



CIHR IRSC

Canadian Institutes of Health Research Instituts de recherche en santé du Canada

Strategy for Patient-Oriented Research

A discussion paper for a 10-year plan to change health care
using the levers of research

February 2010

STRATEGY FOR PATIENT-ORIENTED RESEARCH

Canadian Institutes of Health Research
160 Elgin Street, 9th Floor
Address Locator 4809A
Ottawa, Ontario K1A 0W9 Canada
www.cihr-irsc.gc.ca

Also available on the Web in PDF and HTML formats
© Her Majesty the Queen in Right of Canada (2010)

STRATEGY FOR PATIENT-ORIENTED RESEARCH

Table of Contents

EXECUTIVE SUMMARY	4
STRATEGY FOR PATIENT-ORIENTED RESEARCH	6
Purpose	6
Introduction	6
What is patient-oriented research?	7
Why is patient-oriented research important?	8
PART I: THE PROBLEM	8
Threats to Canada’s competitiveness and capacity in patient-oriented research	10
How other countries have responded to competitive threats to patient-oriented research	16
Canada’s competitive advantages in patient-oriented research	17
Summary	18
PART II: THE STRATEGY	18
Overall goal of the Strategy	18
Component 1: Research environment and infrastructure: a matrix model	19
Component 2: Developing human capacity for patient-oriented research	22
Component 3: Strengthening organizational, regulatory and financial support for clinical trials	23
Component 4: Identifying and promoting use of best practices in health care	23
Coordination and governance	24
CONCLUSIONS	25
REFERENCES	26

STRATEGY FOR PATIENT-ORIENTED RESEARCH

President's Advisory Board, Strategy for Patient-Oriented Research

Sally Brown, RN, MHS

CEO, Heart and Stroke Foundation of Canada

Krista Connell, BPT, MHSA

CEO, Nova Scotia Health Research Foundation

Catriona McMahon, MD

VP, Medical Affairs, Astra Zeneca.

Roger Palmer, PhD

Director, Public Management, University of Alberta

Brian Postl, MD

President and CEO, Winnipeg Regional Health Authority

Dorothy Pringle, RN, PhD

Former Dean of Nursing, University of Toronto; Executive Lead, Ontario Ministry of Health and Long Term Care Initiative, Health Outcomes for Better Information and Care (HOBIC)

Sarah Pritchard, MD

VP, Global Medical Affairs, Baxter Healthcare International

Jean Rouleau, MD

Dean, Faculty of Medicine, University of Montreal

Arthur Slutsky, MD

VP, Research, St Michael's Hospital, Toronto

Aubrey Tingle, MD

Past President and CEO, Michael Smith Foundation for Health Research

Susan Zimmerman, LLB, LLM

Executive Director, Interagency Secretariat on Research Ethics, Tri-Council Initiative

Strategy for Patient-Oriented Research

Paul Hébert, MD

Strategic Lead and Special Advisor to the President, CIHR

Joe Pater, MD

Advisor

Sue Geffken-Graham, MPH

Assistant Director, Strategy for Patient-Oriented Research

STRATEGY FOR PATIENT-ORIENTED RESEARCH

EXECUTIVE SUMMARY

Objectives

This discussion paper drafted by the Canadian Institutes of Health Research (CIHR) proposes the following nationwide Strategy for Patient-Oriented Research as a broad outline for consultation. Patient-oriented research refers to the continuum ranging from the initial human studies of a new drug or device to research evaluating the implementation of simple or complex interventions in the health-care system. The proposed Strategy includes the evaluation of new and current diagnostic approaches, treatments, devices and practices (often referred to as clinical research), as well as the synthesis, dissemination and integration of this new knowledge into the health-care system. A major focus will be to compare new discoveries with existing therapies to determine which interventions are most beneficial.

Canada must increase its investments and better coordinate its efforts in patient-oriented research to improve the quality, accessibility and cost-effectiveness of its health-care system. However, the success of the Strategy depends not only on the support of the federal government, but also on widespread buy-in from major stakeholders including research institutions (universities, hospitals, community centres), clinician scientists, the private and charitable sectors and provincial and territorial governments.

The proposed Strategy has four major components:

- improve the research environment and infrastructure;
- set up mechanisms to better train and mentor health professionals and non-clinicians;
- strengthen organizational, regulatory and financial support for multi-site studies; and
- support best practices in health care.

Context

Health professionals and consumers want evidence-based care. Governments also want health-care systems that are financially sustainable and cost-effective. However, evidence comparing different approaches is either lacking or not used by practitioners or decision makers. This results in overuse and underuse of drugs, diagnostic tests, surgical procedures and preventive health measures. Without high-quality evidence comparing effectiveness, it is difficult to establish guidelines and, ultimately, implement best care practices. Patient-oriented research and its effective dissemination is a key element towards these goals.

There are several factors contributing to the lack of a sustained Canadian momentum in patient-oriented research. These factors include the lack of an overall vision and priorities, insufficient financial support, inadequate clinician-researcher training, mentorship and career support, declining private-sector investments, and important systemic barriers that delay and impede research efforts involving patients.

Yet, Canada possesses significant strengths in patient-oriented research which, if properly harnessed, could significantly increase its international competitiveness in the field. These strengths include: 1) a highly qualified workforce and high-quality health-care system and research environment; 2) a unique competence in systematic reviews; 3) a record of research breakthroughs and high-impact clinical studies; and 4) population-based administrative databases as a basis for research.

Strategy for Patient-Oriented Research

The proposed Strategy comprises four major components:

STRATEGY FOR PATIENT-ORIENTED RESEARCH

(1) Improve research environment and infrastructure

The first component is the creation of patient-oriented research units and networks. We suggest that a key to success will be to build upon existing clinical research excellence and develop new Support for People and Patient-Oriented Research and Trials (SUPPORT) units integrated with health care. Each unit will offer core services to a region's health system to support research excellence. Each SUPPORT unit will be expected to:

- support leading-edge patient-oriented researchers and programs;
- educate and support health-care professionals interested in evaluating the quality, accessibility and cost-effectiveness of care and developing new research programs; and
- implement the standards for research involving research participants.

SUPPORT units will provide a multidisciplinary team of health-care professionals, methodologists, biostatisticians, social scientists and data managers to help investigators design relevant research (including observational and interventional studies), conduct statistical analyses, manage data and meet regulatory standards. Most importantly, all SUPPORT units will be integrated into clinical or care settings to be readily accessible to support a wide spectrum of research and knowledge translation activities.

To further enhance the research environment and infrastructure, the Strategy also proposes to create multidisciplinary patient-oriented research networks to bridge SUPPORT units across thematic areas such as mental health, primary health care and chronic disease management. The purpose of these networks is to:

- link multidisciplinary scientific expertise along a theme of research;
- develop major multicentre projects and programs of thematic research;
- offer mentorship to young researchers; and
- assist in the oversight of research.

(2) Set up mechanisms to better train and mentor health professionals and non-clinicians

The second component of the Strategy is to initiate more health-care professionals in the core methods of clinical research and provide training support for clinical epidemiologists, biostatisticians, methodologists and health economists to improve our research and leadership capacity nationwide. Support will also be provided to develop training programs for research coordinators, project managers and other support personnel. Career training and salary awards programs will be designed to build capacity in patient-oriented research within SUPPORT units.

(3) Strengthen organizational, regulatory and financial support for multi-site studies

The third component of the Strategy is to eliminate systemic barriers that produce inefficiencies in the development and implementation of patient-oriented research such as significant delays created by complex multicentre ethics review processes. We will therefore work with our partners to harmonize the review of applications to shorten the approval process. Similarly, the Strategy will lead the development of a template and guidance document for industry-academic contracts.

(4) Support best practices in health care

The fourth component of the Strategy aims at teaming guideline developers with health-care professionals to promote the rigorous development of high-quality, evidence-informed practice guidelines and encourage policy-makers, institutions, health-care professionals and consumers to adopt them. By linking guideline developers and other stakeholders involved in patient-oriented research activities, Canada will be uniquely positioned to improve the breadth and quality of its guidelines and their impact on health outcomes.

