TOPS AT TAVR
U-M is a leader in transcatheter aortic valve replacement

ALSO:
- Testing how transcranial magnetic stimulation for depression works
- Bilateral mastectomy chosen more frequently than clinically indicated
- Early onset prostate cancer more aggressive
- Treating twin-to-twin transfusion syndrome with fetoscopic laser surgery
- Interventional neuroradiology repairs pediatric neurovascular malformations
- The high cost of treating hepatitis C
New hope for pancreatic cancer

A new Phase I/II study will look at adding the Wee1 inhibitor AZD-1775 to standard gemcitabine plus radiation therapy for patients with unresectable pancreatic cancer. This study builds on almost 20 years of research at the University of Michigan focused on improving the treatment of unresectable pancreatic cancer.

The study, which is the first to test this combination of AZD-1775 with radiation and gemcitabine in patients with pancreatic cancer, stems from laboratory research led by Theodore Lawrence, M.D., Ph.D. It is based on the finding that normal cells have two ways to protect themselves from DNA damage produced by chemoradiation, but pancreas cancer cells have only one way. In preclinical studies, inhibiting the Wee1 kinase by AZD-1775 cancels out the one remaining protection that cancer cells have, causing only the pancreatic cancer cells to die. Normal cells remained relatively unaffected in this model.

**NEW METHODS FOR CLINICAL TRIAL PARTICIPATION**

It's a classic Catch-22. The gold standard for clinical trials of new treatments involves random assignment of participants, but many candidates aren't willing to accept 50/50 random odds. The trial's recruitment lags, slowing the effort to improve treatment through research.

That's why University of Michigan physicians are leading efforts to test and adopt an approach that takes some of the “random” out of the process, while preserving the ability to compare treatments. Instead of every patient receiving a randomly chosen treatment, the approach adjusts the odds as the study progresses. If early results suggest better efficacy from one of the candidate treatments, each new patient’s odds of getting that option increase. It’s called response-adaptive randomization, or RAR.

In the journal Stroke, U-M researchers report the results of how 418 emergency department patients responded to the two approaches to trial design. The researchers asked the patients to imagine they had just suffered a stroke, showed them a video describing a study that needed stroke patients, and asked them whether they would volunteer for that study if they had really just had a stroke.

Half the patients saw a video describing a classic randomized study, and half saw the same video but with an added section describing an RAR approach. Only 54 percent of the people shown the first video said they would volunteer for the study. But 67 percent of those shown the RAR video said they’d enroll.

If the results play out in real emergency stroke studies, this 13-point difference could make a big difference in the pace of medical research, says William Meurer, M.D., M.S., the U-M emergency physician who led the study.

“Although this is a hypothetical scenario, it shows we might increase recruitment for acute stroke studies using a response-adaptive randomization design,” Meurer says. “This could be especially important in emergency situations, when patients or their loved ones have just minutes to consider options.”

**READ** Get linked to the journal article in *Stroke* at *Colleagues in Care Online* at med.umich.edu/cic.

**STUDY** Find out about clinical trials in any specialty that could benefit your patients at umclinicalstudies.org.
TOP FLOOR

Pelvic Floor Disorders Clinic expands access

The multidisciplinary University of Michigan Pelvic Floor Disorders Clinic’s nationally and internationally recognized physicians are uniquely qualified to address problems resulting from muscle laxity in the pelvic floor, such as organ prolapse and urinary or fecal incontinence. Comprehensive services include medical and surgical treatments, some of which employ minimally invasive techniques that can be performed in the office or on an outpatient basis.

The main clinic, located at U-M’s Von Voigtlander Women’s Hospital in Ann Arbor, has recently been joined by two additional locations, in Northville and Midland.

Megan Schimpf, M.D., associate professor of Obstetrics and Gynecology, who is board certified and fellowship trained in female pelvic medicine and reconstructive surgery, stresses that many pelvic floor problems viewed as incurable by older generations of women can now be successfully treated. Newer approaches to treatment used by the clinic are leading to long-term success without some complications that women may have heard about. The physicians at U-M have experience and success in treating women who have problems despite several surgeries for this problem before, including women who have had surgical complications.

“We have had great success in restoring pelvic anatomy without the use of mesh,” Schimpf says. “Women report that we can give them their lives back.”

