

Among the questions Pitt researchers are turning to computer models to help answer: What is a good death?

THEY ANSWER QUESTIONS CLINICAL TRIALS CAN'T

BY MICHAEL FITZGERALD

MEDICAL SUPER MODELS

A patient is telling his doctor about episodes of shortness of breath and chest pain, telltale signs of angina.

"So, you said you're having chest pain five times a week," the doctor notes. "I have a couple of options for medications for you. One will cure you, but I have to tell you that there are side effects, including, very rarely, death. The other won't cure you, but it will reduce your pain."

The patient doesn't pause even a moment before responding. "Does the second one cause death?"

"No," says the doctor.

"That's the one for me, then," says the patient.

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The doctor is curious. "Why, when there's less than a 1 percent chance of dying?"

"Doctor, bad things always happen to me. If someone is going to die from this, it'll be me."

Most people don't think much about luck when it comes to health care. But for some people, whether or not they feel lucky matters, says Carol Stockman, who heard this story from a physician she interviewed. Stockman is an experimental economist and a research assistant professor in health policy and management in the University of Pittsburgh's Graduate School of Public Health.

"The role of luck was not really anything I had ever thought about before," she says, speaking with an economist's mind-set. "I believed people behaved rationally—you did your calculations and made your highest utility choice." But in talking to doctors, she found otherwise.

Stockman is studying what you might call the Eeyore effect: what people choose when they believe they're not lucky.

The answer may help explain some disparities in treatment preferences.

For instance, African Americans with heart problems choose life-saving procedures like bypass operations less often than whites, even when researchers control for type of insurance, income levels, location, physician bias, and levels of pain. Stockman wonders, do African Americans feel especially lucky or unlucky, and how might that influence their healthcare decisions? Might such perceptions contribute to the disparities?

These are the kind of questions Mark Roberts encourages people to ask. Roberts, associate professor of medicine, health policy and management, and industrial engineering, is chief of the School of Medicine's Decision Sciences and Clinical Systems Modeling Section.

Stockman's questions can't be answered with clinical trials. It's a complicated issue. There may be multiple right answers—or none. This may be true anytime you ask the question, *How do patients make decisions?* Likewise, resource and cost questions often can't be studied in randomized clinical trials. But many such questions can be modeled using computers, and researchers at Pitt, notably those associated with or collaborating with Roberts' group (like Stockman), keep expanding their use of mathematics to try to capture the nuances of medicine and health care.

Some of the questions Roberts and his colleagues are asking:

Can predictive models show the best combination of drugs to give HIV-positive patients when antiretrovirals stop working?

How do you get the best results for patients undergoing in vitro fertilization, ensuring that a patient with enough money for only one such procedure has the best chance of conceiving—or that couples can lower their odds of twins or triplets?

Is it more cost-effective to invest in quickly identifying an outbreak of bioterrorism or in the preparation required to respond to it?

Roberts would tell you that in the end this effort has little to do with computers. It's about helping people—doctors, patients, policy makers—make better decisions about health care.

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Two doctors have coffee after rounds. Some of the patients they've just seen won't be leaving the ICU until they leave this world.

"You know, we talk a lot about quality of life for our patients. What do you think they might trade to have a better death?"

"What do you mean?"

"Well, instead of lying around in a hospital bed for months, getting worse and worse, what if people could guarantee an excellent experience at the end of their lives? Would they trade some part of their healthy lives?"

The question wasn't just a sign the doctors—Derek Angus, professor with appointments in the Departments of Critical Care Medicine, Medicine, and Health Policy Management, and Robert Arnold, the Leo H. Criep Professor of Patient Care—needed to cut back on their caffeine. After more discussion, they approached Cindy Bryce, a policy analyst and assistant professor of medicine and of health policy and management, to see if she would be interested in looking at the economics involved.

Bryce thought the questions they were raising were pretty good. Worthy of study, in fact.

From that caffeine-stimulated encounter has come a significant, National Institutes of Health–funded examination of the calculus of cost-effectiveness, which has traditionally boiled down to measuring cost of care versus lives saved. Hospice care may actually shorten a life, which makes it look very expensive relative to other kinds of care. But hospice care may be less painful and make for an overall easier, more peaceful death for some patients. With other researchers at Pitt, Carnegie Mellon University, and the University of Toronto, Bryce crafted a study that may ultimately shift how some healthcare dollars get spent.

First the researchers had to find out how patients would define excellent end-of-life care. Essentially, they wanted to know: What is a good death? To get at this fuzzy question, they asked people about four facets of end-of-life care: level of pain and symptoms, control over conditions in the hospital, control over treatment choices, and emotional and financial family support received.