STRATEGY FOR PATIENT-ORIENTED RESEARCH

STRATEGY FOR PATIENT-ORIENTED RESEARCH

Purpose

This discussion paper opens a new dialogue between CIHR and its partners across Canada on how best to support and invest in patient-oriented research. It outlines the underlying rationale and proposes a strategy to improve health care via patient-oriented research. We propose to partner with all stakeholders – the provinces, the private sector, health charities, universities and research institutes, scientists and, above all, health-care professionals who deliver care – to better target and coordinate investments in research and to break down barriers to conducting and applying patient-oriented research. Our aim is to transfer research and scientific evidence into health-care practice and thereby improve the health of Canadians. Our premise is that greater integration of research-based evidence will improve Canadians' health and Canada's health-care system.

Introduction

Research focused on patients and other users of health services is the cornerstone of evidence-based health care, a modern construct of clinical care largely pioneered in Canada.¹ While science has provided the underpinning for the application of health interventions, comparative evaluations of those interventions that provide guidance as to when and on which patients to apply them has lagged. The delivery of high-quality, timely and appropriate care requires an understanding of:

- what puts an individual at risk of disease (including understanding genetic predisposition, novel biomarkers and social determinants of health);
- how best to make a diagnosis;
- the patient's prognosis for a given condition;
- the optimal choices of therapies and patient-care strategies; and
- how best to facilitate the use of best practices by the health system, health-care professionals, patients and the public.

Health-care professionals and policy-makers need evidence on how to deliver the best care in a cost-effective manner. This requires efficient translation of research innovations from bench to the bedside. It also calls for the evaluation and synthesis of existing knowledge and proper implementation of clinical research findings. For instance, the use of a simple 19-item checklist developed by the World Health Organization has significantly decreased deaths and complications in routine elective surgeries.²

To achieve transformative changes aimed at improving health through research, we propose a strategy to:

- improve the Canadian research environment and infrastructure for patient-oriented research along the entire continuum of health interventions and care;
- set up mechanisms to better train and mentor health-care professionals and others engaged in research through the creation of sustainable patient-oriented career paths;

STRATEGY FOR PATIENT-ORIENTED RESEARCH

- break down bureaucratic barriers to patient-oriented research by strengthening the organizational, oversight and financial support for clinical studies; and
- develop processes for supporting the identification, development and application of best-practice guidelines in health care.

We propose to achieve these goals by building partnerships with research institutions and universities, provinces and territories, health charities, the private sector and several departments and agencies of the federal government including Health Canada, the Public Health Agency of Canada and Industry Canada.

What is patient-oriented research?

Patient-oriented research refers to a continuum of research ranging from the initial human studies of a new drug or device (“first-in-patient”) to research that evaluates the implementation of interventions in the health-care system. The term therefore includes the evaluation of new and current diagnostic approaches, treatments, devices or practices (often referred to as clinical research), as well as the synthesis, dissemination and integration of this new knowledge into the health-care system. A major focus of patient-oriented research is comparing new discoveries with existing therapies (Fig. 1, right box) to determine which interventions are most beneficial as part of usual care (effectiveness or pragmatic trials). Comparative effectiveness research complements studies designed to demonstrate the efficacy and safety of new drugs or devices prior to their initial use in clinical practice (Fig. 1, left box). Patient-oriented research can be conducted by clinician researchers from all health-care professions (e.g., nursing, medicine, chiropractic, pharmacy and all other allied health professions) as well as non-clinicians who conduct applied health research (e.g., clinical epidemiologists, biostatisticians, health economists, anthropologists, sociologists, social and behavioural scientists and biomedical scientists). Patient-oriented research can be undertaken in all settings including the community (including primary and long-term care) and hospital settings (tertiary care).

Figure 1: Developing versus comparing therapies

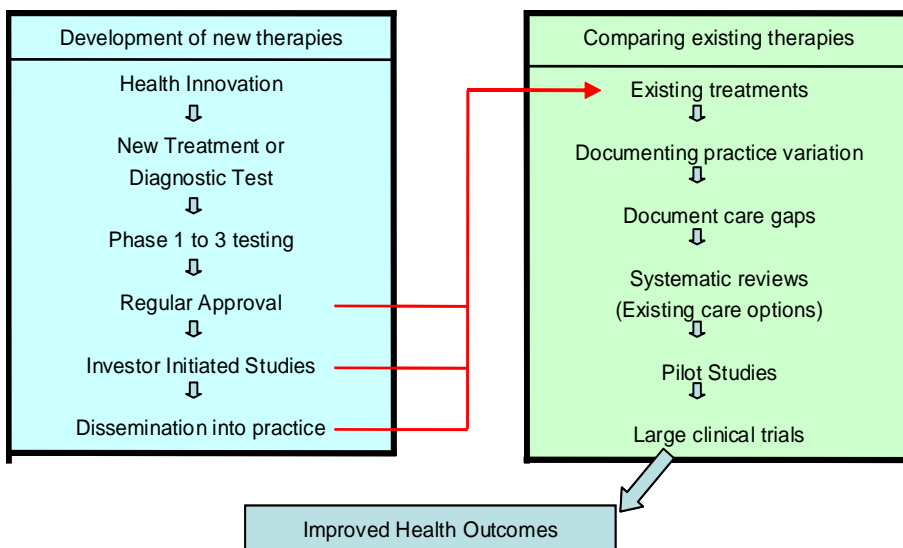


Figure 1: This figure shows a simplified schematic of the chain of steps before a drug or device is proven to save lives or decrease morbidity. The many steps often take 15 to 20 years for new interventions and five to seven years if comparing existing therapies.

STRATEGY FOR PATIENT-ORIENTED RESEARCH

Why is patient-oriented research important?

Better health for Canadians

Investments in health research have led to the development of a vast array of preventive, diagnostic and treatment interventions for health. But the use of interventions such as drugs, procedures and public health measures often varies dramatically among and between different health-care professionals and institutions. Without high-quality evidence on comparative effectiveness, it is difficult to establish guidelines for appropriate care. This lack of evidence may be one of the major drivers for variations in care.³⁻⁸ Indeed, several studies⁹⁻¹¹ have demonstrated that less than 60% of bedside decisions on general medical services have the support of the required level of evidence. Consumers and health-care professionals have a right to expect that important health decisions are made on the basis of solid science.

We believe that participation in integrated research programs should become part of the fabric of health care in Canada. Patients treated in institutions that are actively involved in research have better health outcomes.^{12, 13} Creating this culture of enquiry within our health-care system – in and of itself – will benefit the Canadian population.

Economic benefits and sustainability of Canada's health-care system

Patient-oriented research establishes not only which new discoveries should be brought to market but also compares new discoveries with existing therapies, providing information on outcome and cost effectiveness. In doing so, it generates new knowledge that may have important economic dividends. Other jurisdictions have recognized the importance of research to underpin system sustainability. The Obama administration recently invested in comparative evaluations as a means of improving care and minimizing costs in the American health-care system. They argue that savings from research will offset the costs of health reform.¹⁴ In the United Kingdom, where large comparative studies were developed, this same rationale is used to inform health decisions for the National Health Service. This premise is, in large part, the basis for the mandate of the UK National Institute for Health Research,¹⁵ for whom 53% of investment in research and development is targeted specifically at the infrastructure for clinical studies and systems research.¹⁶ In short, patient-oriented research is not only important for health-care professionals, it also provides evidence for health funders so that resources may be allocated to the most effective interventions and diagnostic procedures.

PART I: THE PROBLEM

Despite some measure of success – most notably in cardiovascular care,^{17, 18} critical care,¹⁹ stroke,²⁰ HIV,²¹ care of pre-term infants,²² pain management,²³ and oncology²⁴ – Canada is rapidly falling behind other industrial countries in terms of capacity to undertake patient-oriented research. For the reasons outlined below, within the next few years we will not be able to generate the evidence to address key sustainability questions in areas such as mental health, primary health care and chronic disease management. Failing new action, Canada will also rapidly lose its competitive advantage in developing novel therapies and evaluating them in patients.

