Craig Shulstad knows the hospital halls well. As a University of Minnesota undergraduate, he daily went through University Hospital—as it was then known. “I lived in Frontier Hall, so I would take a shortcut through the hospital every day on my way to class,” he says.

“But I never thought I’d be back regularly, as a guinea pig,” he says with a laugh.

Shulstad is enrolled in a study investigating a new medication for high cholesterol, and despite laughing at his comment, he takes his involvement as a clinical study participant seriously. “This is something that I can do to help improve my health and science,” he says.

As part of the two-year study, he returns to Fairview-University Medical Center every three months for blood work and other tests; every six months he undergoes an ultrasound of his carotid artery, to check for plaque buildup. “I used to faint at the thought of getting my blood drawn,” he says, “but now, it doesn’t bother me. Especially when I know I’m contributing to research.”
Advancing knowledge, improving treatments

Shulstad is one of thousands of people who participate in more than 2,000 health-related clinical trials at the University of Minnesota each year. The National Institutes of Health defines a clinical trial as “a research study in human volunteers to answer specific health questions.” Clinical trials help determine whether new drugs or treatments are both safe and effective and determine the best way to use a standard treatment.

Cardiologist Daniel Duprez, lead investigator on the study, hopes to prevent or reduce the risk of heart attacks and strokes by effectively managing a person’s lipids, or cholesterol levels. A host of treatment options already exist to keep a person’s cholesterol levels in check, such as drugs known as statins. Yet Duprez believes that “we can do even better.”

The trick, he thinks, may be to actually raise cholesterol levels—at least the “good” kind, known as HDL. “There are already a number of successful treatments for lowering the bad type, or LDL,” he says, “but we haven’t done much in the way of potentially increasing one’s HDL.”

Duprez’ study is testing a drug that may do just that.

“We hope to find that the drug in question will be effective at raising HDL levels, and that raising a person’s HDL levels will have a positive effect on their health,” findings that could help several million people, he says.

Shulstad was already on medication that was effectively managing his cholesterol levels. So, why participate in a clinical trial? “Because I know medication can keep getting better,” he says.

Clinical trials are only part of a broad range of clinical research, which the NIH describes as patient-oriented. Clinical research also includes: experiments that provide greater understanding of normal human physiology; epidemiologic studies that look at diseases in populations; behavioral studies; outcome research that examines how treatments work in the real world; and, health services research.

Because the University is involved in all areas of clinical research, it must maintain equally wide-ranging support. A major resource is the General Clinical Research Center (GCRC). The center is one of 70 GCRCs nationwide, funded by the NIH to support clinical investigations.

“While our primary mission is to support NIH-funded researchers,” says center director Elizabeth Seaquist, “we also have a strong training mission” for investigators just starting their research careers. The GCRC provides a dedicated space for clinical research as well as services such as nursing staff trained in research protocols and statistical assistance. (The AHC’s Research

“Participant safety is of utmost concern.” — Moira Keane

Kristine Ensrud directs the Epidemiology Clinical Research Center, which conducts ground-breaking research in areas such as osteoporosis, diabetes, and cardiovascular disease prevention.

“T HIS IS A ONE-STOP-SHOP FOR RESEARCHERS’ NEEDS,” SAYS ELIZABETH SEAQUIST, GENERAL CLINICAL RESEARCH CENTER DIRECTOR.
Services Organization also aids researchers and those outside the University with an array of services.)

“I simply wouldn’t be doing my research now if it wasn’t for the GCRC,” says Seaquist, an endocrinologist who began studying diabetes in the early 1980s with GCRC support. “One of the best things about the GCRC is that researchers like me can grow their work and develop their own team.” Seaquist discovered that some people have a genetic predisposition to diabetic complications. She currently has three NIH grants and 10 staff supporting her research.

Protecting participants

A GCRC seed grant to investigate the clinical use of tea tree essential oil was awarded to Linda Halcon, a School of Nursing professor. She studies whether tea tree oil speeds the process of healing chronic wounds.

Collaborating with orthopedic surgeon Marc Swiontkowski and infectious disease expert Dean Tsukayama, Halcon devised a pilot study with subjects recruited from Fairview-University Medical Center and Hennepin County Medical Center. Participants come in weekly for four weeks, during which time their wound is physically measured and monitored for skin irritation from the twice-daily application of a gel containing tea tree oil.

