March 2017

Aurora Research Institute Patient-Centered Research Annual Report, 2014

Follow this and additional works at: https://digitalrepository.aurorahealthcare.org/ahc_books

This Document is brought to you for free and open access by the Aurora Health Care at Aurora Health Care Digital Repository. It has been accepted for inclusion in Aurora Health Care Books, Documents, and Pamphlets by an authorized administrator of Aurora Health Care Digital Repository. For more information, please contact aurora.libraries@aurora.org.
Purpose, Vision, Values

**Purpose:**
We help people live well through innovative research.

**Vision:**
Offer more treatment choices and improve patient outcomes through research and innovation.

**Values:**
- Every patient and community deserves the best care
- Resources should be managed responsibly
- A healthy workplace is built through accountability, teamwork and respect

**Value Proposition:**
Innovative research centered on improving choices and outcomes for patients

- A premier destination health care system offering more treatment options for patients
- Research that is patient-centered and held to the highest standards of quality and ethics
- Attract talented and innovative clinicians focused on finding better ways to help patients
- Educational outreach that not only touches individuals, but transforms the health of communities
- National recognition and reputation for innovative research through scholarly publication and presentations

The information presented in this annual report is intended for general information and educational purposes. It is not intended to replace the advice of your own physician. Contact your physician if you believe you have a health problem.
Table of contents

President’s welcome message ........................................................................................................................................ 3
Aurora’s Way Forward .................................................................................................................................................. 4
Research Business Services ........................................................................................................................................ 5
Clinical Trials Department ........................................................................................................................................ 7
Sponsored Programs Office/Investigator-Initiated Research Department ................................................................. 9
Regenerative Medicine/Laboratory Research ........................................................................................................... 11
Journal of Patient-Centered Research and Reviews .................................................................................................. 13
Research recognition events ....................................................................................................................................... 14
Education and philanthropy ......................................................................................................................................... 15

Cardiovascular research ................................................................................................................................................ 19
  CIRCA ....................................................................................................................................................................... 23
  Research highlights .................................................................................................................................................... 25
  Cardiovascular volumes ........................................................................................................................................... 33
  Cardiovascular publications .................................................................................................................................. 34

Oncology research ........................................................................................................................................................ 37
  TORQUE .................................................................................................................................................................. 41
  Early Phase Cancer Research Program .................................................................................................................. 43
  Research highlights .................................................................................................................................................... 44
  Oncology volumes ..................................................................................................................................................... 47
  Oncology publications ............................................................................................................................................ 48

Neurosciences research .................................................................................................................................................. 49
  Research highlights .................................................................................................................................................... 51
  Neurosciences volumes ............................................................................................................................................ 56
  Neurosciences publications ..................................................................................................................................... 56

Additional strategic research ......................................................................................................................................... 57
  Precision Medicine research .................................................................................................................................. 59
  Orthopedic research and volumes .......................................................................................................................... 61
  Women’s Health research and volumes .................................................................................................................. 63
  Aurora UW Medical Group research ....................................................................................................................... 65
  Center for Urban Population Health ........................................................................................................................ 67
  Research highlights .................................................................................................................................................... 69
  Additional strategic publications .............................................................................................................................. 71
President’s welcome message

We are excited to present the Aurora Research Institute 2014 Patient-Centered Research Annual Report, a gauge of recent innovative research achieved throughout Aurora Health Care.

Such achievements include implantation of the first leadless pacemaker in Wisconsin and study of an innovative way to remove brain clots through coordination of a nationwide clinical trial. Aurora was awarded several competitive federal grants – one for participation in the National Cancer Institute Oncology Research Program (NCORP), which expands local access to clinical trials, and another for the SMARTCare project, which aims to advance cardiovascular care while saving costs. Other highlights include receiving National Institutes of Health funding to study genetic testing as a means to offering precision (personalized) medicine, and renewal of a U.S. Department of Defense grant to continue our Knowledge-Based Nursing Initiative.

Through the partnership with Discovery World, our cardiovascular researchers educated the community in a direct, interactive way. Our philanthropic efforts were returned as His Highness Sheikh Khalifa bin Hamad Al Thani, Tim and Vivian Sullivan, and so many others gave generous gifts to support research.

Our successes are too numerous to recount here. Paging through this report, I trust you will be as proud as I am of all the tremendous research at Aurora.

For our patients who span the globe, Aurora Research Institute represents innovative research centered on improving choices and outcomes that change not only the lives of individuals, but transform the health of populations. Our Journal of Patient-Centered Research and Reviews helps advance scientific breakthroughs to patients and medical professionals spanning more than 70 countries and six continents.

On behalf of Aurora Research Institute and its newly formed board of directors, I am pleased to provide this highlight of our 2014 outcomes and, as always, I welcome your feedback.

Helping people live well through innovative research,

Randall Lambrecht, PhD
Senior Vice President, Aurora Health Care
President, Aurora Research Institute

Aurora Research Institute
Board of Directors

Aurora Research Institute is governed by a board of directors that consists of Aurora Health Care leaders who oversee the strategic and financial decisions that shape the institute’s future.
CONTRIBUTING TO AURORA’S WAY FORWARD

2015 AND BEYOND

AURORA RESEARCH INSTITUTE ENGAGES ...

Caregivers
- With regular learning opportunities
- Through relevant research-related news

Researchers systemwide and beyond
- Through quarterly publication of Journal of Patient-Centered Research and Reviews
- With more than 180 scientific journal articles/textbook chapters and more than 130 abstracts published last year
- By offering intramural grant opportunities totaling more than $530,000 annually for heart and cancer studies
- With recognition for outstanding research efforts

Patients and survivors
- With treatment options they can’t get elsewhere
- Through programs that lead to better outcomes and promote adoption of healthy lifestyles

Generous donors
- To enhance research on the aging heart and research performed by fellows
- To provide educational opportunities and advance medicine

Communities and stakeholders
- With the Aurora Health Satellite through a partnership with Discovery World
- Through public outreach, collaboration with American Heart Association
- At speaking engagements for the Clinical Trials Education Network of Wisconsin and others

Policymakers
- For development of SMARTCare software to improve care for patients with stable ischemic heart disease
- Through designation as a National Cancer Institute Community Oncology Research Program site to expand cancer clinical trial offerings
- With nursing education through a U.S. Department of Defense grant

AURORA RESEARCH INSTITUTE ENHANCES ...

- Care for the people Aurora serves by providing more choices and improved outcomes through innovative research
- Data analysis with digital analytics staff and biostatistician support
- Health care savings by managing finances responsibly

AURORA RESEARCH INSTITUTE GROWS ...

- The Wisconsin First strategy by being the first in Wisconsin to offer the latest treatments through research like a leadless pacemaker and stem cell therapies

AURORA RESEARCH INSTITUTE TRANSFORMS ...

- Research into new treatment options for the people Aurora serves
- Populations through collaboration with Center for Urban Population Health

AURORA RESEARCH INSTITUTE INNOVATES ...

- New technologies and treatments of care delivery like the integrated surgical approach to remove brain clots
Kurt Waldhuetter
Vice President, Research Business Services

Waldhuetter leads the Research Business Services team, which is responsible for Aurora Research Institute's business operations and planning as well as pursuing collaborative opportunities.

Research Business Services

Senior research business analyst Julie Basquin, MS, serves as a liaison to the Finance Department and helps facilitate resource planning for Aurora Research Institute, with budget planning and financial monitoring and reporting services.

2014 expenditures: $16.5 million

- Foundation support: $1,406,576
- Grants and awards: $2,152,504
- Clinical programs: $837,361
- Other: $400,287
- Institutional investment: $7,144,899
- Industry contracts: $4,607,127
Biorepository and Specimen Resource Center

*Powered by ORBIT (Open-Access Robotic Biorepository and Informatics Technology)*

Led by **Natalie Polinske, MS**, the Biorepository and Specimen Resource Center (BSRC) provides leftover and prospectively collected tissue and blood samples for research uses ranging from Alzheimer’s disease to ovarian cancer to congestive heart failure.

More than 100,000 patients have consented for their leftover biospecimens to be used for research purposes.

The BSRC is powered by ORBIT (open-access robotic biorepository and informatics technology) and supported by the Research Analytics team, led by **Andy Marek**. Through Aurora Health Care’s electronic health record database, Research Analytics aids in the transformation of data into new knowledge and medical-decision support.

---

**Fostering innovation**

Aurora Health Care caregivers often come up with new ways that could achieve better health outcomes, reduce costs or redefine the patient experience. Research business innovation manager **Don Conrad** reviews intellectual property for commercialization consideration.

*In 2014:*

- 16 biospecimen requests fulfilled
- 868 biospecimens distributed

---

**Clinical Trials Business Services and Grant Contracting**

Contract services are vital to deliver investigational treatment options to patients.

Led by **Katie Richter**, the Clinical Trials Business Services team assists with contract budgeting, including medical coverage analysis, and contract negotiations. Contract services also are necessary to facilitate the acceptance of grant funding.

*In 2014:*

- 78 grant contract agreements completed
- 46 clinical trial contract agreements completed
- 64 confidentiality disclosure agreements completed

---

*Research associate Anne-Marie McAnelly works with a blood sample.*

*The Clinical Trials Business Services team at work.*
Clinical Trials Department

Sara Planton, BSN
Director, Clinical Trials Department

Planton runs the Clinical Trials Department, which provides access to cardiovascular, oncology, neuroscience and other investigational treatments before they are available elsewhere. More than 300 active drug, device, procedure and registry clinical trials are supported by over 70 caregivers, including managers, coordinators, specialists and educators. More than 1,100 patients enrolled in a clinical trial throughout Aurora Health Care in 2014.

Cardiovascular team

Led by Wendy Schmidt, RN, the Clinical Trials Department cardiovascular team coordinates clinical trials in the areas of cardiac surgery, interventional cardiology and electrophysiology and for conditions such as pulmonary hypertension, peripheral vascular disease, structural heart disease, heart failure and other cardiovascular disease conditions.

“The most exciting experience for my team is to have the opportunity to provide cutting-edge technology to cardiovascular patients and families and see many trial outcomes advance to FDA approval for commercial use,” Schmidt said.

Oncology team

The oncology team, led by Jan DeBartolo, MSN, coordinates clinical trials on breast, lung, colorectal, prostate, gynecologic, hematologic, renal cell and other cancers.

“Aurora Health Care was the recipient of an NCORP grant,” DeBartolo said. “More trials will be opened in shorter time frames. Thirty-three new cancer trials were approved in 2014. There were 28 more enrollments in cancer clinical trials in 2014 over 2013. We anticipate an even larger degree of change in 2015.”
Manager Carol Tutino, BSN, MS, leads the neurosciences team, which coordinates clinical trials on brain cancer and surgery, stroke, epilepsy and interventional radiology. She also oversees AsthmaNet studies and orthopedic and women’s health research.

“In 2014, stroke studies were opened to support Aurora St. Luke’s certification as a Comprehensive Stroke Center. MiSPACE, a minimally invasive technique to remove blood clots from the brain, was opened as a multicentered registry study with Aurora St. Luke’s as the coordinating center,” Tutino said.

A joint venture between BayCare Clinic and Aurora Health Care, Aurora BayCare Medical Center offers the latest clinical trials, which are held to the same high standards as throughout the Aurora system. The team is led by Annette Paul.

“2014 was a building year with a push for innovative, physician-driven studies that cover multiple specialties and continued growth in orthopedics research,” Paul said.
Sponsored Programs Office/Investigator-Initiated Research Department

Vani Nilakantan, PhD
Director, Sponsored Programs Office and Investigator-Initiated Research Department

Dr. Nilakantan directs the Sponsored Programs Office (SPO) and leads the Investigator-Initiated Research (IIR) Department. The SPO serves as a central coordinating hub for Aurora Health Care’s externally and internally funded research and other projects. The IIR Department facilitates studies in which the researcher takes responsibility for all aspects of the project as sponsor. Dr. Nilakantan also oversees the Animal Research and Care Program.

Sponsored Programs Office

The goal of the SPO team is to assist principal investigators in their efforts to secure extramural research funding (pre-award) and ensure compliance with regulations, terms and conditions (post-award).

In 2014, the SPO tracked awards totaling $5,161,750 – a success rate of 30%, which is nearly double the pay line rate for National Institutes of Health research projects. The SPO also is responsible for administering three intramural grant award programs (two cardiovascular and one cancer) and supported the funding of 14 pilot grants totaling $533,686 in 2014.

The team includes a dedicated program administrator to manage Aurora’s National Cancer Institute Community Oncology Research Program award of $3.87 million over five years. The funding will help expand access to cancer clinical trials in Wisconsin (see page 39).
Across the Aurora system, researchers are engaged in investigator-initiated research and are invested in developing ideas and studies that lead to patient-centered outcomes.

The IIR Department facilitates such research with senior research scientists with diverse expertise in areas of cancer, cardiovascular, epidemiology, pharmacogenetics and informatics. The scientists and senior biostatisticians are aligned with the clinical system programs and collaborate with internal (cancer, cardiovascular, women’s health, neuroscience, etc.) and external (University of Wisconsin’s Milwaukee and Madison campuses, Harvard University, Vanderbilt University, Medical College of Wisconsin, etc.) investigators, and conduct their own investigator-initiated research.

The work done by the IIR Department is supported by intramural (cardiac awards, cardiovascular surgery award, cancer care award) and extramural funding from federal (National Institutes of Health, Department of Defense), industry (Genentech Inc.) and foundations (Rock River Cancer Research Foundation).

The IIR team also supports investigators with development of methods, study design and execution of research.

**In 2014:**

- 16 manuscripts published
- 50+ abstracts presented/accepted by the team

**Research regulatory specialist, associates and coordinators**

Available to all Aurora researchers, the research regulatory specialist ensures compliance of investigator-initiated research with federal regulations and helps investigators with Institutional Review Board and Institutional Animal Care and Use Committee submissions.

- Project-dedicated research associates and coordinators support sponsored investigator-initiated research studies.

**Animal research and care program**

**David Krum, MS,** oversees operation of the Electrophysiology Basic Research Laboratory and the animal research and care program.

The animal program abides by the Institute for Laboratory Animal Research standards outlined in the Guide for the Care and Use of Laboratory Animals, the Public Health Service policy for all vertebrate animals and the U.S. Department of Agriculture’s Animal Welfare Act. All research protocols are supervised by Aurora’s Institutional Animal Care and Use Committee.
Regenerative Medicine Center/
Laboratory Research

Nina Garlie, PhD
Director, Regenerative Medicine Center

Dr. Garlie leads the Regenerative Medicine Center. Research conducted through the center is directed at using the body’s own healing and immune processes to develop new treatments for life-threatening diseases. The center also includes translational research laboratories that focus on a variety of specialties. Laboratory manager Bob Stoltz, MBA, MT, oversees lab staff, which includes associates, assistants, technologists and technicians.

Regenerative Medicine Center

The Regenerative Medicine Center, located at Aurora St. Luke’s Medical Center, integrates research and clinical care in an environment conducive to innovation. Physicians and research scientists work together to develop personalized approaches to treat diseases, learning from the patient’s body and its ability to recognize and fight disease, then heal and regenerate.

The center houses the Autologous Stem Cell Transplant Program, an accredited clinical service providing expert coordinated care and high-quality stem cells for patients with cancer. The goal of this 20-year program is to continually research and develop the best treatment approaches to improve outcomes for transplant patients.

Results from a research study conducted by this lab in 2014 suggests that the stem cell collection procedure for patients undergoing stem cell transplantation can be shortened without affecting the ability to reach target numbers of stem cells required for successful transplant.

Transplant and Histocompatibility

Led by Martin Oaks, PhD, the scientific focus of the Transplant and Histocompatibility Research Laboratory is to characterize the antigens and antibodies that are relevant to long-term survival of solid organ transplants.

A primary research area for the lab is the characterization of the anti-inflammatory (healing) properties of certain subpopulations of antibodies found in transplant patients. These antibodies are decorated with unique sugar structures that appear to engender them with the ability to suppress rejection of the transplanted organ.

A second area of interest is characterization of harmful versus innocuous antibodies that are reactive with antigens present on transplanted organs. Recent findings identified antibody populations that are believed to be not harmful to the transplant, and work continues to characterize the reactivity and molecular targets of these antibodies.
Endocrinology

The focus of the Endocrine Research Laboratory, led by Hershel Raff, PhD, is hypothalamic-pituitary-adrenal function.

As part of a basic research study, investigators are evaluating the development of neonatal adrenal function and the role of the hypothalamus and pituitary therein. The pituitary-adrenal adaptation to critical illness is a clinical research focus. New laboratory approaches to evaluate endocrine function in patients is another area of study for this lab.

Neurosciences

The Neurosciences Research Laboratory was developed in late 2014 to initiate a brain tumor stem cell bank in collaboration with Aurora’s Biorepository and Specimen Resource Center.

Tumor samples obtained from patients undergoing brain surgery are analyzed in the lab to identify, isolate and expand cancer stem cells. Testing of these samples and expansion of this research program will be the goals of this lab in 2015.

Cardiovascular

Laboratory-based research of the Sheikh Khalifa bin Hamad Al Thani Center for Integrative Research on Cardiovascular Aging is on pages 23 and 24. Clinical and preclinical cardiovascular work with stem cells is on pages 25 and 26.

Oncology

Targeted laboratory-based research includes experimental cancer therapeutics and immunotherapy.

