI when they joined the HCSRN several years ago.

Long-time Collaboration Continues Despite the Distance

Dr. Joseph Mazza, Senior Emeritus Research Scientist

As part of the Marshfield Clinic Emeritus Program, Dr. Joseph Mazza assists in providing current staff with guidance, assistance and mentoring as well as engaging in research himself and continuing to publish papers. Launched in 2011, the program aims to keep former healthcare and research staff connected to MCHS, their colleagues and the community.

One example of this is the connection Dr. Mazza maintains with long-time collaborator Dr. Steven Yale, former Director of the Clinical Research Center at MCRI and a General Internist. Both have been involved in clinical research and education at MC/MCRI and combined have published hundreds of peer review articles. Despite the physical distance (Dr. Yale now resides in Florida while Dr. Mazza remains in Wisconsin), over the past two years their rewarding partnership has resulted in 4 manuscripts. Both continue to stay in close contact and look forward to collaborating on research projects in the future. Recent manuscripts include:

- Erythrocyte Sedimentation Rate and C-Reactive Protein Measurements and Their Relevance in Clinical Medicine in WMJ
- Thromboembolic complications following a first isolated episode of superficial vein thrombosis: a cross-sectional retrospective study in J Thromb Thrombolysis
- Treatment-Related Cardiovascular Outcomes in Patients with Symptomatic Subclavian Artery Stenosis in Cureus
- The Clinical Significance of Relative Bradycardia submitted to WMJ (5/17)

Compliance Notes

The following article - "Don't 'shun' your research compliance officer" appears here with permission from the Health Care Compliance Association. Contact HCCA at 952-405-7937 with reprint requests. It originally appeared in the May 2017 issue of Compliance Today.

Don't "shun" your research compliance officer
by Kelly M. Willenberg, DBA, RN, CHRC, CHC, CCRP

Do you "shun" your research compliance officer? Merriam-Webster's Dictionary states the meaning of shun as "to avoid deliberately and especially habitually."

I meet research compliance officers around the country who feel as though people purposely avoid them. I sometimes see people who think if they keep away from a Research Compliance Office, then they are safe from any scrutiny. Are you like this?

Research is an emo"shun"al issue at some institutions. Compliance can invoke an agitated feeling amongst peers. This is unfortunate for research compliance officers, because they have a tremendous amount of responsibility. Is it because people are scared of what it means? My experience is that people are emotional about research compliance, because they have a lack of understanding of the consequences. Intense feelings come from that anxiety. How can you direct these feelings toward a positive outcome? Educate and train your team members on compliance in a positive manner and avoid the emotions involved with it.

Research compliance officers have to consider their role in a logical, sensible way. They are trying to be ra"shun"al! They are usually logical in their thinking. Sometimes a gut feeling by a research compliance officer is all I need to dig further when my team is performing an audit or review. Being rational sometimes is the best course of action, even when it's intense.

Staff need to understand that they can choose to embrace compliance if they want to. Voli"shun" is the cognitive process by which an individual makes the decision to commit to a particular course of action. Volition is using one's will and choosing to accept compliance. I sometimes tell clients to embrace research compliance and find physician champions who will not be irra"shun"al about process improvement. Many times, bringing the right champion into the fold is one of the necessary solu"shuns."

Horace is quoted as saying "While fools shun one set of faults, they run into the opposite one." All sites have faults or imperfections in research compliance. The goal of your research compliance officer is to help eliminate errors, correct imperfect"shuns," and transform weaknesses into strengths. Do not allow them to go at it all alone. Meet compliance head on with intent and collaboration, and you will turn your shortcomings into a solu"shun!"

Compliance Presentation
The Office of Research Compliance's June meeting of the Quality Improvement/Best Practices Workgroup included a presentation that discussed the definitions of research, human subjects and non-human subjects research, as well as the defining characteristics of proposed activities that are determined to be Exempt or are able to be reviewed via the IRB Expedited review mechanism. This presentation was recorded and may be downloaded for viewing.

