

# Population Health Research Institute

RESEARCH REPORT • 2006



Hamilton Health Sciences





## The health of our people...the health of all people



**Dr. Salim Yusuf**

In the last century, life expectancy has doubled globally from about 30 years in 1900, to about 60 years by the year 2000. At no time in the history of mankind have such impressive gains been made in preventing and treating disease and improving human longevity. These remarkable advances have been made possible by improved social and economic circumstances, and advances in our ability to prevent premature death and disability from childhood and adult diseases — through health research.

Yet these advances pose new challenges this century. There are stark differences in the health of different people, between societies and within societies, marked inequities in research investments and efforts into solving diseases of the wealthy compared to diseases of the poor. Improving health requires a shift in paradigm from the sole investigation of biologic phenomena to one that explores the complex interactions of societal and policy influences on human behaviours and lifestyles, risk factors, and ill health and disability.

The Population Health Research Institute (PHRI) has been created with such a broad vision — it explores the role of multiple societal influences in health, investigates the risk factors for cardiovascular diseases, diabetes and obesity throughout the life course, and where appropriate, evaluates both emerging as well as overlooked (but promising) therapies or preventive strategies. A range of disciplines and methodologies are often brought to bear on most problems tackled by the PHRI. Our projects are based on global collaborations and succeed because of the dedication and commitments of a well-knit team in Hamilton and superb collaborators worldwide. Our goals are the improvement of health of all peoples of the world, utilizing the knowledge gained through careful and innovative research. This report is a testament to the dedication of our entire team in Hamilton and our collaborators worldwide.

### **Dr. Salim Yusuf**

*Director, Population Health Research Institute  
Chief Scientific Officer, Hamilton Health Sciences  
Professor of Medicine, McMaster University*

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**Editors:** Liisa Morley, Salim Yusuf and PHRI Staff

**Graphic Designer:** Michelle Sharp, Media Production Services

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**Photographers:** Cyprian Estrada, Peter Foulds, Bridget Greer, Irma Long, Robert Tatlock and Martin Wissenz  
(Photo of Andre Lamy by Dr. ER Jeans)

# Improving Health Through Research



**Murray T. Martin**



**William B. MacLeod**



## Hamilton Health Sciences

### Research at Hamilton Health Sciences

Hamilton Health Sciences is committed to advancing excellence in health care through research and education to benefit the people and communities we serve. By emphasizing multidisciplinary and collaborative research that enhances our main clinical programs, we strive to share our knowledge beyond borders, while promoting the adoption of best practices within Canada and around the world.

Hamilton Health Sciences currently administers a significant number of research projects, representing contributions from the federal and provincial government and corporate and not-for-profit sponsors. The research framework at Hamilton Health Sciences is dependent on interaction between fundamental, translational and clinical knowledge transfer and health services research platforms. In order to engage research at all levels, Hamilton Health Sciences provides resources to help researchers obtain funding through federal and provincial agencies such as the joint Canada Foundation for Innovation (CFI) and Canadian Institutes of Health Research (CIHR), the Ontario Research Fund (ORF) and other peer-reviewed infrastructure programs.

Providing our researchers with facilities that meet their unique needs, and fostering an environment of collaboration and discovery is an important aspect of the research culture at Hamilton Health Sciences. Currently, we are constructing a new 165,000 square foot institute that will be dedicated to advancing research in cardiac, vascular and stroke care.

Under the leadership of Drs. Salim Yusuf and Jeffrey Weitz, the innovative Cardiac, Vascular and Stroke Research Institute will unite new and existing clusters of scientists in one collaborative and integrated program. As a world-renowned cardiologist and director of the Population Health Research Institute, Dr. Yusuf has led numerous studies that have resulted in reductions in premature heart disease and improvements in the outcomes for people with heart disease here in Hamilton and around the world. Similarly, as one of the world's foremost experts in thrombosis and director of the Henderson Research Centre, Dr. Weitz has contributed significantly to the basic understanding of how blood clots form and how to treat them.

Together, Drs. Yusuf and Weitz will lead their teams in new and collaborative directions and continue to pioneer research related to these global health issues in Hamilton and around the world.

#### **Murray T. Martin**

*President and Chief Executive Officer  
Hamilton Health Sciences*

#### **William B. MacLeod**

*Vice President, Research and Corporate Development  
Hamilton Health Sciences*



## Research at McMaster University

At McMaster University, we believe that in health sciences education, research and practice, we are here to question, to learn, to discover and to communicate. Every day we live our well-earned reputation as Canada's most research-intensive and innovative university.

Across the city of Hamilton — on campus, at our affiliated institutes and centres including the Population Health Research Institute, and at our academic hospital partners Hamilton Health Sciences, St. Joseph's Healthcare Hamilton and St. Peter's Health System — researchers are working on more than 1,500 health research projects worth practically \$300 million a year.

McMaster researchers continually pursue medical breakthroughs in our laboratories, develop them into better health care and integrate them into the practice of health care professionals. McMaster's culture of innovation fosters a commitment to discovery and learning in teaching, research and service that is both inspiring and engaging.

McMaster University's Faculty of Health Sciences, the Population Health Research Institute and our academic hospital partners share the same deep commitment to:

- Improving excellence in health care research with improved global research methodologies;
- Pioneering discoveries that will translate into advanced health care;
- Maintaining a vision that includes better health for people around the world, not just in our home region or in Canada.

In fact, the Population Health Research Institute's success and international renown is a superb example of quality research having global impact on prevention and treatment practices worldwide.

Our Faculty thrives on a team approach to health care that represents a true partnership between the wider community and the University.

We congratulate the Population Health Research Institute on its continuing dedication and pursuit of excellence as we work together to advance health through learning and discovery.

### **John G. Kelton, MD**

*Dean and Vice President, Faculty of Health Sciences  
McMaster University*

### **Stephen M. Collins, MD**

*Associate Dean, Research, Faculty of Health Sciences  
McMaster University*



**John G. Kelton**



**Stephen M. Collins**



## Working collaboratively to improve the health of the populations of the world



The Population Health Research Institute (PHRI) coordinates large, international clinical trials, population health studies and outcomes research. Founded in 1999 under the directorship of Dr. Salim Yusuf, the PHRI evolved from the successful Preventive Cardiology and Therapeutics Research Program (established in 1992) at the Hamilton Civic Hospitals Research Centre, located in Hamilton, Ontario.

Originally formed with a focus on cardiovascular disease (CVD), the PHRI has since expanded to explore innovative projects in a variety of areas including diabetes, obesity and societal influences on health, with specific emphasis on variations by ethnicity and geographic region. The Institute is also involved in researching risk factors for heart disease in urban and rural populations, developing countries and throughout the life course.

Affiliated with Hamilton Health Sciences and McMaster University, the PHRI collaborates with more than 1,000 clinical sites in 66 countries around the world, and is regarded as a pre-eminent centre for research into international health and training for young researchers. The goals of the PHRI are to understand the causes of chronic diseases and how they can be prevented or treated. While its primary role is to provide leadership in international health research, the PHRI also plays an active role in the education of individual researchers, and in building capacity internationally for the development of global research programs.

### Several of the discoveries made by scientists at the PHRI have influenced prevention and treatment practices worldwide.

#### INTERHEART

From 1999 to 2006, PHRI researchers collaborated with investigators from 52 countries to investigate the causes of heart attacks globally, in the INTERHEART study. In a series of papers in the *Lancet*, the study reported that nine easily measurable and modifiable risk factors (inset) could explain over 90 per cent of the risk of a heart attack globally and in all regions and major ethnic groups of the world. These studies emphasized that avoidance of tobacco, daily consumption of fruits and vegetables and regular exercise could potentially avoid two-thirds of heart disease. The results also indicated that tobacco (smoking even one cigarette per day increases the risk of myocardial infarction (MI) by five per cent) and abnormal lipids were the two most important risk factors globally, and that the markers of abdominal obesity and hip size (waist-to-hip-ratio) are far more predictive than body mass index (BMI) in predicting MI. Furthermore, stress and psychosocial factors were found to be important risk factors for MI.

#### OASIS Series (1 to 6)

In a series of studies, investigators led by PHRI demonstrated that a new antiplatelet drug (clopidogrel) added to the benefit of aspirin in patients with imminent heart attacks. This study (CURE or OASIS-4) led to the adoption of this useful therapy worldwide. The year 2005 saw the release of the world's largest study on acute coronary syndromes (ACS). This Canadian-led study, named OASIS-5/MICHELANGELO, involved researchers from 41 countries and proved that a new anti-thrombotic therapy (to prevent blood clots), fondaparinux, is safer, causes less bleeding, and is as effective as the traditional therapy used in preventing heart attacks, death and ischemia (death of heart tissue) in the short-term. These

effects translated into reductions in mortality in the long-term. The study findings demonstrate that the therapy should be the new drug of choice for patients with acute coronary syndromes who are already receiving aspirin and clopidogrel, a blood-thinning drug that helps to prevent blood clots to prevent strokes and heart attacks in patients at risk for these problems. Equally important, the study highlights the clinical importance of avoiding bleeding.

#### HOPE

One of the most notable clinical studies conducted by the PHRI was the HOPE (Heart Outcomes and Prevention Evaluation) study that was cited by the American Medical Association as being among the top ten medical discoveries in 2000, and the most cited article in clinical medicine that year. This study demonstrated the value of ramipril, an ACE inhibitor, in reducing deaths, heart attacks and stroke, thus improving the lives of people around the world by refining and clarifying clinical practice guidelines. This line of research is continuing to be pursued in ongoing studies that include more than 30,000 patients (ONTARGET and TRANSCEND) and the HOPE-3 study that is following 10,000 individuals.

#### SHARE and PURE

Many of the population health studies the PHRI has been involved in have also led to significant health benefits for people around the world. The SHARE (Study of Health Assessment and Risk in Ethnic groups) study for example, led by Drs. Sonia Anand and Salim Yusuf, examined CVD risk factors among populations of varying ethnic origin. Ultimately it added new information to the body of knowledge about why South Asians and aboriginal people are at increased risk of CVD in comparison to other ethnic groups. This work is continuing through the large PURE study; involving 135,000 individuals from 16 countries examining the effects of societal changes on CVD.



With sponsorship from the World Heart Federation and the World Health Organization (WHO), the PHRI is also actively involved in establishing cardiovascular research programs in developing countries.

Analysis shows that more than 80 per cent of CVD occurs in low- and middle-income developing countries, yet the overwhelming majority of data on risk factors and prevention of CVD is derived from developed countries with primarily white, European populations. With varying lifestyles and social circumstances, it is unclear whether data from Western countries is applicable to other regions of the world.

This concern has been addressed through two important studies – the first, INTERHEART, involved about 30,000 people in 52 countries. This study indicated that nine modifiable risk factors accounted for more than 90 per cent of the global burden of heart attacks. This information provides a firm basis for a global strategy on CVD prevention. The second study, PURE (Prospective Urban Rural Epidemiological study), examines the hypothesis that CVD rates are increasing in developing countries due to changes in urbanization and industrialization. This study is currently taking place in 15 countries and will involve 135,000 individuals.

An important area of research for the PHRI is explaining the relationship of elevations of blood glucose and cardiovascular disease. The DREAM and ORIGIN studies are exploring new ways of preventing and treating diabetes. Another emerging area of research is the assessment whether environmental influences during pregnancy and early childhood predispose a child to developing risk factors for cardiovascular disease. This project (FAMILY study) involves extensive collaboration between pediatricians, cardiologists and epidemiologists.

Other major programs include: preventing perioperative cardiac events, new antithrombotics and atrial fibrillation, better treatments for heart attacks and unstable angina, efficient care for heart failure patients, new approaches to prevention of atherosclerosis and its complications and investigating the causes of strokes worldwide.

With a staff of about 200 individuals, the PHRI includes a wide range of research personnel including physicians, nurses, epidemiologists, research coordinators, biostatisticians, computer programmers, data management assistants and administrative staff.

With the aid of funding from generous donors, the Population Health Research Institute will soon move into a new and state-of-the-art building at the Hamilton General Hospital site. The facility, named the Cardiac, Vascular and Stroke Research Institute (CVSRI), will allow for the consolidation of cardiac with vascular thrombosis research into one facility, ultimately providing additional resources for population, clinical and basic research. For more information regarding the CVSRI, see page 76.



## Highlights

## Special infrastructure and expertise to support research



The success of any research endeavour depends critically on an infrastructure that can assist the development and sustenance of multi-dimensional studies that are both single and multi-centre.

**The PHRI has substantial expertise in all administrative aspects and coordination of large studies. These include:**

- Statistical support with 12 statisticians and statistical programmers;
- Computing support with 10 programmers, a network of over 120 computers, 14 servers, each with at least 2Gb of RAM and in excess of 400 Gb of data stored, automated data back-ups, standardized operating procedures, automated randomization programs, etc. Ongoing efforts are aimed at developing new programs and data management systems;
- Extensive laboratory facilities with experience in shipping bloods frozen from over 50 countries. At present, about one million aliquots are in storage;
- Capabilities for drug packaging and distribution for medium-sized studies.
- Data management of large volumes of forms using the DataFax system (at peak work load, up to 100,000 records have been processed in one week);
- Administrative, legal, and financial support for developing and negotiating contracts and managing funds.

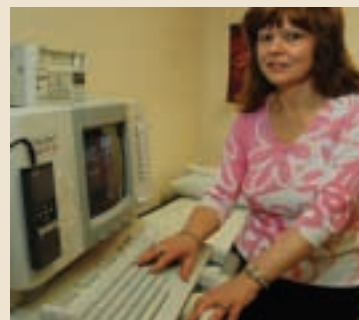
### Biobank and Proteomics Laboratory

In collaboration with the PHRI, the Clinical Trials and Research and Proteomics Laboratory has developed the capacity for storage of a large number of blood samples in liquid nitrogen. At present, approximately one million samples from 150,000 participants are stored at  $-160^{\circ}\text{C}$ . These blood samples are matched to patient clinical status and outcomes, and are used to test new hypotheses as they emerge. The Biobank has recently been expanded to accommodate 40 large storage tanks, each holding approximately 55,000 vials. For more information on this facility, see page 38.



### Vascular Research Imaging Laboratory

The Vascular Research Imaging Laboratory has been the core lab for a number of multi-centre international studies and is used for both epidemiologic studies and interventional trials. Here, expertise in various aspects of vascular imaging and analyses has been developed for carotid B mode ultrasonography (forearm vascular blood flow and cardiac echocardiography). New uses being developed include vascular imaging in children to evaluate early changes in blood vessel wall and function. For more information on the laboratory, see page 40.





The Population Health Research Institute depends critically on a global team of collaborators with researchers from 66 countries, spanning six continents, including:

**North America:**

Canada, Guatemala, Mexico and United States of America

**Europe:**

Austria, Belgium, Bulgaria, Baltic Republic, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Netherlands, Norway, Poland, Portugal, Slovakia, Spain, Sweden, Switzerland, Turkey, Ukraine and United Kingdom

**Asia:**

Bahrain, Bangladesh, China, Democratic Socialist Republic of Sri Lanka, Hong Kong, India, Iran, Israel, Japan, Kenya, Kuwait, Malaysia, Nepal, Pakistan, Philippines, Qatar, Russia, Singapore, South Korea, Sultanate of Oman, Taiwan, Thailand and United Arab Emirates

**South America:**

Argentina, Brazil, Chile, Colombia and Peru

**Africa:**

Benin Republic, Botswana, Cameroon, Democratic Republic of Congo, Egypt, Mozambique, Nigeria, Republic of Seychelles, South Africa and Zimbabwe

**Australia:**

Australia and New Zealand

**Major collaborating research institutions include:**

- The International Clinical Epidemiology Network (INCLEN);
- The University of Oxford, United Kingdom;
- Estudios Clínicos Latinoamérica (ECLA), Rosario, Argentina;
- Instituto Dante Pazzanese de Cardiologia, Sao Paulo Brazil;
- St. Johns Medical College, Bangalore, India;
- University of Cape Town, Rondebosch, South Africa;
- World Hypertension League and Fu Wai Hospital, Beijing, China;
- Linda Richardson, United Kingdom;
- Duke University Medical Center, Durham, North Carolina USA;
- Associazione Nazionale Medici Cardiologi Ospedalieri (ANMCO), Firenze, Italy; and
- Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto miocardico (GISSI Group), Milan, Italy.

## International Collaborations

## Endowed Chairs

A great strength of the PHRI is the interdisciplinary nature of its research and collaboration with other divisions in the department of medicine and other departments at Hamilton Health Sciences and McMaster University; in addition to extensive collaborations nationally and internationally. Accordingly, many of the career awards and chairs reflect this interdisciplinary approach. These include:



**Salim Yusuf**

Heart and Stroke Foundation of Ontario Research Chair in Cardiovascular Diseases



**Hertzell Gerstein**

Population Health Research Institute Chair in Diabetes and Cardiovascular Diseases



**Sonia Anand**

Eli-Lilly May Cohen Chair in Women's Health



**Heather Arthur**

Heart and Stroke Foundation Endowed Chair in Cardiovascular Nursing Research



**John Eikelboom**

Canada Research Chair in Cardiovascular Medicine



**Stuart Connolly**

Salim Yusuf Chair in Cardiology



**Arya Sharma**

Canada Research Chair in Cardiovascular Obesity Research and Management



**Martin O'Donnell**

William J. Walsh Chair in Internal Medicine

HOPE Research Chair in Peace Through Health

**To be appointed**

Efforts continue to establish endowed chairs in innovative areas to provide productive researchers with stable salary support in order to protect their time devoted to research.

## Career Development and Awards

Researchers at the PHRI have influenced practice guidelines around the globe. It is no surprise that they have garnered an extensive list of achievements and awards including:

## 2006

- Teaching Excellence Award, McMaster University: *Janice Pogue*
- Scientific Director, Canadian Obesity Network: *Arya Sharma*
- International Lecture of the American College of Cardiology: *Salim Yusuf*
- Jack Hirsh Award for Outstanding Academic Achievement, McMaster University Department of Medicine: *Salim Yusuf*
- Canadian Association of Physicians of Indian Heritage Award: *Salim Yusuf*

## 2005

- Induction into McMaster University Alumni Gallery of Distinction: *Sonia Anand*
- Rick Gallop Award for Research Excellence, Heart & Stroke Foundation of Ontario: *Arya Sharma*
- Michael Smith Prize in Research Finalist, CIHR: *Salim Yusuf*
- Elected Fellow of the Royal Society of Canada: *Salim Yusuf*

## 2004

- American Association for Clinical Chemistry Award for Outstanding Contributions to Clinical Chemistry: *Matthew McQueen*
- Premier's Research Excellence Award (PREA), Ontario Provincial Government: *Parminder Raina*

## 2003

- DRC Gold Medal Oration Award, Chennai, India: *Hertzel Gerstein*
- Somogyi-Sendroy Award by the Upstate New York Section of the American Association for Clinical Chemistry (AACC): *Matthew McQueen*
- Canada's Top 40 Under 40: *Shamir Mehta*
- Paul Wood Silver Medal; British Cardiac Society: *Salim Yusuf*
- Heart and Stroke Foundation Of Canada Lecture: *Salim Yusuf*
- R.T. Hall Professorship, Australian New Zealand Society of Cardiology: *Salim Yusuf*
- Population Sciences Lecturer, European Society of Cardiology, Vienna: *Salim Yusuf*

## 2002

- Induction into McMaster University Alumni Gallery of Distinction: *Hertzel Gerstein*
- Teaching Excellence Award, McMaster University: *Janice Pogue*
- Louis and Artur Lucian Award for Research in Circulatory Disease: *Salim Yusuf*
- Ignacio Chavez Inaugural Lecture; World Congress of Cardiology, Sydney: *Salim Yusuf*

## 2001

- Canadian Society Internal Medicine Young Investigator Award: *Sonia Anand*
- Prix Galien Canada Research Award: *Salim Yusuf*

## 2000

- Gustav Nylin Medal, Swedish Society of Cardiology: *Salim Yusuf*

## 1999

- Cardiovascular Society Young Investigator Award: *Sonia Anand*
- Canadian Diabetes Association Young Scientist Award: *Hertzel Gerstein*
- Canadian Diabetes Association Frederick G. Banting Award: *Hertzel Gerstein*
- National Health Scholar, NHRDP, Health Canada/CIHR: *Parminder Raina*
- Career Research Award of the Canadian Cardiovascular Society, 1999: *Salim Yusuf*
- Sol Sherry Award, International Society of Thrombosis & Haemostasis: *Salim Yusuf*

## 1998

- Outstanding Service Profession, Canadian Academy of Clinical Biochemistry: *Matthew McQueen*

## 1997

- Heart and Stroke Foundation Endowed Chair in Cardiovascular Research, 1997: *Salim Yusuf*

## 1996

- Canadian Society of Clinical Investigators Award: *Sonia Anand*

## 1995

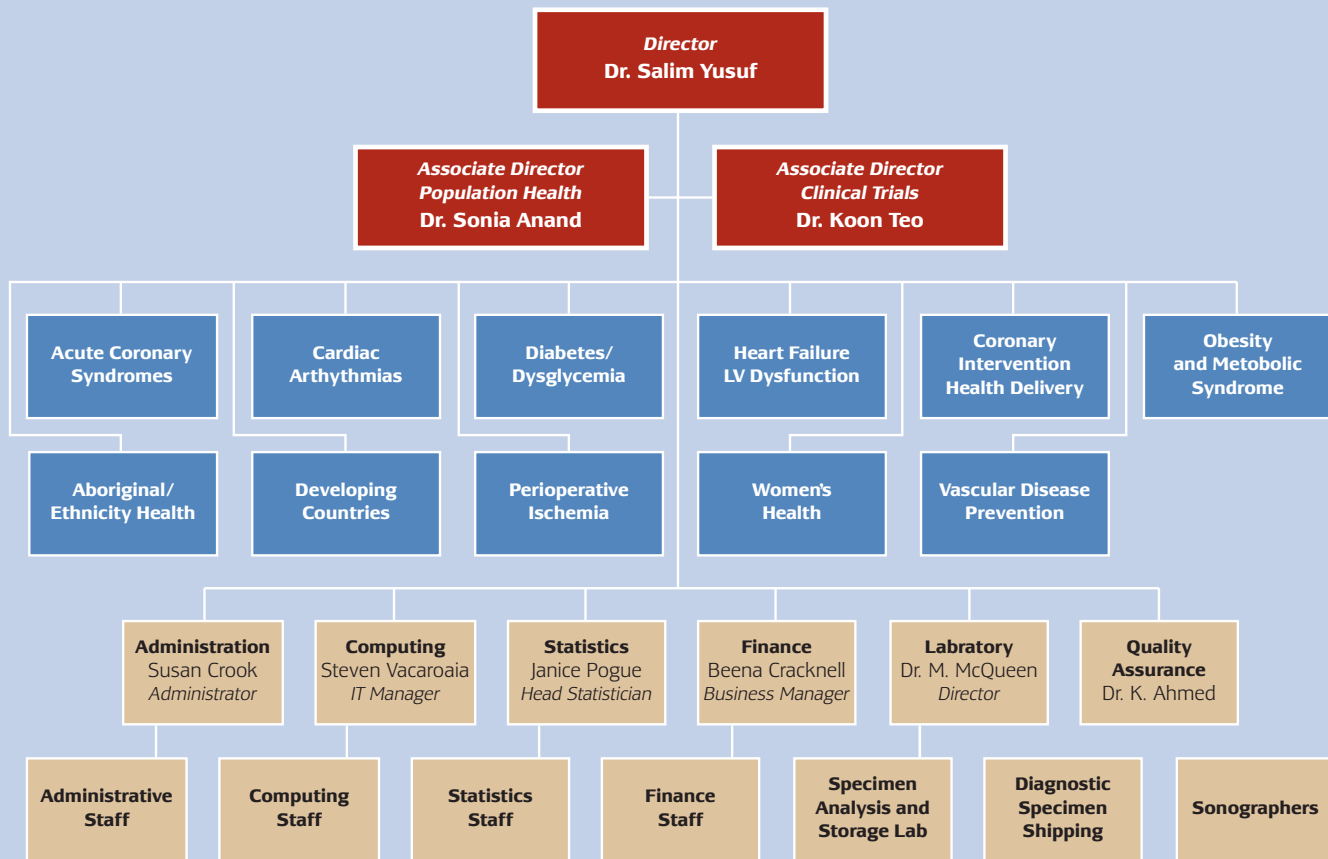
- Career Scientist Award, R. Samuel McLaughlin Centre for Gerontology, McMaster University: *Parminder Raina*

## Career Scientist and Research Fellowship Awards

- CIHR Senior Scientist Award: *Salim Yusuf*, 1994 to 2004
- CIHR Clinician Scientist Award: *Sonia Anand*, Phase 1: 1998-2002, Phase 2: 2002-2008
- CIHR Senior Health Research Fellowship: *Stephanie Ounpuu*, Phase 1: 2001 to 2003
- CIHR Senior Research Fellowship Award: *P.J. Devereaux*, Phase 1: 2003-2004, Phase 2: 2004-2006
- CIHR Doctoral Research Award: *Lisa Cronin*, 1999-2001
- CIHR New Investigator Award: *Shamir Mehta*, 2003-2008
- CIHR New Investigator Award: *P.J. Devereaux*, 2006-2007
- CIHR New Investigator Award: *Marek Smieja*, 2006-2011
- CIHR Investigator Award: *Parminder Raina*, 2004-2009
- CIHR Fellowship, *Philip Jong*, 2000-2004
- Ontario Ministry of Health Career Scientist Award: *Robert McKelvie*, 1989-1999
- Ontario Ministry of Health Career Scientist Award: *Catherine Demers*, 2003-2008
- Ontario Ministry of Health Career Scientist Award: *Heather Arthur*, 1998-2005
- Heart and Stroke Foundation of Canada Doctoral Research Award: *Linda Kelemen*, 2001-2002
- Heart and Stroke Foundation of Canada Doctoral Research Award: *Juan Carlos Villar*, 2002-2004
- Heart and Stroke Scientific Research Corporation of Canada Research Fellowship Award: *Catherine Demers*, 1998-2001
- Heart and Stroke Foundation of Canada Research Fellowship Award: *Sonia Anand*, 1996-1998
- Heart and Stroke Foundation of Canada/CIHR Research Fellowship Award: *Philip Jong*, 1999-2002
- Heart and Stroke Foundation of Canada Research Fellowship Award: *Shamir Mehta*, 1998-2000
- Heart and Stroke Foundation of Canada Research Fellowship Award: *Marek Smieja*, 1998-2001
- Heart and Stroke Foundation of Canada/CIHR Research Fellowship Award: *P.J. Devereaux*, 2000-2003
- Heart and Stroke Foundation of Canada Research Fellowship Award: *John Eikelboom*, 2000-2001
- Heart and Stroke Foundation of Canada Research Fellowship Award: *George Heckman*, 2001-2004
- Heart and Stroke Foundation of Canada Research Fellowship Award: *Stephanie Ounpuu*, 1998-2000
- Heart and Stroke Foundation of Canada/AstraZeneca Canada Research Fellowship Award: *Jeff Healey*, 2004-2005
- 4th ICPC/HSFC/CCS Fellowship Preventive Cardiology Research Award: *Katherine Morrison*, 2002-2005

A number of individuals have received training awards from the Heart and Stroke Foundation of Ontario/Canada and the Medical Research Council/Canadian Institutes of Health Research. In addition, the PHRI has provided partial salary support or research support to a number of trainees and faculty members.