They found, among other things, that almost three out of four people would give up time, as much as two years, for less suffering at the end of their lives. If people knew they would die at about 80 and could have a one-month period of exceptional care before dying, they would, on average, surrender more than eight months of their lives in exchange.

Bryce is aware such questions raise other questions. "Whose values do we care about?" she asks. "Society is the big gold standard. But a lot of research shows that what patients value and what society values is different."

She acknowledges that some people question whether quality can be measured but believes that using models to help analyze decisions is valid and useful for doctors helping patients with hard decisions. How does this work translate to the clinic? A doctor may never punch patient-decision parameters into a software program (though that could happen as well), but the efforts of decision scientists can help a doctor understand how her patients make choices and what's important to them as they do.

Bryce is also involved in the best known and most advanced research on decision making under way at Pitt. Led by Roberts, she and others have since 1997 published a series of papers that ask challenging questions about



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Choices, choices. Decision scientists help doctors, patients, and policy makers with tough healthcare decisions.

liver transplantation. Among them: Should the sickest patients receive new livers, or the patients most likely to benefit? Should we maintain the current regional system, where transplant candidates in one of 11 regions typically get access only to livers donated in their region, or should we distribute livers nationally? And when is the best time to give a patient a transplant?

Their research has fueled national debate on these and other questions related to liver transplantation.

"It's truly groundbreaking," says Stephen Pauker, associate physician-in-chief at Tufts-New England Medical Center, founder of Tufts' Center for Clinical Decision Making, and one of Roberts' early mentors. (Pauker published several seminal papers in the decision-making field.)

Groundbreaking is exactly what Wishwa Kapoor, Falk Professor of Medicine and chief of the Division of General Internal Medicine, wanted when he began encouraging Roberts to pursue research into decision making. Roberts came to Pittsburgh in 1992 to run the internal medicine residency program at UPMC Shadyside. Prior to that, he had been an instructor of medicine and a research fellow at Harvard Medical School with a research focus on how doctors make decisions.

Kapoor knew that Roberts was one of the best decision-science researchers in the nation—Pauker calls him "a mainstay of the field, and one of the best modelers we have." Kapoor also knew that questions involving resource allocation were becoming more and more important in health care.

"It comes up in everything we do," Kapoor says. "If we have some new treatment that is really, really expensive, is it cost-effective to use it? Or if we have something that is cheap but doesn't improve quality of life or quality of care, should we keep using it? Decision sciences is one way of objectively looking at it."

Kapoor saw an opportunity for Pitt to become a leader in national policy discussions, and he's been right. Since Roberts established his section in 2000, the group has produced more than 40 published papers, with another 20 submitted or in process—and those are just the ones Roberts is coauthoring.

Not long after he came to Pitt, a cautious Andrew Schaefer walked into a doctor's cluttered, book-filled office.

He sat down and immediately announced, "I see I've come to the right place."

Schaefer, now an assistant professor in both industrial engineering and medicine, was hoping to find a doctor willing to apply industrial engineering techniques to health care. In graduate school, Schaefer says, "the conventional wisdom was that there are great problems in medicine, but you can never find an MD to work with you."

In that office, he knew he'd found the MD, because he was sitting eye level with Martin Puterman's *Markov Decision Processes*, a mathematics text engineers use to help resolve questions whose answers vary depending on circumstances. He knew that if a doctor had a copy of Puterman, there had to be work they could do together.

That doctor was, of course, Mark Roberts, and he and Schaefer have found plenty of uses for mathematical techniques from the world of industry to look at supply-chain questions like donor organ allocation. They've also used the predictive math of finance to determine when patients might need certain treatments.

Schaefer has taken to calling such research "therapeutic optimization." By next August,

he hopes to start a Center for Therapeutic Optimization at Pitt—another place for doctors to collaborate with those outside their disciplines on tough questions.

It certainly won't hurt Pitt's reputation in decision sciences. As Schaefer says, "This is the time to be doing this stuff, and Pitt is the place to do it."

He admires Roberts' cross-disciplinary finesse, which has helped build Pitt's reputation in the field.

"The thing that's amazing about Mark is he can think about problems as an MD or as an engineer or as an economist or as a statistician. And then he can turn around and explain difficult concepts from one of those areas to experts in another," says Schaefer.

That's no surprise to Eileen O'Keefe, Roberts' wife of 20 years, who says he can talk to anyone: "He'd be my worst nightmare on a plane. He's the kind of guy who can sit down and talk to you for the entire flight."

Roberts' parents say he has always been able to do this, even when the family spent two years in Lahore, Pakistan—there, he became relatively proficient in Urdu and would lead other kids on jaunts.

"Mark goes to these conferences, and he's like the mayor," says his wife. "He's slapping so-and-so on the back, talking to everyone."

