

“The mission statement around here is to make health care in the future better than it is today.”



### RABENECK PUTS COLONOSCOPIES UNDER MICROSCOPE

The research in which Linda Rabeneck engages is what she likes to call “policy relevant,” a label that suggests it has very real-life consequences. “We set the bar very high here, and we’re trying to do research that’s not just, ‘Oh gosh, that’s intriguing.’” It is also, she says, identifiable for her level of involvement in its nuts and bolts. “I’ve always taken a dim view of folks who are making broad policy statements but not contributing to the area,” Rabeneck, who is also a senior scientist, says. “I think to fully understand the field you have to be working in it and contributing to it.”

Rabeneck has engaged in both recently, in the service of more accurately defining the limitations and applications of colorectal cancer research. A colonoscopy is the final common pathway for any abnormalities revealed through a colon cancer screening test. But while it may be the best tool available for detecting polyps and cancer in the colon, it’s still some distance from perfect. It was Rabeneck’s dismay over stories from colon cancer patients about colonoscopies that missed their diagnoses that spurred her to research investigating their accuracy.

Focusing on 2,654 patients newly diagnosed with cancer on the right side of their colon (the most technically difficult to reach) who had surgery for their cancer between 1997 and 2001 and a colonoscopy in the preceding three years, Rabeneck honed in on the last colonoscopy before the diagnosis, and considered the interval. If the colonoscopy was within six months of the diagnosis, she determined, it found the cancer. But for those diagnosed between six months and three years after their test, the “miss rate” was alarming. Specifically, it was 4%: the cancer in 105 of 2,654 patients had been overlooked by the very test undertaken to find it.

The results of this retrospective cohort study were published in *Gastroenterology* in 2004.

The translation of this grim fact to the reality of a patient’s life is easy, says Rabeneck. It means now, in addition to explaining the various physical risks of the procedure (e.g., bleeding, a punctured bowel), a doctor must include noting the possibility that, “If you have cancer, there’s a small chance I might miss it.”

Rabeneck, about whom SRI senior scientist Dr. Thérèse Stukel admires, “her intellectual curiosity, her absolute rigour in doing research and her openness to comments from [others],” has also investigated the issue of setting an upper-age cutoff for colonoscopy screenings. Currently, international recommendations say these tests should begin at age 50, but nobody’s ever put a ceiling on them. They should, believes Rabeneck, who has a strong family history of the disease. A person’s likelihood of developing colon cancer rises beyond the age of 50, but his life expectancy goes down. And, again, colonoscopies are not without risk.

Her study, published in *The Journal of the American Medical Association* in 2006, examines the trade-off, and concludes that a colonoscopy screening lends an 80-year-old only 15% of the expected gain in life expectancy that it does younger patients. This finding, says Rabeneck, “should be factored into decision-making about whether elderly patients should be screened.”

### SRI SCIENTIST GIVES CHOLESTEROL-REDUCING DRUG NEW LIFE IN DEFENCE AGAINST SEPSIS

Don Redelmeier’s understanding of clinical epidemiology smacks of some dissatisfaction. “There really are many things wrong with current health care, and we want future health care to be better,” says the senior scientist, who holds a Canada Research Chair in Medical Decision Sciences and is cross-appointed to the Institute for Clinical Evaluative Sciences (ICES).

But Redelmeier, whom SRI senior scientist and colleague Dr. Michael Schull describes as “one of the few people who can manage to create broad interest in his research,” is not about to let the flaws go untreated. “The mission statement around here,” he says, “is to make health care in the future better than it is today.”

Examples of this early declaration in action are legion. Among the more recent is his research on the connection between statins and sepsis.

In general, people with hardening of the arteries take a statin, a drug that lowers fat levels in the blood, to reduce their cholesterol. A possible underlying predisposition to sepsis is not a consideration in its prescription. Similarly, the risk of contracting sepsis has nothing to do with cholesterol count. Sepsis, a rare but serious bacterial infection, visits its victims in response to other factors, like if they have cancer, compromised immune systems or just lousy luck, and develop pneumonia or a kidney infection.

Jumping to preclinical models from experiments outside of the clinical epidemiology realm, Redelmeier noted that pretreatment with statins extends survival and sometimes even promotes complete recovery from blood-poisoning sepsis.

He extended this research to people, considering 60,000 Ontarians with hardening of the arteries, some of whom were taking a statin, some of whom were not. Taking care to peer-match them in terms of other risk factors, Redelmeier followed-up these people—a mean age of 74, 56% men, 16% living in rural Ontario—for a median duration of five years between 1997 and 2002. Findings, published in *The Lancet* in 2006, were revealing. He observed that those who were taking statins had a 20% lower risk of developing or dying from sepsis than those who were not.

“That’s a big deal,” he says, closing his eyes for emphasis, leaning his long body back in his chair, “because sepsis can be a very unpleasant disease: lethal (the case fatality rate of sepsis is at least 20%) and expensive to treat.” What’s more, he notes that current clinical treatment for sepsis is “not always satisfactory.” Statins, he concluded, might prove a feasible method for preventing at least some cases.

That his work revealed a new use for drugs whose relevance was previously assigned to another application cements Redelmeier’s conviction that research of medications that are now being used more broadly under normal community circumstances, might reveal characteristics—surprising harms or benefits—that weren’t anticipated. This impulse makes sense to Schull, who calls Redelmeier “a very serious guy superficially,” but says, “deep down, Don and his research are like a kid in an amusement park: He sees all this opportunity to go on the rides.”



DR. DONALD REDELMEIER