

DRUG INNOVATION FUND TO ADVANCE RESEARCH INTO VALUE OF MEDICINES APPROVED FUNDING FOR RESEARCH PROPOSALS FROM 2007/08 REVIEW CYCLE

In April 2007, the Ministry of Health and Long-Term Care announced the establishment of the Drug Innovation Fund (DIF) with \$5 million available annually to provide Ontario researchers with stable, long-term funding needed to perform evidence-based research that will demonstrate the positive role of new and existing drugs in reducing non-drug health care expenditures within the health care system.

The mandate of the Drug Innovation Fund is to:

- Generate strong, high-quality, independent scientific evidence on the impact and value of new and existing drugs across the healthcare system, by linking drug interventions to health or system outcomes.
- Support linkages between researchers, clinicians and drug policy decision makers to ensure the timely and effective application of relevant evidence-based scientific information and to support the objectives and priorities of the Ontario Public Drug Programs.
- Support and develop research capacity in the area of drugs and health outcomes in Ontario.

The three areas of research that the ministry is interested in focusing on include:

- Impact of Drug Access and Utilization
- Optimal Use of Drugs
- Drug Adherence

Information gained from this research will support drug policy decision making in Ontario, in addition to capacity building and knowledge transfer, which are also important objectives of the Fund.

In response to our July 18, 2007 invitation for potential research grants through the DIF, the ministry received 37 Letters of Intent (LOI) from 25 different principal investigators representing various institutions and universities from across Ontario. All LOIs were reviewed and evaluated by a 9-member Joint Academic and Relevance Review Panel. Of the 37 LOI evaluated, 13 were invited to submit a full research proposal to the ministry, which were also evaluated by the Panel.

Based on the recommendations of the Panel, the ministry finalized its decision and will fund 8 research proposals, totalling about \$3.8 million. The following is a list, with a brief description, of the specific research proposals that will receive funding from the DIF for the 2007/2008 review cycle:

“Personalized Medicine and Optimal Warfarin Anticoagulant Therapy in Ontario”

Principal Investigator – Richard Kim

Sponsoring Institution: London Health Sciences Centre

Summary:

It is currently estimated that adverse drug reactions are the 4th leading cause of death among hospitalized patients. Many drugs in clinical use, such as the oral anticoagulant (blood thinning drug) warfarin, have a narrow margin of safety, and require frequent monitoring or dose adjustments. Personalized medicine represents the integration of data in relation to a patient’s genetic makeup, specifically Single Nucleotide Polymorphisms (SNPs) in the genes that affect drug disposition or response, together with environmental influences and disease states to identify more precise treatment options for an individual patient. In this application, a practical “real world” assessment of the role and

relevance of SNPs in the genes responsible for warfarin metabolism (CYP2C9) and the target for warfarin effect (VKORC1) is proposed, through the synergistic collaboration between researchers with complementary expertise in pharmacogenomics and anticoagulation therapy. Specifically an optimal algorithm for warfarin therapy which includes CYP2C9 and VKORC1 genotypes will be identified and studied in our hospital- and outpatient-based populations, to test the hypothesis that individualized therapy for warfarin that includes such genomic information will reduce the time needed to reach desired level of anticoagulation and the bleeding risk from excess warfarin effect. The key benefit from this research for Ontario is the potential of this proposal to generate a new paradigm for managing our patients on warfarin that will save health care delivery costs, while increasing the overall quality of life for our patients by reducing unnecessary or unexpected clinic visits and the number of bleeding related hospitalizations.

“The cost-effectiveness of cancer drugs: Providing evidence of the value of medicines in delivering expected outcomes”

Principal Investigator: Jeffrey Hoch, Murray Krahn

Sponsoring Institution: St. Michael’s Hospital

Summary:

If we gave a cancer patient a new treatment, how much longer would she live? How much more would the new treatment cost? Decisions about whether Ontario should pay for new cancer drugs are frequently based upon the most recent data from short-term studies on special populations. Often, these study results are the only information that decision makers can use to guess at the value of new cancer medicines. Cost-effectiveness analyses showing the extra cost of the extra patient benefit are likewise created from best guesses. As a result, it is possible that new cancer drugs that look promising in terms of cost and survival when studied under scientific conditions may not deliver expected outcomes when used in the “real world”.