Schimpf also points out that while not immediately life-threatening, pelvic floor disorders are socially debilitating; women with these concerns generally do not discuss them with family or friends and can become very isolated. The new locations and large team of providers will permit more access for patients who may not have been able to be seen before.

“Referring physicians should know that we are strongly motivated to help these patients and we have an armamentarium of new therapies that we choose from based on each specific woman’s needs,” Schimpf says. “We do everything we can to get them seen as soon as possible.”

Call M-LINE at 800-962-3555 to refer patients to the Pelvic Floor Disorders Clinic.

Golden anniversary

First transplant recipients help celebrate U-M Transplant Center’s 50th year

Identical twin sisters Janice and Joan Ottenbacher were just 15 years old when they unexpectedly became part of a groundbreaking surgery at the University of Michigan. Janice was dying; her kidneys failing. Joan agreed to donate a kidney. And as their parents waited anxiously, the twins successfully survived the first kidney transplant ever done in Michigan.

Fifty years later, both are healthy and thriving. They both became nurses, got married, and had children and grandchildren.

This summer, the twins joined the University of Michigan community in celebrating the 50th anniversary of the Transplant Center. Since the twins’ transplant in 1964, the University of Michigan Transplant Center has done more than 10,126 organ transplants, of which 1,077 were for pediatric patients. Only about a dozen centers nationwide have done that many procedures.

“I should have not been here, if it weren’t for God’s hand in our life and the technology and the doctors and nurses at the hospital 50 years ago,” says Janice Ottenbacher Schroeder, who now lives in Craig, Colorado.

At that time, transplant was very new and often limited to identical twins because immunosuppressant drugs weren’t needed to prevent the donor from rejecting the organ.

About 400 to 450 transplants are done at U-M annually. Kidney transplants have the highest volume, followed by liver, heart, lung and pancreas.

MORE Find out more about the transplant program at U-M and watch a video at uofmhealth.org/transplant.
The 10-seat hyperbaric oxygen treatment chamber that recently opened at the U-M Comprehensive Wound Care Clinic adds a key treatment modality to the clinic’s armamentarium.

CONSOLIDATED CARE

Multidisciplinary wound care clinic addresses multiple patient needs

More than five million Americans are treated annually for chronic wounds that do not heal. Such wounds can result from a number of factors, including diabetes, poor circulation, trauma, vascular disease or immobility. Foot ulcers affect more than 15 percent of people with diabetes and account for more than half of all lower extremity amputations.

The University of Michigan Health System’s Comprehensive Wound Care Clinic, opened in fall 2013, addresses the needs of these patients with a focus on wound healing, limb preservation, and prolonging and improving the quality of life. The clinic takes a multidisciplinary approach to the evaluation and treatment of non-healing wounds.

A variety of treatment modalities, such as the latest in biologic dressings, are part of the everyday care arsenal employed by the clinic’s practitioners. The newest addition to the clinic, a 10-person, multi-place hyperbaric oxygen (HBO) therapy chamber, opened in late September. The clinic will initially run two HBO sessions daily.

The intensive oxygenation provided to damaged tissues during HBO treatment hastens healing. “Not every wound patient needs HBO,” says Steven Haase, M.D., plastic surgeon and programmatic medical director for Wound Care. “But those who do really benefit from it.”

“The goal of this multidisciplinary clinic is to serve all patient needs in one facility,” continues Haase. The clinic offers a wide array of specialties, including general surgery, plastic surgery, family medicine, physical medicine and rehabilitation, podiatry and physical therapy wound care. In addition, support services such as social work and nutrition services are available on-site.

Patients who are referred to the clinic by their primary care providers are triaged by the clinical staff and assigned to the appropriate care provider, says Melissa Peterson, MSN, ambulatory care administrator. Electronic medical records keep referring physicians apprised of treatment plans and patient progress.

“Our staff is passionate and committed to wound care,” says Haase. “Because we generally see patients regularly over weeks or months, we strive to build good long-term relationships with each of them.”

“This clinic is a medical ‘home’ for patients with chronic wounds,” Peterson adds. “We make sure they get consistency and the responsive follow-up they need.”

M-LINE To refer a patient to the Comprehensive Wound Care Clinic, call M-LINE at 800-962-3555.

WATCH View a video introduction to the Comprehensive Wound Care Clinic at med.umich.edu/cic.
STOP THE CYCLE

Teen dating violence study shows the importance of screening

Dating during the teen years takes a violent turn for nearly one in six young people, a new study finds, with both genders reporting acting violent or experiencing violence within their dating relationships.