Clinical research networks organized along thematic lines (e.g., the NCIC Clinical Trials Group,²⁵ the HIV Clinical Trials Group²⁶ and the Canadian Critical Care Trials Group²⁷) have led to publications in high-

STRATEGY FOR PATIENT-ORIENTED RESEARCH

profile journals and, in some instances, have affected health-care practice in Canada. These networks, however, are limited to a few diseases. As well, while significant increases in Canadian health research investments over the past 10 years have resulted in biomedical discoveries and advances, there has been limited uptake of these research results into clinical practice.

Although there have been some successes, two major concerns have arisen:

- Investment in research is uneven and does not always reflect the priorities important to Canadians, burden of illness, costs to the system or expertise among Canadian researchers.
- There is limited accountability and evaluation of ongoing relevance/importance of research programs and no uniform standards.

Canada faces a dual challenge in the knowledge translation continuum referred to as the two “Death Valleys” (Fig. 2). Knowledge translation involves facilitating the use of research findings and innovations including the commercialization of discoveries. Valley 1 refers to the decreasing capacity to translate the results of basic research to the bedside, as well as capacity to successfully commercialize our health discoveries. Valley 2 refers to the limited capacity to synthesize, disseminate and integrate research results into clinical practice. These two valleys must be bridged if Canada is to bring evidence to bear to encourage a sustainable health-care system and to enhance our ability to commercialize discoveries and innovations derived from research.²⁸

Figure 2: The two “Death Valleys” of the clinical translational continuum

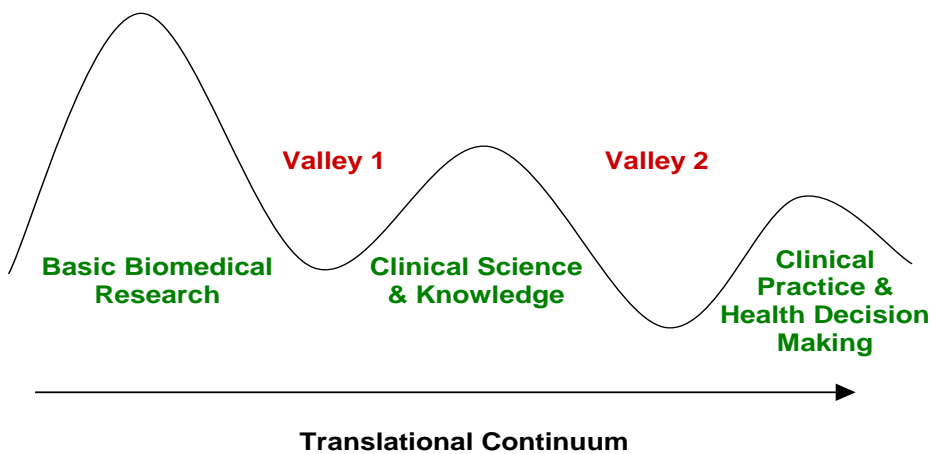


Figure 2: This figure illustrates the points at which Canada experiences decreased capacity to translate research results to the next stage, affecting, first, our ability to commercialize research results (Valley 1), and, second, our effectiveness at moving results into clinical practice (Valley 2) *Figure from Steven Reis, University of Pittsburgh and Harold Pincus, Columbia University.*

STRATEGY FOR PATIENT-ORIENTED RESEARCH

Threats to Canada's competitiveness and capacity in patient-oriented research

Six major CIHR-commissioned reports on clinical research²⁹⁻³⁴ have emphasized that Canada has significant deficits in the leadership and coordination of patient-oriented research efforts, especially clinical studies. At present, patient-oriented research investments are scattered. While based on excellent proposals, few investments reflect an overall strategy or established, agreed-upon priorities. Less than 6% of Canadian publications from CIHR-funded health research present the results from clinical studies – despite the potential enormous impact of such publications on clinical care.

All of these clinical research surveys³⁵ reveal major challenges and structural barriers to the sustainability and growth of patient-oriented research. These challenges include requirements for complex and multiple ethics reviews and contract processes, shortages of health-care professionals engaged in research and the lack of an overall nationwide strategy. There are also deficits in:

- financial support;
- infrastructure;
- training and career support;
- governance and coordination; and
- private sector investments.

Financial support

Patient-oriented research is underfunded in Canada, with approximately 6% (\$60 million) of the current CIHR budget devoted to it. On a per capita basis, CIHR's investments in health research overall are markedly lower than those made by the US National Institutes of Health, the UK National Institute of Health Research or Australia's National Health and Medical Research Council (Fig. 3).

Figure 3. Comparative international spending in health research

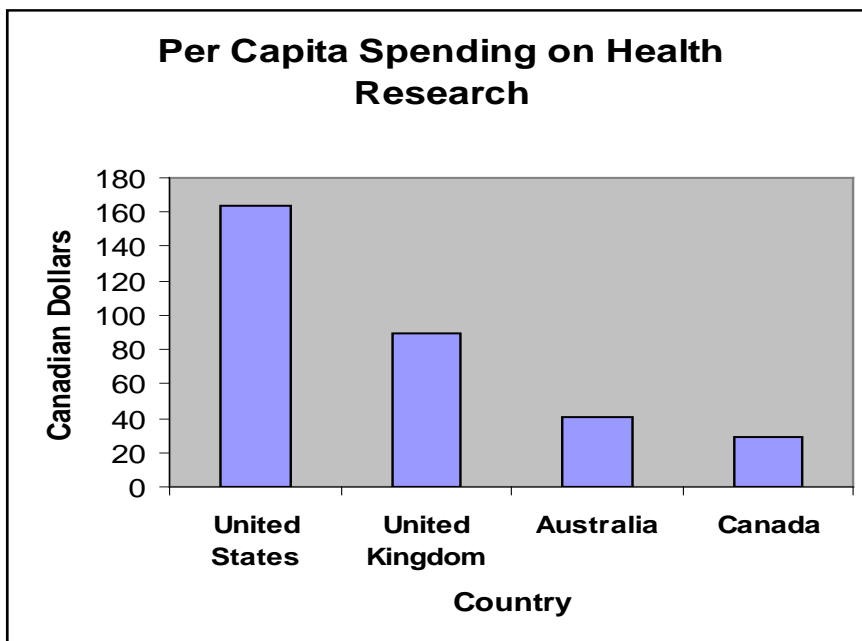


Figure 3: This figure compares the per capita spending on health research for the United States, United Kingdom, Australia and Canada. All figures are based on estimated budgets for 2010-11, converted to Canadian dollars. Data for the United Kingdom includes spending by the Medical Research Council, National Institute of Health Research and Wellcome Trust.

STRATEGY FOR PATIENT-ORIENTED RESEARCH

In any given year, half of the \$60 million that CIHR invests in patient-oriented research supports approximately 25 small- to medium-sized clinical trials. It is difficult, however, to publicly fund large multi-site studies because they have become much more expensive due to additional rules governing research and increased administrative requirements.³⁵ Yet, there is a growing need to conduct intervention studies that are large enough to address important clinical issues and undertake observational research projects that can identify health gaps across many centres. These studies involve large numbers of patients who receive health-care services in many settings across the country and beyond. The results from such trials provide the basis for firm recommendations about patient diagnosis, prognosis and treatment. Because of the ever-increasing costs and limited public funds, prospective investigators must identify a combination of potential private sector partners, public agencies and charities to assemble the required funds for major projects. This process can take several years, even for practice-changing research.

This tight funding situation has been compounded recently by a decrease in indirect financial support from the university and hospital sectors. University departments traditionally have supported salaries and protected time for research, while hospitals have allowed researchers the use of clinical laboratories and diagnostic tests. However, because of budgetary constraints in all provinces and territories, institutions have moved to a cost-recovery approach. Equipment, facilities and personnel are no longer available to clinical researchers without funding to reimburse the institutions, thereby reducing the capacity to conduct patient-oriented research.

Although the most serious threat to the sustainability of patient-oriented activities is the limited amount invested in it, the lack of investment in areas of high disease burden is also a major concern. Historically, Canada has invested research dollars in areas of excellence, but not nearly as significantly in areas such as mental health, primary health care or on complex chronic diseases such as diabetes and cancer care.