Experimental cancer therapeutics

Researchers are working on new mechanism-based drugs to treat various cancers. The goal is to develop new approaches to prevent or treat cancers through a better understanding of the genes and pathways underlying their pathogenesis.

Research areas of interest include tumor proliferation, invasion and metastasis, cell signaling, apoptosis, angiogenesis, protein-protein and protein-DNA interactions, and epigenetic alterations in the cancer. The hope is to provide novel therapies that avoid or overcome chemotherapeutic drug resistance and most importantly, prolong the lives of cancer patients.

Immunotherapy

Monocytes may have both positive and negative roles in cancer development and therapy. Researchers are exploring the role of monocytes in killing cancer cells when stimulated by antibodies. Findings show a necessity for high levels of antigen expression for monocytes to become activated. This may partially explain why antibodies used against HER2/neu are not effective in breast cancers that do not overexpress the antigen.

Monocytes also may inhibit the immune response, thus assisting in tumor growth and spread. Researchers are studying methods in which immune suppression may be inhibited so we can improve immunotherapy of cancer.
The fourth issue of Journal of Patient-Centered Research and Reviews (JPCRR) capped off an impressive first year for Aurora Health Care’s scientific journal.

Largely funded by a generous donation from the Robyn Temkin Memorial Fund and led by Editor-in-Chief Dennis Baumgardner, MD, JPCRR was launched in February with a melanoma-themed issue overseen by guest editor Michael Thompson, MD, PhD, and immediately caught the eyes of researchers around the world, spurring well-received submissions from health centers in Oklahoma, Texas, Tennessee, Canada and Italy.

The regional research community also took note of Aurora’s entry into publishing, and JPCRR received praise from health professionals across Wisconsin in an April feature by Milwaukee Journal Sentinel.

Capitalizing on that early momentum, JPCRR launched an interactive website and Twitter feed (@JPCRR), resulting in thousands of article downloads over just a few months. An issue focused on the burgeoning field of cardio-oncology, overseen by guest editors Charles Bomzer, MD, and Bijoy Khandheria, MD, provoked positive feedback from readers in Ireland, India, Taiwan and the Democratic Republic of the Congo.

“The broad scope of topics makes JPCRR an appealing source of clinical guidance to both primary care physicians and multidisciplinary specialists,” Dr. Baumgardner said.

Following its successful debut, JPCRR plans to further grow its author, audience and article diversity in 2015. The journal’s double-blind peer-review process ensures unbiased evaluations of a manuscript’s scientific strengths and weaknesses.

It is important to recognize that JPCRR is first and foremost dedicated to improving patient care. Everyone from patients to students to clinicians can access journal content from current and archived issues at www.aurora.org/jpcrr.

Original submissions to JPCRR are welcome at any time.
Caregivers recognized for achievements in research

Recognizing achievements in research is one way Aurora Research Institute engages researchers throughout Aurora Health Care.

The Research Awareness Committee coordinated the institute's fifth annual Greater Milwaukee Clinical Research Recognition Event on Sept. 10, 2014, at Aurora St. Luke's Medical Center. The event highlights achievements in research by Aurora caregivers in the Greater Milwaukee area.

2014 Greater Milwaukee award recipients

Clinical Trials Research Award
Thomas Saphner, MD
Michael Thompson, MD, PhD

Investigator-Initiated Research Award
Anthony DeFranco, MD

Collaborative Research Award
Judy A. Tjoe, MD

Senior Investigator Award
Daniel O'Hair, MD

New Investigator Award
Michael Anderson, MD

Innovation Award
Amin Kassam, MD

Research Champion Award
A. Jamil Tajik, MD

Research Service Award
Anthony Chambers, BSN
Lisa Klement
Maharaj Singh, PhD

2014 Green Bay award recipients

Medical Educator of the Year Award
Erik Johnson, MD

Medical Education Curriculum Development Award
Cardiology Department

Research Fellow in Sports Medicine
Rebecca Yde, DPT
Joe Woldt, DPT
Kate Jochimsen, DPT

Principal Investigator of the Year Award
James Gapinski, MD

Innovation Award
Robert Limoni, MD

Research Support Award
Ashley Heesacker
Jean Dill, NP
Denise Barnes, RN

Greater Milwaukee area award recipients: (back row, from left) Thomas Saphner, MD, and Anthony Chambers, BSN, and (front row, from left) Maharaj Singh, PhD, Michael Anderson, MD, Judy A. Tjoe, MD, Michael Thompson, MD, PhD, Daniel O'Hair, MD, Lisa Klement and Amin Kassam, MD. (Not pictured: Anthony DeFranco, MD, and A. Jamil Tajik, MD.)

Aurora BayCare Medical Center held its sixth annual Fall Research and Medical Education Reception on Oct. 15, 2014, at Aurora BayCare Orthopedic and Sports Medicine Center. The event highlights achievements in research and education by Aurora and BayCare Clinic caregivers in the Green Bay area.

2014 Green Bay award recipients

Medical Educator of the Year Award
Erik Johnson, MD

Medical Education Curriculum Development Award
Cardiology Department

Research Fellow in Sports Medicine
Rebecca Yde, DPT
Joe Woldt, DPT
Kate Jochimsen, DPT

Principal Investigator of the Year Award
James Gapinski, MD

Innovation Award
Robert Limoni, MD

Research Support Award
Ashley Heesacker
Jean Dill, NP
Denise Barnes, RN

Before the ceremony in Green Bay, Robert Limoni, MD, unveiled several orthopedic innovations he is bringing to market.

Before the ceremony in Green Bay, Robert Limoni, MD, unveiled several orthopedic innovations he is bringing to market.
Aurora Research Institute cultivates future health care researchers

Education and outreach are important tenets of research. That’s why Aurora Research Institute offers many research opportunities for students over the summer.

Seven talented student interns gained valuable insights to the different components of the institute and, in turn, offered support on a variety of research initiatives during the Summer Student Intern Program. The program accepts students from around the country who spend 8-10 weeks conducting patient-centered research projects.

“Our investigators value the support the students provide to further the institute’s patient-centered research,” said Vani Nilakantan, PhD, director of Investigator-Initiated Research/Sponsored Programs Office for Aurora Research Institute. “And having the clinical research experience they gain at Aurora on their resumes will open many doors for these students.”

Institute investigators also mentored five students who were afforded a 10-week opportunity to gain hands-on, biomedical research experience because of the generosity of medical staff, who donate to Aurora Health Care Foundation’s Medical Staff Endowment Fund.

“The researchers give their time to these students to make a difference,” said Hershel Raff, PhD, of the Endocrine Research Laboratory.

Not only does the institute provide these summer student program opportunities, but it supports inquisitive volunteers who benefit from working with and learning from experienced investigators at the Sheikh Khalifa bin Hamad Al Thani Center for Integrative Research on Cardiovascular Aging (CIRCA) at Aurora St. Luke’s Medical Center.
Meet the summer student interns

**THERESE (TESS) BATTIOLA**
Mentors: Arshad Jahangir, MD; Ekhsno Holmuahmedov, PhD  
Year/University: junior/University of Wisconsin-Madison  
Project: Review records for appropriate shocks in patients who received an implantable cardioverter-defibrillator (ICD) and determine the possible association of echocardiographic measures of cardiac function to ICD shock

**LYDIA GARLIE**
Mentors: Scarlet Shi, PhD; Vinay Thohan, MD  
Year/University: junior/University of Wisconsin-Madison  
Project: Investigate the differential effect of simvastatin on atrial and ventricular fibroblasts from the human heart

**ALESSANDRA DEFRANCO**
Mentors: Arshad Jahangir, MD; Farhan Rizvi, PhD; Ekhoon Holmuahmedov, PhD  
Year/University: junior/Mount Holyoke College, South Hadley, Mass.  
Project: Investigate the differential effect of simvastatin on atrial and ventricular fibroblasts from the human heart

**ZACHARY GRESE**
Mentors: Natalie Polinske, MS; Anne-Marie McAnelly  
Year/University: graduate/Marquette University, Milwaukee, Wis.  
Project: Examine the effects of long-term storage at -20 C, multiple freeze thaw cycles and ambient transport of blood specimens by identifying the quantity and quality of DNA present

**MACK GUENTHER JABLONSKI**
Mentor: Hershel Raff, PhD  
Year/University: junior/Lawrence University, Appleton, Wis.  
Project: Evaluate the function of the adrenal gland in a rat model of premature birth

**SOIBHAN KELLEY**
Mentors: Vani Nilaikan, PhD; Sara Planton, BSN  
Year/University: senior/University of Rochester, N.Y.  
Project: Compare postoperative acute kidney injury rates between geriatric patients receiving cardiac and abdominal procedures; set up templates for quarterly clinical trials dashboard

**KINGSHUK MAZUMDAR**
Mentors: Arshad Jahangir, MD; Ekhsno Holmuahmedov, PhD  
Year/University: sophomore/Union College, Schenectady, N.Y.  
Project: Evaluate differences in sensitivity of naive and activated fibroblasts to apoptotic cell death stimuli

**ALEX REDDY**
Mentors: Andy Marek, John Klehm  
Year/University: sophomore/University of Wisconsin-Milwaukee  
Project: Write an internal web application allowing biorepository staff to access specimen metadata and manage studies

**JUSTIN ROUNTREE**
Mentor: Ahmed Dalmar, MD  
Year/University: junior/Carroll University, Waukesha, Wis.  
Project: Evaluate HER2/neu overexpression in women with primary diagnosis of Stage IV breast cancer

**STEVE SAWYER**
Mentors: Judy A. Tjoe, MD; Sanjay Kansra, PhD  
Year/University: second year, Creighton University School of Medicine, Omaha, Neb.  
Project: Identify predictive biomarkers in early stage breast cancer

**PAYDEN WHITE**
Mentors: Vicki Soerens; Julie Walters; Katie Klein; Joe Grundle; Kurt Walduhuetter  
Year/University: sophomore/University of Wisconsin-Madison  
Project: Update research website content, review new Intellectual Property Policy and assist with a multitude of clerical and administrative projects

**MELISSA WONG**
Mentor: John Richards, PhD  
Year/University: senior/Washington University in St. Louis, Mo.  
Project: Evaluation of immune cell-mediated tumor killing using herceptin as a model

**CIRCA summer volunteers**
- Esha Afreen, Marquette University, Milwaukee, Wis.
- Adil Bhatia, Brookfield Academy, Brookfield, Wis.
- Madeline Bireley, University of Wisconsin-Madison
- Zachary King, Johns Hopkins University, Baltimore, Md.
- Nate Kluge, University of Wisconsin-Madison
- Nick Kluge, University of Minnesota, Minneapolis
- Kennedy Ringelberg, University of Wisconsin-Madison
- Ramali Siddiqui, University of Wisconsin-Madison
- Fong Wang, Concordia University Wisconsin, Mequon, Wis.
- Callie Weers, Northwestern University, Evanston, Ill.

**Carl Kaiser** (teacher), Marquette High School, Milwaukee
Caregivers who care

In an organization dedicated to improving outcomes for patients, it’s not surprising to find that Aurora Research Institute caregivers have big hearts.

Throughout 2014, in a variety of ways, those caregivers supported agencies and funds with missions to change lives for the better.

Discovery World
(see page 21 for full story)

Aurora Research Institute's Nina Garlie, PhD, and Arshad Jahangir, MD, coordinated a unique educational outreach opportunity, Aurora Health Satellite: Your Mighty Heart, at Discovery World, Milwaukee’s science and technology center.

From March through May, medical and research experts invested countless hours, sharing their knowledge as part of an interactive exhibit and through heart health educational workshops that featured innovative research and medical procedures at the frontier of cardiovascular health.

American Heart Association

Aurora Research Institute has strong ties with American Heart Association. In September, Vani Nilakantan, PhD, captained a walking team and spearheaded a community outreach booth for the Milwaukee Heart Walk & Fun Run. More than 40 institute caregivers, including Nina Garlie, PhD, and Arshad Jahangir, MD, and their family members and friends supported the institute’s team and booth. The booth featured Aurora Health Care volunteers teaching heart anatomy using pig hearts, performing ECGs using AliveCor technology and providing information on healthy foods.

Aurora Research Institute and its caregivers raised $1,125 for AHA through the walk.
Aurora Partnership Campaign

Aurora Research Institute caregivers contributed **more than $23,500** to a variety of public agencies, including **$18,588** to Aurora Health Care Foundation through its 2014 Aurora Partnership Campaign. Available throughout October and November, the campaign offers a way for Aurora caregivers to support more than 1,600 charitable funds.

**Great Basket Events**

One way to support the campaign is to contribute a basket to one of the hospitals’ Great Basket events. Another way is to buy raffle tickets for those baskets.

**Sara Planton, BSN**, collected funds and created the Aurora Research Institute basket, with a building innovation theme, for the Aurora Sinai Medical Center event. The basket had a value of $85 and featured Legos, K’nex, Mega Bloks and Cra-Z-Art toys to represent creative thinking. The basket helped raise **$1,341** for the neonatal intensive care unit at Aurora Sinai.

For the Aurora St. Luke’s Medical Center event, **Jennifer Cooper, RN**, spearheaded the Cardiovascular and Gastroenterology Research basket and **Diane Gentilini** and **Jill Barz** the Regenerative Medicine Center basket. The baskets were valued at about $100 each and featured items to enjoy a day snuggling on the couch and create an Italian dinner, respectively. They helped raise **$3,360** for Aurora St. Luke’s Greatest Needs Fund and **$380** for the Family-to-Family Thanksgiving program.

**Penny Wars**

For Aurora Sinai’s first-ever Penny War, **Sara Planton, BSN**, spearheaded a penny jar for the institute in September. Twenty teams competed; team members put pennies in their team jar and silver coins or paper money into other teams’ jars. In total, the initiative raised **$856** for the Milwaukee Homeless Veterans Initiative.

**Townsend Street School Students**

On behalf of Aurora Research Institute, **Vicki Soerens** and **Julie Basquin, MS**, coordinated the adoption of **10 students** who attend Townsend Street School for Christmas to provide gifts to students who are less fortunate. About 97% of the students at the school are living at or below the poverty line or are homeless.

In total, Aurora adopted **276 students**, the most since the program began in 2009, fulfilling wishes for warm clothes, action figures and dolls.
Cardiovascular research

A. Jamil Tajik, MD
President, Aurora Cardiovascular Services
Director, Aurora Cardiac Specialty Centers

Dr. Tajik leads a multidisciplinary team of specialists who coordinate cardiovascular care at Aurora Health Care.

Cardiovascular fellowship research

Suhail Allaqaband, MD
Program Director, Clinical Research for the Cardiovascular Disease Fellowship Program

M. Fuad Jan, MD
Associate Director, Clinical Research for the Cardiovascular Disease Fellowship Program

Noreen Wynn
Aurora Cardiovascular Services Fellowship Research Manager

Sara Walczak
Research Regulatory Specialist

Cardiovascular Leadership Council Research Committee

Suhail Allaqaband, MD
Tanvir Bajwa, MD
Indrajit Choudhuri, MD
Anthony DeFranco, MD
**Arshad Jahangir, MD (CHAIR)**
M. Fuad Jan, MBBS, MD
Bijoy Khandheria, MD
David Kress, MD
David Krum, MS
Randall Lambrecht, PhD

Mark Mewissen, MD
Imran Niazi, MD
Vani Nilakantan, PhD
Sara Planton, BSN
Wendy Schmidt, RN
Mia Stone, MS, BSN
Nasir Sulemanjee, MD
A. Jamil Tajik, MD
Noreen Wynn

>$1 million in external grant funding awarded in 2014 for investigator-initiated cardiovascular research studies
Jim McKinnon participated in a clinical trial to extend his life. Feeling “super” after surgery, he donned an iconic cape. (See story on page 29.)

>25% of Aurora’s research is cardiovascular-related

~40% of Aurora’s cardiovascular research is investigator-initiated

623 total cardiovascular clinical trial enrollments in 2014

82 open cardiovascular clinical trials as of Dec. 31, 2014
Connecting the community with cardiac experts – **Aurora Health Satellite** provides avenue for personal interaction

Aurora Health Care cardiac specialists volunteered their time and shared their expert knowledge during a unique partnership with Discovery World, Milwaukee’s science and technology center.

As part of the Aurora Health Satellite, called Your Mighty Heart, Discovery World visitors experienced an interactive exhibit and participated in heart health educational workshops featuring innovative research and medical procedures that are the frontier of cardiovascular health.

“The partnership between Aurora and Discovery World provided an exciting opportunity for our cardiovascular researchers and clinicians to work directly with the community in an interactive way, emphasizing wellness and prevention as well as options for those with disease,” said Arshad Jahangir, MD, director of the Sheikh Khalifa bin Hamad Al Thani Center for Integrative Research on Cardiovascular Aging. “The exhibit and workshops were well received with attendees of all ages.”

The interactive exhibit, accessible to more than 75,000 people during an 11-week period, featured a demonstration arena for the public that included opportunities to learn about exciting research being conducted at Aurora and hands-on experiences with heart anatomy and suture incisions on animal hearts. The displays highlighted significant pioneering medical technologies and a timeline reflecting Aurora’s dedication to the Milwaukee community’s health. Aurora volunteers staffed the exhibit Saturdays as a way to connect with the public (more than 9,000 people) and showcase Aurora’s cardiac expertise.