This startling number, drawn from a University of Michigan survey of more than 4,000 adolescent patients ages 14 to 20 seeking emergency care, indicates that dating violence is common and affects both genders.

Probing deeper, the study finds that those with depression or a history of using drugs or alcohol have a higher likelihood of acting as an aggressor or victim.

The findings, from the largest-ever study of the issue in a health care setting, suggest a need for health care providers to ask both young women and men about whether their relationships have ever turned violent, and to guide them to resources. The results were published in the Annals of Emergency Medicine.

“It’s important to think about both genders when trying to identify teen dating violence, especially when there are associated conditions we may be assessing in the health care setting,” says Vijay Singh, M.D., M.P.H., M.S., the study’s lead author and U-M faculty member in Emergency Medicine and Family Medicine. “These data remind us that teen relationships are not immune to violence and should encourage providers to ask adolescent patients about this important issue.”

Singh also co-wrote guidance for primary care providers on screening for intimate partner violence, published in Primary Care: Clinics in Office Practice.

RESOURCES Get linked to resources on teen dating violence to share with patients, along with more information about Singh’s research, at Colleagues in Care Online at med.umich.edu/cic.

The Eyes Have It

New ophthalmology app

A mobile app is now available to help check symptoms, causes and common treatments for some 135 eye diseases and disorders. More than 400 photos and videos illustrate the entries, including sections on eye anatomy and eye screening basics.

The app is an outgrowth of The Eyes Have It, a website created by Jonathan D. Trobe, M.D., professor and neuro-ophthalmologist at the U-M Kellogg Eye Center.

“The program was originally intended for medical students and ophthalmology residents,” says Trobe. “But we soon discovered that pediatricians, internists and many other physicians found it to be a great resource when seeing patients with vision problems. Now the app will make it even easier for them to use.”

DOWNLOAD The app costs $4.99 and is available for iPhone and iPad on iTunes. You can also use the website at kellogg.umich.edu/theeyeshaveit.

Parent pulse

Each month, the C.S. Mott Children’s Hospital National Poll on Children’s Health asks the public about children’s health issues. In the August poll, a nationwide sample of adults ranked the top 10 biggest health concerns for kids. Childhood obesity remains the top health concern for children in 2014, but when asked about national concerns, adults also put school violence and gun-related injuries in the top 10.

GET MORE You can find out more about the National Poll on Children’s Health and browse all the reports at mottnpch.org.
Ray Tollefson is no stranger to battling for his life. The 89-year-old World War II veteran trained as an Army Ranger, and was wounded in the June 1944 invasion of Normandy while attempting to storm Omaha Beach. He was hospitalized for two years because of his wounds. After the war, Tollefson became an accountant and eventually managed one of the largest luxury car dealerships in Detroit. Later in life, his service during the war was recognized and appreciated by several American presidents and the French people he fought to liberate.

Since 1984 — the 40th anniversary of D-Day — Tollefson has attended commemorative events in France every five years. However, in the fall of 2012, Tollefson was diagnosed with aortic valve stenosis by his doctors in the Petoskey area. He began to worry that he might not make the 70th anniversary event, possibly one of the last major commemorative events attended by soldiers who survived Normandy.

Then Tollefson was referred to the University of Michigan. Thanks to the team at the U-M Frankel Cardiovascular Center and the newest TAVR (transcatheter aortic valve replacement) procedure, Tollefson was able to travel to France for the 70th D-Day anniversary in June of 2014. And better still, he is back to living the active life he enjoyed before his diagnosis.

A PERSONALIZED APPROACH
The U-M Frankel Cardiovascular Center has been treating aortic diseases since
The University of Michigan Health System has a long history of superior cardiac care, with significant contributions to both research and clinical care of cardiac valve disease. This includes the latest transcatheter aortic valve replacement procedures (TAVR).

“With all cardiovascular procedures, volume is a key indicator of outcomes,” says G. Michael Deeb, M.D., co-director of the Heart Care Program at UMHS. “Any time outcomes are studied, factors that have a significant positive impact always include a significant volume of procedures.”

“In the last three years at UMHS, we’ve done over 375 TAVRs, including the procedures we did during the multiple clinical trials in which we’ve participated,” explains Deeb. “Currently, we do a minimum of four to six a week, which is also important for skills maintenance. We have excellent volume for a TAVR program that is not based in a very large city.”