Roberts isn't just a social butterfly. He graduated cum laude in economics from Harvard before going to medical school at Tufts (he spent one med school year at Pitt). While getting his MD, he also earned a master's in public policy at Harvard's Kennedy School of Government.

In his third year in medical school, he met a young patient—a contractor with testicular cancer. The cancer was metastatic, but it was also highly responsive to chemotherapy.

The chemo drugs then available would cause patients to vomit 40 or 50 times a day. Patients could reduce that to eight or 10 times a day using Compazine. But a then-new drug, Trilafon, completely eliminated vomiting induced by the chemo. Roberts knew it had been recommended for the contractor.

The contractor, who had secured health insurance for his employees, had neglected to insure himself, figuring that as a 28-year-old he was unlikely to need much medical care.

"He asked all the time about what things were costing," says Roberts.

One day, the patient had to throw up when Roberts was visiting him on rounds. Roberts was startled. "Isn't the Trilafon working?" he asked.

"The Trilafon works great, but it's $370 a dose. The Compazine's $20. For $350 bucks, I'll vomit 10 times."

Roberts was horrified. He later reconsidered: "I thought, why shouldn't he be able to make the decision?"

Roberts was already interested in the policy of health care—he had his Master of Public Policy degree by that point. But interacting with the contractor got him interested in how patients make decisions and trying to optimize those decisions using analytical tools from outside the medical field. Ultimately, he began using sophisticated computer models of the sort common in airplane design and corporate logistics departments.

Bryce jokes that Roberts will look at any complex question and say, "But that's just a trivial matter of programming." Still, Roberts knows that many doctors are skeptical of the models and not without reason. He cites studies showing that doctors make more accurate treatment decisions in a minute or two of looking at a patient than with unlimited time and a full chart and file.

"Our [doctors'] training is not so I can just sit there and remember an algorithm—it's so I can recognize when the patient in front of me doesn't fit the algorithm," Roberts says.

He points out that in the mid-1990s 30 percent of heart attack survivors in Pennsylvania left the hospital without instructions to take an aspirin.

"People forgot, people were too busy," Roberts says. "We're obviously making decisions that are not particularly thoughtful. I want to make those decisions more consistent and thoughtful."

For him, that means ensuring that patients have a hand in the decision making.

He recently saw an elderly patient whose LDL cholesterol levels had reached 150. The models showed there was a 4 percent chance of her having a heart attack in the next 10 years, slightly higher than average. If she were to take the popular drug Lipitor, her odds of a heart attack would drop to 3 percent.

Lipitor would cost her $2,000 a year. He asked the woman if she thought it would be worth it to spend $2,000 every year on Lipitor for the next 10 years, to bring her risk down a percentage point. Or, he asked, would she rather go to the Bahamas every year?

She picked the Bahamas. Roberts says her quality of life will almost certainly be better doing that than taking Lipitor.

But for him, it comes down to this: "She's the only one who can decide whether or not one percent risk is worth $2,000 a year." ■

CHEAP DATE

Viagra might seem like a frivolous drug, a "lifestyle enhancer." But does that mean it isn't cost-effective?

That's what Kenneth J. Smith, assistant professor of medicine, decided to find out five years ago. Smith, at the time a clinician at Mercy Hospital, was frustrated that he had to fill out extra forms to get insurers to consider covering Viagra prescriptions, not something he had to go through for, say, migraine treatments. Yet insurers didn't seem to have any trouble paying for penile implant surgery, which Smith thought was a costlier way to treat erectile dysfunction than the typical lifetime payout for Viagra.

"Insurers didn't feel Viagra was cost-effective," he recalls. "It seemed to me they were using a variety of rationales not to cover it."

So Smith contacted Mark Roberts, associate professor of medicine, health policy and management, and industrial engineering, who is chief of the School of Medicine's Decision Sciences and Clinical Systems Modeling Section. Smith and Roberts, who had collaborated on research since 1993, decided to examine the cost-effectiveness argument. They knew that Viagra was less expensive than surgery, but it also has potential side effects, including heart problems and death. An insurer could argue that the potential for such side effects would make no treatment better than using the drug. To model potential changes in health over time, Smith and Roberts drew on decision models used by industrial engineers.

They examined data from a number of studies on erectile dysfunction. Even adjusting the data so that death occurred much earlier and much more often than what happened in the actual studies, Smith and Roberts found that Viagra was clearly cost-effective when compared to other standard treatments for non-life-threatening conditions that insurance companies routinely cover.

"It skewered popular wisdom," Smith says, and gained national attention. Insurers could find other reasons not to pay for Viagra, but no longer could they say it wasn't cost-effective. —*MF*