

Sunnybrook Launches ROAM Study

By Jim Oldfield

Research will open Canada-wide window into management of anticoagulant warfarin

Two Sunnybrook researchers, Dr. Nicole Mittmann and Dr. Rita Selby, have secured \$1 million from Boehringer Ingelheim for the first prospective, cross-Canada study of warfarin management. The ROAM (Resource Utilization Associated with Oral Anticoagulant Management) study will enroll 600 patients from five provinces, detailing administration of their care, health outcomes, complications and the cost of the therapy to the Canadian health care system.

Warfarin is an anticoagulant (blood thinner) used to prevent strokes and venous blood clots. About 5% of North Americans aged over 65 years take it. But, says Selby, a thrombosis specialist and director of Sunnybrook's coagulation laboratory, "the drug has a narrow therapeutic index, which means that blood levels must be controlled within a certain range to be effective. Unfortunately, much evidence suggests that warfarin is suboptimally managed worldwide."

Although warfarin is safe and effective when used properly, and its administration has improved over its five-decade history, the medication can produce significant interactions with food and other drugs, and about one-half of those who take it have an unpredictable (though manageable) result owing to their genetics.

Inappropriately managed warfarin therapy can result in stroke, bleeding in the brain and death. A 2007 *Archives of Internal Medicine* paper that looked at U.S. death certificates found anticoagulants ranked first in 2003 and 2004 in the "number of total mentions of deaths for drugs causing 'adverse effects in therapeutic use.'" As the main oral anticoagulant in use in Canada and the U.S., warfarin is "the commonest drug resulting in ER visits for adverse events, 73% of which are for bleeding and 44% of which lead to hospital admission," says Selby.

There are two established means of monitoring warfarin therapy. One is through an anticoagulant clinic, where the clinic's only role is to monitor patients on the drug. The other is by routine medical care through general practitioners (GPs) or specialists. In Canada, where there is a paucity of specialized clinics, warfarin is mostly monitored by GPs. Evidence worldwide indicates that though the proportion of time patients spend in their target therapeutic range is similar in both settings, patient outcomes are far better within anticoagulant clinics—less bleeding, fewer recurrent blood clots and lower rates of death.

"Ideally, the results of this study will definitively show a model that either works or doesn't work, and highlight where the failures are," says Mittmann, a scientist at Sunnybrook Research Institute and director of the HOPE—Health Outcomes and PharmacoEconomic—research centre at Sunnybrook.

Patients will keep a detailed diary of the warfarin monitoring process—how often they saw a doctor, how much they paid for parking, when they required lab tests, whether their physician's

office contacted them with lab values (doctors in several provinces aren't reimbursed for such calls, a disincentive for diligent monitoring) and whether they saw a nurse, among other criteria. "Using medical charts alone would be very biased toward obtaining medical data only," says Mittmann. "If we want patient-level data, then we have to go to the patient. It's the only way to look at what's happening in the real world."

Despite the financial burden of conducting a study this size, and typical but substantial challenges recruiting doctors and patients, Selby and Mittmann are optimistic. Says Mittmann, "As a hematologist, Rita does clinical research, and I do pharmacoeconomic research; this study looks at a clinical situation, but collects economic and resource parameters in addition to clinical outcomes. It's a nice marriage of both specialties."