# Career Development and Awards

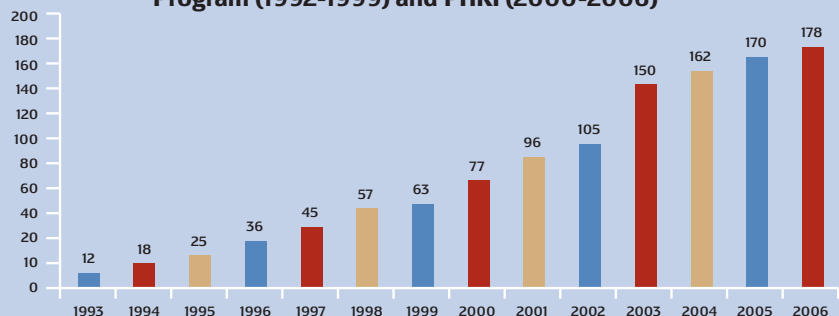


## Research Personnel

The number of research personnel at the PHRI has steadily grown to a team of over 200 health care professionals, including: clinician scientists, physicians, epidemiologists, research coordinators, rehabilitation experts, nutrition scientists, biostatisticians, nutritionists, nurses, computer programmers, data management assistants as well as administrative staff.



**Number of staff in the Preventive Cardiology and Therapeutics Program (1992-1999) and PHRI (2000-2006)**



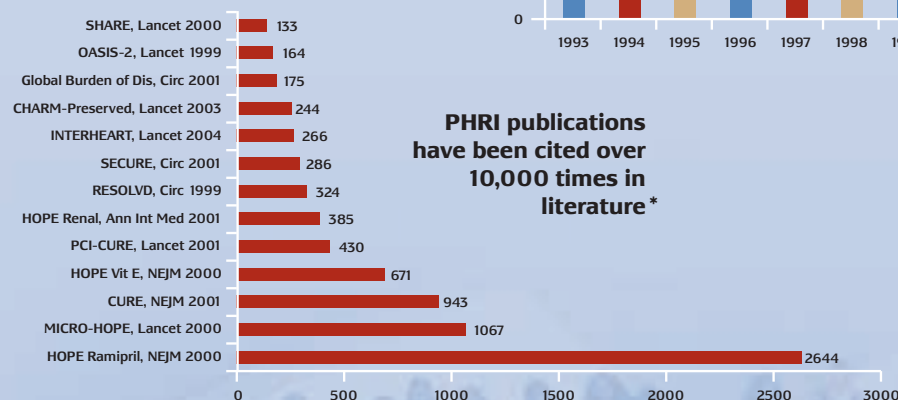
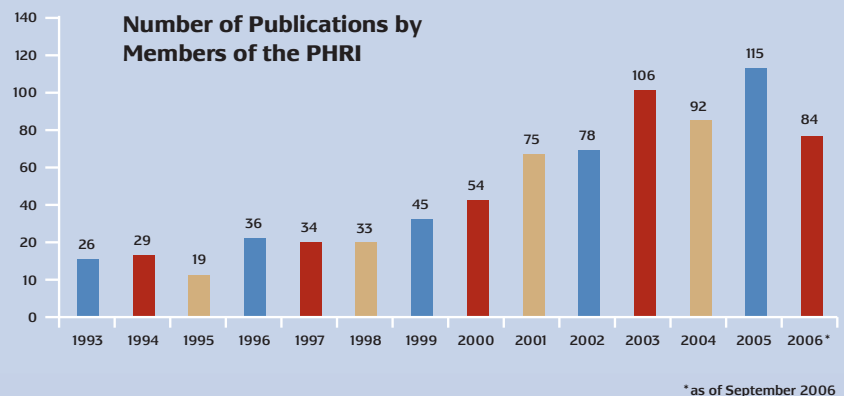


Research out of the PHRI has led to more than 800 publications in the last 10 years in prestigious medical journals such as The New England Journal of Medicine, The Lancet, The Journal of the American Medical Association, British Medical Journal, Circulation, Journal of the American College of Cardiology and The European Heart Journal. Several of the discoveries made by scientists at the PHRI have influenced prevention and treatment practices worldwide.

In addition, a number of PHRI studies have won the acclamation of being considered Classic Papers. In 2005 the INTERHEART study, published in the Lancet, was chosen for inclusion in the anthology "Vintage Papers From the Lancet". The HOPE study was the most cited paper in clinical medicine in November-December 2001, and was considered one of the top ten research advances in heart disease and stroke in 1999 by the American Heart Association, and Harvard Health letter in the year 2000. In addition, the HOPE study led to the drug ramipril being awarded the Molecule of the Year by MMW Pharmaceuticals in 2000.

Lastly, the INTERHEART study (Lancet 2004) has been acknowledged in 2006 as a Hot Paper by Canadian authors, with its top ranking on the Canada's Top 10 Hot Papers list from Essential Science Indicators<sup>SM</sup>.

For a comprehensive list of peer reviewed publications of the PHRI, see page 60.



## Publications and Citations

## Understanding the causes and evaluating new methods of preventing cardiovascular disease



“With common diseases such as CVD, only modest health gains are achievable by treating individuals affected by the disease, and moreover this is quite costly. Instead, our primary focus has to be preventing disease; and the last two or three decades have been a story of remarkable success.”

– Dr. Salim Yusuf



Cardiovascular disease (CVD) is the number one killer globally. Of the 55 million deaths that occur in the world, approximately 35 per cent are due to cardiovascular diseases. The majority of these are due to coronary artery disease or strokes. Furthermore, most of these occur in low and middle-income countries. The increase in cardiovascular disease is a relatively recent phenomenon; it was rare approximately 100 years ago, but is now common in all societies. This marked increase in CVD initially occurred in Western countries, but it is now increasingly being seen in low and middle-income countries, such that over 80 per cent of cardiovascular disease burden is seen in these latter countries. In the future, cardiovascular disease rates are expected to decline in the high-income countries, but the rates of these conditions will continue to increase in low and middle-income countries. Therefore, global efforts are warranted.

The PHRI's work in preventing CVD has taken two directions. The first being: evaluating novel approaches to preventing vascular disease in those who already have established disease or those who are at high risk. The second approach has been to try to understand the causes of heart disease and strokes globally.

### Preventing heart attacks and strokes through novel interventions

#### **HOPE: The Heart Outcomes Prevention Evaluation Trial**

The HOPE trial is a landmark study that has had a major impact on the prevention of heart disease and strokes in individuals who are at high risk. This study, funded by 14 industrial partners (principally Aventis), as well as the Canadian Institutes of Health Research (CIHR), demonstrated that ramipril, an angiotensin-converting enzyme inhibitor, reduced the risk of death from cardiovascular causes, heart attacks, and strokes by about one-fifth. In addition, there were beneficial effects in avoiding heart failure, as well as reducing the progression of renal disease. The study involved over 9,000 individuals from 19 countries, involving 267 centres. The main results were published in the New England Journal of Medicine and The Lancet, along with 50 other publications in various leading journals. The results of the trial have been incorporated into practice guidelines worldwide. If only half the individuals who are eligible to receive this preventive therapy actually receive it, this would have a substantial impact on a global scale. Between one and two million individuals will benefit from this therapy every year.

#### **HOPE-TOO**

In recent times, major emphasis has been placed on the hypothesis that the causes of heart disease could involve the oxidation of bad lipids (low density lipoproteins). Therefore, the concept that antioxidant vitamins may be helpful in avoiding heart disease emerged. HOPE was the first definitive trial to evaluate the role of high doses of vitamin E. Unfortunately: the results showed that vitamin E was not helpful. A follow-up study (HOPE-TOO) indicated that utilizing high doses of vitamin E long-term, might lead to increased heart failure. These results have important implications, as large numbers of people take high doses of vitamin E with the

expectation that there are benefits in preventing cardiovascular disease.

Another emerging hypothesis was that elevations of an amino acid in the blood (homocysteine) increased the risk of cardiovascular disease. A cocktail of inexpensive vitamins, such as folate, vitamin B6 and B12, reduces homocysteine levels substantially. Given the low cost of these vitamins and relative safety, if they benefit patients, even to a modest extent, this would have huge global applicability. Therefore, HOPE-TOO, a trial involving 5,500 high-risk individuals, evaluated homocysteine-lowering versus usual care, on top of best available therapy (funded by the CIHR). After five years of follow-up, this study showed a neutral effect of homocysteine lowering. Subsequent to this study, at least two others have confirmed the results. Along with the HOPE trial, this indicates the importance of reliably evaluating various promising hypotheses in large randomized trials. Only such trials can provide definitive answers as to the worth and safety of various treatments.

#### **HOPE-3**

Recent data indicates that the majority of individuals living in westernized settings, especially in urban areas, are at high risk for cardiovascular disease. This is because most of these individuals have several of the risk factors that predispose to heart disease. A novel concept that has emerged is that by using a combination of lipid-lowering therapy (with a low dose statin), blood pressure lowering (with multiple agents used in low doses) and aspirin in those with vascular disease, would lead to very large reductions in the risk of future events; some have postulated as much as an 80 per cent reduction in the risk of events.

The PHRI is conducting two studies to evaluate this concept. The first of these is the HOPE-3 study, which includes evaluating a low dose statin

## Prevention of Cardiovascular Disease in Broad Populations

(rosuvastatin at 10 mg a day, which reduces low-density lipoprotein (LDL) by 50 per cent), and a combination of two blood pressure-lowering agents used in low doses (candesartan and hydrochlorothiazide), in high risk individuals who are middle-aged and have no evidence of vascular disease. By evaluating the impact of each of these therapies alone, and in combination, by utilizing a 2x2 factorial design, the trial will establish the relative roles of each of these therapies (lipid-lowering or blood pressure-lowering compared to controls), as well as their combination. It is expected that the combination therapy will reduce the risk of future events by at least 50 to 60 per cent. If this is confirmed, this would have considerable public health benefits. The HOPE-3

trial is funded by AstraZeneca and will involve 10,000 individuals from 10 countries who will be followed for about five years.

The second study evaluating this concept is the **Indian Polypill study**, which will test the pharmacological effects of various combinations of therapy on blood pressure-lowering, lipid-lowering, and antiplatelet therapy. This study will be conducted in 60 centres in India, in approximately 1,800 individuals with diabetes or hypertension. If this study shows the desired impact on risk factor levels, as well as safety, then a larger trial utilizing a strategy of a combination pill will be evaluated in large numbers of individuals to assess their impact on clinical events.

## Ongoing Studies

Building upon the HOPE study, the ONTARGET and TRANSCEND studies will be evaluating whether angiotensin receptor blockers are as effective as ACE inhibitors in preventing vascular disease in individuals – similar to those who entered HOPE. This is a particularly important question because angiotensin receptor blockers do not have some of the side effects as ACE inhibitors, such as cough or angioneurotic edema, which limit patients from using these drugs. Equally exciting, will be the evaluation of whether the addition of an angiotensin receptor blocker to an ACE inhibitor (ramipril) will be superior to ramipril alone. In a parallel trial (TRANSCEND), the role of an ARB (telmisartan alone) versus placebo in individuals who cannot tolerate an ACE inhibitor will be evaluated. Collectively, these two trials (which are funded by Boehringer-Ingelheim), involving 31,000 high risk individuals, represents the largest secondary prevention program in the world. Their results are due to be evaluated in the middle of 2008, and are expected to have an important impact on cardiovascular prevention.

### Preventing Vascular Events in People with Dysglycemia

The ORIGIN study evaluates the role of an easily administrable new form of insulin (insulin glargine), as well as fish oil, in preventing vascular

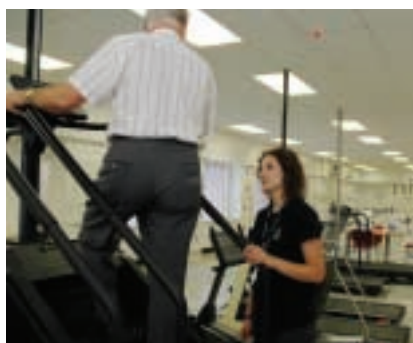
events in 12,500 high-risk people with diabetes. The study, which is funded by Aventis, is being conducted in 40 countries and in 578 centres and is expected to provide results by the year 2010.

The above studies on preventing major vascular events are complemented by studies evaluating the impact of various preventive strategies in preventing the progression of atherosclerosis measured non-invasively. These are outlined in the section on vascular imaging on page 40.

A major thrust of the prevention group is to assess the impact of risk factors globally. Accordingly, the large INTERHEART study, involving 52 countries, has been completed (for details see page 22). Following in its footsteps, PURE study (Prospective Urban Rural Epidemiologic study) is evaluating the societal and genetic causes that lead to the development of risk factors by trying to recruit 135,000 individuals from 15 countries (low, middle, and high-income countries), and follow them for 10 years. This study has received support from six pharmaceutical companies, and additional funding is sought through peer-review grants, both in Canada and internationally. At present, the study has recruited over 50,000 individuals from 11 countries. Further details are provided in the Obesity research section on page 20.

### Research team:

Salim Yusuf, Sonia Anand, Arya Sharma, Eva Lonn, Jackie Bosch, Koon Teo, Matthew McQueen, Hertzell Gerstein, Ingrid Copland, Janice Pogue, Kim Hall, Sumathy Rangarajan, Jane Shannon and Mary Micks



### Key publications:

- The Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *New Engl J Med* 2000; 342(3): 145-53.
- The Heart Outcomes Prevention Evaluation Study Investigators. Vitamin E supplementation and cardiovascular events in high-risk patients. *New Engl J Med* 2000; 342(3): 154-60.
- The Heart Outcomes Prevention Evaluation (HOPE) Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. *Lancet* 2000; 355: 253-59.
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- Bosch J, Lonn E, Pogue J, Arnold JMO, Dagenais GR, Yusuf S for the HOPE/HOPE-TOO study investigators. Long-term effects of ramipril on cardiovascular events and on diabetes: results of the HOPE study extension. *Circulation* 2005; 112: 1339-46.
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- Lonn E, Yusuf S, Dzavik V, Doris IC, Yi Q, Smith S, Moore-Cox A, Derksen C, Magi A, Bosch J, Tartaglia C, Riley WA, Teo KK for the SECURE Investigators. Effects of ramipril and of vitamin E on atherosclerosis: The Study to Evaluate Carotid Ultrasound changes in patients treated with Ramipril and Vitamin E (SECURE). *Circulation*, 2001; 103: 919-925.
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- Teo KK, Öunpuu S, Hawken S, Pandey MR, Valentin V, Hunt D, Diaz R, Rashed W, Freeman R, Zhang X, Yusuf S for the INTERHEART investigators. Tobacco use and risk of myocardial infarction in 52 countries – the INTERHEART study. *Lancet* 2006; 368:647-658.

# Prevention of Cardiovascular Disease in Broad Populations



## Preventing the seeds of obesity and heart disease in children

There has been a dramatic increase in childhood obesity in recent years, which predicts a future epidemic of diabetes, atherosclerosis and its complications (heart attacks and strokes). The development of these risk factors and obesity result from complex interactions between one's genes, physical activity, sedentary behaviour, diet and metabolism.

Understanding why at several periods or "critical phases" in fetal life and childhood, some children become obese and develop risk factors will allow us to develop strategies for prevention – in order that we have more healthy children who grow into healthy adults.



"Parents and society do not expect that their children would be at risk of future heart disease, but the rapidly increasing prevalence of childhood obesity and diabetes leads to heart disease in later life. It is absolutely essential that we learn more about the reasons for this rising prevalence, as we are doing in the FAMILY study."

– Dr. Koon Teo

### FAMILY - The Family Atherosclerosis Monitoring in Early Life Cohort Study

The Family Atherosclerosis Monitoring in Early Life (FAMILY) Cohort Study investigates the environmental, genetic and biochemical factors important in the development of cardiovascular risk factors, obesity and atherosclerosis in childhood. One thousand children and their families (both parents and eldest full sibling, where available) are enrolled when the mother is pregnant and all are followed for 10 years. The study will assess blood pressure, lipids, insulin and glucose and body composition, at three and five years of age and examine their impact on atherosclerosis by age 10, using sensitive

ultrasound measures of the arteries in the neck (carotid).

A CIHR Operating Grant funds the FAMILY Cohort Study, with additional support from the Heart and Stroke Foundation of Canada, Hamilton Health Sciences Research Foundation, American Chemistry Council and the Population Health Research Institute. The team investigating this study involves cardiologists, pediatricians, nutritionists, epidemiologists, obstetricians, experts in allergy and lab medicine and endocrinologists.

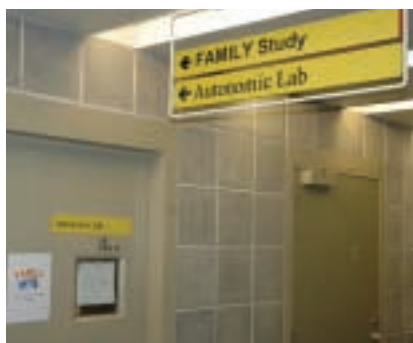
#### Research team:

Katherine Morrison, Koon Teo, Stephanie Atkinson, Warren Foster, Sarah McDonald, Richard Persadie, Barry Hunter, Matthew McQueen, Mike Cyr, Peter Steer, Patrick Mohide, Stephanie Winsor, Judah Denburg and Salim Yusuf



## Childhood Risk Factors





**Why do women with preeclampsia during pregnancy develop more heart attacks and strokes?**

Sarah McDonald, an obstetrician, is working with Salim Yusuf, a cardiologist, to understand why women who had preeclampsia develop more heart disease. These investigations could lead to early prevention in high-risk women.



## Childhood Risk Factors

## Exploring the link between glucose, heart attacks and stroke



"We have clearly shown that dysglycemia is an important risk factor for cardiovascular disease and other health related consequences. If our ongoing studies show that lowering glucose levels with insulin and other therapies mitigates these risks, it will establish pancreatic endocrine dysfunction as a key player in a variety of serious health-related problems."

– Dr. Hertz Gerstein

**D**iabetes is a strong independent risk factor for cardiovascular events. PHRI researchers have shown that the glucose-associated risk of cardiovascular disease (CVD) extends across the range of dysglycemia, from normal glucose levels, right to mild glucose impairment and into the diabetic range.

Researchers at the PHRI are currently focused on several areas related to dysglycemia and CVD. These include: identification of genetic, behavioural, anthropomorphic and social risk factors for dysglycemia, diabetes and cardiovascular disease through the lifecycle; characterization of less-studied consequences of dysglycemia that are related to cardiovascular disease such as cognitive decline, renal dysfunction and erectile dysfunction; and impact of the built environment and urban-rural differences on dysglycemia and CVD.

These factors may be evaluated through the impact of: novel approaches to prevent diabetes with ACE inhibitors, A2 blockers, and/or thiazolidinediones; glucose-lowering to reduce coronary atherosclerosis and cardiovascular events and death in ambulatory settings; insulin-mediated glucose lowering to reduce mortality in coronary care units; and novel computer-based approaches that facilitate self-management of diabetes.

### Key Studies

#### **ACCORD: Action to Control Cardiovascular Risk in Diabetes**

ACCORD is an international National Institutes of Health (NIH) funded trial of 10,251 people with diabetes, who are at high risk for cardiovascular disease. PHRI coordinates the Canadian sites of this study. During a five-year period, the study will determine whether: a therapeutic strategy targeting a HbA1c level less than six percent reduces CV events more than one targeting seven to 7.9 percent; a therapeutic strategy targeting a systolic BP of less than 120 reduces CV events more than one targeting a systolic BP less than 140; the addition of a fibrate to a statin reduces CV events more than a statin alone in the settings of a normal LDL cholesterol level. This trial is also determining the impact of the interventions on eye and kidney disease, cognitive decline, skeletal health, quality of life and health-related costs.

#### **DREAM and STARR: Diabetes Reduction with ramipril and rosiglitazone medication**

DREAM is an international Canadian Institutes of Health Research (CIHR)/Industry funded (GlaxoSmithKline, Sanofi-Aventis and King Pharmaceuticals) trial of 5,269 people at high risk for diabetes. The study aims to determine if either ramipril and/or rosiglitazone reduces diabetes, cardiorenal events, or carotid atherosclerosis. The STARR sub-study is measuring the effect of the interventions on beta cell function, cardiac function, fat distribution and renal disease.

#### **EpiDREAM: Epidemiologic Prospective Study of DREAM Screeners**

The EpiDREAM cohort consists of individuals who were screened for eligibility for DREAM. Information was collected from 22,334 individuals from 21 countries, and 15,760 individuals; including 5,269 individuals in the DREAM trial are being followed prospectively to collect data on incident clinical events, including the development of type-2 diabetes and CVD over five years. All individuals involved in the study provided detailed lifestyle information on dietary intake, physical activity, blood samples and physical measurements. EpiDREAM provides a unique opportunity to analyze the clinical, lifestyle, social and genetic determinants of the four MS-related factors, type-2 diabetes and CVD. This study is funded by the CIHR, industry partners (GlaxoSmithKline, Sanofi-Aventis) and the Heart and Stroke Foundation.