Updates from ORIP/IRB

Lori Scheller,
IRB Administrator

Humanitarian Use Devices (HUD)

In the US, there are two common pathways for medical products intended for very small populations to reach the market. For pharmaceuticals, this pathway is known as orphan drug designation, and is for medicines intended to treat diseases affecting fewer than 200,000 people.

For medical devices, this pathway is known as the humanitarian device exemption (HDE), and is intended for products meant to treat diseases affecting fewer than 4,000 people per year. Devices seeking approval via this pathway are first given designation by Food and Drug Administration (FDA) as a humanitarian use device (HUD), similar to how orphan drug designations. The pathway is unique in that it does not require testing to prove that the HUD is effective for its intended purpose. Rather FDA only requires that a company provide data to show that it is safe – "will not expose patients to an unreasonable or significant risk of illness or injury" – for its intended population. In addition, the devices still need to illustrate a "probable benefit to health".

Use of a HUD for clinical treatment and/or diagnosis of a condition without collection of safety or effectiveness data is not considered human subjects research. However, the FDA still requires an IRB to initially review and approve local HUD use, as well as conduct continuing reviews.

The IRB's "Humanitarian Use Device" procedure for Marshfield Clinic Research Institute outlines the requirements for obtaining an approved HDE, its use and review requirements. Effective June 2017 this procedure has been revised to include the following:

- Name Change from MCRF to MCRI throughout the document
- Sect. 3.2(a) IRB Review currently states that the IRB will consider training and expertise of physicians who use the HUD. This has been changed to also include health care providers.
- Sect. 3.2.(a) Labeling now includes a statement that HUD Labeling shall specify the training requirements for practitioners who may use the device as approved. In addition, the device should be labeled with the fact that it is a HUD, what its approved use is and the reporting requirements if used in an emergency situation, which is 5 business days.
- Sect. 3.2(c) Emergency Use now includes Emergency Use or Off-Label use requirements.

2017 Oral-Systemic Health Conference "The Importance of Integrating Medical and Dental Care for Patients with Diabetes"

The Center for Oral and System Health (COSH) at Marshfield Clinic Research Institute recently hosted the 2017 Oral-Systemic Health Conference at the Kalahari Convention Center in Wisconsin Dells, WI, on June 1st – 2nd. The theme of the conference was "The Importance of Integrating Medical and Dental Care for Patients with Diabetes."

Back left to right: Yvonne Cerne, Nadine Punke, Dr. Ingrid Glurich, Dr. Neel Shimpi, Dixie Schroeder, Dr. Amit Acharya, Annie Steinmetz, Harshad Hegde, Alok Sagar Panny, Dr. Adham Abdelrahim Front left to right: Katelyn Kleutsch, Callahan Katrak

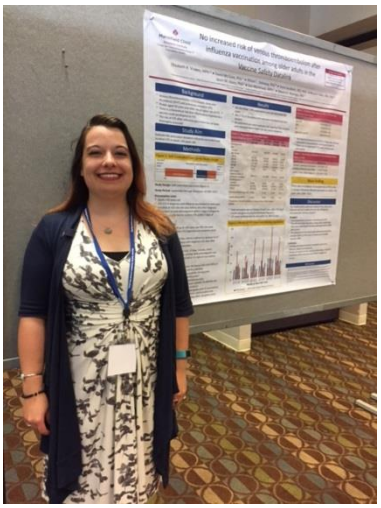
Over 100 healthcare professionals including medical and dental providers, scientists, and executive leaders throughout Wisconsin and surrounding states came together to network and learn more about this important topic. This conference featured two keynote speakers, Dr. Jerry Brown and Dr. George Taylor, along with many other excellent providers and professionals. Strong attendance and positive feedback from attendees attested to the high clinical relevance of this topic and excellence of the program and presenters.

The conference had three main objectives:

1. Discuss the importance of oral health among diabetic patients and the dental providers' key role in screening for dysglycemia
2. Discuss Wisconsin statewide pilot efforts geared towards integrating oral health management of patients with diabetes between medical and dental providers
3. Discuss the potential cost savings and the economics of medical-dental care integration

Dr. Amit Acharya and the COSH team were thankful for the important research grant support from Delta Dental of Wisconsin which made the conference and the COSH research presented at the conference possible.