Infrastructure

Lack of standardized technology platforms is an important infrastructure concern. Some world-class observational databases are already in place in parts of Canada. Electronic data-capture tools facilitate data collection. They allow the sharing of project-based information within networks, the coordination of research activities and the implementation of common standards, as well as easy measurements of outcomes. In addition, these electronic platforms can link to electronic medical records. Developing and linking these platforms will be essential for the success of the Strategy for Patient-Oriented Research. We must seek to provide accurate, broad-based data and timely clinical information along the entire continuum of care. Such information is essential in the early phases of patient-oriented research programs. New investment in the Drug Safety and Effectiveness Network, which introduces post-market monitoring and evaluation of drugs, is a welcome step in extending the evidence base across the continuum of care.

Training and career support

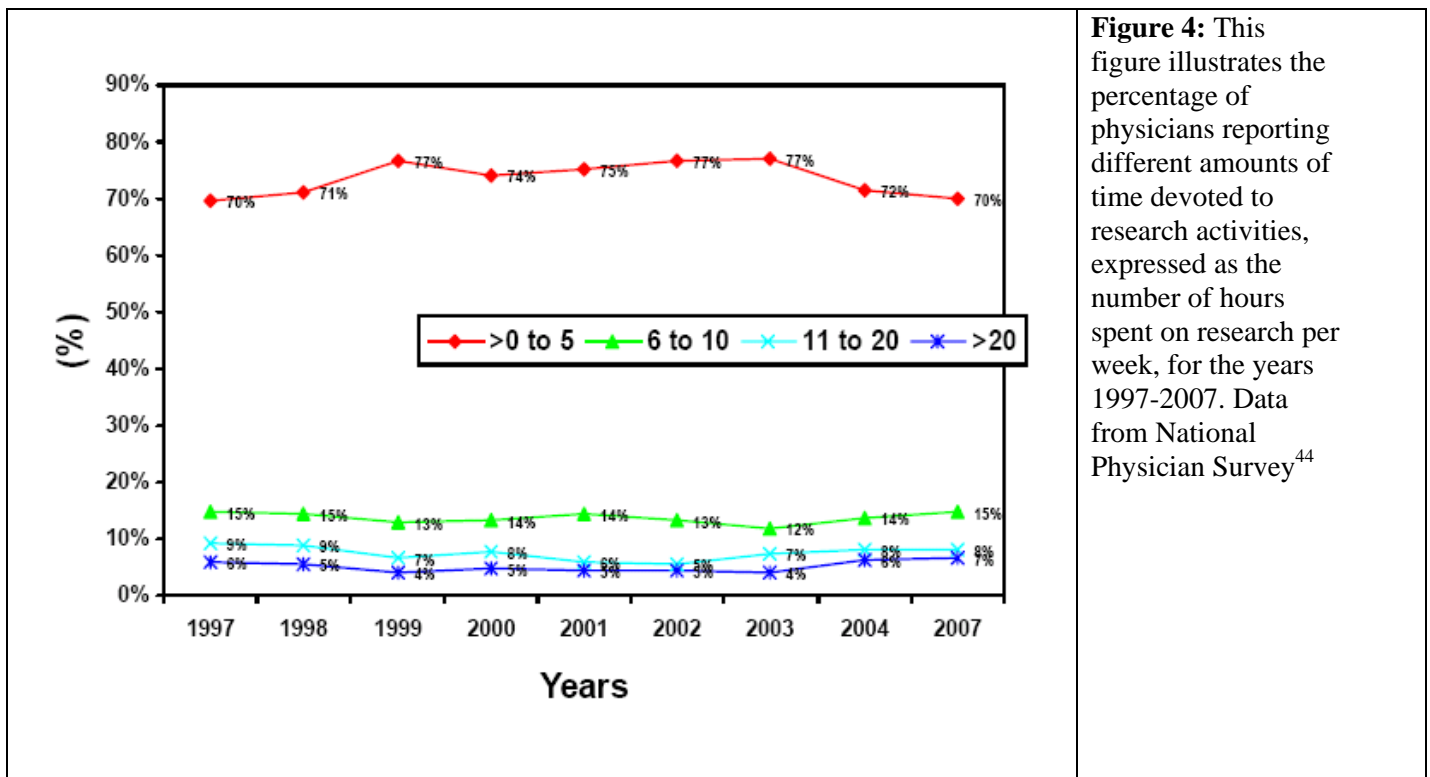
An ideal patient-oriented research scenario should provide technical and methodological support as well as a nurturing, mentoring environment for basic and advanced training. For clinical researchers to thrive, a supportive environment is essential.³⁶⁻⁴¹ Supranational organizations, including the Global Forum for Health Research⁴² and the World Health Organization⁴³ have also emphasized the importance of the research environment.

STRATEGY FOR PATIENT-ORIENTED RESEARCH

Although patient-oriented research centres exist across Canada, few programs support core staff and multidisciplinary teams. The clinical research workforce has not grown since CIHR's creation in 2000, with obvious shortages of biostatisticians, health economists, clinical epidemiologists, social scientists, research nurses and support staff such as trained project coordinators and research assistants. This lack of support for health-care professionals to develop and maintain research careers is a serious threat to patient-oriented research. Without these highly qualified people, patient-oriented research centres cannot offer the necessary support to the local community of health-care professionals and researchers, assist in developing local themes of excellence, and participate in nationwide research efforts. Nor can they coordinate local activities and recruit additional patients in clinical studies.

The next generation of research leaders needs training, support and mentorship. Their research commitment, however, is frequently overwhelmed by clinical and teaching duties because of severe shortages of health-care professionals. Despite CIHR and provincial efforts to address this reality, many reports²⁹⁻³⁴ concur that Canada has failed to adequately deal with this shortage of clinicians in research. In our early consultations with leaders in the research community, the need for non-clinical research staff was repeatedly mentioned as an important threat to the sustainability and growth of patient-oriented research. According to the latest national survey of the Canadian Medical Association, only 4% to 7% of physicians report participating in research more than 20 hours per week. This proportion has remained constant over the last 10 years despite important increases in health research spending from 2000 to 2007⁴⁴ (Fig. 4).

Figure 4. Percentage of all physicians reporting hours of work (hours/week)



STRATEGY FOR PATIENT-ORIENTED RESEARCH

The barriers that prevent physicians from initiating a career in research include:

- few mentors or successful role models;
- limited training opportunities;
- excessive debt loads from medical school;
- heavy clinical workload;
- lack of research time protection from division and department heads;
- poor first experience in research;
- lack of a team environment;
- lack of methodological support;
- inappropriate compensation; and
- lack of a performance-based practice plan that promotes academic success in research.²⁵⁻³⁰

Many of these concerns are not unique to physicians. Nurses, pharmacists, physiotherapists and other allied health professionals face barriers such as hiring practices that favour non-academic roles even in academic institutions, limited access to role models and training opportunities, a lack of support from institutional leaders, resource constraints and major staff shortages.

Data show no sign of an increase in the number of trainees and young health-care professionals entering research careers supported by either CIHR or provincial organizations. Whereas CIHR funding for biomedical scientists has increased by more than 50% over the last five years, its funding of physicians has shown a downward trend (Fig. 5). Similarly, provincial funding of physicians has not increased over the past five years (Fig. 6). Even fewer awards are made to nurses by either CIHR or the provinces, and this category shows a flat five-year trend (Fig. 5 and 6). Overall, while CIHR and the provinces have invested heavily in biomedical research, health-care professionals/clinicians have not seen the same level of support.

