Among its responsibilities, the SRTR reports publicly the outcomes for transplant candidates, recipients and transplant procedure performed in the country. Among its responsibilities, the SRTR reports publicly every six months on the performance of each of the nation’s transplant programs and organ procurement organizations, and yearly on the state of transplantation in the United States.

In addition, it supports the transplant-related research needs of the national Organ Procurement and Transplantation Network, which is responsible for overseeing organ allocation in the United States, while also supporting the needs of HRSA and the U.S. Secretary of Health and Human Services’ Advisory Committee on Transplantation.

In other words, the SRTR is a gold mine for researchers seeking to find ways to improve access and outcomes for transplant candidates, recipients and donors in the United States.

The year 2007 was a blockbuster for research on kidney transplantation at U-M, with several major papers, the initiation of a multicenter study on the outcomes of living lung and living kidney donors, and the adoption by HRSA of a national collaborative project—inspired by U-M research—to attempt to reduce the active U.S. kidney transplant waiting list to zero by the year 2015.

Already in 2008, the U-M team’s work is helping U.S. authorities revise the system by which kidneys are allocated and distributed nationally.

Among the division’s faculty, four play key roles in SRTR. Right from top: Alan Leichtman, MD, and Panduranga S. Rao, MBBS, are co-investigators, while Akinlolu O. Ojo, MD, PhD, is the team epidemiologist. Friedrich Port, MD, MS, an emeritus member of the faculty, is the project director for the SRTR and president of the Arbor Research Collaborative for Health.

Together with U-M transplant surgeons, including Robert Merion, MD, John Magee, MD, and Randall Sung, MD, and numerous research staff, the team delves deep into the data and distills their findings for the entire transplant community to share and use.

For example, this year SRTR published a study showing that a transplant candidate’s place of residence has a significant impact on his or her opportunity to be placed on a transplant waiting list. The analysis also showed that, once listed, a candidate’s location impacted his or her chances of receiving a kidney transplant from a living or deceased donor in a timely fashion.

Certain key changes could increase the chance that an available kidney gets used optimally, says Leichtman, who is also the former chair of the Kidney and Pancreas Transplantation Committee of the Organ Procurement and Transplantation Network.

Appropriate donor-recipient matches can ensure that those kidneys with the greatest potential for long-term survival are directed to those transplant candidates who are likely to live the longest following transplantation, it also ensures that kidneys with more limited-potential survival could be reasonably allocated to candidates with shorter potential lifespans.

Such a strategy would reduce the need for repeat transplantation, and improve the extra years of life potentially achieved from available donors. Additionally, more efficiency could be built into the system for distributing “expanded criteria donor” organs—kidneys that aren’t quite perfect but can improve and prolong a life all the same.

Also in 2007, the U-M Nephrology team and their surgeon colleagues studied the issue of second transplants—and found that 13.5 percent of the kidneys transplanted each year went to people who had already had one transplant, and that 15 percent of people waiting for a new kidney had received one before. This reinforces the importance of better matching between donors and recipients, and better treatment of transplant recipients to reduce the risk that they’ll need another kidney.

The future of transplantation in the making

Right now, more than 75,000 Americans are listed nationally for a kidney transplant. But each year, only about 17,000 Americans receive new kidneys. While thousands die or become too sick to withstand transplant surgery, others just keep waiting.

Fortunately, research at the University of Michigan by Nephrology faculty and their colleagues is helping pave the way for changes in kidney allocation that could lead to improved survival, and to faster and more successful transplantation.

Why is the University of Michigan such a hotbed for kidney transplant research? It’s not just because U-M has one of the best and largest kidney transplant programs in the country. It’s also because the nation’s official organ transplantation registry is based in Ann Arbor at the Arbor Research Collaborative for Health and administered in partnership with co-investigators from the University of Michigan’s Departments of Medicine, Surgery, and Biostatistics.

Organized through a contract from the federal Health Resources and Services Administration (HRSA), this massive database, called the Scientific Registry of Transplant Recipients (SRTR), includes information on every transplant candidate, donor, recipient, and transplant procedure performed in the country.

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This research is being used in the development of new proposed regulations for the allocation and distribution of kidneys around the country, so that the best use can be made of all the available organs each year. This new national allocation system is scheduled to be introduced in 2008.

In the meantime, an effort to maximize kidney transplant opportunities is also under way, with leadership from Dr. Leichtman and others from U-M. Called the 58 DSA (Donation Service Area) Challenge, its aim is to increase the number of kidney transplants performed in the United States annually by 7,000 over the 2006 baseline.

To reach that goal, each DSA—including its participating organ procurement organization, transplant centers, and donor hospitals—is being challenged to optimize the way transplant candidates are treated, and the way potential donor kidneys are identified and made available.