The six workshops explored different cardiac topics and provided nearly 500 registered participants with hands-on opportunities led by Aurora’s medical experts and research teams. Participants took on the role of a researcher, conducting experiments, learning about state-of-the-art technology and hearing personal stories from such patients.

“Our cardiology staff was eager and enthused to educate our community about the latest breakthroughs in research and treatment of heart disease,” said Nina Garlie, PhD, director of the Regenerative Medicine Center, Aurora Research Institute.
Session 1: Cardiovascular Basic and Translational Research  
Led by: Arshad Jahangir, MD  
Mahek Mirza, MD

Session 2: Electrophysiology  
Led by: Jasbir Sra, MD  
Indrajit Choudhuri, MD  
David Krum, MS

Session 3: Cardiovascular Imaging  
Led by: Bijoy Khandheria, MD  
Denise Spiegel, RDCS

Session 4: Heart Failure, Cardiomyopathies and Valve Disease  
Led by: Frank Downey, MD  
Nasir Sulemanjee, MD  
Christina Rivera, NP

Session 5: Cardiovascular Surgery  
Led by: David Kress, MD  
Jonathan Howard

Session 6: Interventional Cardiology  
Led by: Tanvir Bajwa, MD  
Suhail Allaqaband, MD  
Anthony DeFranco, MD  
Cindy Hoyt-Harvey, BSN  
Theresa Briggs, RN
Sheikh Khalifa bin Hamad Al Thani Center for Integrative Research on Cardiovascular Aging (CIRCA)

**Arshad Jahangir, MD**
Medical Director, Sheikh Khalifa bin Hamad Al Thani Center for Integrative Research on Cardiovascular Aging

Dr. Jahangir leads a team of researchers devoted entirely to studying the molecular mechanisms responsible for the aging heart’s decreased stress tolerance and enhanced susceptibility to heart rhythm disorders.

Advancing research ... from bench to bedside

The **Sheikh Khalifa bin Hamad Al Thani Center for Integrative Research on Cardiovascular Aging (CIRCA)**, so named because of a generous **$2 million donation** from His Highness in 2014, is one of a few research centers in the world devoted entirely to study the effect of aging on the cardiovascular system.

Supported by the **National Heart, Lung, and Blood Institute of the National Institutes of Health** throughout 2014, the center’s mission is to support and conduct basic, translational and clinical research on the biology of aging, and to develop predictive, diagnostic and therapeutic interventions to preserve wellness, prevent age-related cardiovascular dysfunction and improve the quality of life of older people.

Publications/presentations

In 2014, the CIRCA team shared its bench, translational and clinical research through manuscript preparation and publication in peer-reviewed journals and abstract presentation at national and international meetings, advancing the collective understanding of the aging heart.

The esteemed meetings included the American College of Cardiology Annual Scientific Session, American Heart Association Basic Cardiovascular Sciences and Annual Scientific Sessions, and Society for Cardiovascular Angiography and Interventions Annual Scientific Sessions.

CIRCA in 2014:

- **9** manuscripts published/submitted
- **20** abstracts presented/accepted
The interest of the CIRCA team was piqued after several large studies raised concerns that testosterone therapy can negatively affect men’s heart health.

Testosterone, a hormone that plays a key role in the development of male sexual characteristics, is important for maintaining health and well-being. Therapy frequently becomes necessary because testosterone decreases as a man ages. Low testosterone can impact cognition, muscle mass and strength, bone density, metabolic function and mood.

After analyzing demographic and health data from 7,245 men with low testosterone levels from 2011 to 2013, CIRCA researchers found that the rate of adverse cardiovascular events in men who received testosterone therapy versus those who did not was the same—meaning the treatment is not causing harm.

“In the absence of prospective data, studies like ours will help ease anxieties around this treatment and provide some information on which physicians can base their prescribing decisions,” said Arshad Jahangir, MD, CIRCA medical director and senior author of the abstract.

The other authors are: Zuber Ali, MD, Danielle Greer, PhD, Robyn Shearer, MS, Ali Gardezi, MD, and Anil Chandel, MD.

The American College of Cardiology invited CIRCA’s researchers to present their findings on testosterone therapy and three other research studies at the 64th Annual Scientific Session.

Findings on testosterone therapy provide valuable bedside information for physicians

Intramural funding

STUDY:
Biomarker-based risk stratification to identify patients at risk for postoperative atrial fibrillation

AWARD:
$50,000, second-year funding

SOURCE:
Aurora Cardiovascular Surgery Research Awards

PRINCIPAL INVESTIGATOR:
Mahek Mirza, MD

STUDY:
A novel calcium entry mechanism in myofibroblast as a therapeutic target for prevention of cardiac fibrosis progression

AWARD:
$50,000 over one year

SOURCE:
Aurora Cardiovascular Surgery Research Awards

PRINCIPAL INVESTIGATOR:
Gracious Ross, PhD

STUDY:
Circulatory biomarkers of extracellular matrix turnover and noncoding RNA as predictor for postoperative heart failure

AWARD:
$50,000, second-year funding

SOURCE:
Aurora Cardiovascular Surgery Research Awards

PRINCIPAL INVESTIGATOR:
Farhan Rizvi, PhD

STUDY:
Cytokine-mediated fibroblast activation increases resistance towards cell death: mechanistic insights and therapeutic implications

AWARD:
$50,000 over one year

SOURCE:
Aurora Cardiovascular Surgery Research Awards

PRINCIPAL INVESTIGATOR:
Ulugbek Negmadjanov, MD
Clinical trials test uses of stem cells

Building on 20 years of experience in cellular therapy, Aurora Health Care investigators are studying investigational treatment options using stem cells to restore normal heart and artery functions.

In the United States, both therapies are limited by federal law to investigational use.

Heart failure

As part of an international clinical trial, investigators at Aurora St. Luke's Medical Center are studying the safety and effectiveness of delivering stem cells via a minimally invasive approach to the lower chambers of the heart, or ventricles, in subjects with chronic heart failure who are already taking the most advanced medications available (clinicaltrials.gov identifier: NCT02032004).

The stem cells (CEP-41750, Teva Pharmaceutical Industries, Petah Tikva, Israel) are obtained from an anonymous healthy volunteer and then expanded in tissue culture before delivery to the heart. The Regenerative Medicine Center team helps prepare the cells for injection. Co-investigator Suhail Allaqaband, MD, and his team perform the stem cell delivery procedures. Half the subjects will receive the stem cells. The other half will receive only medication.

Principal investigator Nasir Sulemanjee, MD, and his team perform screening, study enrollment and follow-up evaluations. They will not know if a subject has received the stem cells to minimize bias in the study.

“Through numerous clinical and preclinical studies, we have come to realize the potential of stem cells to help patients suffering from cardiovascular disease, especially in the treatment of heart failure,” Dr. Sulemanjee said. “This research will help us to further investigate this technology and therapy.”

Over five years, the research team will monitor all enrolled subjects for benefit and improvement in their heart failure, as well as any major adverse cardiac events.

Don Lobacz, RN, and Dena Burke, BSN, are coordinating the clinical trial for Aurora Research Institute.

Critical limb ischemia

Severe blockages in the arteries of their legs, or critical limb ischemia, is caused by a narrowing of the arteries throughout the body, or peripheral arterial disease (PAD).

Through a clinical trial utilizing the MarrowStim PAD Kit (Biomet Biologics LLC, Warsaw, Ind.), principal investigators Tanvir Bajwa, MD, and Richard Carballo, MD, and their team are testing the safety and effectiveness of the investigational treatment for critical limb ischemia compared to a placebo (clinicaltrials.gov identifier: NCT01049919).

The purpose of the research is to establish whether the therapy can prevent or delay major amputation or death in subjects with critical limb ischemia due to severe PAD.

During the single study procedure, a medical oncologist withdraws bone marrow from the subject’s hip. Then, a technical specialist from the Regenerative Medicine Center concentrates the marrow cells using MarrowStim PAD Kit. Immediately thereafter, a vascular surgeon injects the cells into the muscle of the affected limb.

Aurora St. Luke's is the only site in Wisconsin participating in this prospective, multicenter trial.

“Through numerous clinical and preclinical studies, we have come to realize the potential of stem cells to help patients suffering from cardiovascular disease, especially in the treatment of heart failure,” Dr. Sulemanjee said. “This research will help us to further investigate this technology and therapy.”

Over five years, the research team will monitor all enrolled subjects for benefit and improvement in their heart failure, as well as any major adverse cardiac events.

Don Lobacz, RN, and Dena Burke, BSN, are coordinating the clinical trial for Aurora Research Institute.

MarrowStim PAD Kit

MarrowStim PAD Kit is a trademark of Biomet Biologics LLC, Warsaw, Ind.

Caution: The MarrowStim PAD Kit limited by U.S. federal law to investigational use.

Images courtesy of Biomet Biologics LLC
Researchers study technique to deliver stem cells for atrial fibrillation prevention

Scar tissue that develops as a result of heart surgery can cause electrical disturbances to the heart’s rhythm. Patients may require permanent pacemakers to treat these heart rhythm disorders.

Stem cells delivered to the lower chambers of the heart have reduced scar and prevented further scarring in patients with heart disease, but their impact on the upper chambers, or atria, hasn’t been studied.

In collaboration with researchers at the University of Wisconsin-Madison, Aurora Health Care principal investigator Indrajit Choudhuri, MD, is leading a preclinical study using pigs to develop a safe, minimally invasive technique that will allow delivery of stem cells to the atria and enable the researchers to track their retention in the heart tissue.

The purpose of the study is to establish the approach so it can be applied to patients undergoing heart procedures to prevent future heart rhythm disorders and minimize the need for permanent pacemakers.

Pigs are used because their cardiovascular system is similar to that of human. The study received approval by the University of Wisconsin Institutional Animal Care and Use Committee and its protocol is in accordance with the committee’s guidelines.

The first experiments are testing whether injections are feasible during open-chest surgery. Future experiments will test whether stem cells can be injected from inside the heart via catheter.

The researchers are using use fluoroscopy and intracardiac echocardiographic imaging to deliver labeled stem cells, which are tracked via the label with positron emission tomography-computed tomography, more commonly known as PET-CT. Electrograms are monitored during the procedure for electrical disturbances.

About 6 hours after the stem cells are injected, heart tissue samples are evaluated by confocal microscopy to track retention.

“The collaboration with Tim Hacker, PhD, Eric Schmuck, PhD, and Amish Raval, MD, at UW-Madison has been very positive,” said Nina Garlie, PhD, program director of the Regenerative Medicine Center. “Their team has been instrumental in providing protocols, equipment and pigs to move this important project forward. We hope that the knowledge gained from this study will lead to further research to determine whether injected stem cells prevent or reduce atrial tissue scarring.”

Aurora Research Institute awarded $50,000 to this project through the Cardiovascular Surgery Research Awards.

Principal investigators:
Indrajit Choudhuri, MD
Jayant Khitha, MD
Nina Garlie, PhD

Co-Investigators
(Aurora Health Care):
Arshad Jahangir, MD
Bijoy Khandheria, MD
David Kress, MD
Tanvir Bajwa, MD
Jasbir Sra, MD
David Krum, MS
John Hare
Mamatha Pinninti, MD

Injection of porcine mesenchymal stem cells into the atrial appendage of a pig. This was performed under Animal Care and Use Committee approval with full anesthesia.
Institute awards nearly $400,000 for cardiovascular research studies

In 2014, Aurora Research Institute awarded more than $200,000 to Aurora Health Care investigators for new cardiovascular-related research studies.

The purpose of the grants is to provide important seed funding to promote future research of cardiovascular disease, preferably through competitive extramural funding.

The Sullivan Cardiac Research Award for Residents and Fellows provides up to $30,000 per award to residents and fellows under mentorship guidance for patient-centered research of cardiovascular diseases.

Interventional cardiologist Tanvir Bajwa, MD, serves as mentor to all winners of the Sullivan award, which is funded thanks to the generosity of Tim Sullivan, a member of Aurora’s board of directors, and his wife Vivian Sullivan. The Sullivans donated $1 million to support Dr. Bajwa’s cardiac research via the fellowship program.

The Cardiac Research Award provides up to $40,000 per award and the Cardiovascular Surgery Research Award up to $50,000 per award to basic and clinical investigators and fellows for patient-centered research of cardiovascular diseases.

Investigators can apply for second-year funding to continue their projects. Five renewals totaling more than $175,000 were awarded in 2014.

Funds for the Cardiac and Cardiovascular Surgery research awards are available because of the generosity of donors to Aurora Health Care Foundation.

The Scientific Review Committee, which consists of researchers and clinicians, scientifically evaluates proposals based on overall impact of the proposed study; its significance, innovation and approach; and the investigators involved in the research.

Continuing intramural funding

Through the Cardiovascular Surgery Research Awards, Martin Oaks, PhD, received $37,250 in second-year funding to analyze HLA antibodies in patients with ventricular assist devices.
Two Aurora hospitals test SMARTCare

Aurora Health Care is collaborating with the American College of Cardiology on an innovative quality improvement research project, SMARTCare (Smarter Management and Resource Use for Today’s Complex Cardiac Care).

The Centers for Medicare and Medicaid Services in May 2014 awarded the ACC Foundation $15.8 million to test the SMARTCare software. The pilot program incorporates the software into the electronic health record to improve care for patients with stable ischemic heart disease by giving treating physicians the most current information available.

The purpose is to optimize quality of care to improve health outcomes while saving costs.

Anthony DeFranco, MD, an Aurora cardiologist and current governor of the ACC’s Wisconsin Chapter, helped secure the grant.

“To improve coordination of care between specialists and primary care physicians as well as reduce costs without compromising care, health systems need a practical way of implementing rapidly advancing practice guidelines at the bedside,” Dr. DeFranco said. “SMARTCare will enable Aurora to lead the way on value-based care in a way that is feasible for physicians and hospitals and also better for patients.”

A portion of the grant will support the project’s implementation at Aurora St. Luke’s Medical Center and Aurora Medical Center in Grafton. Dr. DeFranco and Aurora executive vice president Patrick Falvey, PhD, will facilitate SMARTCare’s implementation at Aurora as well as for future Wisconsin participants.

Senior grant specialist Toby Wolf and senior sponsored programs specialist Lee Banfi, MBA, CPA, provide post-award grant services on behalf of Aurora Research Institute.

Sullivan Cardiac Research Award for Residents and Fellows

Principal investigator: Daniel Ortiz, MD
Mentors: Tanvir Bajwa, MD, and Mark Mewissen, MD
Co-investigator: Maharaj Singh, PhD
Project: Implement a new tool to assess the possibility for bleeding in patients who undergo treatment for blockages in leg arteries

Cardiac Research Award

Principal investigator: Vinay Thohan, MD
Co-investigator: Scarlet Shi, PhD
Project: Study whether Doppler imaging of heart function can predict outcomes in patients with heart failure who will undergo noncardiovascular surgeries

Principal investigator: Steven Port, MD
Co-investigator: Lily Honoris, MD
Project: Study whether computed tomography angiography can identify plaque in the coronary arteries in patients with end-stage kidney disease

Cardiovascular Surgery Research Award

Principal investigator: Ulugbek Negmadjanov, MD
Co-investigators: Ekhsun Holmuhamedov, PhD, Arshad Jahangir, MD, A. Jamil Tajik, MD, David Kress, MD, Frank Downey, MD, Larisa Emelyanova, PhD, Farhan Rizvi, PhD, and Hao Xu, PhD
Project: Determine how disease causes heart repair cells to produce excessive scar tissue, which leads to complications after heart surgery

Principal investigator: Vinay Thohan, MD
Co-investigator: Scarlet Shi, PhD
Project: Identify clinical factors that may predict the development of gastrointestinal bleeding in patients with left ventricular assist devices (LVADs)

Principal investigator: Nasir Sulemanjee, MD
Project: Determine whether and how kidney disease stages in LVAD placement patients affects outcomes

Additional extramural funding

STUDY: Severe blood transfusion reactions, including pulmonary edema (STRIPE)
AWARD: $309,032 over 21 months
SOURCE: National Heart, Lung, and Blood Institute (via BloodCenter of Wisconsin)
PRINCIPAL INVESTIGATOR: Michael Michalkiewicz, PhD

STUDY: Using system science methods to study cardiac risk in the Somali community
AWARD: $19,065 first-year funding
SOURCE: National Heart, Lung, and Blood Institute (via HealthPartners Institute for Education and Research)
PRINCIPAL INVESTIGATOR: Ahmed Dalmar, MD
Continuing his journey: Patient receives LVAD as destination therapy via clinical trial

Because he felt so good and it was close to Halloween. That’s why Jim McKinnon, 81, of East Troy, Wis., donned a Superman cape in his hospital room at Aurora St. Luke’s Medical Center, where he was recovering from heart surgery.

“A Superman symbolizes strength and energy,” said McKinnon, who was just starting to feel stronger.

McKinnon, through participation in a clinical trial, received a HeartWare left ventricular assist device (LVAD) as destination therapy, meaning he had exhausted all other advanced heart failure treatment options and was ineligible for a heart transplant.

Aurora St. Luke’s is the only site in Wisconsin offering the HeartWare® Ventricular Assist System (Framingham, Mass.) as destination therapy.

“I was at death’s door,” said McKinnon, who could hardly walk at the time.