STRATEGY FOR PATIENT-ORIENTED RESEARCH

Figure 5. Total training and salary awards by CIHR

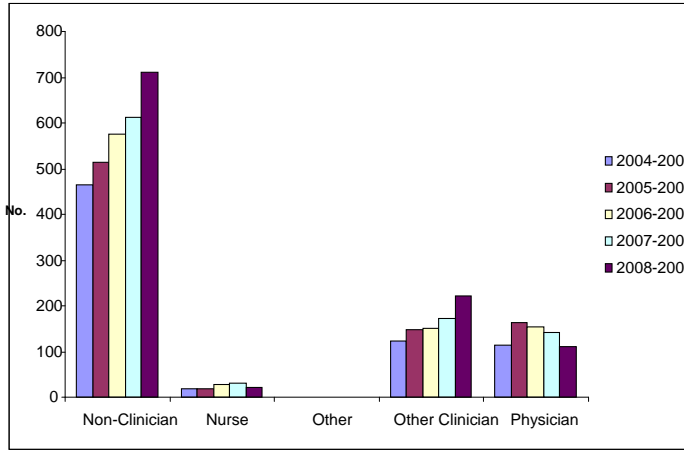
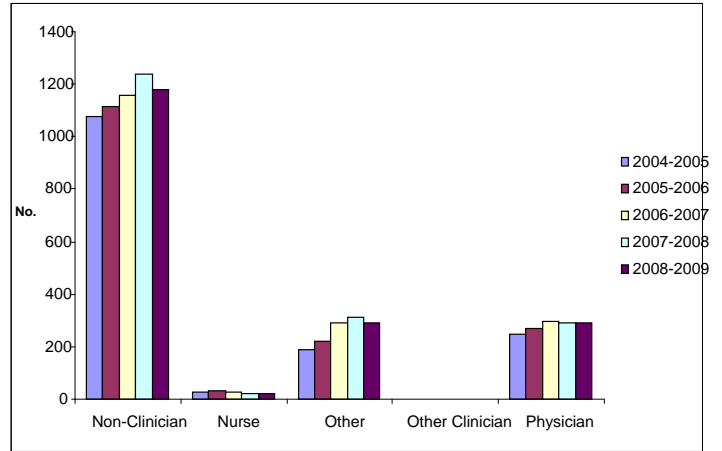


Figure 6. Total training and salary awards by provinces



Sources: (1) Provincial data from NAPPHRO; (2) Canada data from CIHR EIS

Figure 5: This figure contrasts the total number of annual training and salary awards CIHR gave to physicians, nurses and other clinical health-care professionals from fiscal 2004-2005 to fiscal 2008-2009 with those it gave to non-clinician researchers over the same period.

Figure 6: This figure contrasts the total number of annual training and salary awards the reporting provinces (Alberta, British Columbia, Manitoba, Nova Scotia, Ontario and Quebec) gave to physicians, nurses and other clinical health-care professionals with those they gave to non-clinician researchers from fiscal 2004-2005 to fiscal 2008-09.

Governance and coordination

Research programs in Canada are undertaken within the complex regulatory environment that governs the Canadian health-care system. Health is not a single matter assigned by the Canadian Constitution exclusively to one level of government. Multiple jurisdictions have overlapping responsibilities for the funding and regulation of health care. The federal government is responsible for health surveillance, drug regulation and major research programs. The provinces are responsible for planning and financing most health-care services and support the major institutions where patient-oriented research is conducted.

These multiple jurisdictions often make for suboptimal coordination of patient-oriented research, which leads to inefficiencies and under-performance. Most significantly, this ineffective governance structure has meant the absence of pan-Canadian standards. Such standards are critical because research increasingly crosses provincial boundaries. The impact of barriers created by increased regulations and inefficient reviews of ethics and contracts also should not be underestimated. Recent research shows that when guidelines are developed without the participation of researchers, the consequent regulatory burden has the effect of rendering prohibitive the academic research that such guidelines were intended to safeguard.^{45, 46}

STRATEGY FOR PATIENT-ORIENTED RESEARCH

Optimizing the application of best practices and knowledge from patient-oriented research requires seamless integration with all involved partners, various levels of government, charities, academic units, public health and industry. Given the multi-jurisdictional nature of the Canadian health-care system, this will require considerable coordination and cooperation.

Private sector investments

Canada has a strong track record of partnerships between academia and the pharmaceutical industry. The top 10 pharmaceutical companies spent more than \$1.3 billion in research and development in Canada in 2007. Of this amount, they spent \$600 million on clinical trials in Canada, accounting for 78% of their applied research expenditures.⁴⁷ As in other Western countries, however, Canada's growing barriers to enrolling patients and performing trials in a timely and cost-effective manner have led to a shift to conducting clinical trials in developing countries.³⁵ As a result, investments in clinical research and the overall investment in research and development in Canada by the pharmaceutical industry have flattened over the last five years⁴⁸ (Fig. 7).

Figure 7: Number of Clinical Trials between 2003 and 2007 in Canada led or sponsored by pharmaceutical industry

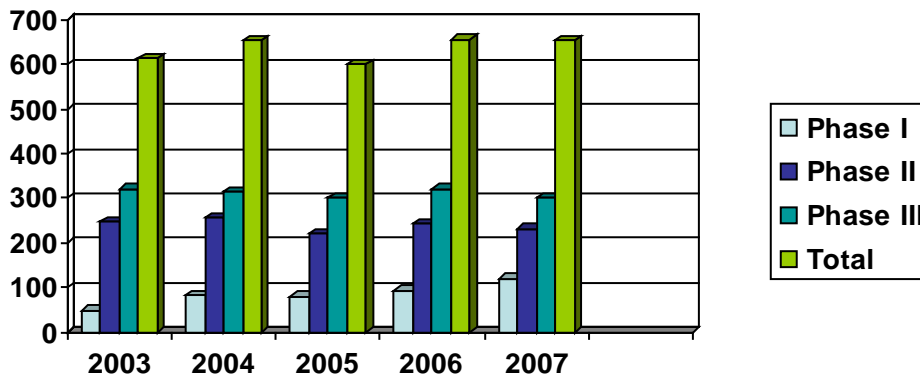


Figure 7: This figure illustrates the lack of growth in the number of industry-led clinical trials and equivalent lack of growth in investment in research, in Canada over the years 2003 to 2007.

Canada's position as a world leader in clinical research is threatened by serious competition from India, China, Brazil and Russia. These countries provide rapid access to large numbers of patients, while conducting research there costs 30% less than in Western nations. The potential to gain access to emerging markets is also quite attractive to industry. China's market, for example, is growing at a rate of 25% per year. The lack of intellectual property protection is no longer a barrier to conducting research in many developing countries. In addition, China and India are investing billions of dollars to provide the infrastructure, capabilities and training necessary to run clinical trials and attract industries. Canada's share of global clinical trials has consequently shrunk to 4.1%, representing an average relative annual growth decline of 12% and placing our country fourth after France, with 4.3%, and Germany, at 5.7%. The United States leads, with 49% of global trials.⁴⁹

STRATEGY FOR PATIENT-ORIENTED RESEARCH

The growth of multinational pharmaceutical companies' in-house research and development investments in Canada has also slowed since 1999 and is proportionately lower than in competitor countries, despite higher revenues. While the 2005 research and development investment by multinational pharmaceutical companies was at 19% of sales in the United States and 25% in the United Kingdom, it was only at 9% in Canada.

When therapies are developed and tested in Canada it ensures that we have first access to new drugs and technologies. It provides opportunities to train our health-care professionals in the use of these drugs and therapies, assists in their dissemination and generates economic benefits. Should the studies fail to show benefit, Canada is then in the best position to make decisions about limiting the use of those drugs and procedures. These investments and partnerships also assist in developing a culture of enquiry by constantly challenging existing approaches to patient care. Consequently, they foster a more knowledge-based workforce.

How other countries have responded to competitive threats to patient-oriented research

Canada is clearly losing ground relative to the investment of other countries in patient-oriented research, which has become a high priority in the United States,⁵⁰ the United Kingdom,⁵¹ Europe (Germany, France, Scandinavia, Italy),^{52, 53} and Australia.^{54, 55} Recognizing the importance of clinical research in securing their national health and international competitiveness, these countries have invested massively in rebuilding their clinical research enterprises to better capture the health benefits and economic potential of this important sector.