#### **ORIGIN: Outcome Reduction with an Initial Glargine Intervention**

ORIGIN is an international industry-funded (Sanofi-Aventis) trial of 12,612 people. The study will determine if either insulin-mediated normoglycemia with glargine insulin or omega 3 fatty acids reduce CV events in people with impaired fasting glucose (IFG), impaired glucose tolerance (IGT), new diabetes or early established diabetes. It will also determine the effect of the interventions on cognitive decline, erectile dysfunction, renal disease, beta cell function, skeletal health and biologic markers.

## Dysglycemia and Cardiovascular Diseases



#### Research team:

Sonia Anand, Stephanie Atkinson, Jackie Bosch, Ami Gafni, Brian Haynes, Alison Holloway, Eva Lonn, Anwar Merchant, Katherine Morrison, Janice Pogue, Koon Teo, Katherine MacDonald, Matthew McQueen, Zubin Punthakee, Rosalie Russo, Jane Shannon, Arya Sharma and Salim Yusuf

#### Key publications:

- Gerstein HC, Yusuf S. Dysglycemia and risk of cardiovascular disease. *Lancet* 1996; 347(9006): 949-950.
- Coutinho M, Gerstein HC, Wang Y, Yusuf S. The relationship between glucose and incident cardiovascular events. A metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. *Diabetes Care* 1999; 22(2): 233-240.
- Heart Outcome Prevention Evaluation (HOPE) Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO HOPE sub study. *Lancet* 2000; 255:253-259.
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- Gerstein HC, Pogue J, Mann JF et al. The relationship between dysglycemia and cardiovascular and renal risk in diabetic and non-diabetic participants in the HOPE study: a prospective epidemiological analysis. *Diabetologia* 2005; 48(9): 1749-1755.



## Dysglycemia and Cardiovascular Diseases



## Addressing the global epidemic of obesity and its consequences



"While preventing obesity through a better understanding of societal and lifestyle determinants is key, we also need to develop and deliver effective treatments to those already struggling with obesity. Exploring the proper use of medications and surgery will be an important area of future research in obesity management."

– Dr. Arya Sharma

Excess body weight, the hallmark of obesity, is well recognized today as a key determinant of health, both at the level of populations, as well as that of individuals. PHRI is actively pursuing a number of key projects aimed at better understanding the environmental, societal, cultural and biological determinant of this global epidemic.

### Landmark studies in obesity at PHRI

#### FAMILY

The fetal and peri-natal determinants of obesity are being explored in the CIHR-funded FAMILY study, a prospective study of 1,000 pregnancies, where the development of excess body weight and metabolic complications of the children will be monitored into early childhood and beyond. This study should lead to novel insights into the relationship between maternal and early childhood determinants of obesity and its consequences. For more information on this study, see page 16.

#### PURE

The Prospective Urban-Rural Epidemiologic (PURE) study will be the largest global study examining the environmental, societal and biological determinants of obesity and other chronic health problems both in developing societies. PURE is designed to examine the impact of urbanization on the development of primordial risk factors (for example: physical activity and nutrition changes), primary risk factors (for example: obesity, hypertension, dysglycemia and dyslipidemia, smoking), and CVD. Urban and rural paired cohorts of over 135,000 individuals will be established in 14 countries with periodic standardized collection of data, bloods and other variables. In addition, DNA will be stored, allowing future exploration of gene-environment interactions. For more information on this study, see pages 15 and 22.



#### INTERHEART

The specific role of abdominal obesity as a risk factor for cardiometabolic disease has been the focus of a number of PHRI projects. The INTERHEART study, which involved 27,500 individuals from 52 countries, identified abdominal obesity as one of the nine global risk factors for myocardial infarction, accounting for around 35 per cent of the population attributable risk.

#### Mol-SHARE

This representative cross-sectional study of ethnic communities in Canada found that South Asian, Chinese and Aboriginal Canadians have a greater susceptibility to the cardiometabolic complications of excess body weight than Canadians of European descent. Following this finding, the Mol-SHARE study is now focusing on whether or not this difference in susceptibility to the metabolic complications of obesity in South Asians is due to molecular differences in fat tissue or skeletal muscle. The Heart and Stroke Foundation of Ontario currently funds Mol-SHARE.

PHRI studies focus on the prevention and treatment of obesity complications. In the HOPE study, a blockade of the renin-angiotensin system with ramipril reduced the incidence of type-2 diabetes by nearly 25 per cent. One reason for this metabolic effect of renin-angiotensin blockade may be the formation of subcutaneous fat cells to serve as a metabolic sink for excess fat. This hypothesis is currently being explored in the TRIM study. The effect of renin-angiotensin blockade on the incidence of type-2 diabetes is also the focus of DREAM, ONTARGET and TRANSCEND.







## Current Studies

**TRIM** (Telmisartan in the Reduction of Intra-Myocellular Lipids) Canadian Institutes of Health Research and Boehringer-Ingelheim, 2004 - 2006  
This study is examining the effect of renin-angiotensin blockade with the angiotensin receptor blocker telmisartan on fat cell growth and skeletal muscle fat deposition in individuals with abdominal obesity.

**MoL-SHARE** (Molecular Study of Health Assessment and Risk in Ethnic Groups): Heart and Stroke Foundation, 2005 - 2007

People who originate from the Indian subcontinent (South Asians), have an increased risk for diabetes and heart disease. It is possible that South Asians may have more body fat than Europeans of similar weight, may deposit more fat in their internal organs (gut, muscle, liver), or have differences in structure and function of fat and muscle tissue compared to Europeans. The aim of this project is to understand whether or not these entities explain the increased risk of South Asians for diabetes and heart disease.

**SOCCER** (State of Obesity Care in Canada Evaluation Registry): Abbott Pharmaceuticals, 2005 - 2008

An observational study of clinical care of patients with obesity, this study assesses the gaps that exist in the management of obesity and its related conditions in obese patients seen by primary care physicians and specialists. The follow-up phase of the study hypothesizes that a compliance and adherence gap exists in patients prescribed pharmacotherapy for obesity.

**Epicard** (Role of epicardial adipose tissue in Coronary artery disease): Heart and Stroke Foundation, 2006

The Epicard study seeks to evaluate whether patients with coronary artery disease (CAD) have more epicardial fat than people without coronary artery disease. This study is also interested in evaluating whether epicardial fat from CAD patients releases more adipokines than subcutaneous fat.

## Key publications:

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- Shubair MM, Kodis J, McKelvie RS, Arthur HM, Sharma AM. Metabolic profile and exercise capacity outcomes: their relationship to overweight and obesity in a Canadian cardiac rehabilitation setting. *J Cardiopulm Rehabil.* 2004 Nov-Dec; 24(6): 405-13.

## The Population Health Research Institute is home to the newly established Canadian Obesity Network

Funded through the federal National Centres of Excellence (NCE) program, this Network is the primary network of Canadian obesity researchers, health professionals, and other stakeholders aimed at preventing and treating the health consequences of excess body weight. This network currently has over 1,000 members from over 25 Canadian universities and over 100 other institutions and organizations..

### Research team:

Arya Sharma, Sally Kohne, Anne Moore-Cox, Paula Carroll, Sue Damjanovic, Mahmood Akhtar, Bilal Ahmed, Kirstin Gorzelniak, Gianluca Iacobellis, Angela Kochan, Brandy Cochrane, Imtiaz Samjoo, Laura Puri, Carol Petryschuk, Natalie Maystrenko, Charlene Wristen, Margo Thompson, Tripat Gill, Sarah Lemieux, Alice Bradbury, Kristi Ward, Navneet Singh, Laura Bateman-Taylor, Sonia Anand and Salim Yusuf



# Obesity

## Addressing the burden of disease on a global basis

Eighty per cent of the global burden of various diseases, including chronic diseases, occurs in low and middle-income countries. Of these, cardiovascular diseases and diabetes-related complications constitute amongst the largest burdens. The PHRI has been exploring the causes of heart disease and strokes globally, and improving management of patients with acute coronary syndromes. The Institute has also initiated studies in conditions, which are commonly neglected in research, such as Chagas disease.

## Studies

### INTERHEART

This study, involving approximately 28,000 individuals from 52 countries, has documented that nine simple modifiable risk factors can account for over 90 per cent of the population's attributable risk for heart disease globally. More importantly, these risk factors appear to have similar predictability in all regions of the world, as well as in all ethnic groups. These findings simplify prevention and suggest that similar approaches to cardiovascular prevention (but with local modifications for varying cultural and economic circumstances) is likely to make a big impact in avoiding heart disease globally.

The number of smokers worldwide is currently estimated to be 1.3 billion, of which 82 per cent live in developing countries. However, most large studies on smoking and heart disease to date have focused on developed countries. In 2006, the INTERHEART study established that all forms of tobacco exposure, such as smoking, chewing tobacco or inhaling second hand smoke, increase the risk of heart attack.

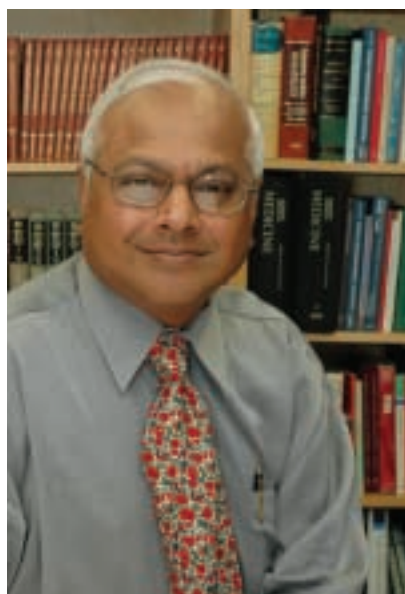
The study found that tobacco use in any form, including sheesha smoking, which is popular in the Middle East, and beedie smoking, common in South Asia, was harmful. Compared to people who had never smoked, smokers had a three-fold increased risk of a heart attack. Even those with relatively low levels of exposure doubled their risk of heart attack; each cigarette smoked per day increased the risk by 5.6 per cent. It also established that the risk of heart attack decreased with time after stopping smoking and exposure to second hand smoke increased the risk of heart attack in both former and non-smokers.

### PURE (Prospective Urban Rural Epidemiologic Study)

In order to assess the reasons of why some individuals develop risk factors for cardiovascular disease, a study examining the influence of societal factors (particularly urbanization) on lifestyle behaviours, which in turn influence risk factors through interactions with genes, is being explored in 15 countries representing low, middle, and high-income regions of the world. The study is expected to involve 135,000 individuals who will then be followed for at least 10 years following the study. The PURE study team has currently recruited over 50,000 individuals from India, China, South Africa, Zimbabwe, UAE, Chile, Argentina, Brazil, Colombia, Sweden and Canada. The study is expected to be initiated shortly in Iran, Poland, Tanzania, and also hopefully in Ghana. This global study will form the platform to assess a variety of additional questions, such as indoor and outdoor pollution, disability and road traffic accidents.

### INTERSTROKE

Strokes are a much more heterogeneous condition than coronary artery disease and may be hemorrhagic or ischemic. Ischemic strokes may be due to a variety of different etiologies, such as small vessel disease or large vessel disease, or embolic causes. The proportion of individuals with strokes who have any of these conditions varies substantially by region. Furthermore, the risk factors for strokes have varying prevalences in different parts of the world. Therefore, we have launched a large case-control study (INTERSTROKE) examining the risk factors for stroke in multiple countries. The pilot study will



“The majority of health problems are global, and in order to have a global impact, we work in 66 countries – tackling some of the most important health challenges.”

– Dr. Salim Yusuf.



## Cardiovascular Diseases and Related Conditions in Developing Countries



involve 1,200 cases of strokes and 1,200 controls from seven countries, and will then be expanded to include about 25,000 cases and 25,000 controls from a larger number of countries.

#### CREATE Registry

The CREATE Registry is the largest registry of practice patterns and clinical course of patients with acute coronary syndromes from a developing country. The study has included approximately 20,000 individuals from about 90 centres in India. The registry documents patterns of practice and forms a benchmark that can be used by clinicians to improve their practice.

#### The CREATE Trial

The CREATE trial is one of the first large randomized trials exclusively done in low and middle-income countries. The trial tested two simple therapies in patients with myocardial infarction, (glucose-insulin-potassium and reviparin, a low molecular weight heparin). The study was conducted in India, China, Latin America, and in Pakistan. Twenty thousand individuals were recruited over three years for this study, all with high rates of follow-up and high data quality. While reviparin demonstrated reduction in mortality and reinfarction, there was an excess of significant bleeding, including intracranial bleeds. The CREATE study showed that glucose-insulin-potassium was found not to have a beneficial effect and its results have created the basis of further trials in these countries.



#### BENEFIT

Chagas disease is a parasitic condition caused by triatomine bugs that affects approximately 15-20 million individuals in Latin America. Given the large population that this condition affects, very little research has been done in regards to its treatment or prevention. The PHRI has initiated a trial of 1,000 individuals (BENEFIT) examining the role of trypanocidal treatment (benznidazole) in individuals with a chronic phase of asymptomatic Chagas disease. The Canadian Institutes of Health Research, as well as the Tropical Disease Research-World Health Organization fund this pilot study.

#### Other Emerging Collaborations

The PHRI is working with investigators in Africa, led by Professor Bongani Mayosi from Cape Town, South Africa, to develop a large trial evaluating the role of steroids in tuberculous pericarditis. A pilot study is expected to be initiated shortly, which will be the basis for a formal submission for a much larger study in multiple countries.

In collaboration with INCLEN and the Canadian Obesity Network (CON), the PHRI is developing a study on the determinants of childhood obesity in 32 countries of the world. The countries represent the entire spectrum from low, to middle, to high-income countries.

#### Research team:

Salim Yusuf, Koon Teo, Matthew McQueen, Carlos Morillo, Shamir Mehta, Martin O'Donnell, Arya Sharma, Rashid Ahmed, Barbara Ramos, Chanchun Xie, Sonia Anand, Kim Hall, Sumathy Rangarajan, Anwar Merchant, Mahshid Dehghan, Romaina Iqbal, Shofiquel Islam, Denis Xavier and Ruth Chen

#### Key publications:

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- Pais P, Pogue J, Gerstein H, Zachariah E, Savitha D, Jayaprakash S, Nayak PR, Yusuf S. Risk factors for acute myocardial infarction in Indians: a case-control study. *Lancet* 1996; 348: 358-363.
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- Steyn K, Sliwa K, Hawken S, Commerford P, Onen C, Damasceno A, Öunpuu S, Yusuf S; INTERHEART Investigators in Africa. Risk factors associated with myocardial infarction in Africa: the INTERHEART Africa study. *Circulation* 2005; 112(23): 3554-61.
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- Teo KK, Öunpuu S, Hawken S, Pandey M, Valentin V, Hunt D, Diaz R, Rashed W, Freeman R, Jiang L, Zhang X, Yusuf S, on behalf of the INTERHEART Study Investigators. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. *Lancet* 2006; 368 (9536): 647-658.



## Cardiovascular Diseases and Related Conditions in Developing Countries



## Exploring differences in heart disease and diabetes between women and men



“Training new investigators to have the methodologic skills to approach sex and gender disparities in health is a major thrust of our program.”

– Dr. Sonia Anand



The Women's Health program at PHRI is focused on the promotion of women's health in the clinical, education and research domains, with specific reference to cardiovascular disease (CVD). On the clinical front of this program, women with risk factors for CVD or established CVD are diagnosed and treated at the Women's Vascular Clinic at McMaster University Medical Centre in Hamilton.

Dr. Sonia Anand leads the Women's Health research program at PHRI. This program area is focused on conducting population-based and clinical trials to understand the broad determinants of type-2 diabetes and CVD among women. The program is also focused on studying breast cancer, access to health care among women and the evaluation of treatment effects of specific medical therapies in women with established CVD.

### The Caring Network

An Interdisciplinary Capacity Enhancement (ICE) grant from the Canadian Institutes of Health Research (CIHR) and Heart and Stroke Foundation of Ontario (HSFO) has allowed the establishment of the Caring Network (2004 – 2008) at PHRI. The projects in this area explore whether and why women have differing outcomes in acute coronary syndromes and the metabolic syndrome.

### Current Projects of the CARING Network

- Catherine Kreatsoulas: Web Based Survey to Detect Gender and Sex Differences in the Referral for Cardiac Catheterization, 2005-06
- Patricia Caldwell: Measurement of Gender Differences in Psychosocial Factors Related to Cardiac Catheterization, 2005-06
- Larry DeKoning: Meta-analysis of Measures of Abdominal Obesity as a Predictor of CVD among Women and Men, 2004-05
- Amandev Aulakh: What constitutes a valid Sex/Gender Subgroup Analysis?

### Current Studies

#### Gender and Ethnic Differences in Hypertension and Diabetes Mellitus

Funded by the Canadian Institutes of Health Research, and led by Naida Khan, this study documents differences in the prevalence and incidence of diagnosed hypertension and diabetes mellitus and their treatment among South Asian, Chinese and other Canadian women and men in BC and Alberta.

#### Biological Determinants of the Differences in Metabolic and Cardiovascular Risk Factors Between South Asians and European Caucasians

See the Obesity Research Program section on page 20 for more details on this study, which is funded by the Heart and Stroke Foundation.

### Long-Term Effects on Diet on CHD risk factors in women

Funded by the Canadian Breast Cancer Research Initiative, and led by Dr. Norman Boyd of the University of Toronto, this study is a dietary intervention trial for the prevention of breast cancer. It compares long-term changes in serum lipid and lipoprotein levels, body weight/composition and C-reactive protein and carotid artery atherosclerosis measured at one time point. The study also characterizes the dietary intakes of these subjects to determine the relationships between dietary measures and risk factors and atherosclerosis measurements.

### Long-Term Outcomes of a Randomized Trial

This study evaluates the effectiveness, cosmetic appearance and long-term outcomes of a shorter, intensive radiation therapy schedule received by over 1,200 women with breast cancer. This trial is funded by the Canadian Breast Cancer Research Initiative and is led by Tim Whelan who collaborates with Sonia Anand.

### ICRH Reducing Health Disparities and Promoting Equity for Vulnerable Populations

Funded by the Canadian Institutes of Health Research, this study compares verified cardiac rehab access in vulnerable populations, including women and ethnic groups following these different operationalizations of referral, by tracking ACS patients for one year, from nine acute care sites from across Windsor to Sudbury. Sonia Anand collaborates with PI, Sherry Grace of York University, on this project.

### Key publications:

- Keshavarz H, Prabhakaran D, Anand S. Metabolic Risk Factors for vascular disease in women. Greer IA, Ginsberg J, Forbes CD. Editors. Women's Vascular Health. University of Glasgow (In Press).
- Yusuf S, Anand S. Hormone replacement therapy: a time for pause. CMAJ 2002 Aug 20; 167(4): 357-9.
- Anand S, Xie C, Mehta S, Franzosi M, Joyner C, Chrolavicius S, Fox K, Yusuf S. Differences in the Management and Prognosis of Women and Men who suffer Acute Coronary Syndromes. J Am Coll Cardiol Nov 15; 46(10): 1845-51.
- Anand S, Razak F, Davis A.D., Jacobs R, Vuksan V, Teo K, Yusuf S. Social disadvantage and CVD: development of an index and analysis of age, sex and ethnicity effects. Int J of Epidemiol 2006.

### Research team:

Sonia Anand, Heather Arthur, Eva Lonn, Madhu Natarajan, Shamir Mehta, Arya Sharma, Hertzfel Gertsein, James Velianou and Salim Yusuf



The Six Nations Reserve in Brant County, Ontario took its present form of 20,000 hectares in 1847, and is now home to over 12,000 Six Nations people. The traditional lifestyle of the Six Nations people included agricultural farming, hunting and fishing, but the increase in permanent settlements during the second half of the 20th century led to their growing dependence on store-bought foods, and an increased dependence on automobiles and other energy-saving devices. This has led to a marked increase in obesity, diabetes and CVD.

Between 1996 and the year 2000, PHRI researchers, led by Dr. Sonia Anand, together with Six Nations Health Services, under the leadership of Ruby Jacobs and A.D. Davis, conducted the Study of Health and Risk Evaluation in Aboriginal Peoples (SHARE-AP) to determine the prevalence of CV risk factors among the Six Nations people. This study confirmed that the Six Nations people suffered a disproportionate burden of risk factors including obesity, diabetes, and CVD. On-going collaborations continue between the researchers and the Six Nations people, and since then the team has conducted all studies on the Six Nations reserve under the leadership of A.D. Davis R.N.

#### Peer-Reviewed Studies

##### SHARE-AP Follow-Up Study

(The Study of Health Assessment and Risk Evaluation in Aboriginal Peoples): Heart and Stroke Foundation, 2003 – 2007

##### SHARE-AP Action

(Study of Health Assessment and Risk Evaluation – Obesity Prevention): Canadian Institutes of Health Research, 2003 – 2005

##### ACADRE

(Aboriginal Capacity and Development Research Environments): Canadian Institutes of Health Research, 2001 – 2002

##### SHARE

(Relation between dietary and serum levels of folate, B12, and plasma B6, and methylene tetrahydrofolate reductase (MTHFR) gene with plasma homocysteine and atherosclerosis in the Study of Health Assessment and Risk in Ethnic groups): Canadian Institutes of Health Research, 2002 – 2003

##### SHARE-AP

(Study of Health Assessment and Risk Evaluation in Aboriginal Peoples) - Dietary Questionnaire Validation: Canadian Institutes of Health Research, 2000 – 2001

#### Research team:

Sonia Anand, Jackie Bosch, A.D. Davis, Hertzell Gerstein, Ruby Jacobs, Eva Lonn and Salim Yusuf

##### SHARE-AP

(Study of Health Assessment and Risk Evaluation in Aboriginal Peoples): Heart and Stroke Foundation of Ontario, 1998 - 2000

##### SHARE

(Study of Health Assessment and Risk in Ethnic groups)- Dietary Questionnaire Validation: Medical Research Council of Canada, 1998 - 1999

##### SHARE

(Study of Health Assessment and Risk in Ethnic groups): Medical Research Council of Canada, 1996 - 1998

#### Key publications:

- Anand S, Yusuf S, Jacobs R, Davis D, Gerstein H, Lonn E, Yi Q. Risk factors, atherosclerosis, and cardiovascular disease among Aboriginal People in Canada: The Study of Health Assessment and Risk Evaluation in Aboriginal Peoples (SHARE-AP) Lancet 2001 Oct 6; 358(9288): 1147-53.
- Anand S, Yi Q, Gerstein H, Lonn E, Jacobs R, Vuksan V, Teo K, Davis B, Monategue P, Yusuf S. The Relationship of the Metabolic Syndrome and Fibrinolytic Dysfunction to Cardiovascular disease. Circulation 2003 Jul 29; 108(4): 420-5.
- Anand S, Razak F, Yi Q, Davis B, Jacobs R, Vuksan V, Teo K, McQueen M, Yusuf S. C-Reactive Protein as a Screening test for Cardiovascular Risk in a Multi-ethnic population. Arterioscler Thromb Vasc Biol 2004 Aug; 24(8): 1509-15.



## Understanding the shift between agriculture and modern culture



“The health problems faced by Aboriginal people in Canada are staggering, and similar to those of developing countries. These problems are due to complex interactions between historical, political and social factors, and require our intensive and whole-hearted efforts to improve the health status of Aboriginal people.”

– Dr. Sonia Anand



## Aboriginal Health

## Testing new anti-clotting therapies to prevent heart attacks



"Results from landmark trials such as CURE, CREATE and Michelangelo OASIS 5 and 6 will prevent tens of thousands of heart attacks, strokes and deaths every year on a global basis. The clinical studies originating at the PHRI have had a remarkable influence on the modern day practice of cardiology globally."