After a decision is made to fund a new cancer drug, data about the drug’s cost as well as patient and health system outcomes are available from various administrative data sources. Linking these data together provides an excellent opportunity to explore the value of cancer medicines in delivering expected health outcomes. Our research will link existing administrative databases and analyze them to provide evidence of the impact of the use of new cancer drugs on both patient and health system outcomes. This research will benefit Ontario by providing real time evidence from real world data, helping to calibrate policies so that we get the most health from each healthcare dollar. This is research that supports the government’s goal of accountability.

“Dementia Treatment and Time to Nursing Home Placement”

Principal Investigator: Sudeep Gill

Sponsoring Institution: Queen’s University

Summary:

This study will examine the use and impact of cholinesterase inhibitors among older adults with dementia. Cholinesterase inhibitors (such as Aricept) are medications that represent one of the few treatment options currently available to manage Alzheimer’s disease and related dementias. They are funded by the Ontario Drug Benefit formulary, but controversy persists regarding the benefits associated with their use and their value given their relatively high cost (approximately \$150 per month). Several US studies have suggested they may help to delay the time to nursing home placement, while a study in the UK suggested little if any impact on time to nursing home placement. Importantly, no Canadian studies on this important question have yet been published. This study will examine the impact of cholinesterase inhibitor treatment on time to nursing home placement among older adults with dementia who are living in Ontario. This research will benefit the Ontario health care system by determining the value being received for relatively expensive drug treatment. This research will serve as a model for future post-marketing research of real-world drug effectiveness.

**“The Ontario Drug Policy Research Network (ODPRN) – Rapid Response Unit (RRU)
Principal Investigator: Muhammad Mamdani, David Juurink
Sponsoring Institution: St. Michael’s Hospital**

Summary:

Drug therapy is a cornerstone of medical practice - the majority of adults in North America will have filled a prescription at some point in their life. The consequent financial investment is substantial: nearly \$9 billion was spent on drug therapy in Ontario in 2005. Drug policy decisions determine the allocation of these substantial yet limited resources and have profound effects on the health of the individuals affected. Critical to optimal decision-making is the availability of timely, high-quality information. Although academic institutions are known to provide the most scientifically rigorous information, they are often criticized for their lack of focus on the specific needs of decision makers and their relatively slow turn-around times. In contrast, commercial research organizations typically focus directly on the needs of their clients and accommodate aggressive timelines, yet are criticized for their high cost and lack of scientific rigor. For these reasons, an academic-based Rapid Response Unit (RRU) focused on drug policy will be established. The two core principles under which the RRU will function are quality and timeliness, which will drive the goal of providing scientifically rigorous information to decision-makers in a timely manner. The RRU will leverage cutting-edge research methodology from the academic-based Ontario Drug Policy Research Network (ODPRN) to provide information on real-world drug safety, effectiveness, and costs to decision makers through a central, dedicated Operational Business Unit. This innovative collaboration will effectively inform policy decisions affecting the lives of Ontarians.

“Providing Evidence on the Impact of Medication on Chronic Obstructive Pulmonary Disease Outcomes: The impact of long acting anticholinergic and long-acting beta agonist medications on patient and health care system outcomes.”

**Principal Investigator: Andrea Gershon
Sponsoring Institution: Institute for Clinical Evaluative Sciences**

Summary:

The proposed study will address the clinical question: in someone with COPD, which long acting inhaled agent should be introduced first? At the current time, for mild disease, the Canadian Thoracic Society guidelines suggest a long-acting beta-agonist (LABA) medication or a long-acting anticholinergic (LAAC) medication. There have been several observational studies on inhaled corticosteroids and therefore we do not propose conducting another one. Instead, we propose that this study examine the effectiveness of LABA and LAAC and compare their effects to each other. .

“Effectiveness And Optimal Use of Biologic Response Modifying Drugs for the Treatment of Rheumatoid Arthritis in Ontario.”