MCRI Scientists and Staff Present at the Annual Vaccine Safety Datalink Meeting



The MCRI Vaccine Safety Datalink (VSD) Team attended the annual VSD meeting May 23-24 in Oakland, CA. MCRI is one of nine health care organizations that participate in VSD. VSD is a collaborative project with CDC to monitor safety of vaccines and conduct studies about rare and serious adverse events following immunization. VSD started in 1990 and MCRI joined VSD in 2001. Presentations by MCRI Scientists/Staff included:

- David McClure, PhD, gave an oral presentation titled, "Feasibility of near real time influenza vaccine safety assessments during pregnancy".
- Elizabeth Vickers, MPH, presented posters on "Investigating Vaccine Safety Outcomes During the Transition from ICD-9 to ICD-10" and "No increased risk of venous thromboembolism after influenza vaccination among older adults in the Vaccine Safety Datalink".
- Burney Kieke, MA, presented a poster on "Flexible Software Infrastructure for Conducting Rapid Cycle Analyses".
- Erica Scotty, MA, participated in a panel discussing MCRI's experience on an NLP project to assessing adverse events following vaccination.

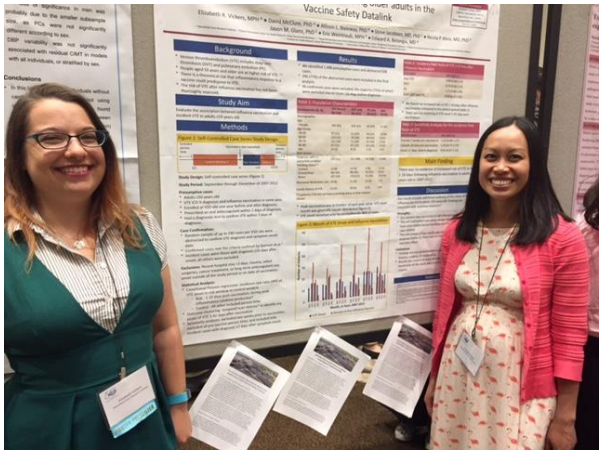
BIRC Director Presents at 3rd Annual CPCP Retreat

On June 1st, Peggy L. Peissig, PhD, Research Scientist, CRIO, and BIRC Director presented at the Center for Predictive Computational Phenotyping (CPCP) Third Annual Retreat hosted by the Wisconsin Institutes for Discovery at UW-Madison. The day-long program featured presentations about using Big Data to improve human health. Also in attendance from BIRC were Eric LaRose, BS; Jon Badger, PharmD; John Mayer, PhD; and Ahmad Pahlavan Tafti, PhD.

Dr. Peissig presented "Entity Matching Using Magellan: Matching Drug Reference Tables" to address the challenge of matching large amounts of non-standardized data, often spelled or abbreviated differently, from multiple sources. Using Magellan and the assumption that drugs with shared active ingredients should have similar 1) efficacy for disease treatment and 2) risk of adverse events, expert review proved validation with 99.18% precision and 95.29% recall. The presentation was based on work done by LaRose, Badger, and Peissig along with Pradap Konda and Dr. Anhai Doan from UW-Madison.

The CPCP's mission is to develop innovative computational and statistical methods and software for a broad range of problems that involve extracting relevant phenotypes from complex data sources and predicting clinically important phenotypes before they are exhibited. The CPCP investigates how to exploit a wide array of data types for these tasks, including molecular profiles, medical images, electronic health records, and population-level data.

CCEPH Scientists Present Research at SER



Huong McLean, PhD and Elizabeth Vickers, MPH attended and presented their research at the 50th Society for Epidemiologic Research (SER) Meeting in Seattle June 20-23. SER brings together epidemiologists from all stages (trainees to senior scientists) to discuss emerging epidemiologic research.