– Dr. Shamir Mehta

The most common presentation of heart attacks or pre-heart attacks, also known as myocardial infarction (MI), and one of the common medical emergencies can be attributed to acute coronary syndrome (ACS). Characterized by severe chest pain, unstable angina and non-Q-wave MI, patients with ACS are at high risk of dying or developing a new heart attack or a stroke.

The ACS Research Program at the Population Health Research Institute is one of the largest programs in the world focusing on the evaluation of new antithrombotic agents and other strategies to improve outcomes in patients with unstable angina/non-ST elevation myocardial infarction (MI) and ST segment elevation myocardial infarction (STEMI).

## Understanding the differences between STEMI and non-STEMI heart attacks

**STEMI** is a serious form of heart attack that derives its name from the elevation of the ST segment on the electrocardiogram. Characterized by irreversible myocardial damage as a result of insufficient blood supply to the heart muscle, STEMI is a form of ACS that accounts for approximately 2.5 million hospital admissions

worldwide and is a major cause of mortality and morbidity in western countries.

**Non-STEMI** is a partial or smaller heart attack, which is not as immediately fatal as an ST elevation MI, but in the long term, these individuals have more frequent heart attacks and require coronary bypass surgery or angioplasty.

## The OASIS Trials and Registries

The **OASIS** (Organization to Assess Strategies in Acute Ischemic Syndromes) trials are a series of randomized controlled trials designed to evaluate the efficacy and safety of various anticoagulant agents. The OASIS-1 and 2 trials evaluated the effects of a direct thrombin inhibitor hirudin (lepirudin n=11,000) versus heparin in patients with non-ST elevation acute coronary syndromes and demonstrated that hirudin was far more effective than heparin in preventing ischemic events. However, bleeding rates were higher with hirudin in this trial. The values of long-term oral anticoagulants were tested, but no overall benefit was seen.

Following this, the **OASIS-3** trial (CREATE) evaluated the low molecular weight heparin reviparin in patients with ST-elevation myocardial infarction in 15,000 patients from India and China with acute STEMI. The trial demonstrated the

superiority of reviparin over placebo in reducing mortality and reinfarction. In collaboration with Estudios Cardiológicos Latin America (ECLA) the ACS group evaluated acute treatment with glucose insulin and potassium infusion and demonstrated that GIK did not affect mortality, thereby settling a long-standing debate.

The **OASIS-4**, CURE (Clopidogrel in Unstable Angina to Prevent Recurrent Events) evaluated the antiplatelet agent clopidogrel in addition to aspirin in 12,500 patients with non-ST elevation ACS and demonstrated that acute and long-term therapy with clopidogrel was superior to placebo in preventing cardiovascular death, MI and stroke. Clopidogrel is now a widely used antiplatelet agent in patients with ACS and is endorsed as a Class I recommendation by both the United States and European ACS practice guideline committees.



# Acute Coronary Syndromes



The **PCI CURE** study evaluated the effects of clopidogrel and aspirin in the subset of 2,600 patients undergoing percutaneous coronary intervention (PCI) in the CURE trial, and found a 30 per cent reduction in death or MI in this group.

The **OASIS-5** trial demonstrated that a new Factor Xa inhibitor (fondaparinux) preserved the short-term benefits of standard therapy with enoxaparin. However, there was a marked reduction in major bleeding approaching 50 per cent. This reduced mortality and strokes at six months. This study involved over 20,000 subjects from 50 countries and is the largest ACS trial ever conducted.

The companion, **OASIS-6** trial, demonstrated that fondaparinux reduced all causes of mortality, in addition to the composite of mortality and recurrent myocardial infarction in 12,000 patients with ST-elevation MI. There was no increase in bleeding with use of fondaparinux in this study.

#### Research team:

Shamir Mehta, Susan Chrolavicius, Madhu Natarajan, Brandi Meeks, Jeffrey Weitz, John Eikelboom, Jack Hirsh, Janice Pogue, Rizwan Afzal, James Velianou and Salim Yusuf

The **OASIS-6** trial marks the first time an anticoagulant agent has been shown to be beneficial in patients with ST-segment elevation myocardial infarction without increasing the risk of bleeding.

The **OASIS-7** trial is a randomized trial of 14,000 patients with non-ST segment elevation ACS referred for early coronary angiography and PCI and is designed to compare a high loading dose of clopidogrel compared with the standard loading dose and will answer the question as to whether high-dose aspirin is superior to low-dose aspirin. This trial will involve over 40 countries worldwide and will evaluate the effects of the higher loading dose strategy and higher aspirin dose in terms of preventing death, MI or stroke.

The **TIMACS** trial is evaluating the optimal timing of intervention in 3,000 high-risk subjects with ACS.

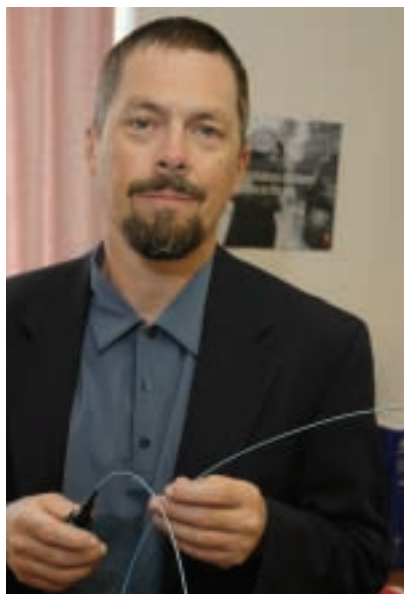
#### Key publications:

- Organization to Assess strategies for Ischemic Syndromes (OASIS-2) Trial Investigators. Effects of recombinant hirudin (lepirudin) compared to heparin in preventing death, myocardial infarction, refractory angina and revascularization procedures in patients with acute myocardial ischemia without ST elevation: A large international randomized double blind study. *Lancet* 1999; 353: 429-438.
- Eikelboom JW, Anand SS, Mehta SR, Weitz JI, Yi C, Yusuf S. Prognostic significance of thrombocytopenia during hirudin and heparin therapy in acute coronary syndrome without ST elevation: Organization to Assess Strategies for Ischemic Syndromes (OASIS-2) Study. *Circulation* 2001; 103(5): 643-650.
- Mehta SR, Chrolavicius S, Afzal R, Pogue J, Granger CB, Budaj A, Peters RJ, Bassand JP, Wallentin L, Joyner C, Fox KA, for the OASIS-6 Trial Group. Effects of fondaparinux on mortality and reinfarction in patients with acute ST-segment elevation myocardial infarction: the OASIS-6 randomized trial. *JAMA* 2006; 295: 1519-1530.
- Yusuf S, Mehta SR, Chrolavicius S, Afzal R, Pogue J, Granger CB, Budaj A, Peters RJ, Bassand JP, Wallentin L, Joyner C, Fox KA: Fifth Organization to Assess Strategies in Acute Ischemic Syndromes Investigators. Comparison of fondaparinux and enoxaparin in acute coronary syndromes. *N Engl J Med* 2006; 354(14): 1464-1476. Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KAA for the CURE Investigators. The Clopidogrel in Unstable angina to prevent Recurrent Events Trial (CURE) Investigators. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med* 2001; 345: 494-502.
- Mehta SR, Yusuf S, Peters RJG, Bertrand ME, Lewis BS, Natarajan MK, Malmberg K, Rupprecht H-J, Zhao F, Chrolavicius S, Copland I and Fox KAA for the Clopidogrel in Unstable angina to prevent Recurrent Events trial (CURE) Investigators. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. *Lancet* 2001; 358: 527-533.
- Yusuf S, Mehta SR for the CREATE Trial Group Investigators. Effects of reviparin, a low-molecular-weight heparin, on mortality, reinfarction, and strokes in patients with acute myocardial infarction presenting with ST-segment elevation. *JAMA* 2005; 293(4): 427-436.
- Mehta SR, Yusuf S, Diaz R, Zhu J, Pais P, Xavier D, Paolasso E, Ahmed R, Xie C, Kazmi K, Tai J, Orlandini A, Pogue J, Liu L for the CREATE-ECLA Trial Group Investigators. Effect of Glucose-Insulin-Potassium infusion on mortality in patients with acute ST-segment elevation myocardial infarction. *JAMA* 2005; 293(4): 437-446.

## Acute Coronary Syndromes



## Understanding the causes of heart rhythm disorders



“Disorders of the heart rhythm are common and harm many people. We are working to find ways to prevent and alleviate the consequences of these problems.”

– Dr. Stuart Connolly

The Cardiac Arrhythmia Research Program at the PHRI focuses on answering questions related to the best clinical management of patients with atrial fibrillation and other cardiac arrhythmias. Atrial fibrillation is the most common serious disorder of the heart rhythm, affecting one per cent of the population; its most serious consequence is stroke.

This research group has focused extensively on the treatment for prevention of stroke in atrial fibrillation and is currently leading two large clinical trials evaluating novel therapies (combination of aspirin and clopidogrel and dabigatran, an oral thrombin inhibitor) for stroke prevention.

The group also is interested in the effects of blood pressure lowering in atrial fibrillation. Blood pressure is the most common cause of atrial fibrillation in Canada and other developed countries. However, the pathophysiologic role of hypertension has not been clearly defined; two studies being led by the group are exploring this issue. Prevention of atrial fibrillation by means of cardiac ablation is one of the promising new frontiers in the treatment of atrial fibrillation. This therapy is now increasingly used, but clinical trials to evaluate its effectiveness are just now being started and the group is leading one of the largest trials in this area. The Radiofrequency Ablation versus Antiarrhythmic Drugs for Prevention of Atrial Fibrillation (RAAFT) study being led by Carlos Morillo and Stuart Connolly is assessing 400 patients and is funded by Johnson and Johnson.

Cardiac arrhythmias are increasingly treated by means of implanted devices, both defibrillators and pacemakers. This research group has a long-standing interest in device therapy for the management of a number of cardiac arrhythmias and is currently conducting the largest study ever done evaluating device therapy for the prevention of atrial fibrillation and evaluating the ability of cardiac arrhythmia devices to detect silent atrial fibrillation, which might place patients at increased risk of stroke.

## Key Discoveries

### DINAMIT (Defibrillators IN Acute Myocardial Infarction Trial)

The DINAMIT trial demonstrated the lack of benefit of implantable defibrillators in patients with recent acute myocardial infarction. This large, multi-national trial defines one of the key limitations of implantable defibrillator therapy as prophylactic therapy and its findings have been incorporated into all major treatment guidelines.



### OPTIC (The Optimal Pharmacologic Therapy in Implantable Cardioverter defibrillator patients)

This international study demonstrated the benefits of combining anti-arrhythmic drug therapy with defibrillators for improving the outcomes of patients with life threatening ventricular arrhythmias. It also dispelled a major myth regarding the lack of safety of amiodarone in defibrillator patients.

### ACTIVE W

This study was the largest randomized trial of antithrombotic therapy in atrial fibrillation. The results of the study, which have recently been presented, showed that a regimen of clopidogrel plus aspirin is not as effective as warfarin for prevention of vascular events in atrial fibrillation.

### Research team:

Stuart Connolly, Carlos Morillo, Jeffrey Healey, Girish Nair, Susan Chrolavicius, Ellison Themeles, Janice Pogue, Peter Tent and Salim Yusuf





## Research Studies

**ACTIVE** (Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events) is a research program that includes three clinical trials, all related to the risk of vascular events in patients with atrial fibrillation. ACTIVE is currently the largest clinical trial program in atrial fibrillation, with more than 14,000 patients enrolled.

**ACTIVE-A** evaluates whether clopidogrel and aspirin is superior to aspirin in 7,500 patients.

**ACTIVE-I** evaluates whether irbesartan reduces the risk of vascular events in 9,000 patients with atrial fibrillation and is funded by Sanofi-Aventis and Bristol Myers Squibb.

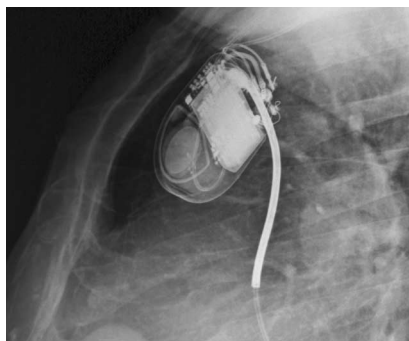
**ASSERT** (The Asymptomatic Atrial Fibrillation and Stroke Evaluation in Pacemaker Patients and the AF Reduction Atrial Pacing Trial) evaluates the prognostic significance of asymptomatic short episodes of atrial fibrillation detected by pacemakers in high-risk patients. ASSERT is the largest study ever to evaluate atrial overdrive pacing in atrial fibrillation and evaluates asymptomatic atrial fibrillation as a risk factor for stroke.

**I-PACE** (Irbesartan Pacemaker Study) evaluates the mechanisms by which irbesartan could reduce the risk of developing atrial fibrillation in patients with pacemakers who also have intermittent atrial fibrillation. Funded by Bristol-Myers Squibb and Sanofi-Aventis, this study will enroll 200 patients.

**RE-LY** The RE-LY study will be one of the largest trials of therapy for stroke prevention in atrial fibrillation and will involve 15,000 patients from 50 countries. Sponsored by Boehringer-Ingelheim, it evaluates the role of Dabigatran, a direct thrombin inhibitor, for the prevention of stroke in patients with atrial fibrillation.

**RAAFT** (The Radio Frequency Ablation vs. Antiarrhythmic drugs for Atrial Fibrillation Treatment) is a randomized trial studying cardiac ablation, versus anti-arrhythmic drugs for first-line management of atrial fibrillation. The study, which will enroll 400 patients, is sponsored by Johnson & Johnson.

**CREDIT** This registry aims to evaluate whether the use of complex testing procedures (performed during the implantation of an ICD that are designed to assure the safety of the implanted device) can be replaced by simpler tests. These procedures are risky, as they require that the heart be put into fibrillation in order to assess whether the device can work appropriately to return the heartbeat to normal. This 500 patient registry is supported by Guidant Canada.



## Key publications:

- Connolly SJ, Kerr CR, Gent M, Roberts RS, Yusuf SM, Gillis AM, Sami MH, Talajic M, Tang ASL, Klein GJ, Lau C, Newman DM on behalf of the CTOPP investigators. Comparison of the effects of physiologic pacing versus ventricular pacing on cardiovascular death and stroke. *N Engl J Med* 2000; 342: 1385-1391.
- Connolly SJ, Gent M, Roberts RS, Dorian P, Roy D, Sheldon R, Mitchell LB, Green M, Klein G, O'Brien B on behalf of the CIDS Investigators. Canadian Implantable Defibrillator Study (CIDS): A randomized trial of the implantable cardioverter defibrillator against amiodarone. *Circulation* 2000; 101: 1297-1302.
- Connolly SJ, Sheldon R, Thorpe KE, Roberts RS, Ellenbogen KA, Wilkoff BL, Morillo C, Gent M on behalf of the VPS II investigators. The Second Vasovagal Pacemaker Study (VPSII): A double-blind randomized controlled trial of pacemaker therapy for the prevention of syncope in patients with recurrent severe vasovagal syncope. *JAMA* 2003; 289:2224-2229
- Hohnloser SH., Kuck, KH, Dorian, Roberts RS, Hampton R, Hatala R, FainE, Gent M, Connolly SJ, on behalf of the DINAMIT Investigators. Prophylactic Use of an Implantable Cardioverter-Defibrillator after Acute Myocardial Infarction. *N Engl J Med* 2004; 351: 2481-2488.
- Connolly SJ, Dorian P, Roberts RS, Gent M, Bailin S, Fain ES, Thorpe K, Champagne J, Talajic M, Couto B, Gronefeld GC, Hohnloser SH: Optimal pharmacological Therapy in Cardioverter Defibrillator Patients (OPTIC) Investigators. Comparison of beta-blockers, amiodarone plus beta-blockers, or sotalol for prevention of shocks from implantable cardioverter defibrillators: the OPTIC Study: a randomized trial. *JAMA* 2006; 295(2): 165-171.
- ACTIVE Writing Group on behalf of the ACTIVE Investigators; Connolly S, Pogue J, Hart R, Pfeffer M, Hohnloser S, Chrolavicius S, Pfeffer M, Hohnloser S, Yusuf S. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial. *Lancet* 2006. 367(9526): 1903-12.



# Cardiac Arrhythmia

## Exploring new procedures in cardiac care

The Interventional Cardiology Research Program at the Population Health Research Institute is a multidisciplinary program that focuses on evaluating pharmacologic therapies and the role of invasive and new procedures in patients with acute coronary syndromes (ACS). Accompanying this, the Health Care Delivery Program at PHRI is studying waiting lists and queues for cardiac catheterization. (See page 36 for more information).

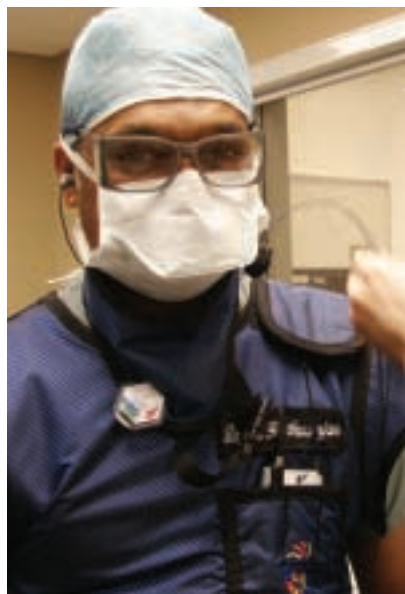
The role and timing of invasive procedures in patients with ACS is currently being evaluated in a large, randomized trial of 3,000 patients. The TIMACS (Timing of Intervention in Patients with Acute Coronary Syndromes) study is jointly funded by the Canadian Institutes of Health Research (CIHR) and industry.

Patients with ACS will be randomized to an early invasive strategy involving heart catheterization and PCI within 24 hours of randomization, versus a delayed strategy after a period of medical stabilization with pharmacologic therapy. The primary outcome of the trial is the composite of death, myocardial infarction (MI) or stroke. The results of this trial are expected to help guide the optimal approach to managing patients with acute coronary syndrome.

The current OASIS-7 trial, led by Dr. Shamir Mehta, will evaluate the effects of a high clopidogrel loading dose regimen in 15,000 patients with ACS who will be managed with an aggressive invasive strategy, with catheterization and intent for PCI within 24 hours of randomization. In addition, the trial will be the world's first large-scale comparison of high versus low dose aspirin therapy in these patients.

### Key publications:

- Mehta SR, Steg G, Granger CB, Bassand J-P, Faxon DP, Weitz JI, Afzal R, Rush B, Peters RJG, Natarajan MK, Velianou JL, Goodhart DM, Labinaz M, Tanguay J-F, Fox KAA, Yusuf S. for the ASPIRE Pilot Investigators. A randomized blinded trial comparing fondaparinux with unfractionated heparin in patients undergoing contemporary percutaneous coronary intervention. The Arixtra Study in Percutaneous Coronary Intervention: A randomized evaluation (ASPIRE) Pilot Trial. *Circulation* 2005; 111: 1390-1397
- Natarajan MK, Velianou JL, Turpie AG, Mehta SR, Raco D, Goodhart DM, Afzal R, Ginsberg JS. A randomized pilot study of dalteparin versus unfractionated heparin during percutaneous coronary interventions. *Am Heart J* 2006; 151(1): 175
- Mehta SR, Eikelboom JW, Rupprecht H-J, Lewis BS, Natarajan MK, Yi C, Pogue J, Yusuf S. Efficacy of hirudin in reducing cardiovascular events in patients with acute coronary syndrome undergoing early percutaneous coronary intervention. *Eur Heart J* 2002; 23: 117-123
- Mehta SR, Cannon CP, Fox KAA, Wallentin L, Boden WE, Spacek R, Widimsky P, McCullough PA, Hunt D, Braunwald E, Yusuf S. Routine versus selective invasive strategies in patients with acute coronary syndromes: A collaborative meta-analysis of the randomized trials. *JAMA* 2005; 293(23): 2908-2917
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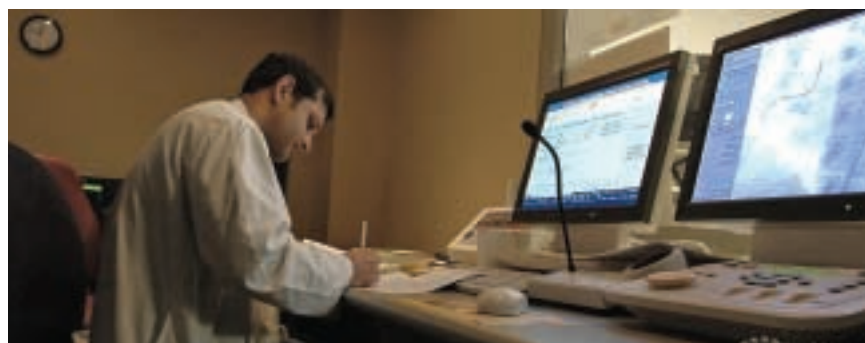


"The future of coronary interventional research involves looking at how we can provide this technology for a broad population in a timely, affordable and safe manner. Through our clinical trials we understand what works, but we have to focus on how and when to target specific populations."

– Dr. Madhu Natarajan

### Research team:

Shamir Mehta, Madhu Natarajan, James Velianou, Mike Rokoss, Nick Valettas, Dave Crosby and Doug Holder



## Coronary Interventions

Chronic heart failure (CHF) is a clinical problem of increasing importance. Overall, CHF affects approximately two per cent of the population, but this increases rapidly with age. In spite of new medical interventions, age-adjusted death rates and the rates of important morbidity like hospitalizations have increased over the last few decades. It is estimated that approximately one-third of all hospital bed-days used are because of cardiac diseases associated with CHF. For individuals over 65 years of age, CHF is the most common reason for hospitalization. It can be foreseen that chronic heart failure will become an increasing problem in the aging population in the industrial world. Despite new and efficacious treatment strategies, mortality and morbidity rates remain unacceptable. Thus, there is a strong need for improved medical therapy.

The Heart Failure Research Group has evaluated diverse areas, ranging from the effects of exercise training, the impact of heart failure on cognitive function and various drugs, such as angiotensin receptor blockers and growth hormones. Novel areas include documenting and understanding the causes of frailty and cognitive dysfunction in heart failure patients. This research group has become increasingly interested in understanding the role of exercise in heart failure. A majority of work completed in this area occurs in the Heart Function Clinic at Hamilton Health Sciences and is composed of a group of physicians, including a geriatrician and nurse clinicians.

The group has made major contributions in evaluating ACE inhibitors and angiotensin inhibitors and angiotensin receptor blockers with heart failure, through the conduct of the RESOLVD and CHARM trials.

Members of this group are also involved on the executive committees of two large international multi-centre trials. The first, funded by Bristol Myers Squibb/Sanofi-Aventis, is the IPRESERVE study, which is examining the effects of irbesartan on clinical outcomes in 4,100 HF-PSF patients. The second is the HF ACTION study, funded by the National Institutes of Health (NIH), which is examining the effects of exercise training on mortality and morbidity in 3,000 heart failure patients.