**Principal Investigator: Claire Bombardier
Sponsoring Institution: University Health Network**

Summary:

There is an urgent need to ensure universal and appropriate access to optimal treatment, as many new, expensive drugs enter the market. Biologic response modifying drugs (BRMs) for the management of rheumatoid arthritis (RA) provide a good example. Because the cost of BRMs can be 40-50 times higher than traditional RA treatments, access to BRMs may be limited even for patients with private drug coverage. In addition, the long-term safety and real-world effectiveness of BRMs remain largely unknown. The Ontario Biologics Research Initiative (OBRI) involves the collaboration of stakeholder groups representing rheumatologists, patients and researchers. The goals of the OBRI are to determine

the effectiveness and safety of BRMs for the treatment of adults with RA in Ontario, and to develop and evaluate a range of strategies to promote best practices and post-marketing surveillance in usual care. Our proposal will address the Drug Innovation Fund targets of determining the impact of drug access and utilization and optimal use of drugs by providing an infrastructure to support data collection and knowledge translation. This will be accomplished through the collection and analysis of effectiveness, safety and health care utilization data, and the provision of patient and physician feedback. This proposal has been developed as a result of national and provincial policy initiatives to monitor the effectiveness and safety of newly developed drugs, in order to inform policies regarding their optimal use and will be an innovative model for other drugs.

“Epidemiology, Medication Treatment Patterns, Clinical Outcomes, Healthcare Resource Utilization, Costs And Cost-Effectiveness Associated With The Management Of Diabetes And Associated Risk Factors In Primary Care Practices In South-Western Ontario: A Large Real-World Cohort Analysis.”

Principal Investigator: Robert Petrella

Sponsoring Institution: University of Western Ontario & St. Joseph’s Health Care Centre

Summary:

Diabetes is a chronic, highly prevalent, condition that is associated with significant morbidity, mortality and health care resource costs. As a result, diabetes has been identified as a priority area for the current Ontario government. The government is also committed to an evidence-based platform for future policy direction and development. Although essential for demonstrating safety and efficacy of interventions, evidence from randomized controlled trials of diabetes interventions may be limited due to artificial trial conditions or concerns about generalizability to the Ontario setting. As a result, ‘real world’ data on the management and long-term outcomes of patients with diabetes in Ontario is essential for evidence-based policy development.

The existence of a large database of primary care patients (approximately 170,000 to date) in South Western Ontario (SWO) represents a unique opportunity to study the effectiveness and cost-effectiveness of various management strategies for patients with diabetes in Ontario. Created in 2000, the database contains real world Ontario longitudinal observational data, has important information not available from other administrative databases (e.g. laboratory values and diagnostic test results) and is large and diverse enough to address important sub-group populations (i.e. urban/rural, patients with various co-morbidities). Since 2007, data from 2 clinical practices primary serving First Nations individuals are also collected. This database will allow for a rigorous assessment of the impact of drug access by patients with diabetes, the assessment of the optimal use of drugs in diabetic patients, and diabetic drug adherence in a large real world population-based setting in SWO. In addition, data can be extracted in order to populate the Ontario Diabetes Economic Model (ODEM), which will allow for the estimation of both short- and long-term effectiveness and cost-effectiveness of various diabetes management alternatives.

“Individualizing Drug Therapy: A Quantitative and Qualitative Pilot Study to Determine the Impact of a Personalized Benefit/Harm Assessment on Patients’ Decisions Regarding Warfarin”

Principal Investigator: Anne Holbrook

Sponsoring Institution: Father Sean O’Sullivan Research Centre, St. Joseph’s Healthcare

Summary:

Warfarin is a commonly used blood thinner that is very effective in reducing stroke risk in patients with atrial fibrillation (AF), an abnormal heart rhythm affecting more than 5% of the senior population. However, warfarin also increases the risk of major bleeding. Until recently, information about warfarin was based on summaries of clinical trials providing average rates for decreasing strokes and increasing bleeding. Within the last year, it has become possible to predict which patients may be more likely to

benefit from warfarin and which patients may be likely to have a bleed, which if in the brain, is usually disabling or fatal. It is very important to identify patients for whom the risk of harm outweighs expected benefit, and vice versa. Our study is a decision-making exercise in the senior population to determine how decisions to take warfarin would differ and why, depending on information patients receive about warfarin's benefit and harm: the typical, "average" information about warfarin's effect vs. information tailored to the individual. Many patients may make different treatment decisions if they are presented with their own benefit:harm profile rather than the average, as few people are identical to the "average patient". Since it is widely held that patients must be fully informed of their own risks and benefits of therapies, it is important to evaluate what impact this individualized information has on patients' decisions to accept treatment or not.