His cardiologist Ali Khan, MD, referred McKinnon to John Crouch, MD, a cardiovascular and thoracic surgeon. Crouch and Frank Downey, MD, principal investigator for the HeartWare clinical trial at Aurora St. Luke’s, discussed McKinnon’s eligibility for the trial.

“He is a very outgoing and positive individual,” Dr. Crouch said. “He was an ideal patient.”

Dr. Crouch and his team presented McKinnon with his options, which were limited due to his age. He could continue with medication, try a U.S. Food and Drug Administration-approved LVAD (HeartMate II, Thoratec Corp., Pleasanton, Calif.), which weighs about 10 oz., or enroll in the clinical trial for the possibility to receive the HeartWare LVAD as a destination therapy.

Taking a chance

Because of his small stature, McKinnon chose enrollment in the clinical trial (clinicaltrials.gov identifier: NCT01966458) with hopes of receiving the HeartWare LVAD, which is half the weight of the FDA-approved model. Through randomization, he had a 66% chance of receiving the miniature device, which is limited by U.S. federal law to investigational use for the destination therapy indication.

“That was a lifetime decision, a life-saving decision,” McKinnon said.

Limited options

Five million Americans a year experience a level of heart failure at varying degrees.

For 14 years, McKinnon suffered with heart failure. During that time, the retired State of Wisconsin Department of Transportation employee underwent two bypass surgeries, received multiple stents and developed a heart rhythm disorder – his kryptonite that caused his heart failure to worsen. Suddenly, drugs stopped working against the disease.
McKinnon was randomized to receive the HeartWare device, and Crouch performed the surgery. Aurora St. Luke’s has performed more LVAD procedures than any other hospital in Wisconsin.

McKinnon will need the device, which is connected to his heart, for the rest of his life. The LVAD system pumps blood from the left side of the heart into the aorta, the large blood vessel that carries blood from the heart to the rest of the body.

McKinnon must carry the system’s controller in a small carrying case around his waist. Ralph, as McKinnon calls his controller in memory of his late father who died of a heart attack at 49, is connected to the LVAD by a small cable that passes through McKinnon’s skin above his stomach. All three of his children are trained to change the wound’s dressing, which must be done every other day.

The controller runs the pump and provides text messages and audible alerts to help better manage the system. The controller is powered by two small batteries or can pull energy from a wall outlet.

Feeling super

About a month after receiving the LVAD, McKinnon wanted to celebrate how well he was feeling. So as part of an inside family joke, his daughter brought him a Superman cape.

“It means I can get to my grandson’s wedding next October,” McKinnon said of his new lease on life. “It’s a joy to see my (younger) grandchildren and have them call me ‘bapa.’”

Though he still needs to return to Wisconsin for regular follow-up visits, the snowbird met his goal and made it to Florida for the holidays.

“As part of his follow-up for the study, I need to see Jim at 3 months, 6 months and 1 year and then every 6 months for the study,” said Cheryl A. Zywicki, RN, who is coordinating the clinical trial for Aurora Research Institute.

He may not be as fast as a speeding bullet, but he is able to breathe easier when walking across a room. Considering how he felt before the surgery, it’s almost as if he really could leap a tall building in a single bound.

McKinnon’s results should not be used to predict outcomes of the clinical trial. Researchers are documenting incidence of stroke. Data collection is ongoing.
Miniature pacemaker technology under review

Advances in technology have allowed pacemakers to shrink from the size of a pocket watch to a AAA battery or vitamin capsule.

Aurora Health Care researchers were the first in Wisconsin to implant these miniaturized pacemakers – that do not require leads – as part of ongoing international clinical trials. In the United States, the Nanostim™ leadless pacemaker (St. Jude Medical Inc., St. Paul, Minn.) and Micra™ Transcatheter Pacing System (Medtronic Inc., Minneapolis, Minn.) are limited by federal law to investigational use.

Instead of an incision to the skin of the chest, subjects undergo a minimally invasive procedure via a vein in the leg, eliminating the need for a surgical pocket under the skin.

The goals are to reduce complications, including device pocket-related infection and lead failure, and improve quality of life.

Anthony Chambers, BSN, is coordinating both clinical research trials for Aurora Research Institute.

Nanostim™ clinical trial

Principal investigators Imran Niazi, MD, and M. Eyman Mortada, MD, and their team are studying the safety and effectiveness of the Nanostim™ leadless pacemaker in subjects indicated for a single-chamber ventricular pacemaker (clinicaltrials.gov identifier: NCT02030418).

All subjects enrolled in this prospective, multicenter clinical trial will receive the device, which is about the size of a AAA battery and weighs 2 grams.

“This is a revolutionary technology,” Dr. Niazi said. “By avoiding invasive surgery and using interventional techniques for implanting pacemakers, we could reduce patient discomfort and cost significantly. Surgical risk – such as infection – and recovery time in the hospital is greatly reduced. This new technology has the potential to have an enormous impact on cardiac care for the nearly 700,000 people worldwide who receive pacemakers each year.”

Drs. Niazi and Mortada and their team are documenting complications, pacing thresholds, R-wave amplitudes, and response during graded exercise testing.

Micra™ clinical trial

Principal investigators Jasbir Sra, MD, and Vikram Nangia, MD, and their team are studying the safety and effectiveness of the Micra™ Transcatheter Pacing System in subjects who have a Class I or II indication for a single-chamber ventricular pacemaker (clinicaltrials.gov identifier: NCT02004873).

All subjects enrolled in this prospective, multicenter clinical trial will receive the device, which is about the size of a vitamin capsule.

Drs. Sra and Nangia and their team are documenting major complications and pacing capture threshold success.
Electrophysiologists literally wrote the book

FDA approvals

Aurora Research Institute was instrumental in bringing the following innovations to market through participation in clinical trials.

**CoreValve (Medtronic Inc.)**
The first in Wisconsin to implant the artificial aortic valve nonsurgically, Aurora researchers refined the transcatheter aortic valve replacement approach with development of a TAVR program and dedication of hybrid cardiovascular operating rooms. Though FDA approved for patients who are not candidates for surgery, clinical trial participation at Aurora continues for patients at intermediate to very high risk for surgery.

**Turbo-Tandem System (Spectranetics Corp.)**
One of the first sites in the state to participate in the EXCITE clinical trial, Aurora St. Luke’s Medical Center clinicians have the expertise to use the FDA-approved Turbo-Tandem System to treat narrowing of the arteries in patients who had been previously treated with stents. The laser technology removes plaque that causes arteries to narrow.

**IN.PACT Admiral drug-coated balloon (Medtronic Inc.)**
The only site in Wisconsin to participate in the IN.PACT SFA II clinical trial, Aurora St. Luke’s Medical Center has the ability to treat patients who suffer from peripheral artery disease with the drug-coated balloon.

**CardioMEMS HF System (St. Jude Medical Inc.)**
The system wirelessly measures and monitors pulmonary artery pressure and heart rate to reduce hospital readmissions for patients with heart failure. After it had been studied via clinical trial at Aurora a few years ago, the system received FDA approval in July. Aurora clinicians are developing a program to implement use of this device for patients with heart failure.

Electrophysiologists literally wrote the book

Aurora Cardiovascular Services electrophysiologists [Jasbir Sra, MD]{/} and [Masood Akhtar, MD]{/}, edited and contributed to a textbook that uses cases to keep readers engaged.

“Practical Electrophysiology,” published by Cardiotext Publishing (Minneapolis, Minn.), features detailed discussion of fundamental electrophysiology aspects and includes more than 70 case studies with multiple-choice questions.

“It is difficult to stay current with the ever-changing field of electrophysiology,” Dr. Sra said. “Despite that, there are fundamentals that students of electrophysiology need to understand. We hope this textbook proves a useful tool.”

The book includes contributions from other Aurora physicians (see Cardiovascular Appendix, page 34) and specialists from around the world.

Dr. Masood Akhtar Cardiac Research Fund

To honor Aurora Health Care’s own electrophysiology pioneer, the [Aurora Health Care Foundation]{/} established the Dr. Masood Akhtar Cardiac Research Fund in 2014.

Donors can advance cardiac research with contributions to the fund, which will support Aurora's cardiovascular research program activities, including speakers and educational/training programs.

[Masood Akhtar, MD]{/}, former president of Aurora Cardiovascular Services, created one of the first accredited electrophysiology fellowship programs and played a key role in developing Aurora's other cardiovascular fellowship programs.

Since stepping down as president, Dr. Akhtar has concentrated on electrophysiology research and teaching as a clinical professor of medicine for the University of Wisconsin School of Medicine and Public Health at Aurora Sinai and Aurora St. Luke's Medical Centers.
## Cardiovascular volumes – systemwide

### Cardiovascular surgery

<table>
<thead>
<tr>
<th>Procedure</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary artery bypass graft (CABG) total</td>
<td>794</td>
<td>920</td>
<td>926</td>
</tr>
<tr>
<td>CABG on pump</td>
<td>653</td>
<td>722</td>
<td>768</td>
</tr>
<tr>
<td>CABG off pump</td>
<td>141</td>
<td>198</td>
<td>158</td>
</tr>
<tr>
<td>Valve replacement</td>
<td>430</td>
<td>491</td>
<td>572</td>
</tr>
<tr>
<td>Aortic valve replacement</td>
<td>364</td>
<td>373</td>
<td>446</td>
</tr>
<tr>
<td>Mitral valve replacement</td>
<td>56</td>
<td>112</td>
<td>107</td>
</tr>
<tr>
<td>Other valve replacement</td>
<td>10</td>
<td>6</td>
<td>19</td>
</tr>
<tr>
<td>Valve annuloplasty (open)</td>
<td>101</td>
<td>116</td>
<td>101</td>
</tr>
<tr>
<td>Cardiac ablation – open (MAZE)</td>
<td>94</td>
<td>100</td>
<td>95</td>
</tr>
<tr>
<td>Valve repair</td>
<td>80</td>
<td>98</td>
<td>76</td>
</tr>
<tr>
<td>Mitral valve repair</td>
<td>61</td>
<td>77</td>
<td>61</td>
</tr>
<tr>
<td>Other valve repair</td>
<td>19</td>
<td>21</td>
<td>15</td>
</tr>
<tr>
<td>Patent foramen ovale/atrial septal defect closure total</td>
<td>60</td>
<td>64</td>
<td>75</td>
</tr>
</tbody>
</table>

### Vascular medicine

<table>
<thead>
<tr>
<th>Procedure</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral vascular intervention</td>
<td>2,041</td>
<td>1,906</td>
<td>1,709</td>
</tr>
<tr>
<td>With stent</td>
<td>1,063</td>
<td>1,024</td>
<td>954</td>
</tr>
<tr>
<td>Without stent</td>
<td>978</td>
<td>882</td>
<td>755</td>
</tr>
<tr>
<td>Endarterectomy</td>
<td>496</td>
<td>480</td>
<td>504</td>
</tr>
<tr>
<td>Carotid endarterectomy</td>
<td>292</td>
<td>307</td>
<td>303</td>
</tr>
<tr>
<td>Other endarterectomy</td>
<td>204</td>
<td>173</td>
<td>201</td>
</tr>
<tr>
<td>Other endovascular procedure</td>
<td>465</td>
<td>507</td>
<td>365</td>
</tr>
<tr>
<td>Lower extremity bypass</td>
<td>178</td>
<td>165</td>
<td>174</td>
</tr>
<tr>
<td>Amputation</td>
<td>162</td>
<td>163</td>
<td>172</td>
</tr>
<tr>
<td>Below knee</td>
<td>108</td>
<td>104</td>
<td>120</td>
</tr>
<tr>
<td>Above knee</td>
<td>54</td>
<td>59</td>
<td>52</td>
</tr>
<tr>
<td>Abdominal aortic aneurysm repair</td>
<td>202</td>
<td>162</td>
<td>172</td>
</tr>
<tr>
<td>Endovascular</td>
<td>160</td>
<td>128</td>
<td>132</td>
</tr>
<tr>
<td>Open</td>
<td>42</td>
<td>34</td>
<td>40</td>
</tr>
<tr>
<td>Thoracic aortic aneurysm repair</td>
<td>115</td>
<td>93</td>
<td>99</td>
</tr>
<tr>
<td>Endovascular only</td>
<td>29</td>
<td>17</td>
<td>22</td>
</tr>
<tr>
<td>Open only</td>
<td>86</td>
<td>76</td>
<td>75</td>
</tr>
<tr>
<td>Both</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Vessel intervention</td>
<td>294</td>
<td>291</td>
<td>63</td>
</tr>
<tr>
<td>Surgical occlusion of vessels</td>
<td>278</td>
<td>275</td>
<td>49</td>
</tr>
<tr>
<td>Other vessel resection</td>
<td>16</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>Carotid stenting</td>
<td>91</td>
<td>69</td>
<td>28</td>
</tr>
</tbody>
</table>

### Interventional cardiology

<table>
<thead>
<tr>
<th>Procedure</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart catheterization total</td>
<td>10,822</td>
<td>10,359</td>
<td>9,394</td>
</tr>
<tr>
<td>Cardiac catheterization</td>
<td>8,485</td>
<td>7,959</td>
<td>7,049</td>
</tr>
<tr>
<td>Angiogram without pressures</td>
<td>2,337</td>
<td>2,400</td>
<td>2,345</td>
</tr>
<tr>
<td>Coronary intervention</td>
<td>3,109</td>
<td>2,812</td>
<td>2,567</td>
</tr>
<tr>
<td>With stent</td>
<td>2,952</td>
<td>2,653</td>
<td>2,441</td>
</tr>
<tr>
<td>Without stent</td>
<td>157</td>
<td>159</td>
<td>126</td>
</tr>
<tr>
<td>Myocardial biopsy</td>
<td>743</td>
<td>432</td>
<td>343</td>
</tr>
<tr>
<td>Endovascular aortic valve replacement</td>
<td>48</td>
<td>55</td>
<td>187</td>
</tr>
<tr>
<td>Patent foramen ovale/atrial septal defect closure total</td>
<td>50</td>
<td>65</td>
<td>60</td>
</tr>
<tr>
<td>Balloon valvuloplasty (percutaneous)</td>
<td>45</td>
<td>37</td>
<td>40</td>
</tr>
<tr>
<td>Transapical mitral valve replacement (TMVR)</td>
<td>7</td>
<td>3</td>
<td>17</td>
</tr>
<tr>
<td>Transapical aortic valve replacement (TAVR)</td>
<td>20</td>
<td>57</td>
<td>14</td>
</tr>
</tbody>
</table>

### Electrophysiology

<table>
<thead>
<tr>
<th>Procedure</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardioversion</td>
<td>1,259</td>
<td>1,243</td>
<td>1,175</td>
</tr>
<tr>
<td>EP study</td>
<td>1,139</td>
<td>1,114</td>
<td>1,130</td>
</tr>
<tr>
<td>Pacemaker</td>
<td>1,007</td>
<td>941</td>
<td>1,059</td>
</tr>
<tr>
<td>Ablation – percutaneous</td>
<td>1,091</td>
<td>1,062</td>
<td>1,050</td>
</tr>
<tr>
<td>Cardiac mapping</td>
<td>963</td>
<td>974</td>
<td>839</td>
</tr>
<tr>
<td>Defibrillator</td>
<td>856</td>
<td>830</td>
<td>804</td>
</tr>
<tr>
<td>Tilt testing</td>
<td>713</td>
<td>650</td>
<td>553</td>
</tr>
<tr>
<td>Lead extraction</td>
<td>50</td>
<td>39</td>
<td>68</td>
</tr>
</tbody>
</table>

## Top 50 ranking third year running

Continuing the streak, the cardiology and heart surgery department at Aurora St. Luke’s Medical Center, Milwaukee, was the only heart program in Wisconsin nationally ranked by U.S. News & World Report in its 2014-15 evaluation of the nation’s best hospitals.

Aurora St. Luke’s cardiology and heart surgery department ranked 41st nationally among 708 programs that qualified for review. This is the third year in a row that it was the only heart program in the state ranked among the nation’s top 50.
Cardiovascular publications

2014 Aurora-authored, peer-reviewed

Journal articles, book chapters, monographs


Oncology research

James Weese, MD
Vice President, Aurora Cancer Care

Dr. Weese leads a multidisciplinary team of specialists who coordinate cancer services at Aurora Health Care.

Research Steering Committee for Medical Oncology

- Michael Mullane, MD
- Dhimant Patel, MD
- Rubina Qamar, MD (CHAIR)
- Antony Ruggeri, MD
- Thomas Saphner, MD
- Corey Shamah, MD
- Michael Thompson, MD, PhD
- Thomas Zukowski, MD

Cancer Leadership Council Research Committee

- Marija Bjegovich-Weidman, MSN
- George Bobustuc, MD
- Jan DeBartolo, MSN
- Carla Fuentes
- Nina Garlie, PhD
- Neha Glandt
- Peter Johnson, MD
- Amin Kassam, MD
- Randall Lambrecht, PhD
- Ali Mahdavi, MD
- Gary Neitzel, MD
- Vani, Nilakantan, PhD
- Dhimant Patel, MD (CO-CHAIR)
- Sara Planton, BSN
- Rubina Qamar, MD
- Richard Rovin, MD
- Ajay Sahajpal, MD
- Thomas Saphner, MD
- Michael Thompson, MD, PhD (CO-CHAIR)
- Judy A. Tjoe, MD
- Carol Tutino, BSN, MS
- James Weese, MD

>$3.9 million in external grant funding awarded in 2014 for oncology research studies
349 total oncology clinical trial enrollments in 2014

77 open oncology clinical trials as of Dec. 31, 2014 (excludes open trials in follow-up)

~45% of Aurora’s research is oncology-related

>10% of Aurora’s oncology research is investigator-initiated

Yvonne Kidandi, a breast cancer survivor, challenged herself by joining Team Phoenix to train for a triathlon. (See story on page 42.)
Aurora Research Institute received a highly competitive grant in 2014 to further its efforts of connecting individuals to cancer research taking place in their communities.