But more than just volumes, it’s important for all cardiac care that referring physicians and patients evaluate the overall institution. “It’s important to have a programmatic-based commitment from that institution, because TAVR is a multifaceted, multidisciplinary procedure,” says Deeb. “For example, CMS requires a multidisciplinary clinic to evaluate patients for the TAVR procedure, and U-M adheres to that requirement.”
TAVR was initially tested and approved for use in patients with prohibitive surgical risk. However, TAVR is currently being evaluated for use in patients with moderate risk for open surgery, which may expand treatment options to patients who may benefit from the minimally invasive approach of this procedure.

THE NEXT PHASE
Tollefson came through the TAVR procedure without complications. In fact, after the procedure, he rested a few days at his daughter’s house in Ann Arbor, and then drove himself 300 miles home to the Petoskey area.

Here was a witty, sharp, vibrant man who was shackled down and was not able to live to his full potential. It felt like we unshackled him by doing the TAVR procedure.

Stanley J. Chetcuti, M.D.

These days, Tollefson stays busy, because now he can accomplish in an afternoon what would have taken him all week before the procedure. He also recently returned from a two-week Alaskan cruise.

“I think Mr. Tollefson felt like a caged animal when I saw him. Here was a witty, sharp, vibrant man who was shackled down and was not able to live to his full potential. It felt like we unshackled him by doing the TAVR procedure,” says Chetcuti. “Physically, he was limited by his valve problem. However, we were able to take care of that, without the incapacitation of a prolonged surgical procedure or a prolonged recovery period.”

During the June 2014 D-Day events, Tollefson was interviewed on national television about his experience at Omaha Beach, and he also met the president. “It meant so much to the whole team to see Mr. Tollefson sitting there,” says Chetcuti. “He sent me some pictures from Normandy, and they are now some of my most prized possessions.”

“I had complete confidence in Dr. Chetcuti and the entire team,” says Tollefson. “Every one of the people on the team treated me like family. And, the operation was amazing. I have had more bad side effects from a visit to the dentist’s office than I did from the TAVR surgery, so it was a fabulous thing. It was truly unbelievable.”

ONLINE Read more about TAVR and watch a video about its use at the U-M Frankel Cardiovascular Center at Colleagues in Care Online at med.umich.edu/cic.

REFER Refer patients for evaluation for TAVR by calling M-LINE at 800-962-3555.

Nation’s first transcatheter tricuspid valve replacement

The University of Michigan Frankel Cardiovascular Center is the first heart center in the nation to perform catheter-based percutaneous implantation of the Edwards SAPIEN valve to replace a patient’s tricuspid valve. On August 11, the tricuspid valve replacement was successfully completed by a cardiac team that included cardiac surgeon Steven Bolling, M.D., interventional cardiologist Stanley Chetcuti, M.D.; interventional cardiologist Daniel Menees, M.D., and cardiac surgeon Matthew Romano, M.D.

The team replaced the 47-year-old patient’s stenotic valve to improve blood flow on the right side of her heart. Her tricuspid valve had previously been replaced using animal tissue, which added to the complexity of her case. However, because of the less invasive catheter-based approach, the patient was discharged after only a two-day hospital stay.

Catheter-based percutaneous interventions can reach the heart without opening a patient’s chest, giving older, frail, high-risk surgical patients, non-operable patients and patients with complex health conditions more options for treating severe heart defects. While the transcatheter technique for aortic valve replacement (TAVR) has quickly become the preferred procedure for patients at prohibitive risk for open surgical intervention, transcatheter tricuspid valve-in-valve implantation is just beginning.
A national discussion

Cost shouldn’t be a barrier to a cure for hepatitis C

The treatment of hepatitis C virus infection has reached a crucial juncture, because new screening guidelines and more effective medications have the potential to improve the health outcomes of hundreds of thousands of Americans. “Hep C is a leading cause of liver failure, liver cancer and liver transplant in the U.S. and Michigan,” says Robert John Fontana, M.D., medical director of Liver Transplantation at UMHS. “Hep C is contagious before symptoms appear, so screening those at higher risk is essential to combating this disease.”

However, controversy has surrounded hep C treatments because of the timing of two events. First, in 2012 the CDC issued recommendations to screen all Baby Boomers for hep C (see sidebar). A year after this recommendation, new, better tolerated and more effective hep C drugs debuted on market. However, these drugs are extremely expensive, a fact magnified by the large pool of potential patients.