#### Research team:

Robert McKelvie, Koon Teo, Ernest Fallen, Catherine Demers, George Heckman, Heather Arthur, Karen Harkness, Catherine Chant-Gambacort and Salim Yusuf

#### Key publications:

- McKelvie RS, Yusuf S, Pericak D, Avezum A, Burns RJ, Probstfield J, Tsuyuki R, White M, Rouleau J, Latini R, Maggioni A, Young J, Pogue J for the RESOLVD Pilot Study Investigators. Comparison of Candesartan, Enalapril, and their combination in congestive heart failure: randomized evaluation of strategies for left ventricular dysfunction (RESOLVD) pilot study. *Circulation* 1999; 100: 1056-64.
- Jong P, Yusuf S, Rousseau MF, Ahn SA, Bangdiwala SI. Effect of enalapril on 12-year survival and life expectancy in patients with left ventricular systolic dysfunction: a follow-up study. *Lancet* 2003; 361: 1843-8
- McKelvie RS, Teo KK, Roberts R, McCartney N, Humen D, Montague T, Hendrican K, Yusuf S. Effects of exercise training in heart failure patients: the Exercise Rehabilitation Trial (EXERT). *Am Heart J* 2002; 144(1): 23-30.
- Roccaforte R, Demers C, Baldassarre F, Yusuf S, Teo K. Effectiveness of Research Management Programmes in Improving Clinical Outcomes in Heart Failure Patients. *Eur J Heart Failure* 2005; 7: 1133-44.
- McKelvie RS, Rouleau J-L, White M, Afzal R, Young JB, Maggioni AP, Held P, Yusuf S. Comparative impact of enalapril, candesartan or metoprolol alone or in combination on ventricular remodeling in patients with congestive heart failure. *Eur Heart J* 2003; 24(19): 1727-1734.
- Heckman GA, Misiaszek B, Merali F, Turpie I, Patterson CJ, Flett N, McKelvie RS. Management of heart failure in Canadian long-term care facilities. *Can J Cardiol*, 2004; 20(10): 963-969.
- Yan RT, White M, Yan AT, Yusuf S, Rouleau J-L, Maggioni AP, Hall C, Latini R, Afzal R, Floras J, Masson S, McKelvie RS, and Randomized Evaluation of Strategies for Left Ventricular Dysfunction (RESOLVD) investigators. Usefulness of temporal changes in neurohormones as markers of ventricular remodeling and prognosis in patients with left ventricular systolic dysfunction and heart failure receiving either Candesartan or Enalapril or both. *Am J Cardiol* 2005; 96(5): 698-704
- Demers C, McMurray JJV, Swedberg K, Pfeffer MA, Granger CB, Olofsson B, McKelvie RS, Östergren J, Michelson EL, Johansson PA, Wang D, Yusuf S. Impact of Candesartan on Non-Fatal Myocardial Infarction and Cardiovascular Death: Results from the Candesartan in Heart Failure-Assessment of Reduction in Mortality and Morbidity (CHARM) Program. *JAMA* 2005;294: 1794-1798.

## Combating the decline of the heart muscle



"Paradoxically, as the treatment of cardiac diseases improve, the prevalence of heart failure escalates; the aging population also contributes to this increasing prevalence. Over the first part of the twenty-first century, the increasing prevalence of heart failure associated with the high morbidity and mortality rates makes it urgent to find improved ways to combat the growing epidemic of heart failure."

– Dr. Robert McKelvie



## Heart Failure



## Evaluating vascular events in patients undergoing non-cardiac surgery



“Perioperative cardiovascular events represent a major population health issue and may surpass the annual incidence of non-operative cardiovascular events in the coming decades.”

– Dr. P.J. Devereaux

Over 500,000 Canadian adults undergo non-cardiac surgery requiring hospital admission annually. Although non-cardiac surgery provides important benefits, it is associated with major adverse vascular events. To address this, the PHRI has initiated a research program evaluating the epidemiology, risk prediction, monitoring strategies, and risk modification of perioperative vascular events. This multidisciplinary research team has expertise in perioperative vascular medicine and represents the fields of anesthesia, cardiology, emergency medicine, gastroenterology, intensive care, internal medicine, laboratory medicine, respirology, statistics, stroke, surgery and thromboembolism.

### POISE

This research group is currently leading the world's largest perioperative cardiovascular randomized controlled trial; the POISE Trial is a 10,000 patient randomized controlled trial evaluating the effects of beta-blocker therapy in patients undergoing non-cardiac surgery. Currently funded by the Canadian Institutes for Health Research (CIHR), the POISE Trial has randomized over 7,500 patients in 185 centres in 22 countries, and will be completed in 2007. The POISE Trial is by far the world's largest perioperative cardiovascular clinical trial to date and will address the fundamental question: whether a beta-blocker can prevent premature death and heart attacks and cardiac arrests around the time of surgery.

The trial has also established an international perioperative research group that will undertake further studies to test interventions to make surgery safer for the millions of adults worldwide who undergo non-cardiac surgery annually. Preliminary research is currently underway to inform the feasibility of undertaking a prophylactic perioperative aspirin trial.

### Current studies are also assessing:

- The incidence of major vascular events (for example: vascular death, nonfatal myocardial infarction, nonfatal cardiac arrest and nonfatal stroke) at 30 days post surgery;
- An optimal clinical model to predict major vascular events at 30 days post surgery;
- The proportion of patients 30 days post surgery with perioperative myocardial infarctions that may go undetected without troponin monitoring;
- The relationship between postoperative troponin measurements and the one year risk of total mortality;
- If perioperative non-invasive pharmacological cardiovascular stress testing (for example: dipyridamole stress perfusion imaging or dobutamine stress echocardiography) has additional predictive value, beyond clinical variables, for the occurrence of major perioperative cardiovascular events in patients undergoing major hip and knee surgery.

### Key publications:

- Devereaux PJ, Yusuf S, Yang H, Choi PTL, Guyatt GH. Are the recommendations to use perioperative  $\beta$ -blocker therapy in patients undergoing noncardiac surgery based on reliable evidence? *CMAJ*. 2004; 171: 245-247.
- Devereaux PJ, Beattie WS, Choi PTL, Badner NH, Guyatt GH, Villar JC, Cinà CS, Leslie K, Jacka MJ, Montori VM, Bhandari M, Avezum A, Biasi Cavalcante A, Giles JW, Schricker T, Yang H, Jackobsen CJ, Yusuf S. How strong is the evidence for the use of perioperative  $\beta$ -blockers in non-cardiac surgery? A systematic review and meta-analysis of randomised controlled trials. *BMJ*. 2005; 331: 313-321.
- Devereaux PJ, Goldman L, Cook DJ, Gilbert K, Leslie K, Guyatt GH. Perioperative cardiac events in patients undergoing noncardiac surgery: a review of the magnitude of the problem, the pathophysiology of the events and methods to estimate and communicate risk. *CMAJ*. 2005; 173: 627-634.
- Devereaux PJ, Goldman L, Yusuf S, Gilbert K, Leslie K, Guyatt GH. Surveillance and prevention of major perioperative ischemic cardiac events in patients undergoing noncardiac surgery: A review. *CMAJ*. 2005; 173: 779-788.
- The POISE Investigators. Rationale, design, and organization of the PeriOperative Ischemic Evaluation (POISE) Trial: A randomized controlled trial of metoprolol versus placebo in patients undergoing noncardiac surgery. (In Press *Am Heart J*).

### Research team:

P.J. Devereaux, Homer Yang, Gordon Guyatt, Peter Choi, Launi Greenspan, Susan Chrolavicius and Salim Yusuf





The Peace through Health program is a collaboration between the Centre for Peace Studies at McMaster University and the PHRI and is focused on the exploration of how the health sector can contribute to peace, based on the proposition that peace is the responsibility of all sectors in society.

In 1991, following the Gulf war against Iraq, an International Study Team, including several people from McMaster University, visited Iraq and gave an early report of the impact of war and sanctions on the Iraqi population. When the first of the wars in the Balkans broke out, concerned individuals from McMaster University's Centre for Peace Studies, and the then Centre for International Health came together to consider how we might contribute to ameliorate an increasingly terrible situation.

From there, the idea of Peace Through Health gradually formed. It began with a wish to carry out field projects simultaneously, reflecting on and analyzing what we were doing, and to evaluating when possible. Group members then began work on an epidemiologic project on the physical and mental health of children in the occupied territory of Gaza, an epidemiologic study of child mental health in Sri Lanka, and an intervention on mental health and peace building for war-affected children in Croatia. The Sri Lankan work evolved into an unusual and wonderful intervention - the Butterfly Garden - a healing garden where children from several sides of ethnic divides come together to grow, create, sing and dance and tell stories.

The Croatian work was evaluated in a controlled trial and showed evidence of effectiveness in both mental health and in reducing ethnic hatred.

The PHRI has now become the "health leg" of peace through health. This association gave birth to two international conferences: the McMaster-Lancet Challenge Conference Peace through Health, which occurred in October 2001; and the Peace through Health: Learning from Action conference in May 2005.

At McMaster University, Peace through Health is a collaborative effort between various academic units, including Centre for Peace Studies, the PHRI, School of Rehabilitation Sciences and colleagues from other universities. The PHRI has been very



instrumental in creating a HOPE Chair for Peace through Health at McMaster University, which is currently under recruitment.

#### Key publications:

- MacQueen G, Santa-Barbara J, Neufeld V, Yusuf S, Horton R. Health and peace: time for a new discipline. *Lancet* 2001; 358(9288): 1183-4.
- Neufeld V, Yusuf S. The McMaster-Lancet health and peace conferences. *Lancet* 2004; 364: 311-12.
- Yusuf S, Anand S, MacQueen G. Can medicine prevent war? *BMJ* 1998; 317(7174): 1669-1670.

#### Research Profile

**Joanna Santa Barbara** is the past-president of Physicians for Global Survival Canada and past vice-president of International Physicians for Prevention of Nuclear War. Joanna teaches a course in the Peace Studies program at McMaster, and has been engaged in work on mental health and peace building in relation to war-affected children in Croatia, and in Afghanistan. The Afghanistan work also includes peace education focused on national reconciliation and non-violence. Joanna was awarded the Order of Ontario for her work in Peace Studies and peace activism.

#### Peace through Health Team:

*Executive:* Khursh Ahmed, Vic Neufeld, Joanna Santa Barbara, Rob Stevens and Jackie Bosch.

*Member/Contributors:* Neil Arya Carrie Bernard, Caecilie Buhmann, Jackie Bosch, Robbie Chase, Sheila Harms, Graeme MacQueen, Alex Mihailovic, Edward Mills, Gjorgi Nikoloski, Andrew Pinto, Seddiq Weera, Don Woodside and Salim Yusuf.

*Students:* Megan Arthur, Heather Farrell, Britt Lehman-Bender, Ryan Marks, Nik Pai, Jeff Santa Barbara and Avita Sooknanan.

## Collaborating to achieve peace



(Left to right) Jackie Bosch, Joanna Santa Barbara and Khursh Ahmed.

"People working in population health look at the big picture. They see the influence on health of such factors as war, poverty, ecological degradation, community and cultural disintegration, poor governance and human rights abuses. They ask the question of how one can act on these macro-determinants of health from the health sector. Clearly you need to work with other disciplines and with people affected by these factors. Peace through Health is an exploration of how you can do this. We're just at the beginning of this, but it's revealing very interesting approaches."

- Joanna Santa Barbara

# Peace Through Health

## Lessening the burden of cognitive decline



"By studying both the causes of cognitive decline, as well as treatments simultaneously, we are developing an understanding of how best to delay and hopefully prevent the devastating effects of this process."

– Jackie Bosch

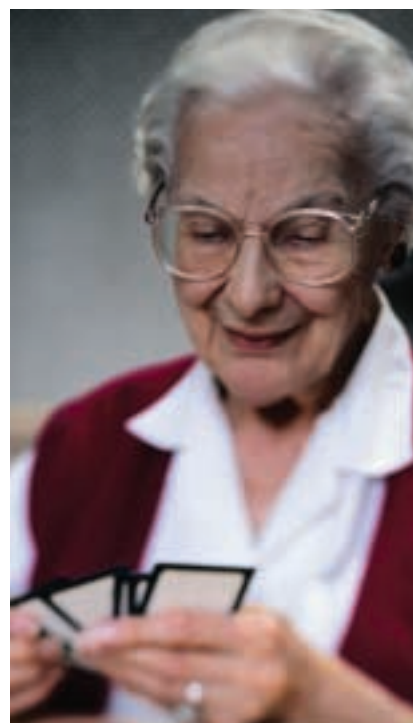
Vascular and metabolic abnormalities can also affect cognitive function. This program area relates to many of the various research programs of the PHRI and measurement of cognitive function is incorporated into many of its studies. Understanding the effect of treatments, which modify CV risk factors on cognitive function and the relationship to clinical outcomes provides new avenues to improve the health of patients.

Historically, studies that have examined cognitive function have tended to use lengthy and costly neuropsychological assessments. While the validity of these tests is established, such procedures are impractical in large, international trials. Therefore, streamlined methods for assessment were implemented. In particular, the PHRI has now administered the Mini Mental State Exam in six studies, enrolling over 55,000 participants. While realizing the value of this tool as a screening instrument for dementia, there is a lack of sensitivity for detecting change in those without overt dementia. Because of this, the PHRI have started to explore the best combination of reliable, valid, simple and internationally available to tools that can provide this information.

The morbidity associated with cognitive decline is not only costly, but also devastating for both the individual and family. By studying potential methods of reducing cognitive decline, as well as understanding the fundamental role of cognitive decline in other disease processes, it is hoped that this burden can be lessened.

### Research team:

Jackie Bosch, Hertzell Gerstein, Parminder Raina, Martin O'Donnell, Koon Teo, T. Cukierman-Yaffee, Eva Lonn, P. Sheridan and John Eikelboom



# Cognitive Function

Decision makers struggle with the challenge of how to best allocate resources made available to health care, amidst the rapidly increasing competition for resources. Economic evaluation provides an evidence base for decision makers in addressing whether to fund a particular intervention in the context of maximizing health gains within available resources.

The Health Economics team at the PHRI provide economic evaluations of new drugs or therapeutic intervention for the treatment of cardiovascular diseases, as well as the evaluation of health care delivery in Canada and worldwide.

Large, multi-national trials involving many countries, in over five continents add a new level of complexity for health economists as the sample size is fragmented and distributed between countries with different health care systems. The inevitable problem of variation of resources consumed, and unit costs from one country to the other (inter-country variations) and also within a single country (intra-country variations) could be described as “system effect”. This “system effect” limits the applicability of the analysis to any of the participating countries and represents a methodology problem of modern clinical trials. The Health Economics team is well versed in this issue and can offer potential solutions to provide an economic evaluation of trials involving more than 40 countries around the world.

## Related projects

ORIGIN, ONTARGET, POISE, WAVE, TIMACS, CORONARY

### Research team:

Andre Lamy and Amiram Gafni

“The reality of the economic problem we face is that we cannot do everything we wish to do: we need to identify and differentiate between those things that are worthwhile and cost-efficient, and those which are not.”

– Dr. Andre Lamy



## Maximizing health gains within available resources

### Key publications:

- Lamy A, Jonsson B, Weintraub WS, Zhao F, Chrolavicius S, Bakhai A, Culler S, Gafni A, Lindgren P, Mahoney E, Yusuf S; The CURE Economic Group. The cost-effectiveness of the use of clopidogrel in acute coronary syndromes in five countries based upon the CURE study. *Eur J Cardiovasc Prev Rehabil*. 2004 Dec; 11(6): 460-5.
- Lamy A, Yusuf S, Pogue J, Gafni A; Heart Outcomes Prevention Evaluation Investigators. Cost implications of the use of ramipril in high-risk patients based on the Heart Outcomes Prevention Evaluation (HOPE) study. *Circulation*. 2003 Feb 25; 107(7): 960-5.
- Mahoney EM, Mehta S, Yuan Y, Jackson J, Chen R, Gabriel S, Lamy A, Culler S, Caro J, Yusuf S, Weintraub WS for the CURE Study Investigators. Long-term cost-effectiveness of early and sustained clopidogrel therapy for up to 1 year in patients undergoing percutaneous coronary intervention after presenting with acute coronary syndromes without ST-segment elevation. *Am Heart J*. 2006 Jan; 151(1): 219-27.
- Lamy A, Gafni A. Is positron emission tomography for the management of potentially operable non-small cell lung cancer an efficient use of Quebec health care resources? *Can Respir J*. 2005 Jan-Feb; 12(1): 11-2. No abstract available.
- Weintraub WS, Mahoney EM, Lamy A, Culler S, Yuan Y, Caro J, Gabriel S, Yusuf S for the CURE Study Investigators. Long-term cost-effectiveness of clopidogrel given for up to one year in patients with acute coronary syndromes without ST-segment elevation. *J Am Coll Cardiol*. 2005 Mar 15; 45(6): 838-45.



# Health Economics



## Evaluating cardiac care research in order to build a stronger health care environment



“The greatest benefits to our patients over the next decade will probably be derived from fully implementing what we have already learnt from clinical trials.”

– Dr. Madhu Natarajan

The Health Care Delivery (HCD) research program at PHRI is aimed at evaluating how medical and surgical interventions deemed efficacious in clinical trials can be applied in an effective and efficient manner to the general population. The projects to date have been closely related to Coronary Interventions (CI). For more information regarding research related to coronary interventions, see page 30.

Examples of questions asked include: is the information received through research being provided effectively to the population at large? Are we efficiently using available resources?

The Health Care Delivery Team is currently collaborating with Dr. Eva Lonn (Director of the Vascular Research Imaging Laboratory) on the ACTIVATE study. Together, the groups are planning to integrate novel techniques for the non-invasive study of atherosclerosis, including multislice CT angiography and MRI imaging. Additionally, in collaboration with the Vascular Research Imaging Laboratory, the group, under the direction of Dr. Madhu Natarajan, is evaluating the use of intracoronary ultrasound for the assessment of coronary atherosclerosis. See page 40 for more information related to research at the Vascular Research Imaging Laboratory.

## Research conducted in the domain of Health Care Delivery addresses three main areas:

### Addressing current obstacles in health care

Waiting lists for medical procedures are a common phenomenon and pose important challenges for health systems around the world. The PHRI was able to secure two grants from the Chedoke Foundation and The Canadian Health Services Research Foundation (CHSRF) to further our understanding of the management of waiting lists for cardiac catheterization and coronary angioplasty in the Central South Region of the Province of Ontario.

### Monitoring outcomes

The evaluation of outcomes in procedures and continuous quality improvement is key to research being conducted in this area. To monitor PCI outcomes, the research team has introduced EZ-CQI: an e-based system for continuous quality improvement at the user level. EZ-CQI is an interactive model for care that incorporates interaction with all stakeholders; including

physicians, nurses, pharmacists, and hospital administrators. A monthly, quarterly and yearly reporting structure is utilized in a simple to use, e-based format. While developed for use in evaluating and reporting information related to coronary interventions, it is forecasted to be applicable to all medical and surgical therapies.

### Introducing new therapies into standard practice

Continuous quality improvement is also necessary in order to introduce new therapies into the broad population. The PHRI is currently tackling local and regional issues regarding the access to primary or direct angioplasty for myocardial infarction. With a peer-reviewed grant from The Change Foundation of Ontario, in collaboration with the Ministry of Health of Ontario, a pilot project has been successful in implementing change in the management of myocardial infarction therapy in the region.

## Knowledge transfer

An important relationship exists between knowledge learned in research related to coronary interventions and health care delivery. While HCD primarily evaluates the outcomes of CI research, innovative discoveries can also be made when transferring knowledge learned from HCD in order to start new clinical trials.





#### Research team:

Madhu Natarajan, Shamir Mehta, Tej Sheth, Amiram Gafni and James Velianou

#### Key publications:

- Natarajan MK, Mehta SR, Holder DH, Goodhart DR, Gafni A, Shilton D, Afzal R, Teo K, Yusuf S. The risks of waiting for cardiac catheterization: a prospective study. *CMAJ*. 2002; 167(11): 1233-1240.
- Natarajan MK, Yusuf S. Primary angioplasty for ST-segment elevation myocardial infarction: Ready for prime time? *CMAJ*. 2003; 169:32-35.
- Natarajan MK, Gafni A, Yusuf S. Determining optimal population rates of cardiac catheterization: a phantom alternative? *CMAJ*. 2005 Jul 5; 173(1): 49-52.
- Ahmad M, Schwalm JD, Velianou JL, Natarajan MK. Impact of routine in-hospital assessment of low-density lipoprotein levels and standardized orders on statin therapy in patients undergoing percutaneous coronary interventions. *J Invasive Cardiol*. 2005 Oct; 17(10): 518-20.
- Labinaz M, Swabey T, Watson R, Natarajan M, Fucile W, Lubelsky B, Sawadsky B, Cohen E, Glasgow K; The CCN Consensus Panel on Access to Urgent PCI for ST Segment Elevation Myocardial Infarction. Delivery of primary percutaneous coronary intervention for the management of acute ST segment elevation myocardial infarction: summary of the Cardiac Care Network of Ontario Consensus Report. *Can J Cardiol*. 2006 Mar 1; 22(3): 243-50.



# Health Care Delivery

## A repository for testing future hypotheses into biomarkers for vascular disease, diabetes and obesity



"It is exciting to see the interaction between innovative laboratory analyses and excellent clinical investigation answering clinically relevant questions, challenging accepted wisdom, or raising more questions."

– Dr. Matthew McQueen



The Clinical Trials Research and Proteomics Laboratory at the Hamilton General Hospital was established more than 20 years ago. It underwent a major expansion in the early 1990s in response to the needs of the large multi-national studies such as the HOPE (Heart Outcomes and Prevention Evaluation) Study, INTERHEART and the many subsequent studies in cardiovascular disease and diabetes organized by the PHRI.

Extensive expertise has been developed in the shipping (utilizing unique vapour shippers), receiving, storage, and analysis of large numbers of samples, given the volume of processing from more than 50 countries. The clinical trials conducted at the laboratory have been supported by peer-reviewed grants from Canada and the United States and as well by the pharmaceutical industry. The laboratory has independently received contracts for organizational and analytical support for pharmaceutical industry-funded clinical studies, from diagnostic companies for analysis in clinical trials, and as a specialized referral laboratory for research contract organizations and commercial laboratories. Arising from the experience gained in these large studies, the laboratory has been selected to provide the biological sample storage and laboratory facilities for a Canadian Longitudinal Study on Aging, which is a collaboration of ten Canadian universities, presented to the Canadian Institutes for Health Research (CIHR) and the Canadian Foundation for Innovation (CFI).

A Biobank was established at the laboratory because of the many biological samples being collected for large clinical studies. Currently, the Biobank is storing over one million samples from 150,000 participants; with the samples being stored in liquid nitrogen at  $-160^{\circ}\text{C}$ . The Biobank has recently been expanded to accommodate 40 large storage tanks, each holding approximately 55,000 vials.

Under the leadership of Dr. Joseph Macri, a state-of-the-art proteomics laboratory has been established at the Hamilton General site in order to further basic research into biomarkers for vascular disease, diabetes, obesity and the responses to therapy. One of the functions of this particular laboratory is a proteomics referral service for small-scale clinical studies. In order to expand capacity towards high throughput proteomics, which would facilitate research in the large clinical studies, an application for infrastructure funding has been put forth.

The INTERHEART genetic study has been a major development for the laboratory in the last three years and has allowed collaboration with the PHRI, Genome Quebec and McGill University. The INTERHEART Study is a large genetic epidemiology study examining the role of approximately 1,600 single nucleotide polymorphisms (100 genes) with DNA purification from 15,000 participants. In addition, the laboratory collaborates with McGill University on the large EpiDream study, which involves 24,000 individuals – exploring the gene environment interaction for the metabolic syndrome.

The laboratory has also been involved in collaborative and basic research into the role of glycosylated hemoglobin (HbA1c) in the diagnosis and early prediction and monitoring of vascular complications of dysglycemia. This laboratory is leading an international collaboration to develop reference material and a reference method for measuring microalbuminuria.

### Research team:

Matthew McQueen, Joseph Macri, Cynthia Balion, Kim Hall, Judith Keys, Josephine Baldwin, Karen Bamford, Linda Carr, Janet Feduszcak, Anna Miller, Sandra Chesal, Liz Clelland, Marlene Popp, Elise Shore, Heather Walker and Ann Walker



## Biobank and Proteomics Laboratory

The risks of developing common diseases such as cardiovascular disease and diabetes are attributable to the complex combination of factors such as lifestyle and environment, combined with genetic factors. Most PHRI studies routinely collect consent for future genetic analysis and a buffy coat (from which DNA is extracted) from all participants in order to facilitate future population genomics evaluations. Currently, DNA or buffy coats have been stored in over 100,000 individuals.

## Understanding the role genes play in disease

### Genomic studies at the PHRI are very unique thanks to:

- Their large size;
- Careful measurement of environmental factors (such as diet and physical activity), which allows the study of gene-environment interactions;
- Ethnic diversity.

Laboratory staff at the PHRI extract DNA using a Gentra Robot and are presently collaborating with the McGill University Genome Quebec Innovation Centre, which is conducting the high through put genetic analysis.