Halcon has gained valuable information from the process. “Preparing for the study took longer than I had imagined,” she says. She had to obtain FDA approval to use tea tree oil as an investigational new drug (IND). She gained assistance from Harvey Arbit, director of the University’s IND/IDE Assistance Program. Arbit’s extensive experience in drug development, clinical research, and regulatory affairs helped ensure Halcon’s application met FDA approval. Halcon and her team then had to submit their research protocol to the University’s Institutional Review Board, or IRB.

“The IRB reviews all research projects involving human participants,” says IRB director Moira Keane. “We do this in order to ensure that two broad standards are upheld—first, that participants are not placed at undue risk, and second, that they give uncoerced, informed consent to their participation.”

Investigators are required to submit to the IRB their research plan, or protocol, including plans for data safety, recruitment, and consent forms. The IRB then reviews for regulatory requirements and ethical principles, before sending it to the IRB committee for final approval. “We give thoughtful review for every proposal,” says Keane. “The questions we ask are very deliberate. Participant safety is of utmost concern.”

These clinical trial participants contribute to new knowledge about devastating conditions. A possible drug treatment for the most common cause of deteriorating eyesight in elderly patients, macular degeneration, is being investigated by ophthalmologist Timothy Olsen.

Collaborating with Deborah Ferrington, Olsen is identifying specific protein modifications that occur in age-related macular degeneration (AMD). Additionally, he seeks to improve the drug delivery systems required for the disease. “Currently, getting the drug to the macula is difficult,” says Olsen. “The macula is very small, about one-tenth the surface of your fingernail. But if we can figure out which protein to target, we hope to develop new treatments for this blinding disorder.”

“We typically receive 30 new applications a week for medical research,” says Moira Keane, director of the Institutional Review Board.
Seeking answers

Community-based research is the focus of the University’s Epidemiology Clinical Research Center, or ECRC. The facility, administered by the School of Public Health, brings together researchers exploring a wide range of health concerns, including cardiovascular disease, obesity, and women’s health.

Center director and physician Kristine Ensrud leads a number of studies examining the safety and efficacy of drugs that have potential for preventing and treating osteoporosis. “Until recently there were no treatments for osteoporosis, except hormone therapy,” she says. In part because of recent studies demonstrating that hormone therapy can cause other health problems for some postmenopausal women, “we are currently evaluating other agents,” she says.

Oral health is the focus of another study. Microbiologist Joel Rudney wants to track down the pathogens responsible for periodontal disease. “Dentists know that cleaning below the gumline eliminates disease-producing bacteria,” he says, “but the bacteria always come back. So what I want to know is: where are they coming from?” Rudney suspects they lurk inside cells at reservoir sites in the mouth and emerge to re-colonize.

By taking cheek cells from dental patients, he found those cells had been invaded by multiple species of bacteria. “The whole thing is much more complicated than we originally thought,” says Rudney. His findings have implications for treatment. “If we block the invasion of one species, what about all the others that might also invade?” Although he doesn’t have an easy answer, Rudney hopes continued research will lead to better oral health.

Clinical research is also being carried out in the College of Veterinary Medicine. Two veterinarians, Sofia Morales and Ned Patterson, are working in different areas to improve the health of dogs.

Some of Morales’s patients have been admitted to the intensive care unit at the University’s Veterinary Medical Center. “Dogs are good at hiding their illnesses,” says Morales. “It’s in their instinct not to look like prey.” The problem with that, she says, is oftentimes by the time it’s evident something is wrong, something’s really wrong.

By testing a dog’s thyroid levels, Morales hopes to better understand the severity of the illness, and also, the dog’s chances of pulling through. “We currently don’t have a lot of data to explain to owners whether their dog with X disease will have an X percent likelihood of making it,” she says. “I hope this study will help owners make informed decisions about their pets.”

Patterson investigates epilepsy in dogs. “One to five percent of all dogs have epilepsy,” says Patterson, “which is as common as it is in people.” He is part of the Canine Epilepsy Research Consortium, a collaboration of institutes searching for the genes responsible for epilepsy in dogs. “There’s currently no diagnostic test for epilepsy,” Patterson says. “Once we have a gene, we’ll begin tailoring potential drugs for treatment.”

Which is a perfect example of how clinical research works—moving from basic science findings to testing a treatment, and bringing that safe, effective treatment to the patient.

For more information on clinical trials, see www.ahc.umn.edu/research/trials.