



The ability to run multinational trials is part of the expertise and experience that cardiologists Dr. Patrick Lawler (left), Dr. Michael Farkouh and Dr. Jacob Udell bring to the PMCC's cardiac clinical work and research.

Finding global solutions to cardiovascular disease

The Peter Munk Centre of Excellence in Multinational Clinical Trials is uniquely positioned to study the world

By **Kira Vermond**

CORONARY HEART DISEASE. It doesn't care if you're Canadian, American or living in India, Kenya or Spain. Political boundaries mean nothing to a condition that kills an estimated 3.8 million men and 3.4 million women globally each year.

So why shouldn't cardiac clinical trials and research also break geographic barriers?

That's part of the thinking behind the Peter Munk Centre of Excellence in Multinational Clinical Trials, launched in

2011 and one of seven Centres of Excellence established by the Peter Munk Cardiac Centre (PMCC) to transform the way patients with cardiovascular disease are treated around the world.

"We bring innovation and what we call the 'one-stop shop,'" says Dr. Michael Farkouh, the Peter Munk Cardiac Centre Chair in Multinational Clinical Trials, who came back to Canada in 2010 after working in the United States for 20 years, including 10

years directing the Mount Sinai Cardiovascular Clinical Trials Unit in New York City.

"When we develop new drugs and new devices, we have the ability that most centres in the world do not have to go from the early concept in innovation all the way to the large clinical trial," he says.

That's partly due to Dr. Farkouh's own experience running large multinational trials. While phase one and phase two trials typically involve smaller numbers of people chosen with very specific medical parameters in mind, multinational trials examine outcomes in thousands or even hundreds of thousands of people worldwide.

Take the FREEDOM Trial, co-led by Mount Sinai Hospital in New York and the Peter Munk Chair in Multinational Clinical Trials. It showed that when diabetic patients with multivessel coronary artery disease have bypass surgery, they live longer and are less likely to experience complications than those who undergo angioplasty.

The Tailored Antiplatelet Initiation to Lessen Outcomes Due to Decreased Clopidogrel Response After Percutaneous Coronary Intervention (TAILOR-PCI) study is another large trial the PMCC is currently co-leading with the Mayo Clinic. It's meant to determine whether patients with stents should receive the drug Plavix or another prescription.

Thirty per cent of people are actually unable to metabolize Plavix. They have a genetic variation in a liver enzyme that prevents it. Ultimately, the drug is next to useless for them.

But what if you could tell – through rapid genotyping – who is a good candidate for that standard medication and who should receive an alternate medication that's more effective for them?

The TAILOR-PCI study team uses genotyping technology – a quick cheek swab – in some of the 6,000 patients enrolled in the trial to see if genetic testing before prescribing medication after angioplasty leads to better patient outcomes. So far, the team has signed up more than 4,000 patients in Canada, the U.S. and South Korea.

"It's about trying to show that individualizing care is the way

to go," says Dr. Farkouh. It's also the first and largest trial of individualized medicine that the U.S. National Institutes of Health (NIH) has sponsored, he explains.

The beauty of multinational trials is not merely the vast scope, but also how the data is actually collected and analyzed, says Dr. Patrick Lawler, a cardiologist, Boston native and new recruit to the centre who is a leading expert in preventing atherosclerosis cardiovascular disease.

Dr. Lawler says he was drawn to the PMCC because the centre's focus is unique: a strong interest in developing pragmatic clinical trials that intersect with real-world evidence by pulling data from actual clinical cases.

In a pragmatic clinical trial, a study could look at how blood in blood banks is used. Are patients being given the newest blood or the stock that has been shelved the longest? (Think milk growing nearer to its expiration date.) Then, when you follow these patients through their electronic health records afterward, what are the outcomes?

"These kinds of pragmatic trials are trying to make use of the fact that our health-care system is increasingly digital, electronic and connected," says Dr. Lawler. "In theory, this should be a more efficient system. The trials should cost a lot less money and they should be faster."

And as the TAILOR-PCI trial shows, the centre also specializes in precision medicine that focuses on making medicine more individualized for patients.

So why leave his full-steam-ahead career in Boston to come to the PMCC in Toronto?

"You know, I think what I was excited about was the spirit of innovation and creativity here. There's an environment that encourages scientific risk-taking," he says.

Dr. Jacob Udell, a cardiologist with expertise in women's health, diabetes and novel ways to protect patients from heart disease, arrived in Toronto from Boston in 2012, also at Dr. Farkouh's urging. Dr. Udell says he, too, was impressed with the Centre of Excellence when he saw an opportunity to join an emerging group ready to use big data in Canada and beyond.

"I want to leverage the power of our health information system in Canada and the U.S. to try to

build a better wheel," he says.

One major study he has in the works looks at whether giving people with weak immune systems a more concentrated dose of flu vaccine will give them cardio protection. The outcome could be the difference between life and death for those with kidney disease, diabetes, cardiovascular disease and those with obesity who are underprotected by the regular shot.

The teams participating in the study have already completed one flu season. The results will be recorded in 2020.

Teamwork and collaboration are obviously paramount if large multinational clinical trials are to succeed. And Dr. Udell says the centre is working with nurses, nurse co-ordinators, lead administrators and senior leadership at the PMCC and Toronto General Hospital, as well as teams across the country and beyond.

"This couldn't have happened without everyone coming to the table," he says. "It's going to take work and rolling up our sleeves, but we're on the precipice of doing something pretty cool that will open the floodgates for many trials to come." ▾

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