Utilizing various designs, including cross-sectional, case-control and prospective cohort studies, a number of large-scale population genomic studies are underway at the PHRI. These include:

- The INTERHEART genetics study, in which an Illumina panel of 100 candidate genes (1536 SNPs) was created in order to study the genetic associations of acute myocardial infarction and its key intermediate phenotypes in 22,000 participants;
- The EpiDREAM genetics study, which involves samples from about 25,000 people screened for entry into the DREAM clinical trial, from 21 countries around the world. This study is designed to investigate the genetic and gene-environmental associations with metabolic syndrome-related factors and type-2 diabetes;
- Population studies for which genetic materials are currently being stored include PURE, that has a target of 135,000 individuals from 15 countries (with 50,000 participants currently recruited) and the FAMILY study which is aimed to involve 1,000 families, of which about 450 families have been recruited;
- Several large clinical trials, such as ONTARGET and TRANSCEND, are evaluating ACE I and ARB; this study currently has over 10,000 participants with DNA stored. The DREAM study is evaluating ACE I and rosiglitazone in 5,200 individuals (all with DNA stored).

### Key Investigators:

Sonia Anand, Hertzell Gerstein, Jackie Bosch, Salim Yusuf, Changchun Xie, in collaboration with Tom Hudson, Jamie Engert and Daniel Gaudet at McGill University



## Population Genomics



## Standardizing methods to assess vascular disease



“Being able to measure atherosclerosis noninvasively and repeatedly in the same person gives us unique insights into how the early seeds of atherosclerotic disease grows and can be influenced by how we live or by treatments.”

– Dr. Eva Lonn

The Vascular Imaging Laboratory of the Population Health Research Institute has standardized methods for the non-invasive assessment of sub-clinical atherosclerosis, endothelial function and left ventricular structure and function.

Major techniques used in the laboratory include quantitative B-mode carotid ultrasonography with measurements of carotid intima-media thickness (IMT) of the extra cranial carotid arteries and assessment of carotid plaques, studies of brachial reactivity or flow-mediated dilation of the brachial artery which are an in vivo assay of endothelial function, studies of endothelial function using pulsed arterial tonometry and echocardiographic studies of cardiac structure and function. The laboratory has used these techniques in epidemiological studies evaluating associations between various risk factors and vascular structure and function and in clinical trials, which have evaluated the effect of various interventions on atherosclerosis. Additionally, this research group has conducted studies evaluating determinants of left ventricular size and function and the effects of various interventions on these parameters of cardiac function.

A number of investigators have studied various aspects of cardiovascular and metabolic diseases and their relationship to vascular and cardiac structure and function. These studies have ranged from patients with advanced cardiovascular disease, to general population studies and to investigations in people with other conditions which may increase the risk of atherosclerosis, such as HIV, obese subjects and people with chronic obstructive pulmonary disease. More recently, the laboratory has started a program of atherosclerosis imaging in children. This program is aimed at detecting early stages of atherosclerosis in a pediatric population and defining cardiovascular risk factors at very young ages.

**The laboratory serves as a core and training laboratory for many collaborators in Canada and in 15 additional countries.**

The PHRI is planning to integrate novel techniques for the non-invasive study of atherosclerosis, including multislice CT angiography and MRI imaging. New members of the PHRI, including Drs. T. Sheth and J. Grynspan will provide leadership in the development and implementation of such novel imaging techniques. Additionally, the team will be collaborating with interventional colleagues under the leadership of Dr. Madhu Natarajan in the use of intracoronary ultrasound for the assessment of coronary atherosclerosis.

**Peer-reviewed grants that have used techniques performed in the Vascular Imaging Laboratory as a major component of the methodology employed to address various aspects of cardiovascular disease include:**

- **SECURE** (Study of Evaluate Carotid Ultrasound Changes in Patients Treated with Ramipril and Vitamin E): Medical Research Council of Canada-Industry Program
- **SHARE-AP** (Study of Heart Assessment and Risk in Ethnic Groups): Medical Research Council of Canada
- **SHARE** (Study of Health Assessment and Risk in Ethnic Groups): First Nations – Medical Research Council of Canada
- **FATE** (Firefighters And Their Endothelium): CIHR/Research and Development Program
- **Assessing the Value of Screening for Asymptomatic Left Ventricular Dysfunction**: Heart and Stroke Foundation of Canada
- **STARR** (Study of Atherosclerosis with Ramipril and Rosiglitazone): Heart and Stroke Foundation
- **Non-Invasive Assessment of Atherosclerosis and its Determinants in HIV-Infected People**: Ontario HIV Treatment Network
- **The Canadian HIV Vascular Study**: Canadian Health Research Institutes of Health Research
- **HART** (Homocysteine Lowering and Atherosclerosis Reduction Trial): Canadian Institutes of Health Research

**The Vascular Research Imaging Laboratory is the core laboratory for a number of industry-funded studies, including:**

- Modulation of Arterial Reactivity Using Amlodipine and Atorvastatin by Ultrasound Examination (MARGAUX)
- Brachial Artery Vascular Endothelium Reactivity (BRAVER)
- Glucose Reduction in Atherosclerosis Continuing Evaluation (GRACE); Atherosclerosis Substudy of the ORIGIN Trial
- Echocardiographic Substudy of the ORIGIN Trial
- Echocardiographic Substudy of the DREAM Trial



### Key publications:

- Lonn E, Yusuf S, Dzavik V, Doris I, Yi Q, Smith S, Moore-Cox A, Bosch J, Riley WA, Teo KK, for the SECURE Investigators. Effects of ramipril and of vitamin E on atherosclerosis: results of the prospective randomized Study to Evaluate Carotid Ultrasound changes in patients treated with Ramipril and vitamin E (SECURE). *Circulation* 2001; 103:919-925.
- Anand S, Yusuf S, Jacobs R, Davis AD, Gerstein H, Montague PA, Lonn E. Risk factors, atherosclerosis, and cardiovascular disease among Aboriginal People in Canada (SHARE-AP). *Lancet* 2001; 358: 1147-53.
- Gerstein H, Anand S, Yi Q, Vuksan V, Lonn E, Malmberg K, McQueen M, Yusuf S, for the SHARE investigators. The relationship between dysglycemia and atherosclerosis in South Asian, Chinese and European individuals in Canada: A randomly sampled cross-sectional study. *Diabetes Care* 2003; 26: 144-149.
- Lonn E, Shaikholeslami R, Yi Q, Bosch J, Sullivan B, Tanser P, Magi A, Yusuf S. Effect of ramipril on left ventricular mass and function in normotensive high-risk patients with preserved left ventricular ejection fraction: a sub study of the HOPE trial. *J Am Coll Cardiol* 2004; 43:2200-2206.
- Yan R, Anderson TJ, Charbonneau F, Title L, Verma S, Lonn E. Relationship between carotid intima-media thickness and brachial artery flow-mediated dilation in middle-aged healthy men. *J Am Coll Cardiol*; 2005; 45: 1980-1986.

### Research team:

Eva Lonn, C. I. Doris, M. J. Sabine, Sandy Smith, Rose Djuric, Laura Newkirk, Marion Armstrong, Lynda Avolio and Lorraine Desjardins



## Vascular Research Imaging Laboratory

## IT infrastructure supporting global health research



"The Computing mission is to facilitate the efficient use of computer information technologies in the PHRI research community, by providing training, outreach, and supporting the use of hardware and software resources."

- Steven Vacaroaia



The Computing Group at the Population Health Research Institute provides data and document management support for the rapidly evolving research and administrative activities at the Institute. A mix of 25 Unix and Windows servers and 180 workstations are used to accommodate these needs. The range of activities include:

### Data Management for Clinical Studies

PHRI research studies typically involve over 1,000 collaborating centres around the world, located in 66 countries. PHRI receives approximately 1.5 million case report forms yearly via fax from these centres. The primary data collection tool used for this function is DataFax, a system which automatically interprets the fax images, which are visually verified and checked for quality control by data entry staff before they are stored in databases for further tracking and statistical analysis. If errors are detected, quality control is sent back to the source to make corrections. The systems tracks expected data on events according to a study-specific timeline. A new version of data fax, which has additional capabilities for electronic data capture and transmission, is expected to be evaluated relatively soon.

### Data Entry via Web

In some cases, data entry is conducted directly via secure web connections. This approach provides immediate feedback for data entry errors, missing data and designated reports. Other technologies (such as hand-held devices) are being developed to accommodate emerging data entry needs.

### Randomization Support

Studies requiring randomized allocation of treatment to patients use a custom-designed software, called Automated Randomization

System - AReS to allocate treatment through a simple telephone interface. AReS operates in 10 languages and handles approximately 50,000 allocations a year from collaborating centres around the world.

### Custom Programming

Computing has a team of Unix and Windows programming staff to create customized applications for special needs, for example, web-based systems, data capture, quality control, data analysis and reporting.

### Secure Network

Given the confidential nature of the data being shared on studies, Computing maintains a secure, high-speed (1 Gb/Sec) network. System integrity is ensured by two independent backup systems. Currently, there is a Storage Attached Network array (SAN) with the capacity of 14 Terabytes, using RAID 5 technology, which allows quick replacement of any of its disks without needing to bring down the system.

### Regulatory Requirements

In addition to the general Standard Operating Procedures (SOPs) used at PHRI, Computing follows a set of SOPs relevant to computing and data management to comply with various regulatory requirements for clinical research. These include staff training, system validation, backups and system security and traceability.

### Computing Team:

Steven Vacaroaia Adam Molnar, Andrew Renner, John Raso, Khursh Ahmed, Laura Bray, Les Farago, Nicholas Lake, Pash Hrnica, Serguei Pavlov, Vidya Patil and Vlad Gasic

## Research Profiles

**Khursh Ahmed** is a Senior Computer Consultant and Quality Assurance Manager at PHRI. Prior to taking this role, he served as the Manager for Computer Services Unit in the Faculty of Health Sciences and as a faculty member in the Department of Clinical Epidemiology at McMaster University for over 25 years. Other than developing computer applications for health research, he is actively involved in Peace through Health, international health and quality assurance.

**Steven Vacaroaia** is the Manager of Computing Group at PHRI. He holds a Master's degree in Engineering and professional certifications in a number technologies (UNIX, Windows, networking and computer security) and has over 20 years experience in computers.



The biostatistics and statistical programming staff at the PHRI collectively hold expertise in the conduct and analysis of large-scale multinational clinical trials, registries and community-based epidemiology projects. As biostatisticians, the group recognizes the importance of the information obtained from large trials and population health studies. Collecting large amounts of data enables PHRI to find true moderate effects of a treatment or moderate risk factors that will influence the lives of many people with common diseases.

PHRI's biostatisticians have in-depth knowledge of clinical trials methodology, meta-analysis, and multivariate methods in epidemiology and survival analysis. This group produces the statistical analysis seen in publications of major journals. The biometrics programmers have been responsible for the database set-up for projects, collectively enrolling hundreds of thousands of participants; they have collectively written and validated tens of thousands of checking programs. All team members hold positions of responsibility working in a team environment on large scale, scientifically important studies.

The group consists of 11 biostatisticians and three biometrics programmers. The majority of these skilled individuals have been with PHRI for four years or longer. The group includes two PhDs, nine Masters, and three B.Sc. level individuals, with appropriate degrees in statistics/biostatistics for the biostatisticians and computer science for the biometrics programmers.



**"Only by collecting large amounts of data are we able to find true moderate effects of a treatment, or moderate risk factors which can influence the lives of many people."**

**- Janice Pogue**

#### Statistics Team:

Janice Pogue Rizwan Afzal, Hongmei (Emily) Dai, Shofiquil Islam, Mark Molec, C Purnima, Rao-Melacini, Leanne Santarelli, Patrick Sheridan, Peter Tait, Changchun Xie, Xiaochun (Sean) Yang, Xiumei Yang, Xiaohe (Michelle) Zhang and Feng Zhao



## Analyzing information on hundreds of people from around the world to improve health

#### Key publications:

- Pogue, J. & Yusuf, S. Cumulating Data and Evidence from Trials: Utilizing Sequential Monitoring Boundaries for Cumulative Meta-Analysis. *Controlled Clinical Trials* 1997, 18, 580-593.
- Pogue, J., Yusuf, S. Overcoming the Limitations of Current Meta-Analysis of Randomized Controlled Trials. *The Lancet* 1998, 351, 47-52.
- ACE-inhibitor Myocardial Infarction Collaborative Group. (Member of coordinating centre) Indication for ACE-inhibitors in the early treatment of acute myocardial infarction: systematic overview of individual data from 100,000 patients in randomized trials. *Circulation* 1998, 97, 2202-2212.
- Pogue J, Yusuf S. Data Monitoring in the RESOLVD (Randomized Evaluation of Strategies for Left Ventricular Dysfunction) Pilot Study: when reasonable people disagree. DeMets D, Furberg CD, Friedman LM. *Data Monitoring in Clinical Trials: A Case Studies Approach*. New York: Springer, 2006.
- Pogue J, Sackett D, Wyse DG, Yusuf S. Data monitoring in the Heart Outcomes Prevention Evaluation and Clopidogrel in Unstable Angina to prevent Recurrent ischemic Events trials: avoiding important information loss. DeMets D, Furberg CD, Friedman LM. *Data Monitoring in Clinical Trials: A Case Studies Approach*. New York: Springer, 2006.



# Statistics

## Balancing a global budget



“Balancing the books and making every dollar stretch ensures that we get the greatest impact for the efforts of all our researchers globally.”

– Beena Cracknell

Finance Manager of the PHRI, received her Certified General Accountant designation in 1994 and began at PHRI the same year.

The finance team is responsible for all financial and contractual activities of our studies. The team assists in the preparation and negotiation of budgets and contracts with funders (pharmaceutical companies and granting agencies), national coordination offices, study sites and other vendors. The team manages the overall study budget in three functional currencies (USD, CAD, EURO) which, in addition to the central PHRI operating costs, includes payments to support worldwide study sites, national coordinators and payments related to investigator and study committee meetings. Another function within the department includes formulating required reports to funders, principal investigators and auditors.

PHRI's finance team uses the Investigator Fee System; an in-house developed system that bases payments on the data received from the study sites for payments to study sites and national coordinators. Every quarter, the Finance department processes over 4,000 payments to over 50 countries. To give an idea of the scope of a new study, the department may be required to execute around 700 contracts within a six-to-nine month period to get a project started.

### Research finance team:

Beena Cracknell Vijay Vasudeva, Lynn Stuart, Brigita Miljevic, Inosha Witharana, Sara Avery, Stephanie Mackenzie, Brett Debastiani and Kevin Gelata



The Administrative team at the Population Health Research Institute is comprised of Susan Crook, Administrator, Khursh Ahmed, Quality Assurance Manager and Judy Lindeman, Senior Research Administrative Assistant.

## Administration and Human Resources

Sue's principal area of responsibility is that of a human resource administrator, liaising with both Hamilton Health Sciences' and McMaster University's Human Resource Departments. Other major responsibilities include overseeing the planning and allocation of space, including any necessary renovations, as well as relocation and purchasing of equipment and office furnishings for both faculty and staff. Sue Crook has been an employee of the PHRI since March 1997. Her responsibilities at that time centred chiefly around administrative support to the Director. However, due to the Institute's accelerated expansion and Sue's increasing involvement in human resource and operational activities, Sue's position has evolved to that of Administrator for the Institute.

Khursh develops and implements security policies in compliance with government agencies, develops and maintains the Institute's Standard Operating Procedures, including insuring that PHRI studies follow regulatory requirements, as well as maintenance of any required documentation. Khursh is instrumental in the conduct of internal audits and assists study teams with external audits. Khursh also ensures that the Institute's computing activities follow policies and guidelines.

Judy provides administrative support to the Director of the Institute. Judy's experience and knowledge provide a very important resource not only for the Director, but for the entire group as well by providing invaluable assistance and guidance in many areas.

### Administration and Human Resources Team:

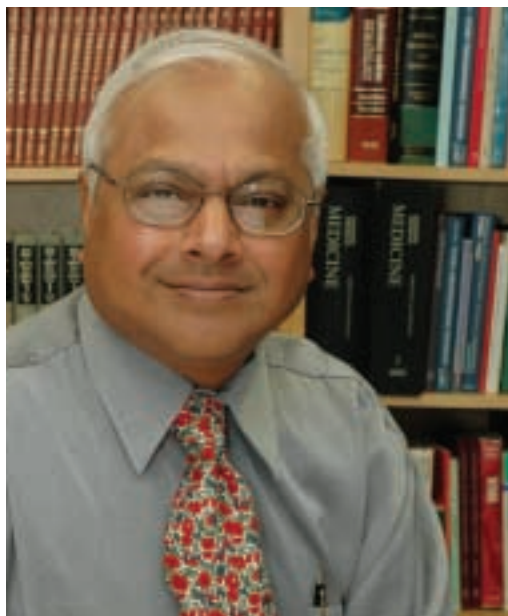
The administrative team works closely with all study teams and departments within the PHRI including Computing, Statistics, and Finance.



(Left to right) Susan Crook, Khursh Ahmed and Judy Lindeman.

## Administration and Human Resources





**Salim Yusuf**  
**Director, Population Health Research Institute**

Having published more than 500 articles, Dr. Salim Yusuf is among the top cited medical scientists in the world, with several articles regarded as citation classics. His work has made a major impact on the health of people in every continent of the world. The Director of the Population Health Research Institute (PHRI), and previous Director of the Division of Cardiology, Dr. Yusuf is also a Professor in the Department of Medicine at McMaster University and a Joint Member of the Department of Clinical Epidemiology & Biostatistics. He was also named as the inaugural Chief Scientific Officer at Hamilton Health Sciences in 2006. Dr. Yusuf graduated from St. John's Medical College in Bangalore, India, followed by clinical training in cardiology and epidemiology as a Rhodes Scholar at Oxford. A holder of a Heart and Stroke Foundation of Ontario Research Chair, Dr. Yusuf was a Senior Scientist of the Canadian Institutes of Health Research and was recently inducted as a Fellow of the Royal Society of Canada. He has received several prestigious research awards, including the Prix Galien in 2001, the Lucian Award, the Paul Wood Medal in 2003, the Population Health Lecturer of the European Society in 2004, the finalist of the Michael Smith Prize in 2005, the International Lecturer award of the American College of Cardiology in 2006 and the Bradford Hill Lecturer of the University of London in 2006.

## Sonia Anand

**Associate Director of Population Health, Population Health Research Institute**

Dr. Sonia Anand is a clinician-scientist and vascular medicine specialist. The Associate Director of Population Health, Dr. Anand is focused on conducting population-based studies and clinical trials in the areas of cardiovascular risk factors in different ethnic groups, population genomics, women's health and peripheral vascular disease. An Associate Professor of Medicine at McMaster University, she has been a member of the PHRI since its inception. Dr. Anand completed her Masters and PhD in Health Research Methodology from McMaster University; following which she completed a clinical fellowship in Vascular Medicine at the Brigham and Women's Hospital in Boston, Massachusetts. Dr. Anand holds a Canadian Institutes of Health Research Clinician-Scientist Phase 2 award and was named the endowed May Cohen Eli-Lilly Chair in Women's Health Research at McMaster in 2001.



## Koon Teo

**Associate Director of Clinical Trials, Population Health Research Institute**

Dr. Koon K. Teo is a Professor in the Department of Medicine and Associate Member in the Department of Clinical Epidemiology and Clinical Biostatistics at McMaster University. A cardiologist at Hamilton Health Sciences, Dr. Teo has considerable experience in large cardiovascular clinical trials and epidemiology studies. He was a Medical Scholar of the Alberta Heritage Foundation for Medicine Research at the University of Alberta, prior to relocating to Hamilton in 1999. Dr. Teo's publications include 200 peer-reviewed articles, 224 abstracts and 16 book chapters on clinical cardiology, physiological studies and clinical trials. He is committed to trials and epidemiology studies and has focused on methodology and meta-analyses of thrombolysis, beta-blockers, nitrates, magnesium, antiarrhythmic agents, ACE inhibitors and aspirin. He is also interested in outcome research studies in acute myocardial infarction, congestive heart failure, atrial fibrillation and risk factors modification.



# Principal Investigators

## Heather Arthur

Holder of the Heart and Stroke Foundation of Ontario Chair in Cardiovascular Nursing Research, Dr. Heather Arthur completed her PhD in Medical Sciences at the University of Toronto. She is Co-Director of the Cardiac and Vascular Nursing Science Unit (CVNSU) at Hamilton Health Sciences and is a Professor in the School of Nursing, Faculty of Health Sciences at McMaster University. A Nurse Fellow of the European Society of Cardiology and President of the Canadian Association of Cardiac Rehabilitation, Dr. Arthur's research is primarily focused on behavioural cardiology. She is interested in psychosocial factors that contribute to the risk and recovery from cardiac illness and women's cardiovascular health. She has a strong interest in the development of research capacity and is the director of the FUTURE Program for Cardiovascular Nurse Scientists, which is part of the Strategic Training Initiative in Health Research, a national program supported by CIHR and its partners.



## Stephanie Atkinson

Dr. Stephanie Atkinson directs an internationally recognized research program in pediatric nutrition and bone metabolism, particularly pertaining to prematurely born infants and children with bone disorders secondary to pediatric diseases or drug therapy. A Professor in the Department of Pediatrics and an Associate Member in the Department of Biochemistry and Biomedical Sciences at McMaster University, she is also a Special Professional Staff member at McMaster Children's Hospital, part of Hamilton Health Sciences' family of hospitals. Her current research includes a birth cohort study that is investigating early determinants of obesity, cardiovascular disease and diabetes in children; investigations of "late effects" on body composition and bone mass in former premature infants and survivors of pediatric cancers or epilepsy; and family interventions to prevent obesity in Aboriginal children. Dr. Atkinson was recently elected President of the American Society for Nutrition and has received numerous prestigious awards that have paid tribute to her distinguished services and success in the field of nutrition in Canada.



## Stuart Connolly

Dr. Stuart Connolly is the Director of the Division of Cardiology at McMaster University and holds the Salim Yusuf Chair in Cardiology. Having completed his cardiology training at the University of Toronto, he then completed sub-specialty training in cardiac arrhythmia at Stanford University. Dr. Connolly led one of the major clinical trials evaluating implantable defibrillator for prevention of sudden death (CIDS) and was involved in the early development of warfarin for prevention of stroke in atrial fibrillation. He also led several trials related to optimal use of pacemaker therapy, including a major clinical trial of dual chamber versus single chamber pacing (CTOPP) and trials evaluating pacemaker therapy for the treatment of vasovagal syncope. His current interests continue to be in the evaluation of antithrombotic therapy for atrial fibrillation and novel aspects of device therapy.





## Catherine Demers

An Ontario Ministry of Health and Long Term Care Career Scientist, Dr. Catherine Demers is an Associate Professor in the Department of Medicine and Division of Cardiology at McMaster University. Her area of interest and expertise includes the management of heart failure in the community, in the primary care setting and the effect of cognitive impairment in elderly heart failure patients. She is currently the PI of a cluster of randomized clinical trials evaluating a primary care based model of heart failure management. Dr. Demers also led a pilot clinical trial evaluating the effects of human recombinant growth hormone on functional capacity, cardiac function, and quality of life in patients with advanced heart failure symptoms.

## P.J. Devereaux

Following residency training in Calgary and Dalhousie, Dr. P.J. Devereaux completed a PhD in Health Research Methodology at McMaster University, where he is currently an Assistant Professor in the Departments of Medicine and Clinical Epidemiology and Biostatistics. The holder of a Canadian Institutes of Health Research New Investigator Award, his clinical research is focused on perioperative vascular medicine in patients undergoing non-cardiac surgery. He is the Co-PI of the POISE trial; the world's largest cardiac randomized controlled trial in patients undergoing non-cardiac surgery to date. He is also the PI of several other ongoing perioperative vascular studies evaluating risk estimation, monitoring, and interventions for perioperative vascular events. Dr. Devereaux has published over 60 peer reviewed papers and 20 editorials, book chapters and commentaries.