The National Cancer Institute (NCI), a component of the National Institutes of Health, selected 34 health care organizations it felt best equipped to partner in the NCI Community Oncology Research Program, or NCORP. The program utilizes community sites to increase the number and scope of available clinical trials. As an NCORP community site, Aurora will implement this nationwide effort on a local level with $3.9 million in federal funding over five years.

“NCORP principal investigators Thomas Saphner, MD, and Michael Thompson, MD, PhD, are spearheading the NCORP initiative throughout Aurora Health Care’s extensive footprint under the guidance of the Aurora Research Institute and Aurora Cancer Care.

“This is a transformational grant for Aurora,” Dr. Saphner said. “We are making a statement and commitment to being a national player in cancer research.”

One of the first implementation steps was creating a program administrator position. Neha Glandt, a key player in preparing the NCORP application, was promoted to the position.

The team, which includes clinical trials manager Jan DeBartolo, MSN, then received training at the charter NCORP meeting in the nation’s capital. In addition to NCI-sponsored clinical trials for cancer treatment, symptom control and prevention, Aurora will participate in cancer care delivery research trials designed to determine the best use of resources in cancer care. This is in addition to any enrollments in non-NCI-sponsored trials.

With monthly meetings to track progress and develop informational materials for patients, the team is working toward its goal of ultimately improving patient outcomes by sharing and analyzing all research findings, then applying that new knowledge to individual treatment.

“We want the right therapy delivered to the right patient at the right location – close to home,” Dr. Thompson said.
Providing more options to fight cancer

When Virginia Mortenson of Green Bay was diagnosed with breast cancer in 2007, she didn’t believe it. “I have always had dense breast tissue and I’ve had to go beyond mammograms a couple times for screenings, but it never amounted to anything,” she said.

But this time regular screening, a second mammogram and biopsy confirmed – Mortenson faced stage 1 breast cancer. “That was a bit of a shocker,” Mortenson said. “It all went very quickly – I scheduled an appointment with a surgeon, she and her team were wonderful in explaining what was happening – it’s a lot to take in.”

After surgery and radiation, Mortenson’s doctor recommended a test that examines the tumor to determine likelihood of recurrence. Because she tested “in the middle” for recurrence, Mortenson decided to enroll in a clinical trial for a chance to avoid the side effects and damage caused by chemotherapy’s toxicity.

The trial involved postmenopausal women with estrogen-positive breast cancer, which is what she had. Some women were given traditional chemotherapy plus an estrogen-inhibiting medication while others avoided chemotherapy and only received the estrogen-inhibiting medication to try to prevent the cancer from recurring. Mortenson received only the inhibitor drug and stayed on it for five years. “I avoided chemotherapy. I don’t think it would have been any more effective than the inhibitor,” Mortenson said.

Providing patients with better access to top clinical trials is a key goal of Aurora Health Care’s involvement with the National Cancer Institute Community Oncology Research Program, or NCORP. Aurora was awarded $3.9 million in federal funding over five years to improve cancer research and expand patient access to clinical trials in Wisconsin. “Currently, there is a gap between when treatments or techniques are known to be successful and when they are incorporated as a standard of care,” said Thomas Saphner, MD, a principal investigator spearheading Aurora’s efforts. “A primary goal of our work on this project will be to narrow this gap.”

Mortenson is living proof. The inhibitor she began taking in 2007 is now available even in generic form. “I entered the clinical trial so in the future, women in my position would have more clear-cut data on which to make a treatment decision,” Mortenson said.

Dhimant Patel, MD, is Mortenson’s oncologist. Lori Bowhousen, Kate McPolin, BSN, and Sarah Peterson, RN, provided site coordination for Aurora Research Institute.
TORQUE

Translational Oncology Research: Quest for Understanding & Exploration

Judy A. Tjoe, MD
Medical Director, TORQUE

Dr. Tjoe leads Aurora Health Care’s translational breast cancer research program through TORQUE (Translation Oncology Research: Quest for Understanding & Exploration), using more than 30 years of data from the Cancer Registry and Biorepository and Specimen Resource Center. With a research component, the Team Phoenix breast cancer survivorship program started by Dr. Tjoe falls under the TORQUE umbrella.

Investigator-initiated research

TORQUE investigators hope to find predictors of breast cancer progression and understand the role of estrogen receptors (ER) in development of the disease.

The investigator-initiated research project led by Judy A. Tjoe, MD, and Sanjay Kansra, PhD, involves identification of biomarkers that could predict development of breast cancer.

Abnormal cell growth in the ducts or lobules of the breast (atypical ductal hyperplasia [ADH] and atypical lobular hyperplasia [ALH]) is associated with a three- to fivefold increased risk of future breast cancer, and risk mitigation includes regular imaging or preventive measures.

The goal of the study is to find predictors for those at highest risk for disease progression to limit aggressive treatment options, which are associated with side effects. Findings so far may have ruled out expression of ER, progesterone receptors and human epidermal growth factor receptor-2 (HER2/neu) as possible predictors.

Using a multiplex immunochemistry technique, their work in patients with premalignant breast lesions (ADH and ALH) revealed distinct findings when compared to a similar study on patients with ductal carcinoma in situ that suggested a combination of three biomarkers (the cell cycle regulator p16\(^{INK4a}\), the proliferation antigen Ki-67 and the stress response enzyme COX2) could predict future breast cancer. Additional study is needed.

Digging deeper, investigators are pursuing nonclassical ER and ER-beta as possible biomarkers to predict future breast cancer.

Maharaj Singh, PhD, and Brittany Last provide support for these studies, which are funded by Genentech Inc. and Rock River Cancer Research Foundation.

Cancer rehabilitation specialist Leslie J. Waltke, PT, gave a talk on the role and benefits of cancer rehabilitation at the 2014 China Cancer Congress in Beijing, China. Waltke was invited to present after publishing a review on exercise and rehabilitation to improve cancer outcomes in Journal of Patient-Centered Research and Reviews.
Survivorship program

“It was more of a challenge than breast cancer,” said Yvonne Kidandi, breast cancer survivor and 2014 Team Phoenix athlete. “You have to show up for treatments, but you don’t have to sign up for a triathlon.”

The 14-week Team Phoenix program, led by breast cancer surgeon Judy A. Tjoe, MD, and cancer rehabilitation specialist Leslie J. Waltke, PT, brings together breast cancer survivors to train – under medical guidance – for a triathlon. The purpose is to promote adoption of regular exercise and healthy lifestyle behaviors that not only counter many side effects, but ultimately empower patients and survivors to take control of their health after treatment.

Kidandi’s journey

Kidandi was diagnosed in July 2011 at 27. She had a double mastectomy, reconstruction and eight cycles of chemotherapy.

“My support system was amazing,” Kidandi said. “All of the nurses at the Vince Lombardi Cancer Clinic at Aurora Sinai Medical Center made the experience better.”

Her last treatment was on her birthday in January 2012, giving her two reasons to celebrate. “It was truly a new beginning,” Kidandi said.

After her treatments were finished, she joined Team Phoenix to challenge herself to a new sport. Both athletic and medical coaches oversee the patients’ gradual progression of increased exercise intensity, while cancer rehab physical therapists address any immediate aches and pains from training or the original cancer surgery and radiation.

“My energy level is up, I’m eating better and I’m happier.”

Research component

Patients in the Team Phoenix program volunteer for research efforts done in collaboration with Marquette University.

Findings showed that participation improved quality of life with more endurance capacity, weight loss and less fatigue.

The research is supported by American Cancer Society and an Aurora Cancer Care Research Award (generously funded by Vince Lombardi Cancer Foundation). In 2014, Dr. Tjoe received $25,000 in second-year funding. Research scientists in endocrinology, Hershel Raff, PhD, and immunology, John Richards, PhD, are co-investigators.

The goal of their continued research is to more definitively determine if markers of inflammation, obesity and health are influenced by prescribed exercise in breast cancer survivors exposed to systemic therapy; and investigate mechanisms of cancer-related fatigue and further evaluate exercise as a means to reduce cancer-related fatigue in patients who have undergone treatment.
Early Phase Cancer Research Program

Michael Thompson, MD, PhD
Medical Director, Early Phase Cancer Research Program

Dr. Thompson leads development of early phase (Phase I and II) clinical trials at Aurora Health Care. These therapeutic trials run through the Early Phase Cancer Research Program are designed to test new treatments with the primary aim to benefit patients. Based on statistical power, Phase I trials evaluate safety and Phase II assess efficacy of investigational treatments before they can be tested against the current standard of care (Phase III studies).

Bile duct cancer (cholangiocarcinoma)

As part of a Phase II clinical trial, Aurora Health Care researchers are trying to improve the response to chemotherapy in patients with advanced cholangiocarcinoma, or bile duct cancer. Cholangiocarcinomas represent approximately 10-15% of all primary liver cancers worldwide and the incidence is growing. The five-year overall survival with systemic chemotherapy is about 5% with median survival less than one year after diagnosis.

Led by principal investigator Michael Thompson, MD, PhD, researchers are testing whether the drug nab-paclitaxel, which has proved effective in advanced breast, pancreatic and non-small-cell lung cancers, will improve survival in subjects with advanced bile duct cancer by targeting gemcitabine chemotherapy (clinicaltrials.gov identifier: NCT02181634; sponsor: PrECOG LLC).

The goal is to enroll 70 subjects nationwide. As of March 27, 2015, Aurora had enrolled 3 of the 17 subjects from the more than 20 participating centers. Enrolling physicians were Scott Maul, MD, Corey Shamah, MD, and Umang Gautam, MD, with support from coordinators Liz Sieber, RN, BS, Chris Goebel, BSN, and Kate McPolin, BSN.

Lung cancer

Aurora Health Care is the only health system in Wisconsin – one of nine health systems nationally – participating in an early phase clinical trial on solid tumors and relapsed small-cell lung cancer.

The Phase I portion of the trial determined the maximum tolerated dose of carfilzomib in combination with irinotecan chemotherapy. The Phase II portion of the trial will assess 6-month survival of patients with relapsed small-cell lung cancer treated with this combination therapy (clinicaltrials.gov identifier: NCT01941316; sponsor: Cancer Research and Biostatistics Clinical Trials Consortium).

Michael Thompson, MD, PhD, is Aurora’s principal investigator. Michael Mullane, MD, and coordinator Karen Crone, RN, enrolled Aurora's first patient by the end of 2014. The goal is to enroll 112 subjects nationwide.
Can **curcumin** heal mouth sores?

Combating the toxic effects of chemotherapy with a natural agent is the goal of a collaborative hybrid effort – an investigator-initiated clinical trial – led by sponsor Dhimant Patel, MD.

Oral mucositis is a common complication of chemotherapy that causes mouth ulcers. The ulcers cause pain and nutritional problems because the person cannot eat. Also, the open sores increase risk of infection. In severe cases, the chemotherapy dose needs to be reduced, which interferes with treatment.

Bench research has shown that curcumin, a chemical found in the spice turmeric, can reduce the amount of bacteria and prevent inflammation.

Dr. Patel and his team want to learn if a mouthwash made with curcumin is safe for people to use and can help with oral mucositis due to chemotherapy.

With assistance from Nina Garlie, PhD, director of Aurora Research Institute’s Regenerative Medicine Center, Patel wrote an investigational new drug application, which received Food and Drug Administration approval.

They developed a protocol for the trial and obtained $25,000 in seed money from Vince Lombardi Cancer Foundation in the form of an Aurora Cancer Care Research Award, which is administered by the institute’s Sponsored Programs Office.

Aurora BayCare Medical Center is the only site for this early phase (I/II) trial (clinicaltrials.gov identifier: NCT02300727). The goal is to enroll about 38 subjects, who will be randomized to receive a pharmacy-prepared mouthwash with or without the maximum tolerated dose of curcumin. Subjects will use the mouthwash three times a day for four to six weeks, unless otherwise advised. An initial group of subjects will determine the maximum tolerated dose.

Kate McPolin, RN, Sarah Peterson, RN, and Corinne Zipperer, RN, are coordinating the clinical trial for the institute.

Vaccines in multiple myeloma

Through a generous donation from **Vince Lombardi Cancer Foundation**, Michael Thompson, MD, PhD, received a 2014 Aurora Cancer Care Research Award totaling $25,000 to pursue a study on the immune system response following vaccination in patients with multiple myeloma.

Plasma cells, a type of white blood cell, create antibodies to fight infections. In multiple myeloma, the plasma cells become cancerous and unable to create infection-fighting antibodies. Because of a compromised immune system response, people with multiple myeloma become susceptible to infections, a common reason for hospitalization or death.

Dr. Thompson is performing a group of three related studies with other Aurora investigators. The first is a retrospective review to determine Aurora’s vaccination practice patterns and outcomes. The second is a prospective registry to track vaccinations in myeloma and other blood cancers. The final component is a blood sample collection study to see how people with multiple myeloma compare to controls in response to flu and pneumonia vaccines.

“We believe this work will provide important information about the best way and time to vaccinate patients with multiple myeloma against flu and pneumonia,” Dr. Thompson said.
Finding new cancer treatment options is a personal mission for researcher

Senior research scientist Santhi Konduri, PhD, has a personal vendetta against breast cancer – it claimed her aunt’s life.

“It has happened in my family, and I’m trying to see if this research can help. Will it make a difference for people like her?” she said.

Winner of two Aurora Cancer Care Research Awards in 2014, Konduri and co-investigator George Bobustuc, MD, have found that a new combination of drugs may decrease breast and pancreatic tumor growth without undesirable side effects to healthy cells. Their continued preclinical evaluation could be translated into new treatment options in the future.

“The key appears to be disulfiram.

“Disulfiram is actually an FDA-approved drug for alcoholism; it creates an aversion for alcohol and reverses the inclination to drink,” said Dr. Konduri, principal investigator. “Recently, it has also shown anticancer properties, and when it is combined with chemotherapeutic drugs (temozolomide and cyclophosphamide/gemcitabine and paclitaxel), we can reduce the dosage of chemotherapeutic drugs.”

This is critical as reducing the dose will decrease both unpleasant side effects and cellular/organ damage caused by chemotherapy’s toxicity.

There are only two drugs with FDA approval to treat pancreatic cancer and the survival rates are quite low.

“It’s a very severe disease, partly because people don’t often notice the symptoms until after the disease has spread to other organs,” she said. “We really need new drug combinations to prolong the lives of these patients.”

Vince Lombardi Cancer Foundation generously supports the Aurora Cancer Care Research Award program. Dr. Konduri received a total of $50,000.

Laboratory capabilities spur collaboration

Aurora Research Institute’s ability to study white blood cell (monocyte) function in human samples spurred collaboration with Duke University School of Medicine cancer researchers.

Immunotherapy researcher John Richards, PhD, developed a method to simultaneously characterize how therapeutic antibodies stimulate various immune cells to kill cancer cells.

His multiplex flow cytometry assay has been used to study human mononuclear cells important to the immune system’s response against cancer as well as destruction of tumors.

Visiting Duke researcher Donald McDonald, PhD, wanted to test the hypothesis that inhibitors to the gene CaMKK2 may improve immune cell-mediated killing of tumors. When the gene is deleted in mice, the mice do not develop tumors. In an ongoing collaboration, Dr. McDonald provides CaMKK2 inhibitors to be tested with Dr. Richards’ assay.

“The door has been opened for immunotherapies,” Dr. Richards said. “They get the person’s immune system to fight the cancer.”

The goal of immunotherapy cancer research is, ultimately, to develop new drugs that spur the immune system to eliminate tumors or keep tumors in check.
Researchers look for predictors to detect early heart damage due to chemotherapy

Chemotherapy is a primary weapon in the arsenal against cancer, but some drugs used to treat cancer have the potential to cause damage to the heart.

Principal investigator Rubina Qamar, MD, and co-investigator Scarlet Shi, PhD, are trying to find early prediction methods for patients with breast cancer who are at greater risk for developing heart disease from chemotherapy.

“We hope that early detection in the future leads to early intervention and improves long-term complications from cardiotoxicities,” Dr. Qamar said.

In this study, the researchers are following 150 patients with breast cancer who are being treated with doxorubicin and/or trastuzumab - drugs known to have cardiotoxic effects - for two years beginning with the start of treatment. Echocardiography and blood tests are being used to determine cardiac function and to evaluate potentially predictive biomarkers.

The goal is to detect early signs of injury to the heart before permanent damage occurs, and modify treatment without impacting the effectiveness of cancer therapy.

“The results will help guide cardio-oncology specialists in making treatment decisions,” Dr. Shi said.

Reviews highlight cardiotoxic drugs, new diagnostic techniques

Both cardiologist Bijoy Khandheria, MD, and medical oncologist Charles Bomzer, MD, served as guest editors of the cardio-oncology theme issue of Journal of Patient-Centered Research and Reviews.