“These events sparked a national discussion about the costs of treating hep C,” says Fontana. “However, it’s important to understand that these new drugs are far superior to previous medications, because they are less toxic, easier to use and are 90 percent effective in clearing the virus. For these reasons, we believe these medicines will allow primary care physicians to diagnose and treat patients with hep C, or easily triage patients to local specialists.”

Fontana encourages advocacy to reduce the costs of these medications, as well as encouraging the discovery of more hep C drugs. He is joined in these efforts by Anna Suk-Fong Lok, M.D., director of Clinical Hepatology and associate chair for Clinical Research in the department of Internal Medicine.

“We should be communicating with insurance companies and government payers that these new drugs cure hep C, preventing progression to cirrhosis, liver failure and liver cancer, with enormous potential cost savings,” says Lok. “Short-term, we also are asking drug companies to expand their assistance programs. However, long-term, we are advocating for more research and development of other hep C drugs to lower costs. We believe with pressure from patients and physicians, we can make a difference.”

REFER

Compli- cated or advanced hep C cases can be referred to U-M Digestive and Liver Health by calling M-LINE at 800-962-3555.

ONLINE

Read more about Fontana and Lok’s research and U-M’s hep C treatment capabilities at Col leagues in Care Online at med.umich.edu/cic.

Screen Baby Boomers for hep C

Fewer than 40 percent of all individuals with hepatitis C know they are infected, but hep C is the most common blood borne illness in the U.S., at about four times the prevalence of HIV. In Michigan, nearly 100,000 individuals have hep C, with approximately 500 hep C-related deaths per year.

Additionally, over 50 percent of people infected with hep C are “Baby Boomers,” born between 1946 and 1965, and hep C is five times more prevalent in that demographic. Therefore, the CDC now advises a one-time hep C screening of all Baby Boomers, in addition to other high-risk patients, including injection-drug users and anyone transfused before 1992.
Early onset prostate cancer, a newly identified, more aggressive subtype often linked to genetic mutations

The number of younger men diagnosed with prostate cancer has increased nearly six-fold in the last 20 years, and the disease is more likely to be aggressive in these younger men, according to a new analysis from researchers at the University of Michigan Comprehensive Cancer Center.

Typically, prostate cancer occurs more frequently as men age into their 70s or 80s. Many prostate cancers are slow-growing and many older men diagnosed with early stage prostate cancer will end up dying from causes other than prostate cancer.
More than 1 million men will undergo a prostate biopsy this year, but only about one-fifth of those biopsies will result in a cancer diagnosis. A new urine-based test developed at the University of Michigan Health System improves on traditional prostate cancer screening tools to create a more accurate picture of a patient’s risk of prostate cancer.

The test, Mi-Prostate Score, looks at PCA3 and the T2:ERG gene fusion, a genetic anomaly discovered in the lab of Arul Chin-naiyan, M.D., Ph.D. These two markers are combined with serum PSA to produce a patient-specific prostate cancer risk assessment.

Researchers validated the new test on nearly 2,000 urine samples. Mi-Prostate Score, or MiPS, was significantly more accurate than PSA alone for predicting cancer as well as predicting aggressive prostate cancer.

**TESTING** The test is currently only available at U-M. For information on ordering the MiPS test, call the University of Michigan’s MLabs at 800-862-7284.

**WATCH** Watch a video about the MiPS test at Colleagues in Care Online at med.umich.edu/cic.

But, the researchers found, when prostate cancer strikes at a younger age, it’s likely because the tumor is growing quickly.

“Early onset prostate cancer tends to be aggressive, striking down men in the prime of their lives. These fast-growing tumors in young men might be entirely missed by screening because the time frame is short before they start to show clinical symptoms,” says Kathleen A. Cooney, M.D., professor of Internal Medicine and Urology at the University of Michigan.

“I’M A FIGHTER.”

Peter Rich was 59 when he was diagnosed with stage 4 prostate cancer. His PSA was only 9, but the disease had already spread to his ribs, spine and lymph nodes.

“To think of mortality was devastating. It was like any major loss — shock and numbness,” says Rich, who had to retire from his job as a school social worker because of his cancer treatment.

Rich was diagnosed six years ago. Average survival for stage 4 disease is generally less than three years.