## John Eikelboom

Dr. John Eikelboom's research is credited as leading the way to the development of a new diagnostic tool to assess the effect of aspirin. A Haematologist at Hamilton Health Sciences and an Associate Professor in the Department of Medicine at McMaster University, he completed training in Internal Medicine and Haematology in Perth, Australia and a fellowship in Thrombosis at McMaster University, during which time he completed an MSc in Clinical Epidemiology. Dr. Eikelboom holds a Tier II Canada Research Chair (CRC) in Cardiovascular Medicine from the Canadian Institutes for Health Research. His major research interests include antithrombotic therapies in arterial and venous thrombosis and the mechanisms of variable response to antiplatelet drugs. Through his CRC position, Dr. Eikelboom is investigating the causes of aspirin resistance and is also working on the development of new treatments. Because of the scope of cardiovascular disease and the widespread use of aspirin, even a small improvement in its effectiveness could prevent thousands of heart attacks and strokes each year.

# Principal Investigators



## Ernest Fallen

Dr. Ernest L. Fallen founded and was the former Director of The Regional Cardiovascular Program in Hamilton. An Emeritus Professor in the Faculty of Health Sciences at McMaster University, he is the author of over 100 research publications. His special interests have been in clinical neurocardiology, cardiac PET imaging and heart failure. Dr. Fallen has served on a number of international task forces and executive committees and was the chairman of the first consensus conference of the Canadian Cardiovascular Society. He is currently semi-retired but working actively to complete an interactive web-based textbook of Cardiology.



## Hertzel Gerstein

Dr. Hertzel C. Gerstein is Director of the Diabetes Care and Research Program at Hamilton Health Sciences and is a Professor in both the Department of Medicine and Clinical Epidemiology and Biostatistics at McMaster University. The Population Health Institute Chair in Diabetes Research at the University, he is currently the principal investigator of a CIHR-funded study, and the joint principal investigator of three large international trials focused on the prevention and treatment of diabetes and its consequences, that is following more than 25,000 people. Dr. Gerstein is also the Director of Diabetes Hamilton. He has published over 150 papers, book chapters and editorials, mainly on diabetes-related issues. In 1999, he received the prestigious CDA Young Scientist Award and Frederick G. Banting Award.



## Jeff Healey

Dr. Jeff Healey completed his clinical training in cardiology and electrophysiology at the University of Ottawa Heart Institute. Following this, he began training in clinical research under the guidance of Dr. Stuart Connolly at McMaster University, where he is currently an Assistant Professor of Medicine. His research interests include the relationship between atrial fibrillation and hypertension, emerging risk factors for atrial fibrillation and device therapy for cardiac arrhythmias. He has published 14 peer-reviewed manuscripts in the area of cardiac arrhythmias and device therapy. Drs. Connolly and Healey are currently the co-recipients of a randomized controlled-trials mentoring program grant from the Canadian Institutes of Health Research, which will support Dr. Healey's ongoing development as a clinical trialist in the field of arrhythmia management. He is also currently the co-principal investigator for the IPACE study and is also a steering committee member for the ASSERT trial. His research focuses on the effect of risk factors, and risk factor modification on the development of atrial fibrillation and its complications, such as stroke.



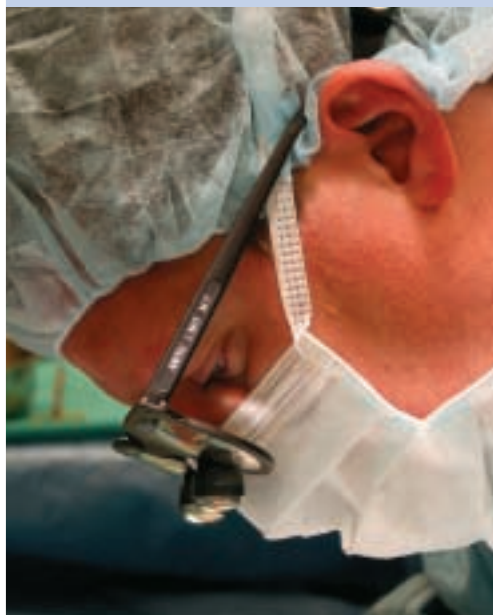


## George Heckman

Originally interested in pursuing a specialty in biomedical engineering, Dr. George Heckman was finally drawn towards Internal and Geriatric Medicine and obtained fellowships in these specialties in 1999 and 2000. An Assistant Professor of Medicine in the Divisions of Geriatric Medicine and Cardiology at McMaster University, his principal research interests are in cardiovascular disease, particularly heart failure, and the geriatric syndromes of frailty, functional impairment, and cognition. Dr. Heckman was the recipient of the 2005 E.J. Moran Campbell Research Award and is the principal investigator of a CIHR funded prospective study of functional, cognitive and neuropsychiatric decline in residents of long-term care with a history of heart failure.

## Andre Lamy

It is highly unusual for a surgeon to worry about costs. But Dr. Andre Lamy's interests combine evaluating new techniques in cardiac surgery (such as off pump bypass) with economic evaluations. Dr. Lamy completed studies in cardiothoracic surgery at the University of British Columbia and training in Heart and Lung Transplantation at Papworth Hospital, in Cambridge, England. A cardiac surgeon, Dr. Lamy's research interests include new techniques in cardiac surgery, such as beating heart surgery, cardiac valve prostheses, atrial ablation surgery and prevention of cardiovascular events after cardiac surgery. He is involved in numerous local and international clinical trials in cardiac surgery and cardiology. Dr. Lamy has an avid interest in clinical research and health economics, including the cost analysis and effectiveness of new drugs for the treatment of cardiovascular diseases. Analyses are performed with patient-level data with micro-costing or modeling. He is also involved in the economic analysis of several clinical trials, as well as peer-reviewed funded trials.



## Eva Lonn

Dr. Eva Lonn is the Director of Echocardiography at Hamilton Health Sciences and the Vascular Research Imaging Laboratory at PHRI. She completed her M.D. degree in Jerusalem, Israel, followed by training in Internal Medicine and Cardiology, a Clinical and Research Fellowship at the University of Toronto and MSc in Health Research Methodology at McMaster University. Dr. Lonn's main research interests relate to ultrasound imaging in atherosclerosis, clinical trials in cardiovascular prevention and cardiovascular epidemiology. She has completed and is currently conducting studies of various interventions such as ACE inhibition, Vitamin E, B Vitamins and glucose lowering in atherosclerosis and cardiovascular prevention. Dr. Lonn is the principal investigator of the recently completed HOPE-2 trial and a member of the International Steering Committee of the HOPE, DREAM and ORIGIN trials and has published over 100 articles in several high impact journals.

# Principal Investigators

## Joseph Macri

A Fellow of the Canadian Academy of Clinical Biochemistry, Dr. Joseph Macri is a laboratory scientist at Hamilton Health Sciences. He obtained his PhD in Biochemistry and a Post-doctoral Diploma in Clinical Chemistry from the University of Windsor. Dr. Macri completed an industrial post-doctoral fellowship at Pfizer Pharmaceuticals using proteomics to identify novel therapeutic targets for heart failure. He is an Associate Professor at McMaster University and is head of the Clinical Proteomics Facility. In 2000, he received the Young Investigator Award from the Canadian Lipoprotein Conference and currently has grants from NSERC, CIHR and CFI. His research is focused on using proteomics to investigate the molecular mechanisms underlying dyslipidemia, diabetes and obesity, as well as identifying novel diagnostic markers and therapeutic targets to detect, monitor and treat these disorders. Dr. Macri has published 16 peer-reviewed articles and has served as a consultant for proteomics to both industry and academia.



## Robert McKelvie

The Medical Director of the Heart Function Clinic and Cardiac Health and Rehabilitation Centre at Hamilton Health Sciences, Dr. Robert McKelvie is a cardiologist and Professor of Medicine at McMaster University. Dr. McKelvie's research in heart failure is focused on the assessment of exercise training and the use of pharmacologic therapy. A study he is currently conducting is assessing the effectiveness of a drug therapy called candesartan to combat heart failure. He held a Ministry of Health Career Scientist Award and has grant-in-aid funding from the Heart and Stroke Foundation of Ontario and Canadian Institutes of Health Research. Dr. McKelvie is a member of a number of scientific review committees and has over 100 peer-reviewed publications to his credit.



## Matthew J. McQueen

Dr. Matthew J. McQueen is the Director of the Hamilton Regional Laboratory Medicine Program and the Clinical Trials Research and Proteomics Laboratory. He received his medical and PhD degrees from the University of Glasgow, Scotland. His main research interests have been in cardiovascular disease with particular emphasis on lipids, lipoproteins, and apo-lipoproteins, as well as the role of biomarkers in the prediction, diagnosis, and management of myocardial ischemia. Dr. McQueen has more than 140 publications and has made more than 300 presentations or invited lectures in 49 countries. In the past ten years, he has been investigator in 34 peer-review funded research studies. He has won numerous national and international awards for his research in clinical chemistry and scientific and professional achievement.







## Shamir Mehta

Winner of the 2003 Canadian Institutes of Health Research New Investigator Career Award, Dr. Shamir Mehta was also recognized as one of Canada's Top 40 Under 40™ in 2004. An Interventional Cardiologist, Dr. Mehta is the Director of Interventional Cardiology and ACS Research at the PHRI. In partnership with Dr. Salim Yusuf, their efforts have led to discovering the benefits of clopidogrel and aspirin, as well as fondaparinux. He completed fellowships in Internal Medicine and Interventional Cardiology at the University of Toronto; following this, he was awarded a Heart and Stroke Foundation of Canada Research Fellowship Award to complete a research fellowship in cardiovascular epidemiology at the PHRI and earned a Master's degree in Health Research Methodology. Dr. Mehta's research involves evaluating new antiplatelet and antithrombotic treatments in percutaneous coronary intervention, acute coronary syndromes and acute myocardial infarction and the role of novel markers of inflammation and hemostasis in patients with ACS. He has published 43 journal articles, 19 journal abstracts and has contributed to the publication of six books.

## Carlos Morillo

Dr. Carlos A. Morillo is a Cardiologist and Electrophysiologist and currently the Director of the Arrhythmia Service at McMaster University. His main research interests are related with the development of clinical trials in the area of cardiac arrhythmias, syncope and treatment of Chagas Disease. Similarly, he has a long-lasting interest in developing new therapeutic approaches for the treatment of atrial fibrillation and autonomic disorders. Dr. Morillo has published 130 articles in peer reviewed journals and is currently focused on the development and implementation of clinical networks that will develop the necessary infrastructure to conduct clinical trials of neglected diseases such as Chagas.



## Katherine Morrison

A pediatric endocrinologist, Dr. Katherine M. Morrison's clinical and research interests relate to the determinants, adverse health consequences and treatment of childhood obesity and lipid disorders in children. Also an Assistant Professor at McMaster University, she completed her medical training at the University of Calgary and Stanford University, followed by a post-doctoral fellowship in Preventive Cardiology at the PHRI. Dr. Morrison is the principal investigator in a study examining the biological, behavioural and social factors that influence the presence of obesity-related health consequences in youth and is co-investigator of the FAMILY study. In collaboration with Dr. Alison Holloway, she is currently examining the impact of in-utero nicotine exposure in an animal model. Another area of research includes examining non-invasive measures of atherosclerosis in youth at high risk for the development of cardiovascular disease.



# Principal Investigators

## Madhu Natarajan

Dr. Natarajan's research interest lies in acute coronary syndromes and health services. The Director of Interventional Cardiology at Hamilton Health Sciences, Dr. Natarajan is also an Associate Professor of Medicine at McMaster University. He completed his training in Internal Medicine and Cardiology at the University of Toronto and Interventional Cardiology at St. Michael's Hospital, Toronto. As a member of the Cardiac Care Network, he has participated in various panels and is a member of the Catheterization/PCI and Operations Working Group Committees. Dr. Natarajan has received peer-reviewed grants from the Canadian Health Services Research Foundation and The Change Foundation of Ontario in projects related cardiac catheterization waiting list registry and primary angioplasty, respectively. In addition, he has been a member of the CURE study Steering committee and is a co-investigator in other ACS trials.



## Martin O'Donnell

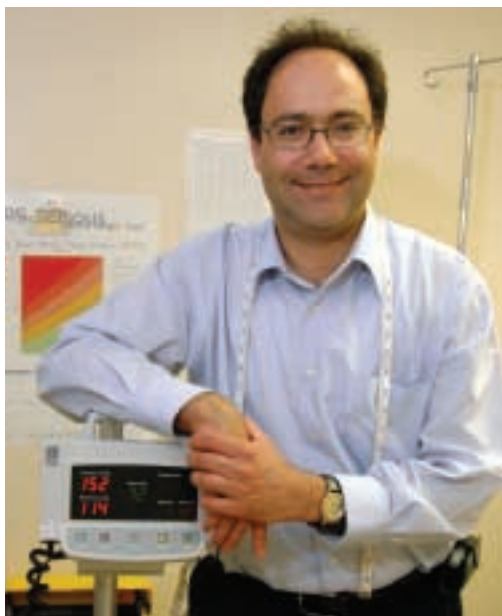
Dr. Martin O'Donnell is an Assistant Professor and William Walsh Chair in Internal Medicine in the Department of Medicine at McMaster University. He completed his undergraduate training and initial clinical training in Internal and Geriatric medicine in Ireland, followed by fellowships in both Geriatric and Thrombosis medicine at McMaster University and training in Stroke medicine at Stanford University. He held a Fellowship award from the Heart and Stroke Foundation of Canada/CIHR and recently received a Clinical Trials Mentoring Program Award from CIHR. Dr. O'Donnell's research career is focused on vascular medicine – stroke medicine in particular. Currently completing a PhD in Health Research Methodology under the supervision of Dr. Gordon Guyatt, he is the principal investigator on numerous research projects, including two clinical trials. He has published numerous peer-reviewed articles, book chapters and reviews.



## Parminder Raina

Director of the McMaster University Evidence-Based Practice Centre, Dr. Parminder Raina specializes in the epidemiology of aging including brain, disability and fall related injuries. He recently was awarded the Ontario Premier's Research Excellence Award in research on aging and holds an Investigator Award from CIHR. Dr. Raina has considerable experience in leading multi-centre population-based research projects, has participated as a site principal investigator on the Canadian Study on Health and Aging and is co-leading the development of a Canadian Longitudinal Study of Aging. Dr. Raina was a founding director of the nationally renowned British Columbia Injury Research and Prevention Unit in Vancouver, British Columbia, where he led the development and implementation of a prospective injury surveillance system in 10 Emergency Departments across British Columbia.





## Arya Sharma

Dr. Arya M. Sharma holds a Canada Research Chair (Tier 1) in Cardiovascular Obesity Research and Management at McMaster University. Trained in Internal Medicine and Nephrology at the Free University of Berlin, his expertise lies in the area of obesity and its impact on cardiometabolic disease. He currently holds funding from CIHR for a New Emerging Team on Obesity and Atherothrombosis from the Heart and Stroke Foundation, as well as industry for a number of clinical trials. Dr. Sharma is also the Director of the federally funded Canadian Obesity Network and is Vice-President of the Canadian Association of Bariatric Physicians and Surgeons. Dr. Sharma has authored and co-authored over 200 scientific articles and book chapters and has lectured widely on the aetiology and management of hypertension, obesity, and related cardiovascular disorders. In 2002 he was the R Douglas Wright Lecturer for the High Blood Pressure Research Council of Australia and in 2005 was awarded the Rick Gallop Award for Research Excellence by the Heart and Stroke Foundation of Ontario.

## Kevin Teoh

Dr. Kevin Teoh obtained his medical degree from The University of Toronto in 1982. A graduate of the Gallie Surgical Program, he completed training in General Surgery and Cardiovascular and Thoracic Surgery from the Institute of Medical Sciences, University of Toronto. Dr. Teoh is the Head of Service for the Division of Cardiac Surgery in the Department of Surgery for Hamilton Health Sciences and the Faculty of Health Sciences, McMaster University. His research interests relate to anticoagulation and hemostasis, inflammatory response to cardiopulmonary bypass and clinical trials in cardiac surgery. In this regard, he has published more than 100 papers.



# Principal Investigators



## Other Faculty Members and Researchers



**Jackie Bosch** is an epidemiologist and occupational therapist, who is an Assistant Professor of Occupational Therapy at McMaster University. She coordinated the HOPE study and manages the DREAM and ORIGIN trials. She has an interest in CV prevention and particularly diabetes, strokes, and CVD.



**Janice Pogue** is the Head Statistician at PHRI, and is Assistant Professor in the Department of Clinical Epidemiology and Biostatistics. Her main research interest is in statistical issues related to clinical trials and meta-analysis. She is directly involved in the design and conduct of large-scale clinical trials in cardiovascular disease and in individual patient meta-analysis. Janice is also interested in issues related to Data and Safety Monitoring Boards and the interim analysis of clinical trials.

## Senior Research Associates



**Susan Chrolavicius** is the manager of several large trials, including CURE, OASIS-5 and OASIS-6, and the two large ACTIVE trials in atrial fibrillation.



**Sumathy Rangarajan** holds a certified clinical research associate certificate and manages large international epidemiological studies, including PURE, INTERHEART 2 and INTERHEART.



**Ellison Themeles** is the manager of several large international drug and device trials in cardiac arrhythmia research including RELY, ASSERT, RAAFT, IPACE and CREDIT.

## Collaborators

**Dr. Jeffrey Weitz** is the Director of the Henderson Research Centre, and collaborates in the area of thrombosis and vascular disease. A clinician-scientist with expertise in thrombosis, Dr. Weitz's research has contributed significantly to the basic understanding of how drugs that interfere with blood clots work.

**Dr. Amiram Gafni** is a Professor in the Department of Clinical Epidemiology and Biostatistics at McMaster University. His research interests are in the areas of economic evaluation of health care programs, modeling of consumers' health care behavior, models of patient-physician decision-making, policy analysis and risk and decision analysis in health. He has published widely in the field of management science and economics on topics related to health.

**Dr. Gordon Guyatt** is an internist and methodologist who collaborates in the area of perioperative ischemia. A Professor of Medicine and Clinical Epidemiology and Biostatistics at McMaster University, Dr. Guyatt coined the term "evidence-based medicine". He has published over 400 peer-reviewed papers in areas of research that include clinical trials, technology assessment, and health policy.

**Dr. Girish Nair:** Dr. Nair joined the faculty of McMaster University in 2004 and is a member of the Division of Cardiology. He plays a supportive role in the clinical trials related to cardiac arrhythmia and is currently enrolled in the Clinical Research Methodologies Master's degree program and is developing expertise in design and management of clinical trials.

**Marek Smieja** is an internist-epidemiologist collaborating in the link between infection, inflammation, and vascular disease.

**Dr. Tim Whelan's** main areas of interest are supportive care and the management of breast cancer. He is principal investigator in several projects evaluating the use of treatment decision aids for women with breast cancer.

## Associates and Collaborators

## Students and Research Fellows

### PhD Students 1996-2006

Sonia Anand, Jackie Bosch (2006-), Larry De Koning (2006-), P.J. Devereaux, Philip Jong (1999-), Angela Kochan (to be completed in 2007), Catherine Kreatsoulas (2006-), Imtiaz Samjoo, Marek Smieja and Juan Carlos Villar.

### MSc Students 1992-2006

Sonia Anand, Amandev Aulakh (2006-), Debika Burman, Ruth Chen (2005-), Brandy Cochrane, Sarah Davies, Catherine Demers, Michael Farkouh, Marcus Flather, Lisa Harrison (2006-), Karen Harkness, Jeff Healey, George Heckman, Katie Hendrican, Linda Kelemen, Shamir Mehta, Patricia Montague, Farouk Mookadam, Anne Moore-Cox (to be completed in Nov 2006), Madhu Natarajan, Dorairaj Prabhakaran, Imtiaz Samjoo, Marek Smieja, Vincent Yacyshyn, Juan Carlos Villar, Andrea Rathe (2005-), Fahad Razak, Rosa Roccaforte, Ross Tsuyuki and Denis Xavier (2005-).

### Post-Doctoral Research Fellows

Deanna Behnke-Cook, Patricia Caldwell, Mario Coutinho: Instituto de Cardiologia, Florianopolis, Brazil, Mahshid Dehghan: Iran, Romaina Iqbal: McGill University, Homa Keshavarz, Patrick Magloire, Catherine McGorrian: Ireland, Katherine Morrison, Stephanie Ôunpuu: University of Guelph, Mamdouh Shubair and Hanan Sokar Todd.

### Research Fellows

Alvaro Avezum (Dante Pazzanese Institute of Cardiology; Sao Paulo, Brazil), Tali Cukierman-Yaffee, Catherine Demers (FRSQ Fonds de la Recherche en Santé du Québec), John Eikelboom (University of Western Australia), Abhinav Goyal (Duke University), Prabhat Jha, Sanjit Jolly, Allan Kitching, Jae-Ki Ko (Korea), Shamir Mehta (University of Toronto), Patricia Montague (McMaster University), Farouk Mookadam (Mayo Clinic), Lucy Nora (St. John's, Bangalore, India), Hans Persson (Sweden), Dorairaj Prabhakaran (All India Institute), Rosa Roccaforte (Italy), Neville Suskin, Juan Carlos Villar (Universidade Industrial de Santander, Colombia), Denis Xavier (Canada-HOPE Scholar; St. John's, Bangalore, India) and Vincent Yacyshyn (Mayo Clinic).

### Visiting Professors

Kerstin Gorzelnik (Germany), Claes Held (Danderyd Hospital, Stockholm Sweden), Klas Malmberg (Karolinska, Sweden), Prem Pais (St. John's Medical College, Bangalore, India) and Rosella Tosini (Italy).

## PHRI Training Awards

The Population Health Research Institute Training Awards have been established to provide funding to encourage and promote individuals who want to participate in PHRI research programs. While working at the PHRI, individuals will partake in the conducting and organizing of clinical trials and epidemiological research studies. All awards are subject to funding availability.

### Categories of awards:

- Medical Fellowship
- Post-doctoral fellowship
- Studentship enrolled in PhD/MD program
- Summer student program
- Peace Through Health Traveling Studentship

Award	Eligibility	Deadline	Stipend	Availability
Post-doctoral Fellowship (PhD)	Must hold a PhD in the field of life sciences or statistics	March 1	\$40,000 per year	1 per year
Medical Fellowship	Completed a medical training and demonstrated real interest and productivity in research	March 1	\$50,000 per year	1 per year
Studentship	Must be currently enrolled in a PhD/MD program	March 1	\$18,000 per year	1 per year
Summer Studentship	Must have completed at least 2 years of an undergraduate degree in life sciences	February 1	\$1,450 per month	3 per year*
Peace Through Health Studentship	Must have a proposal to advance knowledge in PTH through a field study under a supervisor	March 1	\$2,500 per year	2 per year
PHRI International Travel Scholarship	Must be a medical/cardiology student at McMaster University	June 1	\$2,000 per year	1 per year

\* Four months maximum

Preference for all categories of awards is given to those who have worked previously at the Population Health Research Institute. Candidates are asked to submit a CV and two letters of reference, emphasizing research experience and potential. Candidates must identify a supervisor and write a 500-word synopsis of what research they plan to conduct.

### The essay should address the following areas:

- Goals and objectives to be achieved during this period.
- Preparation taken to complete research work?
- How applicants see this experience helping them in achieving short-term and long-term career goals.