Dr. Bomzer provided a review, “Cardiovascular toxicity of common chemotherapy drugs used to treat breast cancer: an overview.” His review identified the most commonly used drugs to treat breast cancer and provided an overview of their potential adverse impact on the cardiovascular system.

Under Dr. Khandheria’s mentorship, Italian author Fausto Pizzino, MD, provided a review, “Diagnosis of chemotherapy-induced cardiotoxicity,” which highlighted new techniques to diagnose cardiotoxicity due to chemotherapy.

Their review notes that use of left ventricular ejection fraction - as recommended by guidelines - is not sensitive in detecting early cardiac damage. Techniques like identifying biomarkers may hold promise for the future, but larger controlled trials are needed.

Both articles stress the importance of close collaboration between cardiologists and oncologists for the correct management of patients who are treated with drugs that have potentially harmful effects on the cardiovascular system. Fostering this collaboration is one of the fundamental principles of Aurora Health Care's Center for Cardio-Oncology Research and Innovation.

The researchers received Aurora Cancer Care Research Awards totaling $50,000 over two years to support this research. Vince Lombardi Cancer Foundation generously supports the award program.
Study tests radiation therapy plus hormone suppression against prostate cancer

External beam radiation therapy is the standard of care for men with prostate cancer as it destroys cancer cells and shrinks tumors. But how do you prevent the cells from growing back? Growing evidence shows that reducing male hormone levels prevents cancer cell growth.

Principal investigator Mitchell Pincus, MD, and his team are studying whether hormone suppression, when added to radiation therapy, is effective in preventing prostate cancer recurrence (clinicaltrials.gov identifier: NCT00567580).

“Some patients treated with hormone suppression drugs and radiation have a greater chance of not having the cancer return when compared to men treated with radiation alone,” Dr. Pincus said.

The clinical trial also is testing whether it is more beneficial to include the pelvic lymph nodes when applying radiation therapy to the prostate bed.

Reducing male hormone levels prevents cancer cell growth

Oncology volumes (new cases) – systemwide

Source: Cancer Registry

<table>
<thead>
<tr>
<th>Primary site of disease</th>
<th>2012</th>
<th>2013</th>
<th>2014*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral cavity</td>
<td>118</td>
<td>131</td>
<td>163</td>
</tr>
<tr>
<td>Lip</td>
<td>6</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Tongue</td>
<td>38</td>
<td>43</td>
<td>51</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>4</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>5</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Other</td>
<td>65</td>
<td>70</td>
<td>87</td>
</tr>
<tr>
<td>Digestive system</td>
<td>1,094</td>
<td>1,036</td>
<td>945</td>
</tr>
<tr>
<td>Esophagus</td>
<td>84</td>
<td>76</td>
<td>80</td>
</tr>
<tr>
<td>Stomach</td>
<td>78</td>
<td>79</td>
<td>79</td>
</tr>
<tr>
<td>Colon</td>
<td>344</td>
<td>318</td>
<td>328</td>
</tr>
<tr>
<td>Rectum</td>
<td>158</td>
<td>155</td>
<td>146</td>
</tr>
<tr>
<td>Anus/anal canal</td>
<td>30</td>
<td>21</td>
<td>23</td>
</tr>
<tr>
<td>Liver</td>
<td>99</td>
<td>82</td>
<td>77</td>
</tr>
<tr>
<td>Pancreas</td>
<td>193</td>
<td>200</td>
<td>189</td>
</tr>
<tr>
<td>Other</td>
<td>108</td>
<td>105</td>
<td>23</td>
</tr>
<tr>
<td>Respiratory system</td>
<td>847</td>
<td>860</td>
<td>956</td>
</tr>
<tr>
<td>Nasal/sinus</td>
<td>6</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Larynx</td>
<td>38</td>
<td>45</td>
<td>34</td>
</tr>
<tr>
<td>Lung/bronchus</td>
<td>789</td>
<td>795</td>
<td>894</td>
</tr>
<tr>
<td>Other</td>
<td>14</td>
<td>16</td>
<td>22</td>
</tr>
<tr>
<td>Blood and bone marrow</td>
<td>540</td>
<td>503</td>
<td>545</td>
</tr>
<tr>
<td>Bone</td>
<td>9</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Connect/soft tissue</td>
<td>43</td>
<td>31</td>
<td>51</td>
</tr>
<tr>
<td>Skin</td>
<td>338</td>
<td>376</td>
<td>460</td>
</tr>
<tr>
<td>Breast</td>
<td>1,173</td>
<td>1,294</td>
<td>1,277</td>
</tr>
</tbody>
</table>

*Complete data not available at time of publication

External beam radiation therapy is the standard of care for men with prostate cancer as it destroys cancer cells and shrinks tumors. But how do you prevent the cells from growing back? Growing evidence shows that reducing male hormone levels prevents cancer cell growth.

Principal investigator Mitchell Pincus, MD, and his team are studying whether hormone suppression, when added to radiation therapy, is effective in preventing prostate cancer recurrence (clinicaltrials.gov identifier: NCT00567580).

“Some patients treated with hormone suppression drugs and radiation have a greater chance of not having the cancer return when compared to men treated with radiation alone,” Dr. Pincus said.

The clinical trial also is testing whether it is more beneficial to include the pelvic lymph nodes when applying radiation therapy to the prostate bed.

Reducing male hormone levels prevents cancer cell growth

Oncology volumes (new cases) – systemwide

Source: Cancer Registry

<table>
<thead>
<tr>
<th>Primary site of disease</th>
<th>2012</th>
<th>2013</th>
<th>2014*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female genital</td>
<td>448</td>
<td>443</td>
<td>578</td>
</tr>
<tr>
<td>Cervix uteri</td>
<td>52</td>
<td>45</td>
<td>75</td>
</tr>
<tr>
<td>Corpus uteri</td>
<td>230</td>
<td>237</td>
<td>291</td>
</tr>
<tr>
<td>Ovary</td>
<td>92</td>
<td>108</td>
<td>127</td>
</tr>
<tr>
<td>Vulva</td>
<td>46</td>
<td>37</td>
<td>63</td>
</tr>
<tr>
<td>Other</td>
<td>28</td>
<td>16</td>
<td>22</td>
</tr>
<tr>
<td>Male genital</td>
<td>801</td>
<td>854</td>
<td>943</td>
</tr>
<tr>
<td>Prostate</td>
<td>760</td>
<td>819</td>
<td>899</td>
</tr>
<tr>
<td>Testis</td>
<td>35</td>
<td>28</td>
<td>38</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Urinary system</td>
<td>570</td>
<td>591</td>
<td>593</td>
</tr>
<tr>
<td>Bladder</td>
<td>327</td>
<td>371</td>
<td>329</td>
</tr>
<tr>
<td>Kidney/renal</td>
<td>226</td>
<td>199</td>
<td>242</td>
</tr>
<tr>
<td>Other</td>
<td>17</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>Brain &amp; central nervous system</td>
<td>197</td>
<td>171</td>
<td>376</td>
</tr>
<tr>
<td>Brain (benign)</td>
<td>6</td>
<td>13</td>
<td>101</td>
</tr>
<tr>
<td>Brain (malignant)</td>
<td>75</td>
<td>71</td>
<td>124</td>
</tr>
<tr>
<td>Other</td>
<td>116</td>
<td>87</td>
<td>151</td>
</tr>
<tr>
<td>Endocrine</td>
<td>190</td>
<td>158</td>
<td>243</td>
</tr>
<tr>
<td>Thyroid</td>
<td>145</td>
<td>130</td>
<td>161</td>
</tr>
<tr>
<td>Other</td>
<td>45</td>
<td>28</td>
<td>82</td>
</tr>
<tr>
<td>Lymphatic system</td>
<td>333</td>
<td>312</td>
<td>317</td>
</tr>
<tr>
<td>Unknown primary</td>
<td>72</td>
<td>66</td>
<td>90</td>
</tr>
<tr>
<td>Other/ill-defined</td>
<td>43</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Total</td>
<td>6,816</td>
<td>6,872</td>
<td>7,592</td>
</tr>
</tbody>
</table>

*Complete data not available at time of publication
Neurosciences research

Amin Kassam, MD
Vice President, Aurora Neurosciences

Dr. Kassam leads the Aurora Neuroscience Innovation Institute team, a multidisciplinary group of specialists who coordinate care for neurological disorders at Aurora.

Neurosciences Research Work Team

Julie Basquin, MS  Vani Nilakantan, PhD  Carol Tutino, BSN, MS
Nina Garlie, PhD (CHAIR)  Sara Planton, BSN  Kurt Waldhuetter
Amin Kassam, MD  Natalie Polinske, MS
Randall Lambrecht, PhD  Bob Stoltz, MBA, MT
17 open neurosciences clinical trials as of Dec. 31, 2014

18 total neurosciences clinical trial enrollments in 2014

Sisters Sarah Socha and Nicole Borley share a birth date and a diagnosis – multiple sclerosis. (See story on page 53.)

~5% of Aurora’s research is related to neurosciences

~5% of Aurora’s neurosciences research is investigator-initiated
Neurosurgeon leads course on latest techniques

Aurora Research Institute in 2014 renovated space in the lower level of the Milwaukee Heart Institute to accommodate the course, which includes hands-on simulation laboratory sessions.

In 2015, new addition to the neurosciences team Richard Rovin, MD, signed on as co-director for the course. Dr. Rovin serves as clinical research director for Aurora Neuroscience Innovation Institute.

Participants earn a maximum 15.5 AMA PRA Category 1 Credits. Aurora Health Care is accredited by the Wisconsin Medical Society. The event is presented through collaboration between Aurora and Academic Event Management.

The course is supported in part by educational grants from NICO Corp., Synaptive Medical, Hitachi Aloka Medical Ltd., KARL STORZ Endoscopy-America Inc. and KLS Martin Group.

Learning brain surgery from Neurosciences Vice President Amin Kassam, MD, well, it’s not brain surgery.

Dr. Kassam leads a two-day course on his minimally invasive 6 Pillar Approach to brain surgery quarterly in the new Aurora Research Institute Innovation Learning Center.

Neurosurgeons, neuroradiologists and neurologists from around the world attend to learn the parafascicular approach to remove tumors and clots from areas deep within the brain, or white matter. The approach pulls together the latest technologies to target treatment.

The course emphasizes economic resource optimization through surgical biometrics.

Abstract highlights

The Society of Vascular and Interventional Neurology invited interventional neurologist Akram Shhadeh, MD, to present two abstracts at its seventh annual meeting in November 2014.

“One abstract reflects our experience with treating ruptured brain aneurysms with a pipeline flow diverter device,” said Dr. Shhadeh, medical director of Endovascular Surgical Neuroradiology for Aurora Neuroscience Innovation Institute. “The second one reflects the benefit of interventional stroke treatment in young patients with no evidence of penumbra on CT perfusion.”

“Treatment of ruptured aneurysm with pipeline” showed that a self-expanding embolization device was safe and effective in treating two patients with ruptured brain aneurysms not amenable to other endovascular or surgical options. Further study is needed to validate this option.

“IA stroke therapy benefits despite lack of ‘penumbra’ on CT perfusion” showed that intra-arterial therapy within eight hours was beneficial in two patients despite a matched lesion without potentially salvageable tissue, or penumbra, visible with computed tomography perfusion imaging.

Ayman Gheith, MD, Rehan Sajjad, MD, Elizabeth Marriott, MD, Molly Zahour, NP, Megan Dibb, NP, and Amin Kassam, MD, were co-authors of the abstracts.
Expanding clinical trial access

Stroke is the fourth leading cause of death in the United States.

Principal investigator Elizabeth Marriott, MD, received a federal cooperative grant making Aurora Health Care the first StrokeNet satellite site in Wisconsin.

The National Institutes of Health Stroke Centers Network, or StrokeNet, is a network of 25 regional coordinating centers and its satellite sites working together to address the three prongs of stroke research: prevention, treatment and recovery.

The University of Wisconsin-Madison, a regional coordinating center, entered agreements with more than 30 health systems, or satellites, in the region to expand patient access to stroke clinical trials.

“We are pleased to combine the latest advances in stroke care with our extensive research team to bring the best available care to our patients,” Dr. Marriott said.

Clinical trials manager Carol Tutino, BSN, MS, is coordinating the program for Aurora Research Institute.
Sisters provide unique data for clinical trials

Born three years apart, sisters Nicole Borley, 26, and Sarah Socha, 23, coincidentally share a birth date.

Though there is no evidence of hereditary risk, they also share a disease – multiple sclerosis (MS).

Both diagnosed at 18, these Green Bay residents have different manifestations of this unpredictable disease of the central nervous system. However, the same Food and Drug Administration-approved drug, Tysabri (natalizumab, Biogen Idec), seems to work for both women.

Both also agreed to participate in observational clinical trials led by principal investigator James Napier, MD, so researchers can learn more about the disease and impact of the drug (clinicaltrials.gov identifiers: NCT00477113 and NCT01070836).

“First diagnosis”

Borley, who gave birth to a girl at the end of April, first knew something was wrong when she had vision problems with her left eye. After going in for a checkup and then to a specialist, she found out she had optic neuritis, an inflammation of the optic nerve. Further testing – including magnetic resonance imaging – showed lesions on her brain. Her diagnosis was MS.

With no previous medical history, Borley was stunned.

“I was numb,” said Borley, who had graduated high school the previous month. “I had never heard of MS. I didn’t know if I was dying or if it was something that could be fixed.”

After being hospitalized for a week, steroid therapy brought back the lost sight in her left eye after three months.

Borley tried different drugs, but flare-ups continued – numbness and tingling in her arms, legs and feet. When the latest drug stopped working, Borley was prescribed Tysabri.

“More lesions were showing up on my brain,” Borley said. “I had more than 40 lesions and a black hole was forming.”
Second diagnosis

Because of her sister’s experience, Socha was suspicious when she went numb along her left side from her shoulder to her foot.

She underwent testing.

“They wanted to rule out other things,” Socha said.

But Socha, a freshman in college at the time, was called home to receive her diagnosis.

“I stole Nicole’s appointment,” said Socha, who had steroid therapy for five days on an outpatient basis.

After suffering side effects from the first drug she tried, Socha was prescribed Tysabri.

Though the sisters began getting the monthly infusions together at Aurora BayCare Medical Center, Socha had to switch to a different schedule because she is JC antibody positive, which means she is more susceptible to a fatal complication – progressive multifocal leukoencephalopathy, a brain infection that can cause death in three days. Now she goes every seven weeks.

“I have decided to continue this treatment even though the risks are extremely high,” Socha said. “Bottom line is this medicine is very effective in keeping my MS flare-ups under control.”

Differences

The difference in how the disease manifests, particularly in members of the same family, is shown in stark contrast between the two sisters.

“Between Nicole and I, it shows that it can be so different,” Socha said.

Borley was able to complete college, got married and works as a high school math teacher. Though she has about 20 more lesions than her sister, she was primarily symptom-free until her pregnancy. After going off the drug for six months, she was prescribed Tysabri during her third trimester and took medical leave because of flare-ups in her dominant right hand and weakness in her right leg.

Socha, who withdrew from college and is limited to working less than 20 hours a week as a PartyLite consultant, needs a walking stick to get around a store. She hopes to one day return to college and is considering a degree in medical transcription.

“Some people you can really tell they have MS, some you can’t,” Borley said. “It doesn’t mean my body is healed (for lack of symptoms).”

“My symptoms are more physically seen,” Socha said. “The walking stick shows something is physically wrong.”

Giving back

No matter how differently the disease affects the women they are committed to making a difference in the course of MS. Through the Brown County MS Walk, the family has raised more than $73,500 over nine years for the National Multiple Sclerosis Society.

Co-captains of Team Coco Loco, the sisters have pulled together as many as 100 members for the annual walk.

“We’ll always do the walk,” Borley said.

Jennifer Homa, MS, is coordinating the clinical trials for Aurora Research Institute. Both trials are expected to wrap up in 2015.
Brain cancer stem cell bank creation to spur new treatment options

Building on Aurora Research Institute’s infrastructure, Neurosciences Vice President Amin Kassam, MD, is creating a brain cancer stem cell bank. His team is prospectively collecting multiple types of brain tumor tissue, including glioblastoma multiforme samples, and storing them in the Biorepository and Specimen Resource Center (BSRC), managed by Natalie Polinske, MS. The bank will provide a needed resource for the research community to use in development of new treatments for brain cancer.

Current standard of care for brain tumors includes chemotherapy, radiation therapy and surgery. However, long-term survival after treatment is a matter of months due to relapse, possibly because of remaining cancer stem cells.

“It is thought that the cells are at the root cause of tumor development and their elimination is critical for effective eradication of tumors in the long term,” Dr. Kassam said.

To initiate this research at Aurora, project coordinator Nina Garlie, PhD, director of the Regenerative Medicine Center, collaborated with scientific advisor Aaron Cheung, PhD, of Synaptive Medical and principal investigator Dr. Kassam to prepare an application for necessary seed money. They were successful in winning a $25,000 Aurora Cancer Care Research Award. Vince Lombardi Cancer Foundation generously funds the program. Polinske wrote a protocol and obtained Institutional Review Board approval to collect leftover brain tumor samples for research purposes. After the patients consent to the research study, senior research scientist Chang-Hyuk Kwon, PhD, and senior research associate Deborah Donohoe identify and characterize cancer stem cells. They will deposit a portion of the stem cells in the BSRC for future research. The remaining stem cells will be studied to develop new therapeutic techniques.