“What we both said when we got the diagnosis was: ‘Well, that’s not acceptable,’” Rich says of himself and his wife, Carol. “I’m a fighter.”

Cooney and Scott Tomlins, M.D., Ph.D., assistant professor of Pathology at U-M, are leading a new study supported by the U.S. Department of Defense to look at DNA of both normal and cancerous prostate tissue of men diagnosed with advanced prostate cancer before age 61. They will be looking at whether these younger men are more likely to have inherited genetic mutations.

Men with a family history of prostate cancer have a two- to three-times greater chance of being diagnosed with prostate cancer. That risk increases for young men with multiple affected relatives. Prostate cancer runs in Rich’s family. Like Rich, his brother was diagnosed in his 50s, and a cousin and uncle had prostate cancer as well.

**A GENETIC LINK**

Previous studies from the Cooney lab showed that men with early onset prostate cancer had more genetic variants than men diagnosed with prostate cancer at a later age. The researchers suggest that genetic counseling or increased surveillance in younger men with a family history of prostate cancer may be warranted.

American men have a 16 percent risk of developing prostate cancer in their lifetime, but only a 3 percent lifetime risk of dying from it. The challenge, Cooney says, is understanding which subset of prostate cancers are most likely to be aggressive and deadly.

“The unexpectedly poor prognosis of advanced-stage, early onset prostate cancer supports the idea that a new clinical subtype might exist in men with early onset prostate cancer. This subtype is more aggressive and requires more specialty expertise, including genetic sequencing,” Cooney says.

**STUDY** For more information on the new, ongoing study, contact the U-M Cancer AnswerLine at 800-865-1125. To read the analysis in Nature Reviews: Urology, visit med.umich.edu/cic.
A therapy for treatment-resistant depression based on magnetic fields, not medications, may offer relief to some patients. But the underlying mechanism for symptom relief from transcranial magnetic stimulation (TMS) has not yet been identified.

A new clinical trial at the U-M Depression Center and Department of Psychiatry is now recruiting volunteers to receive the standard therapy along with advanced medical imaging so that researchers can examine the response.

The study will provide up to 25 TMS treatments to patients who haven’t responded to at least one antidepressant medication, preceded and followed by functional magnetic resonance imaging.

Although all volunteers will receive TMS therapy eventually, some will randomly receive a sham treatment at first, to allow research on the treatment’s potential placebo effect. Those who receive the sham stimulation can go on to receive 25 active treatments after the first phase of the study is completed.

TMS therapy carries U.S. Food and Drug Administration approval, and a growing number of insurers cover it—though many still do not. Study participants receive treatment at no cost to them.

The lack of clearly convincing evidence, and lack of understanding of the root of the therapy’s effects, are why the new study is needed, says its principal investigator, U-M psychiatrist Stephan Taylor, M.D.

“Previous research suggests that TMS may restore balance between the executive functioning areas at the front of the brain and areas involved in emotional responses and negative thoughts,” Taylor says. “We hope that by studying brain function in patients undergoing TMS, and sham TMS, we can help explain what is going on and perhaps illuminate why some patients experience remission after treatment.”

U-M is the only site in the country for the study, which is funded by the National Institutes of Health. The manufacturer of the TMS device contributed funding and the device that will allow the researchers to deliver the sham treatment, but is not involved in the study. U-M’s Functional MRI Laboratory will be used for pre- and post-treatment imaging.

**STUDY** Patients who have failed to respond to at least one antidepressant and are still taking medication may be candidates to participate if they meet other requirements. More information on the TMS study is available at umhealth.me/tms-study, by calling 734-232-0129 or by emailing psych-rtms-study@med.umich.edu.

**TREATMENT** The U-M Department of Psychiatry offers TMS therapy through its Neuromodulation Program, which also offers electroconvulsive therapy and vagus nerve stimulation. For more information, visit psych.med.umich.edu/neuromodulation.
About 70 percent of women who have contralateral prophylactic mastectomy following a breast cancer diagnosis do so despite a very low risk of facing cancer in the healthy breast, new research from the University of Michigan Comprehensive Cancer Center finds.

Recent studies have shown an increase in women with breast cancer choosing this more aggressive surgery, which raises the question of potential overtreatment among these patients.

The study authors looked at 1,447 women who had been treated for breast cancer and who had not had a recurrence. They found that 8 percent of women had a double mastectomy, and that 18 percent considered having one. Results appear in JAMA Surgery.