In 2002, the National Institutes of Health's (NIH) Roadmap identified the need to re-engineer the United States clinical research enterprise. In fiscal 2009, total Roadmap funding grew from \$496 million to \$534 million (as part of the overall \$9 billion NIH invests for clinical trials and other patient-oriented research), and from \$483 million in 2007. In addition to Roadmap funding, the NIH invested a further \$452.4 million in 2009 through two programs administered by the National Center for Research Resources: the General Clinical Research Centers and the Clinical and Translational Science Awards. The United States clinical research enterprise also benefited from investments of \$1 billion from the Department of Veterans' Affairs and \$330 million through the Agency for Healthcare Research and Quality, \$79 million of which was earmarked for patient safety research and \$400 million for clinical effectiveness research. (*Note: these figures are in US dollars.*)

Similarly, in 2003, the United Kingdom began reorganizing clinical research infrastructure to improve efficiency and break down the barriers. At the time, 300 independent National Health Service (NHS) trusts operated independently. This fragmentation made it extremely difficult to conduct multicentre trials. Individual decision-making authority, combined with unreliable recruitment, variations in data management and inconsistent training procedures, caused delays in study timelines and drove up costs. Based on the recommendations from several reports including *Research for Patient Benefit*⁵⁶ and a review of United Kingdom health research funding,⁵⁷ the government implemented two national initiatives to overcome these obstacles: the UK Clinical Research Collaboration and the UK Clinical Research Network (now known as the National Institute of Health Research CRN). The Collaboration is a partnership among the National Health Service, public and private research funders, industry, regulatory bodies, royal colleges, patients groups and academics. It oversees patient-oriented research at a national level. The NIHR Clinical Research Network coordinates eight research networks in England, working in close collaboration with similar

STRATEGY FOR PATIENT-ORIENTED RESEARCH

programs in Scotland, Wales and Ireland. Collectively, these networks cover six topic areas (neurodegenerative diseases, mental health, stroke, cancer, diabetes and medicines for children); primary care; and coordinating centres (which provide comprehensive support for the six topic networks and the primary care network).

The United Kingdom sought the pharmaceutical industry's input and involvement not only to develop common research contracts, but also to ensure research priorities would be aligned and responsive to the industry's needs. The United Kingdom has invested approximately \$2.7 billion in patient-oriented research in fiscal 2008-2009, with a \$179-million increase planned in each of the next two fiscal years.

Canada's competitive advantages in patient-oriented research

Despite serious challenges, Canada has competitive advantages that should allow it to excel on the world stage in the field of patient-oriented research. With leadership, the right level of financial support and creative integration, Canada's advantages can be exploited to ensure the quality and sustainability of our health-care system.

Canada's recognized competitive advantages include:

1. A highly qualified workforce trained in clinical epidemiology, evidence-based medicine and evidence-based practice. One estimate suggests Canada's clinical research workforce comprises 30,000 researchers and research support staff at 17 medical schools, 12 schools of rehabilitation, nine schools of pharmacy, 12 schools of dentistry, 35 university and degree-granting college nursing schools, and 100 teaching hospitals.⁴⁷ Well-trained clinicians and applied health researchers have been able to conduct and participate in groundbreaking studies that have been adopted by the health-care system.^{17-19, 21, 22, 24, 58}
2. Breakthrough publications in many fields.^{16, 17, 24, 47, 58}
3. Strengths in systematic reviews, gathered through Canada's participation in the Canadian Cochrane Centre and Network, including the Cochrane Effective Practice and Organization of Care group, the Canadian Association for Drugs and Technology in Health, and the Canadian Task Force on Preventive Health Care. Systematic reviews are an essential building block for evidence-based practice and a necessary step in the planning process of large comparative trials.
4. A high-quality health-care system and research environment. Since "usual care" is the comparator in clinical studies, high-quality and uniform care is desirable. Our universal system improves referral patterns into regional programs with higher volumes of cases. It also improves overall coordination of care and research, and access to research participants.
5. The availability of large provincial and Canadian population-based observational administrative and research databases. Academia and industry can use these databases to assess existing care patterns, make novel and important associations between interventions and outcomes, and observe practice variation and the burden of a given illness. This makes it possible to identify gaps in health care,

STRATEGY FOR PATIENT-ORIENTED RESEARCH

particularly in the use of treatment options, and highlight drug safety issues and variations in practice patterns.

6. A highly qualified biomedical research community that has collaborated with clinical researchers in personalizing medicine and thus identifying patients at greatest risk of diseases and their complications, patients most likely to respond or not respond to therapy, and patients most likely to suffer side effects with therapy.

Summary

Canada's knowledge-based health-care system is under stress. Extending patient-oriented research throughout the health-care system offers a way to reorganize it, with targeted investments in key programs and infrastructure as well as important human capacity building. Patients, populations, health-care professionals and policy-makers want and deserve research-based evidence to inform decisions on how to improve care and advance the system as a whole. Improvements in health care will come through research and programs that establish best health-care practices while considering system sustainability. System change requires resources to synthesize existing evidence regarding which practices and technologies work best. And when evidence is not available, rigorous evaluations and clinical studies must compare new and existing treatments in order to implement or retain those that do the most good. Innovations can also pay important economic dividends.

At present, patient-oriented research happens all too infrequently. Despite our country's long history and successes in patient-oriented research, we must find ways to better coordinate our efforts and break down barriers if we are to increase our international competitiveness in health research.

PART II: THE STRATEGY

Overall goal of the Strategy

Canada's research community is uniquely positioned to supply the information needed to make the best possible decisions regarding treatment options and choices to be adopted in the health-care system. Evidence is key to effective decision-making, which includes improving health outcomes and making cost-effective policy choices. Indeed, evidence-based practices can provide high standards of care while reducing disparities and costs.

In this context, CIHR is proposing a Strategy to direct partnered financial investments to improve health outcomes and service delivery by:

- enhancing clinical applications and economic impact of health innovations; and
- providing health-care professionals and policy-makers with information on how to deliver high-quality care and services in a cost-effective manner.

The Strategy intends not only to foster translation of research innovations from the bench to the bedside, but also to generate evidence to compare the safety, efficacy and overall cost-effectiveness of current diagnostic and treatment procedures. The Strategy will assist researchers in addressing areas of greatest need (primary

STRATEGY FOR PATIENT-ORIENTED RESEARCH

health care, mental health and chronic disease management) and improving existing areas of excellence. It proposes to identify gaps in treatment and care, provide the best evidence to fill those gaps and conduct new research when existing knowledge is incomplete. We want to build a coalition of federal, provincial and territorial governments, research funders, academic institutions, health charities and the private sector to jointly promote, coordinate and increase funding of patient-oriented research.

To meet these goals, the Strategy will:

- improve the research environment and infrastructure for patient-oriented research;
- set up mechanisms to better train and mentor health-care professionals and applied health researchers engaged in research through the creation of sustainable, patient-oriented career paths;
- strengthen organizational, regulatory and financial support for clinical studies; and
- develop processes to support the identification, development and application of best practices in health care.

Component 1: Research environment and infrastructure: a matrix model

Patient-oriented research units

The core of the Strategy is organized around the creation of specialized research entities referred to as Support for People and Patient-Oriented Research and Trials (SUPPORT) units. Some of these units will be built upon existing clinical research centres across the country while others will be entirely new. The SUPPORT units will:

- support leading-edge patient-oriented researchers and programs;
- educate and support health-care professionals and their respective communities who wish to evaluate aspects of care and develop new research programs; and
- implement the standards for research involving research participants.

SUPPORT units will typically house multidisciplinary teams comprised of health-care professionals, methodologists, biostatisticians, social scientists and data managers to help investigators design relevant research (including observational and interventional studies), conduct biostatistical analyses, manage data and meet the highest regulatory standards. All SUPPORT units will be integrated into clinical or care settings to be readily accessible to support a wide spectrum of research and integrated knowledge translation activities. Integrated knowledge translation involves researchers and knowledge users working collaboratively to identify relevant research questions and undertake solutions-oriented research. Integration is key to engaging the users of the research with researchers to ensure that their investigations are important to major stakeholders.