Poster presenters and associated MCRI authors included:

- No increased risk of venous thromboembolism after influenza vaccination among older adults in the Vaccine Safety Datalink
  Authors: Elizabeth Vickers, David McClure, Edward Belongia
- Mumps and measles antibody responses after receipt of second and third doses of measles, mumps, rubella (MMR) vaccine
  Authors: Huong McLean, Tenisha Hill, Emma Seagle, Edward Belongia

BIRC Paper Accepted to AMIA 2017 Annual Symposium

Elham Sagheb Hossein Pour recently had her paper entitled “Stage-Specific Survivability Prediction Models Across Different Cancer Types” accepted to the AMIA 2017 Annual Symposium. Elham and her advisor at UW-Milwaukee, Dr. Rohit Kate, collaborated on the paper which explains that for the most cancer types, the stages are sufficiently different and it is best to build survivability prediction models for each stage independently. Few exceptions were found when the number of training examples in a stage, for cancer types with consistently low survivability rates overall all stages, were insufficient. They also determined evaluation survivability models (which were built on all stages) by a test set of all stages is overestimated and the best approach is to evaluate such models with test sets of each stage separately. This type of evaluation also leads them to show that survivability prediction varies among the stages and is generally worse for cancer incidences on higher stages. The AMIA 2017 Annual Symposium will be held November 4th-8th in Washington, DC.

Volunteer Opportunity

Hub City Days
The 7th Annual Hub City Days Duathlon **July 28 and 29** is looking for volunteers for multiple opportunities. Volunteers are needed for the Kids Duathlon Friday evening, July 28 and Saturday morning, July 29. The Duathlon benefits Marshfield Clinic Youth Net, a youth development program serving 8-18 year olds living in the Marshfield area. The program targets educational and academic success, development of personal and social skills and participation in recreational activities and supervised community service opportunities. Register here to volunteer.

Upcoming Talks and Presentations

PreventionGenetics Seminar Series
All seminars take place in Helix Hall at PreventionGenetics.

Thursday, July 20th
10:30-11:30am
Speaker: Juan Dong, PhD, FACMG, PreventionGenetics
Topic: NGS Panel Testing for Skeletal, Skin, and Dental Disorders

Grand Rounds (12:15-1:00 p.m. in the Froehlke Auditorium)

There will be no Grand Rounds on July 28th.

Friday, July 7th
Beyond Screening: Medication Management of Transgender Patients
James Meyer, MD, Pediatrics Primary Care, Marshfield Clinic

Friday, July 14th
Oral Health: What Primary Care Providers Need to Know
Deepak K. Neelagiri, DDS, Neillsville Dental Care; Kristie Virden, RDH, Neillsville Dental Care; Srinivas Challa, DMD, MPH Neillsville Dental Care; and Deann Hanson, RDH, Neillsville Dental Care

Friday, July 21st
Journey from CKD to ESRD to Renal Transplant - A Review
Sandesh Parajuli, MD, MBBS, Transplant Nephrologist, UW-Madison

In Addition:

- The next MCRI Full Staff meeting is scheduled for August 3, 2017 at 10:00AM in the Froehlke Auditorium. Questions can be routed or emailed to Jeanette Normington at 1R3 or normington.jeanette@mcrf.mfldclin.edu.
- The next Board of Trustees meeting will be held on September 13, 2017 at 6PM in the Laird 50 conference room.
- For the latest UW-ICTR news, please visit: https://ictr.wisc.edu/news/.
- For updates on the Wisconsin Network for Health Research (WiNHR), please visit: https://ictr.wisc.edu/winhr
- The Marshfield Clinic Research Institute website can be accessed through this link: http://marshfieldresearch.org/.
- Archived issues of *Research Matters* are available online.

Contributors to this issue: Patti Baer, Bobbi Bradley, Yvonne Cerne, Molly Dowden, Dr. Robert Greenlee, Scott Heiberger, Linda Jaros, Stephanie Karl, Dr. Joseph Mazza, Dr. Huong McLean, Elham Sagheb Hossein Pour, Lori Scheller, Laurel Verhagen, Michelle Wellsandt, Frederick Wenzel, Dr. Steve Ziemba.

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