Overall, about three-quarters of patients reported being very worried about their cancer recurring. Those who chose to have double mastectomy were significantly more likely to express concern about recurrence.

“Women appear to be using worry over cancer recurrence to choose contralateral prophylactic mastectomy. This does not make sense, because having a non-affected breast removed will not reduce the risk of recurrence in the affected breast for most women,” says Sarah Hawley, Ph.D., associate professor of Internal Medicine at the U-M Medical School.

In addition to asking about the type of treatment, researchers asked about clinical indications for double mastectomy. Women with a family history of breast or ovarian cancer or with a positive genetic test for mutations in the BRCA1 or BRCA2 genes may be advised to consider contralateral prophylactic mastectomy due to a high risk of a new cancer developing in the other breast. This represents about 10 percent of all women diagnosed with breast cancer.

The study found that among women receiving a double mastectomy, nearly 70 percent did not have any clinical indications and many were candidates for breast-conserving lumpectomy.

“For women who do not have a strong family history or a genetic finding, we would argue it’s probably not appropriate to get the unaffected breast removed,” Hawley says.

A double mastectomy is a bigger operation that is associated with more complications and a more difficult recovery. In addition, most women went on to have breast reconstruction as well. Women might also still need to undergo chemotherapy or radiation therapy after their surgery — treatments that are known to reduce the risk of cancer recurring — which could delay their recovery further.

The researchers say it’s important to educate women better about the risks and benefits of contralateral prophylactic mastectomy, but that surgeons must also be aware of how patients’ worry about recurrence drives their decision-making.
Securing survival

Treating twin-to-twin transfusion syndrome

Twin-to-twin transfusion syndrome (TTTS) is one of the most serious fetal conditions, with survival rates around 5–10 percent without treatment. The University of Michigan C.S. Mott Children’s Hospital and Von Voigtlander Women’s Hospital offers a full spectrum of prenatal care management and treatment options — including fetoscopic laser surgery — to treat TTTS.

Patients with a monochorionic twin pregnancy share a blood supply through the placenta. There is a 10–15 percent risk of unequal sharing leading to development of TTTS. TTTS is defined as polyhydramnios in one baby with an amniotic fluid pocket of 8 cm or more (the recipient), and oligohydramnios or decreased amniotic fluid with a less than 2 cm pocket of fluid in the other (the donor). These twins also have an additional 10–15 percent risk of other complications related to the monochorionic status throughout the whole pregnancy.

“Treating TTTS with fetoscopic laser surgery is the best treatment we can offer for this very serious condition,” says Marjorie “Marcie” Treadwell, M.D., professor of Obstetrics and Gynecology and director of the Fetal Diagnostic Center at University of Michigan Health System. “Currently, UMHS is the only place in Michigan performing fetoscopic laser for TTTS.”

It is important to stress that monochorionic-diamniotic twins should be followed differently than other twin pregnancies. “We recommend an ultrasound at 16 weeks gestation, and ongoing ultrasounds every other week throughout the pregnancy,” explains Treadwell. “The ultrasound should evaluate fluid volumes and blood flow looking for evidence of either TTTS, twin anemia polycythemia syndrome (TAPS) or selective intrauterine growth restriction. Most pregnancies that progress to TTTS will do so around 18 to 24 weeks, but it can happen anytime, even as early as 16 weeks.”

The decision to use laser intervention is based on ultrasound and fetal echocardiogram evaluation that show TTTS progressive or persistent Stage I with cardiac dysfunction, or at Stage II or greater. The laser procedure severs all vascular connections between the babies, creating separate blood supplies. Excess amniotic fluid is also removed from the recipient baby.

“After the procedure, we either co-manage the patient with her referring provider or refer her back completely, depending on the circumstances,” says Treadwell. “Generally, patients will continue the pregnancy and deliver closer to term, with an average of around 33–34 weeks. A stay in the NICU is often required, but these babies generally do well.”

Refer
To refer a patient to the Fetal Diagnostic Center or the Maternal-Fetal Medicine service at the U-M C.S. Mott Children’s Hospital and Von Voigtlander Women’s Hospital, call 734-763-4264 or contact M-LINE at 800-962-3555.

