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Doing the Math

In the world of operations research/applied mathematics, researchers devise formulas to analyze and resolve real-life problems. With this in mind, transplant surgical fellow Dorry Segev asked his wife, mathematician Sommer Gentry, to help him develop an algorithm for a national paired kidney database. The goal: to figure out how to get the greatest number of kidneys to the neediest people—a concept mathematicians call “optimization.”

After doing some research, Gentry, who is completing her Ph.D. at the Laboratory for Information and Decision Systems at the Massachusetts Institute of Technology, found an algorithm that could be adapted perfectly to the paired kidney exchange situation. “If you have 100 people on your list and a lot of them could trade with others on the list, there are literally millions of different arrangements,” she explained. “But if you just go about matching pairs one by one without considering all possibilities [the current model], rare opportunities for hard-to-match pairs will likely be missed.”

Drawing from data describing end-stage renal disease patients eligible for kidney transplantation and their willing and eligible live donors, Gentry and Segev created virtual patients. The main outcome measures were number of kidneys matched, human leukocyte antigen (HLA) mismatch of matched kidneys and number of grafts surviving five years post transplant. When compared with current pairing schemes, the couple’s national PKE model showed that:

- more patients would be transplanted
- transplants made from the matches would be of higher quality (by antigens, by age, etc.)
- highly sensitized patients—the most vulnerable—would be well served by the system
- patients, physicians and transplant centers would have the flexibility of choosing which priorities are highest for the patient in the system (e.g., a patient

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Toward a National Paired Kidney Exchange



Janet Hiller tells Scott and Lisa Keller what to expect from the surgeries. The couple met at a dialysis center but hope they never have to visit one again.

SCOTT KELLER’S PATIENCE WAS wearing thin. The 31-year-old computer draftsman from Kalamazoo, Mich., has focal segmental glomerulosclerosis—a fancy name for hardened kidney tissue that thwarts the organ’s function. Keller’s wife wanted to give him a kidney, but antibodies from previous blood transfusions would likely launch rejection. Keller had been on dialysis for 15 years. With dialysis came extreme fatigue and osteoporosis, a common renal disease side effect.

While waiting for a cadaveric kidney, Keller heard about the paired kidney exchange program at Johns

Hopkins. Paired kidney exchanges (PKEs) provide organs to patients who have a willing, designated biologically incompatible donor. A kidney from this donor is matched to and transplanted into the recipient of a second donor pair, and vice versa. The transplants are performed simultaneously. Since 2001, 22 successful PKEs have been done at Hopkins Hospital.

Keller decided to find out if he and his wife qualified. “I just wanted to feel halfway normal again,” Keller recalls. They flew to Baltimore, underwent tests and joined the Hopkins database for potential pairing. A year later, though,

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Kidney Exchange

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the search had turned up no matches. Contributing to the delay was the dearth of potential donors in the database. How to expand this pool has been a riddle the Comprehensive Transplant Center has long sought to solve.

Now, CTC director **Robert Montgomery** is on a mission to bring together leading transplant centers to launch a *national* paired kidney exchange. The United Network for Organ Sharing approved a proposal



Dorry Segev and Sommer Gentry: The pair behind the pairing scheme.

last fall for such a program. And in March, the inaugural consensus-building meeting took place in Chicago. Subsidized by Margery Pozefsky, a patient who benefited from a transplant at Hopkins, the conference was the first joint effort to launch a national PKE plan.

Leading the program with Montgomery were several other live kidney transplant pioneers, including incoming UNOS president Frank Delmonico of Harvard University, Lloyd Ratner of Columbia University, Michael Rees of Medical College of Ohio, and E. Steve Woodie of the University of Cincinnati. In all, about 100 surgeons, nephrologists, nurse coordinators, regulators, psychiatric professionals, social workers, and informatics and database ex-

perts shared best practices at the two-day meeting.

“The payoff in making these matches is huge,” Montgomery said, as he rattled off alarming statistics. Currently, 60,000 Americans are awaiting kidneys; 3,718 people died last year because suitable organs couldn’t be found in time. But even when there’s a willing kidney donor pair—as in the Kellers’ case—almost a third of potential donor/recipient pairs won’t match because certain antibodies could jeopardize an organ’s survival. “Every day, it’s like looking for a needle in a haystack,” says Janet Hiller, transplant nurse coordinator, a.k.a. “the kidney matchmaker,” for the Incompatible Kidney Transplant Program.

The Hopkins Immunogenetics Lab has long had a computer program that facilitates difficult tissue type matches to potential donors. But, admits Co-Director Sue Leffell, the pool isn’t large enough to match the growing number of people with rare antigens. Instead, many patients opt to

undergo plasmapheresis—the blood filtering process that removes harmful antibodies—so that a loved one with an incompatible blood or tissue type can donate. “By swapping donors from a bigger pool,” Leffell notes, “we can avoid the risks and expense of desensitization protocols for some patients.”

Leffell represents Hopkins on the UNOS Kidney and Pancreas Transplantation Committee, which approves allocation of those organs—and the first committee to endorse a national PKE proposal. Leffell believes one important goal of the plan is to set uniform standards for immunologic testing. “That would eliminate confusion and complications when pairs must travel for matches,” she said.

Immunologic disparities are but one

barrier to creating a national PKE database. Other obstacles include patients’ insurance coverage and willingness to travel, and the availability of plasmapheresis at other centers for those who need it. Ethical and psychosocial issues arise as well—like feeling no emotional connection to a recipient.

Yet, insisted Montgomery, the benefits of a national PKE database far outweigh the barriers. To prove the point, the CTC hired mathematician Sommer Gentry to develop an algorithm (see sidebar), making the most of combinations while respecting patients’ preferences. Meanwhile, focus groups at the conference analyzed obstacles and offered possible solutions.

Hiller hit numerous snags as she tried to match the Kellers with another donor/recipient pair. In the end, she made an unconventional but successful one-on-one match with a man who suited Scott genetically but who had a different blood type. Keller needed to have his spleen removed and plasmapheresis before the transplant, but his prognosis is good.

In May, as Scott received the new kidney, his wife donated one of hers to another compatible recipient. And Hiller had found a third pair to match that day. It took a little longer to orchestrate all this, but, in Hiller’s view, prolonging life for several people simultaneously was worth the extra effort. ■

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who prefers to stay within his own region but who might travel for a better organ.)

Shortened wait times are obvious benefits of a national PKE plan. But the financial incentive is also noteworthy. “Even if only 7 percent of patients awaiting kidney transplantation participated in a national PKE,” Gentry argued, “the health care system could save as much as \$750 million.” ■

Segev and Gentry are lead authors of a paper on the subject, which appeared in the April 20 issue of the Journal of the American Medical Association.