# Students and Research Fellows & PHRI Training Awards

## Acute Coronary Syndromes

Study Name	Goals	No. Patients	Funding Source	Period
<b>1. OASIS-1</b>	Hirudin vs. heparin Long-term effects of warfarin	900 450	Behringwerke	1994 - 1996
<b>2. OASIS-2</b>	Full scale study of OASIS-1 warfarin	10,000 3,000?	Behringwerke	1996 - 1998
<b>3. OASIS-3/ CREATE</b>	LMWH vs. Control in AMI and GIK vs. control	15,000/ 20,000	Knoll and Internal Resources	2001 - 2004
<b>4. OASIS-4/CURE</b>	Clopidogrel + ASA vs. ASA in non-ST elevation ACS	12,000	Sanofi- Aventis/BMS	1999 - 2003
<b>5. OASIS-5 (MICHELANGELO)</b>	Pentaccharide vs. LMWH in non-ST elev MI. Role of invasive strategies	20,500	Organon- Sanofi-Aventis /GSK	2002 - 2006
<b>6. OASIS-6 (MICHELANGELO)</b>	Pentaccharide vs. placebo in ST elevation + GIK vs. control	12,000	Organon/ Sanofi-Aventis /GSK	2002 - 2006
<b>7. OASIS Registry</b>	Patterns of practice and outcomes in 13 countries	14,000	Multiple companies	1999 - 2002
<b>8. CREATE Registry</b>	Patterns of practice in India for ACS	20,000	Aventis, India	2001 - 2005
<b>9. OASIS-7/CURRENT</b>	Comparison of high vs. standard dose clopidogrel and low vs. medium dose ASA in ACS patients	14,500	Sanofi-Aventis /BMS	2006 - 2009
<b>10. TIMACS</b>	Identify the optimal timing of interventions	3,000	CIHR/Industry	2004 - 2008

## Cardiac Arrhythmia

Study Name	Goals	No. Patients	Funding Source	Period
<b>1. Canadian Trial of Physiologic Pacing</b>	Compare ventricular vs. dual chamber pacing	2,600	CIHR	Completed
<b>2. Canadian Implantable Defibrillator Study</b>	ICD vs. amiodarone in preventing sudden death	600	CIHR	Completed
<b>3. ACTIVE-A</b>	Clopidogrel + ASA vs. ASA in Afib	7,500	Sanofi/BMS	2002 - 2008
<b>4. ACTIVE-I</b>	Irbesartan vs. placebo	9,000	Sanofi-Aventis and BMS	2002 - 2008
<b>5. ACTIVE-W</b>	Warfarin vs. clopidogrel + ASA	6,500	Sanofi/BMS	2002 - 2006
<b>6. DINAMIT</b>	ICD in high risk patients	650	St. Jude Medical	2002 - 2006
<b>7. RE-LY</b>	Dabigatran for AF	15,000	Boehringer Ingelheim	2005 - 2009
<b>8. ASSERT</b>	Detection of atrial fibrillation by pacemakers	2,500	St. Jude Medical	2004 - 2008
<b>9. II-PACE</b>	Irbesartan for AF	200	BMS	2005 - 2008
<b>10. RAAFT</b>	Cardiac ablation vs. anti-arrhythmic drugs	400	Johnson and Johnson Inc.	2005 - 2009

Major research projects with significant leadership from members of the PHRI

### Sources of Funding

Although much of the PHRI's funding is generated from collaborations with industry, a number of projects are funded from peer-review governmental and charitable organizations such as:

- Canadian Institutes of Health Research (CIHR)
- U.S. National Institutes of Health (NIH)
- World Health Organization (WHO)
- Heart and Stroke Foundation of Ontario (HSFO)
- Indian Council of Medical Research
- Change Foundation of Ontario

### Industry Partners include:

- Abbott Laboratories • AstraZeneca
- Behringwerke
- Boehringer-Ingelheim
- Bristol-Myers Squibb (BMS)
- Burroughs Wellcome
- Cadila
- Eli-Lilly
- GlaxoSmithKline (GSK)
- Hoechst Marion Roussel /Aventis
- Johnson and Johnson
- King Pharmaceuticals
- Knoll Pharmaceuticals
- Merck Frosst
- Natural Source Vitamin E Association (Henkel Corp, Eastman Chemical and Eisai Corp)
- Novartis
- Organon
- Sanofi-Aventis
- Sanofi-Synthelabo
- Servier
- St. Jude Medical
- Wyeth Ayerst

PHRI Studies



Major research projects with significant leadership from members of the PHRI

## Interventional Cardiology

Study Name	Goals	No. Patients	Funding Source	Period
1. SORT	Registry of all patients referred for cardiac cath	over 40,000	CHSRF, HHS	1999 onwards
2. Primary angioplasty Program in AMI	Registry	1400	Change Foundation of Ontario, Eli-Lilly, HHS	2003 onwards
3. ASPIRE	Pentasaccharide vs. UFH in elective PTCA	300	Organon/ Sanofi-Aventis	2002 - 2003
4. COURAGE	Catheter based PCI + intensive medical therapy vs. intensive medical therapy alone	2287	CIHR, VA and several pharm companies	1999 - 2006

## Heart Failure

Study Name	Goals	No. Patients	Funding Source	Period
1. EXERT	Exercise rehabilitation	180	CIHR	1994 - 2001
2. RESOLVD	Role of ARB	800	AstraZeneca	1996 - 1998
3. CHARM	Role of ARB	7000	AstraZeneca	1999 - 2003
4. X-SOLVD	Follow-up of SOLVD	6,700	Merck-Frosst	2002 - 2003
5. I-PRESERVE	Irbesartan in heart failure	3,600	Bristol-Myers Squibb	2006

## Prevention of Atherosclerosis

Study Name	Goals	No. Patients	Funding Source	Period
1. HOPE	Ramipril & vitamin E to prevent major vascular events	9,500	CIHR, Sanofi-Aventis, King, Astra, Zeneca, Natural Source Vit. E Assoc.	1993-1999
2. HOPE-TOO	Homocysteine lowering	5,500	CIHR	2000 - 2006
3. HOPE-3	Lipid lowering and blood pressure lowering in primary procetin	10,000	AstraZeneca	2006 - 2013
3. ONTARGET	ARB + ACE-I vs. either alone	25,500	Boehringer-Ingelheim	2000 - 2007
4. TRANSCEND	ARB vs. control in ACE-intolerant	6000	Boehringer-Ingelheim	2000 - 2007
5. WAVE	Warfarin vs. control in addition to ASA in PAD	2000	CIHR/ HSFO	1999 - 2005
6. Indian POLYCAP Study	Combining multiple approaches to reduce CV risk	1,600	Cadila	2000 - 2007

## Prevention of Vascular Events Among Diabetic Individuals/Prevention of Diabetes

Study Name	Goals	No. Patients	Funding Source	Period
1. <b>ACCORD</b>	Glucose lowering, BP lowering, Fibrates	10,000	NIH	2001 - 2009
2. <b>ORIGIN</b>	Glucose lowering with insulin, Fish oil	10,000	Sanofi-Aventis	2002 - 2009
3. <b>DREAM</b>	Ramipril/Rosiglitazone in preventing DM in IGT/IFG	5,200	CIHR, GSK, Sanofi-Aventis, King, Wyeth Ayerst	2001 - 2007

## Prevention of Perioperative Ischemic Events

Study Name	Goals	No. Patients	Funding Source	Period
1. <b>POISE</b>	Beta blockers in preventing periop CV events	10,000	CIHR	2001 - 2007

## Trials in Developing Countries

Study Name	Goals	No. Patients	Funding Source	Period
1. <b>BENEFIT</b>	Benznidazole in chronic Chagas disease	1000	CIHR/WHO	2005 - 2009

## Population Health and Epidemiologic Studies

Study Name	Goals	No. Patients	Funding Source	Period
1. <b>SHARE</b>	Ethnic variations in CV disease and risk factors	900	CIHR	1996 - 1999
2. <b>SHARE-AP</b>	Extension to Aboriginal peoples	300	HSFO	1998 - 2000
3. <b>INTER-HEART</b>	International case-control study of MI	28,000	CIHR/HSFO, plus 39 other sources	1999 - 2004
4. <b>Epi-DREAM</b>	Cross-sectional and cohort study of genetic epidemiology for the prediction of metabolic syndrome, diabetes, obesity, and CVD	25,000	CIHR/Sanofi-Aventis/GSK	2002 - 2008
5. <b>PURE</b>	Prospective cohort study of the effects of urbanization	135,000 (planned) 48,000 (recruited)	CIHR/Sanofi-Aventis/Boehringer Ingelheim/AstraZeneca/Servier/GSK/King/Novartis	2001 onwards Planned until 2015
6. <b>FAMILY</b>	Birth cohort study of 1000 families with enrolment of the mother, the foetus, and the family	1,000 families	CIHR	2004 - 2010

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## Organizations

<b>AACC</b>	American Association for Clinical Chemistry
<b>CDA</b>	Canadian Diabetes Association
<b>CFI</b>	Canadian Foundation for Innovation
<b>CHSRF</b>	Canadian Health Services Research Foundation
<b>CIHR</b>	Canadian Institutes of Health Research
<b>CRC</b>	Canada Research Chair
<b>CVNSU</b>	Cardiac and Vascular Nursing Science Unit
<b>CVSRI</b>	Cardiac, Vascular and Stroke Research Institute
<b>CON</b>	Canadian Obesity Network
<b>ECLA</b>	Estudios Cardiológicos Latin America
<b>FHS</b>	Faculty of Health Sciences
<b>FRSQ</b>	Fonds de la Recherche en Santé du Québec
<b>FUTURE</b>	Facilitating Unique Training Using Research and Education Program
<b>GISSI</b>	Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico
<b>GSK</b>	GlaxoSmithKline
<b>HHS</b>	Hamilton Health Sciences
<b>HRC</b>	Henderson Research Centre
<b>HSFO</b>	Heart and Stroke Foundation of Ontario
<b>HSFC</b>	Heart and Stroke Foundation of Canada
<b>ICE</b>	Interdisciplinary Capacity Enhancement
<b>ICMR</b>	Indian Council of Medical Research
<b>ICRH</b>	Institute of Circulatory and Respiratory Health
<b>MOH</b>	Ministry of Health
<b>MRC</b>	Medical Research Council
<b>NCE</b>	National Centres of Excellence
<b>NHRDP</b>	National Health Research and Development Program
<b>NIH</b>	National Institutes of Health
<b>ORF</b>	Ontario Research Fund
<b>PHRI</b>	Population Health Research Institute
<b>WHO</b>	World Health Organization

## Medical and Miscellaneous Terms

<b>ACE</b>	Angiotensin-Converting Enzymes
<b>AreS</b>	Automated Randomization System
<b>ACS</b>	Acute Coronary Syndromes
<b>BMI</b>	Body Mass Index
<b>BP</b>	Blood Pressure
<b>CHF</b>	Chronic Heart Failure
<b>CI</b>	Coronary Interventions
<b>CT</b>	Computed Tomography, or CAT Scan
<b>CV</b>	Cardiovascular
<b>CVD</b>	Cardiovascular Disease
<b>DNA</b>	Deoxyribonucleic acid
<b>HCD</b>	Health Care Delivery
<b>HIV</b>	Human immunodeficiency virus
<b>ICD</b>	International Statistical Classification of Diseases and Related Health Problems
<b>IFG</b>	Impaired fasting glucose
<b>IGT</b>	Impaired glucose tolerance
<b>IMT</b>	Intima-Media Thickness
<b>LV</b>	Left Ventricular
<b>MI</b>	Myocardial Infarction
<b>non-STEMI</b>	non ST Segment Elevation Myocardial Infarction
<b>MTHFR</b>	Methylene Tetrahydrofolate Reductase
<b>PET</b>	Positron Emission Tomography

# Abbreviations and Acronyms

## Medical Terms and miscellaneous

<b>SAN</b>	Storage Attached Network Array
<b>SOP</b>	Standard Operating Procedure
<b>STEMI</b>	ST Segment Elevation Myocardial Infarction

## Study Acronyms

<b>ACADRE</b>	Aboriginal Capacity and Development Research Environments
<b>ACCORD</b>	Action to Control Cardiovascular Risk in Diabetes
<b>ACTIVE</b>	Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events
<b>ASPIRE</b>	Arixtra Study in Percutaneous coronary Intervention: a Randomized Evaluation
<b>ASSERT</b>	The Asymptomatic Atrial Fibrillation and Stroke Evaluation in Pacemaker Patients and the AF Reduction Atrial Pacing Trial
<b>BRAVER</b>	Brachial Artery Vascular Endothelium Reactivity
<b>CHARM</b>	Candesartan Cilexetil in Heart Failure Assessment of Reduction in Mortality and Morbidity
<b>CIDS</b>	Canadian Implantable Defibrillator Study
<b>CORONARY</b>	CABG Off or On pump Revascularization study
<b>COURAGE</b>	Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation
<b>CREATE</b>	Clinical trial of Reviparin and metabolic modulation in Acute myocardial infarction Treatment Evaluation
<b>CTOPP</b>	Canadian Trial of Physiological Pacing
<b>CURE</b>	Clopidogrel in Unstable angina to prevent Recurrent Events
<b>DINAMIT</b>	Defibrillators in Acute Myocardial Infarction Trial
<b>DREAM</b>	Diabetes Reduction Assessment with ramipril and rosiglitazone Medication
<b>Epicard</b>	Role of Epicardial adipose tissue In Coronary Artery Disease
<b>Epi-DREAM</b>	Epidemiologic Prospective Study of DREAM Screeners
<b>EXERT</b>	Exercise Rehabilitation Trial
<b>FAMILY</b>	Family-based Atherosclerosis Monitoring in early life Study
<b>FATE</b>	Firefighters And Their Endothelium
<b>GRACE</b>	Glucose Reduction in Atherosclerosis Continuing Evaluation
<b>HART</b>	Homocysteine lowering and Atherosclerosis Reduction Trial
<b>HOPE</b>	Heart Outcomes Prevention Evaluation
<b>I-PACE</b>	Irbesartan Pacemaker Study
<b>I-PRESERVE</b>	Irbesartan in heart failure with preserved systolic function
<b>MARGAUX</b>	Modulation of Arterial Reactivity Using Amlodipine and Atorvastatin by Ultrasound
<b>MICRO-HOPE</b>	Microalbuminuria, Cardiovascular and Renal Outcomes HOPE substudy
<b>MoL-SHARE</b>	MOlecular Study of Health Assessment and Risk in Ethnic groups
<b>OASIS</b>	Organization to Assess Ischemic Syndromes
<b>ONTARGET</b>	ONgoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial
<b>OPTIC</b>	The Optimal Pharmacologic Therapy in Implantable Cardioverter Defibrillator Patients
<b>ORIGIN</b>	Outcome Reduction with Initial Glargine Intervention
<b>PCI CURE</b>	Percutaneous Coronary Intervention in the CURE trial
<b>POISE</b>	Perioperative Ischemic Evaluation
<b>PURE</b>	Prospective Urban and Rural Epidemiologic Study
<b>RAAFT</b>	Radiofrequency Ablation version Antiarrhythmic Drugs for Prevention of Atrial Fibrillation
<b>RE-LY</b>	Randomized Evaluation of Long term anticoagulant therapy
<b>RESOLVD</b>	Randomized Evaluation of Strategies for Left Ventricular Dysfunction
<b>SECURE</b>	Study to Evaluate Carotid Ultrasound changes in patients treated with Ramipril and vitamin E)
<b>SHARE</b>	Study of Health Assessment and Risk Evaluation
<b>SHARE-AP</b>	Study of Health Assessment and Risk Evaluation in Aboriginal Peoples
<b>SOCCER</b>	State of Obesity Care in Canada Evaluation Registry
<b>STARR</b>	Study of Atherosclerosis with Ramipril and Rosiglitazone
<b>TIMACS</b>	TIMing of intervention in patients with Acute Coronary Syndromes
<b>TRANSCEND</b>	Telmisartan Randomized Assessment Study in ACE intolerant subjects with cardiovascular Disease.
<b>TRIM</b>	Telmisartan in the Reduction of Intra-Myocardial Lipids
<b>WAVE</b>	Warfarin and Antiplatelet Vascular Evaluation
<b>X-SOLVD</b>	EXtended Study Of Left Ventricular Dysfunction



## Abbreviations and Acronyms



## The Cardiac, Vascular and Stroke Research Institute



### CVSRI Vision

To provide an integrated environment where knowledge flows between basic research, clinical research and clinical care, leading to better education and clinical outcomes and improved health of the populations.

Hamilton Health Sciences is an international leader in cardiac, vascular and stroke research. In order to continue pioneering research related to these global health issues, Hamilton Health Sciences is committed to developing a new 165,000 square foot institute dedicated to furthering research in these areas.

The Cardiac, Vascular and Stroke Research Institute (CVSRI) will integrate two of Hamilton Health Sciences' strongest and most innovative research programs: the Population Health Research Institute (located at the Hamilton General Hospital) and the Henderson Research Centre (HRC, currently located at the Henderson General Hospital). This will allow for the development and expansion of these programs, while further capitalizing on the synergies that have already been established between them, and those that have yet to be explored. The CVSRI will unite existing clusters of scientists in one collaborative and integrated program, bringing together about 400 research personnel under one roof. This will further enhance collaborative research using different disciplines from the bench, to the bedside, to the population.

### Future site of the CVSRI



### The Cardiac, Vascular and Stroke Research Institute

The CVSRI will be a state-of-the-art facility, catering to a diverse and multi/interdisciplinary research program. This six-level building will be located next to the Hamilton General Hospital, - an acute care hospital and the regional trauma centre for central south Ontario.

The CVSRI will contain wet labs, a vivarium, research office space and integrated break-out space to encourage collaboration. It's proximity to Hamilton Health Sciences' biobank and Clinical Trials Research and Proteomics Laboratory will be advantageous because these provide one of the country's largest collections of specimens including blood, serum, plasma and cells, and the capacity for high throughput analysis.

Site preparation for the building is scheduled to begin in the fall of 2006; construction will proceed in stages, with initial occupancy in mid-2008 and all areas being open by December 2009.

Vision for the Future



Artist's rendering of the CVSRI to be constructed at the Hamilton General Hospital site (courtesy of Parkin Architects Limited).

#### **Creating synergies between two innovative programs**

Dr. Salim Yusuf, Director of the PHRI, and Dr. Jeffrey Weitz, Director of the HRC and leader of its Experimental Thrombosis and Atherosclerosis Program, are both internationally recognized in their respective fields. Together, they will provide and build a strong foundation for new research at the CVSRI. Dr. Weitz is an internationally recognized hematologist whose research in thrombosis has contributed significantly to our understanding of how blood clots form and how best to prevent or treat them.

The CVSRI will bring these two research leaders and their teams together under one roof, creating numerous benefits and opportunities related to research and ultimately disease control. Since the clinical needs of patients often overlap, through better integration of existing services within the CVSRI, Hamilton Health Sciences will be able to develop clinical, educational and research components related to these critical areas of health care. A more collaborative environment will also enhance new knowledge and improve patient outcomes.

A critical mass of researchers studying at McMaster University will help to position and develop the CVSRI as a centre of excellence for research, mentorship and career opportunity. The

Institute will offer a collaborative work environment for scientists who are responsible for a combined annual project portfolio of over \$100 million per year.

#### **The Henderson Research Centre: leading the way in thrombosis research**

The HRC, which includes dry and wet laboratory space and a vivarium, has three main programs that span a research continuum from basic to clinical, including: vascular biology; clinical thromboembolism; and clinical trials methodology.

The Centre's Experimental Thrombosis and Atherosclerosis Group, which includes the vascular biology program, has a long track record of success in peer-reviewed and industry funding that will continue and expand. This program will move to the General site to further emphasize and galvanize research related to cardiovascular health and stroke. The research group is world-renowned for their work in thrombosis and is gaining national and international recognition for their work in atherosclerosis and cancer. Cancer-related research will continue to grow at the Henderson site, in partnership with the Juravinski Cancer Centre, while its vascular and thrombosis research programs will thrive at the new CVSRI at the Hamilton General Hospital site.

"By combining two very strong and innovative groups, the new Institute will have the ability to rapidly explore innovative lines of research at multiple levels simultaneously; leading to new scientific discoveries and their application to help treat and prevent disease in populations."

- Dr. Salim Yusuf



Vision for the Future



## Help make something great even greater

Hamilton Health Sciences Foundation is proud to support the extraordinary research enterprise within the HHS family.

The Foundation invests more than \$1.5 million annually to support New Investigators Fellowships, Career Research Awards and critically important start up grants that drive the preliminary data collection and research that allows our people to compete for grants in the national and international arenas.

It is important to note that the Foundation is the conduit between generous donors and the research community. Our role at the Foundation is to help donors achieve their philanthropic goals through advancing research.

In addition to the philanthropic support donors offer annually, the Foundation has made a commitment to raise \$25 million to provide the community share of the new Hamilton Cardiac, Vascular and Stroke Research Institute. The Cornerstone of Care Campaign is well underway to raising an overall \$100 million to redevelop Hamilton Health Sciences (HHS). This campaign will transform the face of health care in our region – for today and tomorrow. Health care research in Hamilton is a significant and dynamic part of our economy. We are in a unique position; we have scientists and talent conducting extraordinary work in cramped and less than ideal conditions. We believe that by providing purpose-built space we will transform our research presence on the international stage.

Our redevelopment will signal a new commitment to research at HHS. It will allow us to attract the “best of class” young scientists. It will position us to better compete for national funding and will be a potent stimulus for the local economy.

But most important, it will advance the very essence of our work... delivery of patient care. Research defines the future of health care. Our hospital working hand-in-hand with a fully integrated research program allows our patients to benefit immediately from the new knowledge being generated here, and by research colleagues around the world.

The support of donors in the community is an enormous part of this vision. If we are to move our researchers and their programs forward – and keep them in Hamilton – we require the foresight of philanthropic leaders at an unprecedented level.

Your support will promise research discoveries that will change the way medicine is practiced here – and worldwide.

### **Michael Farrell, FAHP**

President and CEO  
Hamilton Health Sciences Foundation



**Michael Farrell, FAHP**

President and CEO  
Hamilton Health Sciences Foundation

# Contributing to PHRI's Vision





To contribute to the  
Population Health Research Institute's  
research vision, contact:

**Hamilton Health Sciences Foundation**  
P.O. Box 739, LCD 1  
Hamilton, Ontario, Canada L8N 3M8  
(905) 522-3863  
[www.hamiltonhealth.ca](http://www.hamiltonhealth.ca)

## Research at Hamilton Health Sciences

Hamilton Health Sciences is a family of five unique hospitals and a cancer centre, serving approximately 2.3 million residents of Hamilton, Central South and Central West Ontario. With an annual operating budget of more than one billion dollars and affiliations with McMaster University's Faculty of Health Sciences and St. Joseph's Healthcare Hamilton, Hamilton Health Sciences is one of Canada's largest academic teaching hospitals. Together, these institutions are home to several world-renowned research centres/institutes. These include: Population Health Research Institute; Henderson Research Centre; Offord Centre for Child Studies; Centre for Gene Therapeutics; Juravinski Cancer Centre; The Firestone Institute for Respiratory Health, The Brain and Body Institute and the Michael G. DeGroote Institute for Pain Research and Care. Through its close connection with McMaster University's Faculty of Health Sciences, Mohawk College and other post-secondary institutions, Hamilton Health Sciences offers an academic environment where patients benefit from innovative treatments and are cared for by some of the most talented medical professionals working and training in Canada.





*Health Through Knowledge*

**PHRI**

For more information on research at the  
Population Health Research Institute, contact:

**Population Health Research Institute**  
McMaster Clinic, Hamilton General Hospital  
237 Barton Street East  
Hamilton, Ontario, Canada L8L 2X2  
Local (905) 527-7327  
Toll Free: 1-800-263-9428 (North America only)  
[phri@ccc.mcmaster.ca](mailto:phri@ccc.mcmaster.ca) [www.phri.ca](http://www.phri.ca)

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The Population Health Research Institute is affiliated with the academic teaching hospital of Hamilton Health Sciences and McMaster University's Faculty of Health Sciences. For more information on these institutions, contact:



**Office of Integrated  
Research Services**

**Office of Integrated Research Services**  
Hamilton Health Sciences  
1057 Main Street West, Suite 1  
Hamilton, Ontario, Canada L8S 1B7  
(905) 521-2100 ext. 74595  
[www.hamiltonhealthsciences.ca](http://www.hamiltonhealthsciences.ca)



**Committee on Scientific Development**  
McMaster University, Faculty of Health Sciences  
1200 Main Street West, HSC-1B7  
Hamilton, Ontario, Canada L8N 3Z5  
(905) 525-9140 ext. 22258  
[www.fhs.mcmaster.ca/csd](http://www.fhs.mcmaster.ca/csd)