Jennifer Mathieu and Carol Halliday, RN, lead subject enrollment. Richard Rovin, MD, and Melanie Fukui, MD, are co-investigators.

Additional intramural funding

STUDY: Inflammatory markers and oral HPV infection: is there a correlation?

AWARD: $25,000, one year

SOURCE: Vince Lombardi Cancer Foundation (via Aurora Cancer Care Research Awards)

PRINCIPAL INVESTIGATOR: Martin Corsten, MD
Researchers study brain cancer drug as part of international trial

Aurora St. Luke’s Medical Center is the only site in Wisconsin participating in an international clinical trial to study a new immunotherapy drug in the fight against brain cancer.

Principal investigator George Bobustuc, MD, and his team are studying the impact of the vaccine, DCVax-L. (Northwest Biotherapeutics, Bethesda, Md.), on survival in subjects with newly diagnosed glioblastoma multiforme, an aggressive type of brain cancer, compared to controls (clinicaltrials.gov identifier: NCT00045968).

The drug is composed of the subject’s immune system cells (autologous dendritic cells) that have been modified with a tumor antigen (pulsed with tumor lysate antigen) to provoke an immune system response against relapse.

After the tumor has been surgically removed, subjects undergo standard of care treatment – radiation therapy and chemotherapy – as part of this Phase III trial. Two out of three subjects are randomized to also receive the investigational vaccine, while the remaining subjects receive a placebo.

Jennifer Mathieu and Lynda Yanny, BSN, are coordinating the clinical trial for Aurora Research Institute.

Neurosciences volumes – systemwide

<table>
<thead>
<tr>
<th>Source: Aurora Smart Chart and Medipac</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cases</strong></td>
</tr>
<tr>
<td><strong>2012</strong></td>
</tr>
<tr>
<td>Epilepsy cases</td>
</tr>
<tr>
<td>Total stroke cases</td>
</tr>
<tr>
<td>Ischemic stroke</td>
</tr>
<tr>
<td>Transient ischemic attack stroke</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
</tr>
<tr>
<td>Interventional radiology cases*</td>
</tr>
</tbody>
</table>

*Number of individual patients

Neurosciences publications

2014 Aurora-authored, peer-reviewed

Journal articles, book chapters, monographs


Abstracts


Additional strategic research

Aurora Research Institute investigators engage in additional strategic research that includes:

- Precision Medicine
- Orthopedics
- Women’s Health
- Aurora UW Medical Group
- Center for Urban Population Health
- Miscellaneous

>$265,000 in external grant funding awarded in 2014 for additional strategic research
123
total additional strategic research clinical trial enrollments in 2014

21
open additional strategic research clinical trials as of Dec. 31, 2014

>25% of Aurora’s research fits in the additional strategic category

~45% of Aurora’s additional strategic research is investigator-initiated

Subject Hero Award winner Norman J. Schmidt shares his experience with research. (See story on page 62.)
Study incorporates genetic testing to personalize prescription of drugs

In collaboration with Vanderbilt University, principal investigator Michael Michalkiewicz, PhD, and his team are studying the impact of genetic test results incorporated in the electronic health record on prescription of three common stroke prevention and two cancer therapy drugs.

The precision medicine study uses patients’ genetic characteristics to guide prescription of the best drug for the individual that increases drug effectiveness while at the same time reduces the risk of potential adverse effects.

From its National Institutes of Health grant, Vanderbilt awarded Aurora Health Care more than $400,000 over about four years to test whether genetic testing results in better outcomes for patients in need of these particular drugs.

A clinical decision-making support tool will aid physicians with selection of the proper genetic test before they prescribe warfarin, clopidogrel or simvastatin for stroke prevention or erlotinib or vemurafenib for some lung cancers and melanoma. After the results are incorporated in the electronic health record, the tool will inform the provider about the proper

Precision medicine clinical trial

Rubina Qamar, MD, is principal investigator of a clinical trial that offers precision medicine for subjects with non-small-cell lung cancer, the most frequent type of lung cancer.

Aurora Health Care is participating in the Lung-MAP clinical trial, which utilizes genomic profiling to determine the most appropriate of five investigational treatment options for the specific individual with advanced squamous cell lung cancer (clinicaltrials.gov identifier: NCT02154490).

“Squamous cell carcinoma represents about a quarter of all lung cancer diagnoses, but there are currently few treatment options beyond surgery for the disease,” Dr. Qamar said. “The trial will use genomic profiling to match patients to one of five different investigational treatments – four targeted therapies and an anti-PD-L1 immunotherapy – that are designed to target the genomic alterations found to be driving the growth of their cancer. This innovative approach to clinical testing should improve patient access to promising drugs.”
drug and dose based on the individual patient’s genetic test results.

“This project introduces information technology and organizational platforms for implementing personalized treatment based on a patient’s genetic characteristics,” Dr. Michalkiewicz said. “That means a provider will have the information to suggest a switch to an alternate therapy for a patient with a gene-drug interaction.”

Following implementation of the tool, researchers will evaluate changes in prescribing patterns by providers and improvements in outcomes for patients who were genotyped.

Key personnel include Arshad Jahangir, MD, Michael Thompson, MD, PhD, Ahmed Dalmar, MD, Scarlet Shi, PhD, Anthony DeFranco, MD, and Charles Bomzer, MD.

---

### Additional extramural funding

| STUDY: | Innovative programs  
(Integrative Medicine in Residency Program) to help support resident, faculty and staff education along with patient engagement |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>AWARD:</td>
<td>$13,000</td>
</tr>
<tr>
<td>SOURCE:</td>
<td>Weil Foundation Grant</td>
</tr>
</tbody>
</table>
| PRINCIPAL INVESTIGATORS: | Kristen Reynolds, MD  
Rebecca Schultz, NP |

<table>
<thead>
<tr>
<th>STUDY:</th>
<th>PeriData Maintenance and Service</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWARD:</td>
<td>$55,640</td>
</tr>
<tr>
<td>SOURCE:</td>
<td>University of Wisconsin-Milwaukee</td>
</tr>
<tr>
<td>PRINCIPAL INVESTIGATOR:</td>
<td>Andrew Marek</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>STUDY:</th>
<th>Development of the Lakeland Rural Training Track</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWARD:</td>
<td>$53,267</td>
</tr>
<tr>
<td>SOURCE:</td>
<td>University of Wisconsin-Milwaukee’s Eta Nu Chapter of Sigma Theta Tau International</td>
</tr>
<tr>
<td>PRINCIPAL INVESTIGATOR:</td>
<td>Jennifer Fink, PhD</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>STUDY:</th>
<th>Nurse-initiated music therapy in the immediate postoperative period: an evaluation of the impact of music on pain medication doses in the recovery room</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWARD:</td>
<td>$1,000</td>
</tr>
<tr>
<td>SOURCE:</td>
<td>University of Wisconsin-Milwaukee’s Eta Nu Chapter of Sigma Theta Tau International</td>
</tr>
<tr>
<td>PRINCIPAL INVESTIGATOR:</td>
<td>Matthew Beier, MS, RN</td>
</tr>
</tbody>
</table>

---

In this CYP2C19 gene fragment, a G/C mutation is identified, suggesting prescription of prasugrel instead of clopidogrel.
FDA approves new shoulder replacement device

Whether it’s to address a trauma or chronic debilitation, many people benefit from shoulder joint replacement.

In the 60 years since the first shoulder replacement, the design of the device has changed dramatically to prevent complications.

Aurora Health Care orthopedists R. Sean Churchill, MD, and Joseph Davies, MD, wrapped up testing in November 2014 for the latest design, a stemless device called the Simpliciti total shoulder replacement system (Tornier, Bloomington, MN).

The device received U.S. Food and Drug Administration approval early in 2015 as research results from 157 patients at 14 centers nationwide showed outcomes after two years similar to those of previous models with a stem. It is the first stemless shoulder replacement system available in the United States.

“Shoulder replacement is nothing new, and over time, the stem has shortened up,” Dr. Churchill said. “The question became, can we make it even better.”

Previous shoulder replacement devices had stems that went half way down the shoulder bone – to the weakest spot – and a curved piece that fit in the joint. Fractures at that weak spot were frequent, requiring a second shoulder replacement with a stem inserted along the full length of the bone.

Though newer models have shorter stems, the Simpliciti system abandoned it for a coating that allows bone to grow into the device. Any shoulder bone breaks can be treated naturally.

“Orthopedists are all about trying to conserve bone because you are always looking at not this procedure, but the one down the road,” Dr. Churchill said.

Churchill implanted the first FDA-approved stemless shoulder implant in the world March 17 at Aurora Medical Center in Grafton.

Sue Truchan, BSN, coordinated the clinical trial for Aurora Research Institute.
Pathway to more options

During a routine checkup after having his knee replaced in January 2012, Norman J. Schmidt admitted to shoulder pain.

His physician, Joseph Davies, MD, referred him to R. Sean Churchill, MD, at Aurora Medical Center in Grafton for a clinical trial testing a new shoulder replacement option, the Simpliciti total shoulder replacement system.

Schmidt fit the requirements for the trial and consented to participate.

After a successful surgery, Schmidt returned for regular checkups to test range of motion and monitor pain.

"Every day I wake up without pain and it is just great," Schmidt said. "And I don't know what I would have done without him (Dr. Churchill)."

The bionic man also received a new hip in February 2014 at Aurora Medical Center in Grafton.

"Research – if you can be in it and help someone out – why not do it?" said Schmidt, who received the Aurora Research Institute’s Subject Hero Award at the Greater Milwaukee Clinical Research Recognition Event in September.

"Testimony like that from Mr. Schmidt makes it all worthwhile," said Randall Lambrecht, PhD, president of the institute. "It shows we are fulfilling our purpose of providing options for patients."

Orthopedic volumes – systemwide

<table>
<thead>
<tr>
<th>Inpatient Procedure*</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total knee replacement</td>
<td>2,734</td>
<td>2,713</td>
<td>2,904</td>
</tr>
<tr>
<td>Total hip replacement</td>
<td>1,386</td>
<td>1,440</td>
<td>1,705</td>
</tr>
<tr>
<td>Hip replacement with ceramic-on-polyethylene bearing surfaces</td>
<td>374</td>
<td>628</td>
<td>812</td>
</tr>
<tr>
<td>Packed cell transfusion</td>
<td>864</td>
<td>646</td>
<td>544</td>
</tr>
<tr>
<td>Fusion or refusion of 2-3 vertebrae</td>
<td>449</td>
<td>516</td>
<td>506</td>
</tr>
<tr>
<td>Insert spinal fusion device</td>
<td>307</td>
<td>358</td>
<td>428</td>
</tr>
<tr>
<td>Excision or destruction of intervertebral disc</td>
<td>373</td>
<td>491</td>
<td>389</td>
</tr>
<tr>
<td>Open reduction of tibia and fibula fracture with internal fixation</td>
<td>431</td>
<td>652</td>
<td>384</td>
</tr>
<tr>
<td>Hip replacement with metal-on-polyethylene bearing surfaces</td>
<td>274</td>
<td>266</td>
<td>364</td>
</tr>
<tr>
<td>Injection into joint</td>
<td>712</td>
<td>880</td>
<td>322</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outpatient Procedure*</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee arthroscopy/surgery</td>
<td>3,646</td>
<td>956</td>
<td>4,969</td>
</tr>
<tr>
<td>Shoulder arthroscopy/surgery</td>
<td>2,989</td>
<td>936</td>
<td>4,557</td>
</tr>
<tr>
<td>Carpal tunnel surgery</td>
<td>798</td>
<td>280</td>
<td>1,543</td>
</tr>
<tr>
<td>Arthroscopic rotator cuff repair</td>
<td>833</td>
<td>272</td>
<td>1,514</td>
</tr>
<tr>
<td>Wrist endoscopy/surgery</td>
<td>373</td>
<td>184</td>
<td>735</td>
</tr>
<tr>
<td>Incise finger tendon sheath</td>
<td>320</td>
<td>122</td>
<td>703</td>
</tr>
<tr>
<td>Drain/inject joint/bursa</td>
<td>290</td>
<td>61</td>
<td>652</td>
</tr>
<tr>
<td>Arthroscopy biceps tenodesis</td>
<td>372</td>
<td>104</td>
<td>641</td>
</tr>
<tr>
<td>Removal of support implant</td>
<td>264</td>
<td>82</td>
<td>574</td>
</tr>
<tr>
<td>Revise ulnar nerve at elbow</td>
<td>204</td>
<td>63</td>
<td>410</td>
</tr>
</tbody>
</table>

*Top orthopedic procedures performed in 2014
Weight loss during pregnancy in obese women improves maternal, fetal outcomes

Aurora challenges weight gain recommendations for obese women during pregnancy

Pregnancy for obese women comes with increased risks. However, the Institute of Medicine recommends weight gain for all women, the amount depending on prepregnancy body mass index.

Aurora Health Care research, led by principal investigator David Merrill, MD, and co-investigator Callie Cox-Bauer, MD, challenges the recommendation for obese women, with findings showing that weight loss during pregnancy improves outcomes for obese women and their infants.

Dr. Merrill and his team compared outcomes of obese women who lost weight during pregnancy to those who had gained weight and documented newborn outcomes. Obese women who lost weight were less likely to need cesarean delivery or develop preeclampsia. Though there was an increase in small-for-gestational-age newborns, there was a significant decrease in neonatal intensive care unit admissions and a decrease in poor neonatal outcomes.

The researchers found that it may be safe for obese women to lose weight during pregnancy with appropriate surveillance by a health care provider.

Danielle Greer, PhD, and Kiley Bernhard, MPH, contributed to this research. Dr. Cox-Bauer presented the findings at the American College of Obstetricians and Gynecologists Joint District VI, VIII and IX 2014 Annual Meeting and at the American College of Obstetricians and Gynecologist 2015 National Meeting, receiving the Donald F. Richardson Memorial Prize.

Tool may predict risk for postcesarean incision site infection

Knowing which women who undergo cesarean section are more likely to develop an infection at the incision site could lead to fewer infections and better postpartum recovery.

Danish Siddiqui, MD, led a team of researchers in the development of a risk stratification tool to identify women whose postpartum course may be complicated by infections of their cesarean incision.

After comparing two established models, Dr. Siddiqui and his team found that use of chorioamnionitis - an infection of amniotic fluid, body mass index and surgery duration was a more simplified model for predicting infection based on a high-risk population. Further research is ongoing to validate the model.

Nicole Salvo, MD, Dakisha Lewis, MD, Kiley Bernhard, MPH, Danielle Greer, PhD, and Chris Van Mullem, MS, RN, contributed to this research. Dr. Lewis presented the findings at the Central Association of Obstetricians and Gynecologists 2014 Annual Meeting.
Researchers publish findings on vitamin D, preeclampsia in *Endocrine*

There is conflicting evidence on whether vitamin D deficiency leads to preeclampsia, a pregnancy complication associated with high blood pressure.

Principal investigator Danish Siddiqui, MD, and co-investigator Ahmed Dalmar, MD, compared vitamin D and calcium levels in women with preeclampsia to those without on the first day after childbirth.

The researchers simultaneously tested both the inactive (25-hydroxyvitamin D) and active (1,25-dihydroxyvitamin D) forms of vitamin D, something not routinely reported in the medical literature.

Regardless of type, vitamin D levels did not differ between women who had preeclampsia and those who did not on the first day after childbirth.

The findings were published in *Endocrine.*

Hershel Raff, PhD, Suneet Chauhan, MD, and Maharaj Singh, PhD, contributed to this research.