These units will be housed in academic health science centres or regional health authorities, each serving a particular region. For example, each hospital or community care setting served by a SUPPORT unit would have timely access to resources and personnel. To address concerns about developing research along a full continuum of care, SUPPORT units will be provided with resources to link to family practices so that they can collaborate on research initiatives involving complex disease management as well as community, ambulatory and hospital care. These family practices and community health units would assist in designing and implementing research programs, recruiting patients and supporting follow-up activities.

STRATEGY FOR PATIENT-ORIENTED RESEARCH

SUPPORT units will vary in size and field of interest. As illustrated below (Fig. 8), each unit will be endowed with facilities and personnel to support core research, training and knowledge translation.

Figure 8: A matrix model

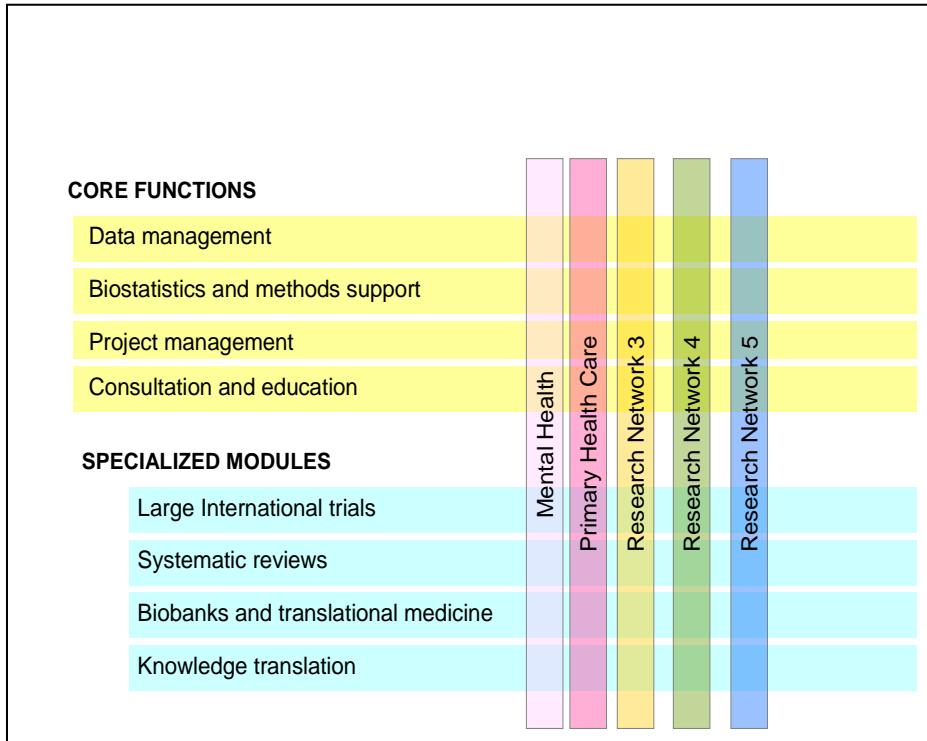


Figure 8: This figure shows the interrelationships of functions and themes within multidisciplinary SUPPORT units. The units are integrated into health-care settings and provide methodological support functions (horizontal elements) to patient-oriented research networks (vertical elements), which will be thematically focused.

In addition, each unit may compete for funding to support one or several specialized modules to strengthen a particular area of expertise. Thus, a small number of SUPPORT units will be equipped to coordinate large international multicentre studies. Others will be provided with the necessary support to conduct systematic reviews or conduct research in knowledge translation to determine how best to increase or speed up the adoption of best practices. Still other units will have the necessary infrastructure to house biobanks and/or carry out translational studies.

SUPPORT units will be encouraged to develop niches of excellence, which will make them competitively attractive internationally. For instance, some may request support to access Canada's large population-based observational databases for analysing existing care patterns, novel and important associations, care gaps, practice variation and the burden of a given illness.

All SUPPORT units will have a common organizational structure and reporting relationship to their parent health institution. This will ensure that regions or hospital foundations and senior administrations provide the space and resources necessary to support patient-oriented research programs.

STRATEGY FOR PATIENT-ORIENTED RESEARCH

Local leadership will ensure that resources promote integration of research activities into the health-care environment. SUPPORT units will be expected to directly improve care in their local setting by providing analytical support to local policy-makers. For example, by examining existing practice patterns, they will identify gaps in care and variations in practice. They will also be well positioned to synthesize the literature to identify best practices to fill these gaps or to carry out new studies, producing outcomes that local policy-makers can put into practice. This will encourage prevention, address transitions in care (from primary care to institutional care and back again) and assist in the management of complex chronic diseases. Thus, SUPPORT units will help fulfill an essential goal of the Strategy: to integrate research across the continuum of care.

Individual SUPPORT units in various parts of the country will initially compete for start-up funds. Renewal of these funds will be contingent on successfully meeting established benchmarks and performance objectives determined by peer review. Initial funding will be based on:

- number and track record of researchers involved;
- size and scope of the proposed infrastructure;
- ability to address areas of high disease burden; and
- integration of the unit in the health-care setting.

Renewal will be based on a number of performance indicators, including:

- number and increase of grants held and studies conducted, completed and published;
- number and increase of patients recruited into patient-oriented research;
- success at and increase in training, recruiting and supporting health-care professionals; and
- adoption of best practices and improvements in health outcomes.

Patient-oriented research networks

As part of the Strategy, CIHR's Scientific Directors and representatives of the various funding partners and stakeholders will identify several major themes for the creation of multidisciplinary research networks. Possible network themes could include mental health, primary health care and chronic disease management. The purpose of these networks will be to:

- create a critical mass of multidisciplinary scientific expertise;
- link relevant SUPPORT and other centres and researchers;
- coordinate overall research activities of the network;
- link to community-based care programs; and
- facilitate continuity in experience.

For example, within an overriding theme of mental health, there could be networks in addiction, schizophrenia, mood disorders and suicide prevention. Similarly, a primary health-care network could tackle specific research programs in the management of complex presenting symptoms (e.g., fatigue, dizziness), chronic disease management and sustainable health-care models. The networks will provide the scientific leadership necessary to direct focused research and specific projects most relevant to Canadians. They will assist in patient recruitment strategies for large multicentre studies and oversee the conduct of those trials.

Clinical research networks will identify research priorities and clinical protocols, assist in the scientific oversight of research programs, support scientists through various teaching and mentorship activities, and foster interdisciplinary research. Each network will receive project-specific support (e.g., methodological

STRATEGY FOR PATIENT-ORIENTED RESEARCH

assistance, data management and statistical services) from one or more SUPPORT units. Over time, we expect that specific SUPPORT units will offer project-based services to the same investigators and clinical networks in order to develop specialization within clinical themes.

To achieve these objectives, each patient-oriented research network will have the resources to ensure leaders have protected time, administrative support and sufficient funding. Networks should expect to:

- have a national leader;
- link to other researchers in their area through regular meetings and planned communication;
- develop a coordinated, nationwide patient-oriented research agenda;
- develop a coordinated funding approach vis-à-vis relevant funders;
- link multiple SUPPORT units that will provide methodological, biostatistical and specific project management assistance;
- assist in conducting research and disseminating results from academic settings into the wider patient-care community;
- provide education and mentorship to emerging researchers in their network;
- coordinate overall project-specific research activities to support their theme;
- ensure maximum efficiency in enrolment in large-scale trials; and
- ensure that each large-scale study meets the highest ethical standards and conforms to national operating standards.

Component 2: Developing human capacity for patient-oriented research

SUPPORT units will require clinical and methodological leadership, support staff and trained clinician researchers. Most academic health science centres conducting clinical research report a critical shortage of biostatisticians and methodologists. There are fewer health-care professionals engaging in patient-oriented research. There is a dearth of international leaders in some critical clinical themes where the burden of disease is great. These shortages hamper the ability to design and conduct practice-changing research.

One of the aims of the Strategy will be to train more health-care professionals and allied non-clinician health professionals, especially those with advanced degrees, in the core methods necessary to carry out research activities. This implies supporting master's and doctoral programs in such areas as epidemiology and biostatistics, as well as health economics and other social sciences, to increase capacity and leadership nationwide. It also implies developing standardized training for research coordinators, project managers and other support personnel.