Doctor bio

Marjorie “Marcie” Treadwell, M.D., received her undergraduate and medical degrees from the University of Michigan. She completed her residency in Obstetrics and Gynecology and her fellowship in Maternal-Fetal Medicine at Wayne State University. She remained in Detroit, based at Hutzel Hospital, for the next 16 years. As director of the Obstetric Ultrasound services for the Detroit Medical Center Hospitals, she pursued her interests in prenatal diagnosis and fetal therapy, in addition to teaching. She returned to the University of Michigan Health System to continue working in the areas of fetal diagnosis and therapy.
The advanced interventional neuroradiology services provided by a team of experienced pediatric neuroradiologists and subspecialty neurosurgeons at University of Michigan C.S. Mott Children’s Hospital are an integral part of the only comprehensive program in the state for the treatment of pediatric neurovascular malformations. One example of pediatric neurovascular anomalies that can be treated at U-M are Vein of Galen malformations.

Vein of Galen malformations can create abnormal dilation of vessels, shunting blood flow from its normal path, which can lead to heart failure, hydrocephalus and subarachnoid hemorrhages. If left untreated, malformations of the Vein of Galen have a high mortality rate. Open surgical repair is possible, but carries high rates of mortality and morbidity. However, endovascular procedures are increasingly being used to successfully treat these malformations.

“Vein of Galen malformations can be detected in utero. However, when a child presents with high cardiac output or hydrocephalus with no clear cause, it’s possible that a malformation in the Vein of Galen is present,” says Joseph Gemmete, M.D., a board certified interventional radiologist at C.S. Mott Children’s Hospital. “To treat this, we insert a small catheter into the abnormal connections, either from the artery or the vein, and block off the abnormal connections with glue or coils. Then we monitor the child to determine if further treatment is required.”

Although Vein of Galen malformations are rare, this condition is just one example of the type of complex pediatric neurovascular anomalies that can be treated at C.S. Mott Children’s Hospital. “We can also handle advanced procedures such as embolization for choroid plexus papilloma, retinoblastomas and other skull-based tumors, as well as cerebral diagnostica,” says Gemmete.

The specialists at C.S. Mott Children’s Hospital can also treat other vascular problems such as lymphatic malformations, venous malformations, spinal hemangiomas, and arteriovenous malformations of the head and neck. These can usually be treated directly through the catheter, or under image guidance with ultrasound or fluoroscopy. Injections such as alcohol or doxycycline may also be utilized.

“Our team includes all the pediatric specialists — including neurosurgeons, neurologists, intensivists, cardiologists, anesthesiologists and the ICU — that are required to deliver this specialized care,” explains Gemmete. “Our volume is high, so we have the expertise here that only a few centers across the country have.”

Interventional neuroradiology techniques are also becoming more commonly used in adult medicine at the University of Michigan. The benefits — less pain, less risk, less blood loss, less scarring and faster recovery times compared with most corresponding open surgical procedures — are the same for adults and children alike.

Many cerebrovascular pathologies in adults can be treated using a simple catheter. “For example, we can block off aneurysms, intracranial arteriovenous malformations and dural arteriovenous fistulas with Onyx glue and/or coils,” explains Gemmete. “We can also embolize many hyper-vascular skull-based tumors and spinal cord fistulas.”

Our volume is high, so we have the expertise here that only a few centers across the country have.

Joseph Gemmete, M.D.
A look at CME courses planned for 2015

**APRIL**
- Advancing Outpatient Diabetes Care

**MAY**
- Updates in Nephrology for the Primary Care Provider
- Internal Medicine Spring Review
- 10th Annual Advanced Liver Disease and Liver Transplantation
- Update on Arrhythmias and Syncope

**JULY**
- 33rd Annual Internal Medicine Update

**AUGUST**
- 28th Annual Cardiology Update
- 28th Annual Pediatric Board Review

**SEPTEMBER**
- Clinical Issues in the Care of Older Adults

**OCTOBER**
- Practical Solutions to Common GI Problems
- Familial Colorectal Cancer: Diagnosis, Genetics and Management
- Contemporary Issues in Multidisciplinary Breast Cancer Management

**NOVEMBER**
- 12th Annual IBD Update for the Practicing Physician
- 28th Annual Update in Pulmonary & Critical Care Medicine

**DECEMBER**
- 17th Annual Liver Disease Wrap-Up

**MORE** Courses listed are tentative and subject to change. Details will be posted at ocpd.med.umich.edu/cme/course-calendar as they become available.