Women’s Health volumes – systemwide

<table>
<thead>
<tr>
<th>Breast Health Procedures</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammography</td>
<td>148,202</td>
<td>158,709</td>
<td>154,539</td>
</tr>
<tr>
<td>Screening</td>
<td>122,601</td>
<td>131,683</td>
<td>128,080</td>
</tr>
<tr>
<td>Diagnostic</td>
<td>25,601</td>
<td>27,026</td>
<td>26,459</td>
</tr>
<tr>
<td>Digital (%)</td>
<td>87%</td>
<td>96%</td>
<td>100%</td>
</tr>
<tr>
<td>Breast ultrasound</td>
<td>15,471</td>
<td>16,155</td>
<td>17,534</td>
</tr>
<tr>
<td>Core biopsy</td>
<td>3,180</td>
<td>3,456</td>
<td>3,373</td>
</tr>
<tr>
<td>Ultrasound-guided</td>
<td>1,941</td>
<td>2,146</td>
<td>2,203</td>
</tr>
<tr>
<td>Stereotactic</td>
<td>1,036</td>
<td>1,188</td>
<td>1,096</td>
</tr>
<tr>
<td>MRI-guided</td>
<td>72</td>
<td>29</td>
<td>41</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>131</td>
<td>93</td>
<td>33</td>
</tr>
<tr>
<td>Breast MRI</td>
<td>1,258</td>
<td>1,372</td>
<td>1,419</td>
</tr>
<tr>
<td>Needle localization</td>
<td>337</td>
<td>391</td>
<td>412</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Obstetrics/Newborn</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital deliveries</td>
<td>12,855</td>
<td>12,883</td>
<td>12,184</td>
</tr>
<tr>
<td>C-section (%)</td>
<td>25.7%</td>
<td>26.2%</td>
<td>27.3%</td>
</tr>
<tr>
<td>Hospital newborns</td>
<td>13,258</td>
<td>13,246</td>
<td>12,523</td>
</tr>
<tr>
<td>Hospital newborn NICU admissions</td>
<td>1,355</td>
<td>1,425</td>
<td>1,406</td>
</tr>
<tr>
<td>Level III unit</td>
<td>1,036</td>
<td>1,101</td>
<td>1,027</td>
</tr>
<tr>
<td>Level II unit</td>
<td>319</td>
<td>324</td>
<td>379</td>
</tr>
<tr>
<td>Average length of stay (days)</td>
<td>15.4</td>
<td>15.7</td>
<td>16.0</td>
</tr>
<tr>
<td>Average daily census</td>
<td>58.0</td>
<td>62.2</td>
<td>61.7</td>
</tr>
</tbody>
</table>

Maternal Fetal Medicine

| Ultrasound                 | 29,236 | 36,850 | 37,987 |
| Office visits              | 2,090  | 3,003  | 3,305  |

<table>
<thead>
<tr>
<th>Gynecology (Primary Diagnostic) Visits</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other disorders of female genital tract</td>
<td>107,981</td>
<td>111,818</td>
<td>112,864</td>
</tr>
<tr>
<td>Routine gynecologic exam</td>
<td>75,177</td>
<td>90,591</td>
<td>89,138</td>
</tr>
<tr>
<td>Contraceptive management</td>
<td>41,195</td>
<td>45,972</td>
<td>47,351</td>
</tr>
<tr>
<td>Inflammatory disease of female pelvic organs</td>
<td>18,918</td>
<td>17,436</td>
<td>17,262</td>
</tr>
<tr>
<td>Benign gynecology</td>
<td>8,045</td>
<td>7,610</td>
<td>7,202</td>
</tr>
<tr>
<td>General fertility management</td>
<td>6,747</td>
<td>6,915</td>
<td>6,727</td>
</tr>
</tbody>
</table>

Surgical Gynecology (Primary Procedures)

<table>
<thead>
<tr>
<th>Hospital procedures</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient (%)</td>
<td>60.2%</td>
<td>68.3%</td>
<td>77.4%</td>
</tr>
<tr>
<td>Laparoscopic (%)</td>
<td>55.2%</td>
<td>55.2%</td>
<td>58.7%</td>
</tr>
<tr>
<td>Laparoscopic assist (%)</td>
<td>11.4%</td>
<td>10.9%</td>
<td>11.2%</td>
</tr>
<tr>
<td>Robotic assist (%)</td>
<td>24.2%</td>
<td>27.8%</td>
<td>26.6%</td>
</tr>
<tr>
<td>Open (%)</td>
<td>16.6%</td>
<td>15.5%</td>
<td>14.5%</td>
</tr>
<tr>
<td>Cancer (%)</td>
<td>10.5%</td>
<td>11.7%</td>
<td>13.7%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Urogynecology surgical procedures</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolapse</td>
<td>835</td>
<td>986</td>
<td>1,092</td>
</tr>
<tr>
<td>Incontinence</td>
<td>692</td>
<td>669</td>
<td>607</td>
</tr>
<tr>
<td>Revision mesh</td>
<td>36</td>
<td>42</td>
<td>33</td>
</tr>
</tbody>
</table>

Source: IDX, EpicPB, Medipac, EpicHB 2012-14
Additional strategic research

Aurora UW Medical Group

**Dennis Baumgardner, MD**
Research Director, Aurora UW Medical Group

Dr. Baumgardner leads the Aurora UW Medical Group research core, which is responsible for supporting, growing and coordinating research and scholarly activity among faculty, students, residents and fellows. Areas of research focus include health care quality improvement and health services, medical education, cardiology, geriatrics, women’s health, healthy lifestyles, health disparities, epidemiology, asthma and other specific diseases.

What’s your worry?

A patient’s greatest health fear may be cancer, but her doctor would rather she focus on her cholesterol levels.

Disagreement on health priorities between patient and doctor is common.

Apparently, disagreement on health priorities is pretty common. In about three of five cases, patients and physicians disagreed about the patient’s greatest health concern, according to research led by principal investigator Dennis Baumgardner, MD, and presented by Jessica Kram, MPH, at the 2014 Wisconsin Research and Education Network Annual Meeting.

To determine the difference in opinions, Dr. Baumgardner and his team reviewed patients’ charts and noted a most important health concern before entering the exam room. During the exam, the physician asked the patient his or her greatest health concern. A total of 94 patients participated in the study.

Of the people who disagreed, the majority (83%) were more concerned about a different particular medical disorder than the doctor had identified. The other patients who disagreed either were worried about finances or violence or had no fears at all.

Men and women equally disagreed with their doctor. Younger patients were more likely to identify the same health concern as their doctor, but difference in age was not statistically significant.

Patients with high blood pressure were twice as likely as patients with other diseases to have a different concern than their doctor.

“People value a doctor who is sensitive to individual needs,” Dr. Baumgardner said. “This study has shown there is potential to identify and address unmet patient concerns and, hopefully, direct that person to relevant health interventions.”

Co-investigators Elizabeth Quiroz, MD, Kiley Bernhard, MPH, Mark Ledesma, MD, and Keren Rosner, MD, contributed to this study, which also was presented at Aurora Health Care’s Quality Roundtable.
Measuring delirium

After showcasing their findings at the American Geriatrics Society 2014 Annual Meeting, Center for Senior Health and Longevity medical director Michael Malone, MD, Ariba Khan, MBBS, MPH, and their team published a manuscript, “Innovative approach to measure delirium in hospitalized older adults using the electronic medical record,” in the Journal of the American Geriatrics Society earlier this year.

Using the Acute Care for the Elderly (ACE) Tracker clinical decision-making support tool within the electronic health record, collaborators compared the delirium marker feature to the standard delirium assessment in hospitalized adults 65 years and older.

The delirium marker combines delirium symptoms documented by nurses, use of physical restraints and pharmacological treatment for delirium.

They found that further work to improve the sensitivity of an automated delirium measure may make it more clinically useful.

Michelle Simpson, PhD, RN, Maharaj Singh, PhD, Mary Hook, PhD, RN-BC, and Yan Geng, MD, contributed to this study, which was also presented locally at Aurora Scientific Day.

Aurora Scientific Day

Aurora Scientific Day, an annual conference held in May, is an opportunity for students, residents, fellows, teaching and research faculty, and other allied health professionals at Aurora Health Care to present research findings.

In 2014, more than 130 people supported research by attending the presentations – 16 judged posters, 13 general posters, 14 oral presentations, two Rieselbach distinguished paper sessions and two innovation projects.

Rieselbach distinguished papers

- Development and validation of a risk score to predict access site hematomas after peripheral vascular interventions – Daniel Ortiz, MD
- Diabetes mellitus is an independent predictor of early mortality in patients at risk of sudden cardiac death – Mahek Mirza, MD

Judged Posters

1st place – Anton Strunets, MD
Increased risk of bleeding with no additional stroke reduction benefit in patients with atrial fibrillation on ASA and dabigatran or ASA and rivaroxaban combination therapy

2nd place – Rayan Yousefzai, MD
Hypertrophic cardiomyopathy with aortopathy: a novel association

3rd place – Mahek Mirza, MD
Noninvasive approach assessing atrial mechanics and serum biomarkers of collagen turnover provides a surrogate for fibrosis and atrial fibrillation

Sanjay Kansra, PhD, presents his study, “Curcumin (diferuloylmethane) induces apoptosis and blocks migration of human medulloblastoma cells,” at Aurora Scientific Day 2014.

Oral Presentation

1st place – Anushree Agarwal, MD
Elevated troponin as a risk marker in hypertrophic cardiomyopathy

2nd place tie – Luke O’Rourke, DO
Association of fetal abdominal-head circumference size difference with shoulder dystocia: a multi-center study

2nd place tie – Rayan Yousefzai, MD
Effect of pulmonary hypertension on patients with aortic stenosis who undergo transcatheter aortic valve replacement

3rd place – David Krum, MS
Determining three-dimensional catheter location using single plane fluoroscopy only
Center for Urban Population Health

Ron Cisler, PhD
Director, Center for Urban Population Health

Dr. Cisler leads the Center for Urban Population Health, a collaboration of Aurora Health Care, University of Wisconsin School of Medicine and Public Health, and University of Wisconsin-Milwaukee. The mission of the center is to advance population health research and education to improve the health of urban communities.

What is population health research?

Population health research focuses on identifying the determinants of health, disease and well-being in a particular population; designing and implementing preventive or treatment interventions; and measuring their effectiveness against health outcomes of the community.

The emphasis is health outcomes research and patient engagement at the intersection of primary care and community health.

Partners

• health centers, hospitals and clinics
• governmental institutions
• community-based organizations
• coalitions and networks
• academic centers and institutions

Dementia wellness project

Alzheimer’s disease is the most common cause of dementia. About 1 in 7 seniors in Wisconsin have Alzheimer’s disease. Currently, 65% of Wisconsin’s 74,000 nursing home residents have dementia, mostly due to Alzheimer’s disease, and the estimated cost of Medicaid-supported long-term care for Wisconsin residents with Alzheimer’s disease was about $1.6 billion in 2010.

Because Alzheimer’s disease is primarily a disease of old age, its prevalence and associated cost are projected to increase exponentially given the unprecedented expansion in the elder segment of the U.S. population. African American baby boomers are at greater risk than non-Hispanic whites of similar ages for Alzheimer’s disease or other dementias. The prevalence of Alzheimer’s disease and other dementias among older African Americans is roughly double than that among non-Hispanic whites, and is significantly higher than that among Hispanics.

In partnership with Milwaukee Health Services Inc. and the Wisconsin Alzheimer’s Institute, UW School of Medicine and Public Health has launched the Dementia Wellness Project for Underserved African American Elders.

The program aims to improve the health and well-being of underserved urban elders and their families by addressing health behaviors, access to care and social and economic factors. Funded by the Wisconsin Partnership Program, this project expands the role of the Dementia Diagnostic Clinic Network.

Bruce Hermann, PhD, is principal investigator with Tito Izard, MD, from Milwaukee Health Services Inc. Teresa Skora is project manager with support from center staff: Michelle Corbett, Gina Green Harris and Stephanie Houston.
African Americans suffer a disproportionate burden of asthma morbidity compared to other ethnicities. One possible explanation for such racial differences in asthma is that African Americans respond differently to asthma therapies as compared to other ethnicities.

The Best African American Response to Asthma Drugs (BARD) trial is comparing four treatment combinations for asthma. Each participant receives a peak flow meter and must complete a daily asthma symptom diary. There are 15 to 18 visits over a 16-month period. Participants, or the parents of minors, complete questionnaires asking about environmental factors, income and quality-of-life issues.

This study is open to enrollment for anyone who has an asthma diagnosis and at least one African American grandparent and is a nonsmoker, on a daily controller medication and at least 5 years old.

The objective of a second asthma study, STep-up Yellow Zone Inhaled CorticosteroidS to Prevent Exacerbations (STICS), is to determine in children receiving low-dose inhaled corticosteroids whether quintupling the dose at the onset of symptoms reduces the rate of severe asthma exacerbations treated with oral corticosteroids.

This study is open to children of all ethnicities from 5 to 11 years of age. Similar to BARD, the STICS study provides all study medication, education and monitoring of asthma symptoms.

The studies are sponsored by AsthmaNet and being conducted in partnership with the Aurora Research Institute Clinical Trials Department, Aurora UW Medical Group and the University of Wisconsin-Madison.

Lisa Sullivan-Vedder, MD, is the principal investigator and Stacie Snap and Mary Briggs-Sedlachek, RN, are coordinators for both studies.

Pediatric asthma research

Obesity intervention

According to the Centers for Disease Control and Prevention, 62.8% of Milwaukee residents are overweight or obese. Ethnic and racial minority groups are disproportionately affected by obesity, particularly African Americans, with 36.8% obese compared to 25.2% of whites.

Interventions have shown limited success at weight reduction in patients from these populations.

The Health Outcomes and Patient Engagement (HOPE) Research Collaborative has been working to develop MyLIFE: a patient-centered obesity intervention for African American women. The MyLIFE project, funded by Center for Urban Population Health, intends to examine the effect of a patient-centered obesity intervention that addresses both individual and community resource issues. Clinically, patients will be engaged in a multidisciplinary manner in areas of primary care, behavioral health, exercise and nutrition.

HOPE partners are Aurora Health Care, Aurora UW Medical Group, Marquette University, Medical College of Wisconsin and University of Wisconsin-Madison.

Ron Cisler, PhD, is principal investigator and Danielle Greer, PhD, Mike Farrell, MD, and Maharaj Singh, PhD, are co-investigators.
In year two of a three-year study, about 850 nurses and 50 nurse leaders at Aurora St. Luke’s Medical Center learned how to use a new evidence-based clinical decision-making support tools in the electronic health record (EHR) system to improve patient outcomes.

Mary Hook, PhD, RN-BC, leads the Knowledge-Based Nursing (KBN) Impact Study, funded by a $1.6 million Department of Defense grant from the U.S. Army Medical Research and Materiel Command. The KBN initiative uses technology to accelerate the adoption of best practices in patient care, which include conducting standardized assessments to detect risks and symptoms, intervening with tailored strategies to address unique patient needs and engaging patients in their care.

“Researchers have found that simply giving information about best practices does not change practice,” Dr. Hook said. “Changes must be adopted, implemented and maintained over time to get the best outcomes. We hope that this study transforms care.”

KBN best practices in six key areas were incorporated in Aurora’s Epic-based EHR system. After performing baseline assessments last year, investigators found knowledge gaps and intervened with various implementation methods to study the best way to improve use of the best practices. Researchers are hoping to eliminate knowledge gaps and increase use of best practices to achieve improved outcomes.

The next steps call for a postintervention assessment and possibly replicating the study at other Aurora Health Care sites. Maharaj Singh, PhD, contributes biostatistical support.

**Additional strategic research**

**Study reaches milestone with training of 900 nurses, nurse leaders in 2014**

The Journal of Physiology invited Hershel Raff, PhD, director of the Endocrine Research Laboratory at Aurora St. Luke’s Medical Center, to write a review on Cushing’s syndrome, a condition caused by too much of the stress hormone cortisol remaining in the body for too long.

Dr. Raff, an endocrinologist with ties to both Aurora Research Institute and Medical College of Wisconsin (MCW), collaborated with MCW endocrinologist Ty Carroll, MD, to publish “Cushing’s syndrome: from physiological principles to diagnosis and clinical care.”

“It is the culmination of my 30 years doing clinical research at Aurora St. Luke’s,” Dr. Raff said.

The review highlights a translational research approach to the condition by first providing a basic physiologic understanding before new diagnostic methods and treatment options can be explored.
As part of collaboration with the University of Minnesota, gastroenterologist Nalini Guda, MD, led research comparing biopsy techniques – conventional fine needle aspiration to the new wet suction technique. The study showed that the new wet suction technique obtained better tissue samples. The findings were presented at Digestive Diseases Week and published in *Gastrointestinal Endoscopy* - “‘Wet suction technique (WEST)’: A novel way to enhance the quality of EUS-FNA aspirate. Results of a prospective, single-blind, randomized, controlled trial using a 22-gauge needle for EUS-FNA of solid lesions.”

The new technique obtained better tissue samples for diagnosis.

This research is changing practice,” Dr. Guda said. “The need to bring patients back for a repeat procedure because of inadequate tissue for diagnosis has decreased.”

Aurora Health Care biostatistician Maharaj Singh, PhD, and gastrointestinal pathologist Timothy Wallace, MD, contributed to the study.

Aurora’s gastrointestinal researchers also had the distinction of securing access to data from the American College of Surgeons National Cancer Data Base. The intent of the study is to determine whether improvements in technology for tumor detection and staging have reduced nationally the number of unsuccessful surgeries in patients with pancreatic cancer.

“No one likes surgery. This research is changing practice,” Dr. Guda said. “It is a difficult disease, and every bit of what we can do for early detection, treatment and palliation will help.”
Aurora St. Luke’s programs rank among nation’s top 50

The gastroenterology and gastrointestinal (GI) surgery department at Aurora St. Luke’s Medical Center, Milwaukee, was the highest ranking GI program in Wisconsin among those nationally ranked by U.S. News & World Report in its 2014-15 evaluation of the nation’s best hospitals.

Aurora St. Luke’s gastroenterology and GI surgery department ranked 39th nationally among 1,586 programs that qualified for review.

Aurora St. Luke’s cardiology and heart surgery (see page 33), diabetes and endocrinology, geriatrics and pulmonology departments also ranked nationally among the top 50 hospitals in their respective categories, contributing to the tertiary care facility’s ranking as one of the best hospitals in the state.

Aurora BayCare Medical Center (Green Bay) and Aurora West Allis Medical Center also were listed as among the best hospitals in Wisconsin.

Research Media and Publishing


Publication is an important research outcome. The team also provides editing and design services for research manuscripts and other research communications.

Thank you!

To the Research Subject Protection Program for its management of the institutional review boards, review of all human subject research submissions and regulatory guidance and support.

To the institutional review board members for the countless volunteer hours they dedicate to ensure the safety and welfare of subjects participating in Aurora research.

Together, these groups help Aurora achieve the highest level of professional and ethical standards in human subject research.

To all the caregivers who contributed data, content and feedback to this report. The hard work and dedication of Aurora’s caregivers are evident on each page.