Other University of Michigan transplant nephrologists are working hard on strategies to improve the lives of patients with kidney disease. In collaboration with surgical colleagues, Diane Cibrik, MD, MS, leads the transplant program’s pharmaceutical research efforts. These investigations ensure that U-M transplant patients get the earliest opportunities to receive the best new medications available to help preserve their kidney transplant function.

Through these efforts, nearly all U-M transplant recipients have the opportunity to participate in studies designed to optimize their post-transplant care. In addition, Dr. Ojo and Crystal Gadegbeku, MD, are involved in a number of important strategy investigations to limit the development of kidney failure, especially in high-risk minority populations, thereby reducing the eventual need for kidney transplantation.

Also of note are the efforts of Silas Norman, MD, to develop protocols for transplant patients at especially high risk for post-transplant infectious complications; and of Fu Luan, MD, to limit post-transplant complications of heart disease and diabetes that may be worsened as a consequence of the required medications that transplant recipients take to prevent rejection. Meanwhile, Dr. Leichtman and Pavan Chopra, MD, are working with colleagues at the Kidney Epidemiology and Cost Center to establish a novel system of Kidney Paired Donation. This allows kidney transplant candidates with incompatible, but otherwise suitable, willing, living donors to find appropriate alternative living-donor opportunities through an exchange of donors and candidates caught in the same situation.

Even as U-M nephrologists lead these efforts, the division continues to train the next generation of kidney transplant specialists, with a transplant nephrology fellowship program that is one of only 17 in the country. In 2007, the program was recertified for another five years, and was praised as a paradigm of training programs. As a hotbed of research, education, and clinical care in kidney transplantation, the division is poised to continue to have a major impact on America’s transplant system.

At the foot of the mountain of kidney disease

Kidney failure costs the United States billions of dollars per year to treat hundreds of thousands of people with drugs, dialysis, and transplants. And that’s not counting the cost of lost workdays, family stress, and lives cut short.

A full 90 percent of those kidney-failure patients have something in common: their end-stage renal disease is rooted in problems with tiny structures inside their kidneys, called glomeruli. Each glomerulus is a hub for the blood-filtering flow that keeps us from drowning in our body’s own toxic waste. When glomeruli get less efficient at their jobs, or fail entirely, the result can be deadly.

But the real problem, it turns out, isn’t with the entire glomerulus. It’s with the podocytes—highly evolved cells within each glomerulus that actually help organize and carry out the blood-filtering process.

Their name means “foot cell,” a name they earned because of their shape. Each podocyte has many protruding “foot processes”—skinny extensions of the cell that interlace with the tiny capillaries that bring blood into each glomerulus. But research is showing they deserve their name for another reason: When you get to the bottom of most kidney diseases, podocytes are the common factor.

This central role has become clear thanks in part to research led by Roger Wiggins, MB, BClin (right), and his colleagues in the Divisions of Adult and Pediatric Nephrology at the University of Michigan.
In recent work, Dr. Wiggins and his podocyte laboratory team were able to show that they could induce kidney disease simply by wiping out a portion of the podocytes in the rat kidney. They did this by developing a transgenic rat with podocyte cells that were made sensitive to the toxin produced by diphtheria bacteria. When podocytes succumbed to the toxin, the glomerulus became leaky and then filled with scar tissue as the body tried to repair it, in exactly the same way as happens in people with common kidney diseases.

These results showed a direct connection between podocyte destruction and the common causes of most forms of kidney failure in people, and set the stage for further work.

Similarly, research by the Wiggins lab team in collaboration with Friedhelm Hildebrandt, MD, and colleagues in the Division of Pediatric Nephrology have shown that a gene mutation leading to a misformed podocyte protein is responsible for nephrotic syndrome and scarring of the glomerulus. In other work, the Wiggins laboratory showed that a high-calorie diet causes podocyte damage and death leading to kidney failure—but that this damage to podocytes can be prevented by restricting how many calories are consumed.

In 2007, Dr. Wiggins published a review article that amasses all the evidence of the podocyte’s importance across a broad spectrum of specific kidney diseases. His work lays out the processes by which podocytes fail, and the causes and effects that lead to a decline in kidney function.

By presenting this unified view of kidney disease, Dr. Wiggins hopes to help physicians understand what they can do to prevent and treat kidney disease in their patients and also to encourage other scientists to focus on productive research into how podocytes become injured and fail. Diabetes, high blood pressure, and genetic predisposition all combine to damage podocytes or make them less efficient, but most of this damage can be prevented or delayed. Blood pressure medicines, effective blood sugar control, and weight control can all help.

These findings are helping bring podocytes to the fore in the search for the causes and potential treatments of kidney disease. For the hundreds of thousands of Americans whose kidneys are failing, and for the millions more whose kidneys are at risk because of diabetes, high blood pressure, and other conditions, those discoveries can’t come too soon.