The Strategy also intends to re-engineer career training and salary awards to build capacity in patient-oriented research for individuals aligned with SUPPORT units. In fact, SUPPORT units are intended to provide an atmosphere of collegiality and support as well as the culture of mentorship that is essential to helping young faculty members acquire the knowledge, skills and aptitude needed to conduct high-impact, patient-oriented research. Awards will be designed to:

- consider different practice plans and remuneration strategies (e.g., alternate payment plans and fee-for-service for physicians) types of positions (e.g., university-based) and sources of support for other health science professions;
- take into account the environment (e.g., the institutional commitment to the applicant and the program they work within) as well as the individual's achievements; and

STRATEGY FOR PATIENT-ORIENTED RESEARCH

- go beyond providing salary support to include recruitment of team members and program development, as well as infrastructure.

Individual awards should require contributions from clinical or academic departments, hospitals, universities and regional or local health authorities as appropriate. They should be linked to regular monitoring of the recipient's performance and the institution's commitment to the researcher.

Component 3: Strengthening organizational, regulatory and financial support for clinical trials

This Strategy will seek to eliminate systemic barriers that produce inefficiencies in the development and implementation of patient-oriented research such as significant delays created by complex review processes. Funders have already streamlined processes by agreeing to a Common CV and, in some instances, a common submission template. We will continue to harmonize the review process and address inefficiencies. Most concerns arise, however, from complex ethics review processes. We will work with partners to implement a common application process and minimize the number of reviews. Similarly, reviews of contracts between industry, investigators and institutions have become laborious and time consuming. With the support and guidance of industry, academic institutions, research funders and research leaders, we plan to develop a template and guidance document for industry-academic contracts. The same should be done for inter-institutional agreements that guide the flow of funds between academic institutions involved in multicentre studies. All interventions designed to improve timeliness and efficiency will be benchmarked and monitored to ensure they are successful in meeting targets.

Conducting clinical investigations is a complex undertaking. As such, clinical studies should be managed using standardized policies and procedures. We will develop a unified set of standards, considered international best practice, which we expect will be adopted across the country. Once developed, they will require adaptation to accommodate local laws and government regulation. The patient-oriented research units and research networks can be used as vehicles for the implementation of standards. Many fields of research will require developing additional policies and procedures because of special circumstances such as the urgency of care to be delivered. There are important challenges in the oversight of clinical research, especially when there is significant risk. Working with our partners, we will streamline the roles and responsibilities of major stakeholders such as ethics committees and data safety and monitoring committees.

Finally, major multicentre projects often require a patchwork of funding. With partners, we hope to develop a unified set of priorities for different levels of government and health charities for publicly funded trials. In doing so, we also hope to facilitate the coordination of reviews of large applications with multiple national and international funding sources.

Component 4: Identifying and promoting use of best practices in health care

Studies consistently demonstrate that when evidence-based practice guidelines are rigorously developed and effectively implemented, both quality of care and health outcomes improve.⁵⁹ Unfortunately, guideline development in Canada is under-resourced and often inefficient, with duplication in the searching and appraising of evidence. Consequently, the quality of guidelines and their implementation varies.

STRATEGY FOR PATIENT-ORIENTED RESEARCH

The Strategy aims at teaming guideline developers with health-care professionals to promote the rigorous development of high-quality, evidence-informed practice guidelines and encourage policy-makers, institutions, health-care professionals and consumers to adopt them. Networks and SUPPORT units will assist guideline developers in searching the literature for evidence, critically appraising it and synthesizing it. Those SUPPORT units with knowledge translation expertise will work with guideline developers to study how best to facilitate practice guideline adoption and use. As with the rest of the Strategy, this best practices initiative will require the active engagement of the provinces and health services providers to ensure that it meets their needs. By linking guideline developers and other stakeholders involved in patient-oriented research activities, Canada will be uniquely positioned to improve the breadth and quality of its guidelines and their impact on health outcomes. No other country currently has such a structure in place to seamlessly link knowledge generators and knowledge translation researchers embedded in the health-care system with national practice guideline developers.

Coordination and governance

A national champion will lead the Strategy for Patient-Oriented Research. The champion, who will manage a national coordinating centre, will report to a board of directors with representatives from all major stakeholders and funders. The board will set priorities for the Strategy. The champion will implement all plans, coordinate activities and ensure communication among the patient-oriented research networks and the individual SUPPORT units. We expect that the proposed governance structure will enhance accountability and ensure that we target and invest in areas of high disease burden and greatest need, maximizing our overall research potential.

As a more formal proposal for governance is developed, the board will ensure that the Strategy is built upon the following principles:

- 1) **Excellence:** Excellence should be the driving force of any research enterprise. We must build on our strengths and expand on existing clusters of excellence. Peer review is key to identifying and promoting excellence.
- 2) **Collaboration and partnership:** Given the current organization of health care and the magnitude of investment and national standards required, success can be achieved only through partnerships and enhanced collaborations with federal and provincial governments, academic institutions, non-governmental agencies, the voluntary health sector and the private sector.
- 3) **Equity:** In order to improve health outcomes, the Strategy must address areas of greatest need. For instance, primary health care, mental health, populations with high disease burden, behavioural and social determinants of health and high-risk and complex disease management should be seriously considered.
- 4) **Integration:** We believe that integrating research activities directly into health care is the only way to introduce a culture of enquiry throughout the health system. Integrating research into clinics and hospital wards was successfully pioneered at McMaster University over 30 years ago. It has been adopted in many areas of the country – making Canada unique. Integration also means that we will focus research activities on the entire continuum of care. For instance, research on congestive heart failure should include the community and primary, secondary and tertiary care settings.

STRATEGY FOR PATIENT-ORIENTED RESEARCH

- 5) **Accountability:** The Strategy will ensure that the highest ethical standards are met and that appropriate standards and monitoring systems are in place. Accountability also refers to producing the desired results – that individuals and institutions deliver on promises accompanying program investments.
- 6) **Flexibility:** It is important that we develop a plan that can accommodate multiple themes of research, regional differences, differing levels of expertise and capacity-enhancing opportunities.
- 7) **Innovation:** The system must promote rapid, high-quality patient-oriented evaluations of practices, techniques, novel drugs and devices.

How will the Strategy for Patient-Oriented Research meet the needs of stakeholders?

For patients and health practitioners:

- Provide easy access to evidence and the ability to generate new evidence.
- Allow academic programs to develop and recruit leaders in areas of research that are most relevant to patients.
- Improve care by facilitating the recruitment of the best and brightest health providers and researchers.

For policy-makers:

- Allow institutions, health authorities and provinces to evaluate new and existing programs as well as health interventions to determine which provide value for money.
- Adopt the concept of a learning health-care system to ensure its long-term sustainability as we face major challenges from a population increasingly affected by chronic diseases.

For basic biomedical scientists:

- Enable better characterization of large populations of patients necessary to better understand the influence of genetic factors on disease predisposition and progression as well as the influence of genetic factors on the risks and benefits of medications.
- Allow new drugs and devices to be tested and commercialized in Canada.

For industry:

- Break down barriers to multicentre research, develop international leadership, enhance research training, implement uniform standards and build an infrastructure that enables access to a large number of patients that will drive pharmaceutical investments into Canada.

CONCLUSIONS

Through partnered investments and planning, we propose to create a nationwide, patient-oriented research enterprise that will promote a culture of enquiry throughout the health system. Making it easier to generate evidence and integrate it into practice will ensure that our health system grows, provides optimal care and is sustainable. The Strategy for Patient-Oriented Research requires a nationwide, coordinated effort to direct investments in major programs, break down barriers to major multicentre studies, and enhance training for clinicians and standards for research.

These programs will ensure that Canada offers the best care possible. They will also enable major academic institutions to hire highly qualified faculty by offering them opportunities in research. They will secure

STRATEGY FOR PATIENT-ORIENTED RESEARCH

access to high-quality patient care through innovative diagnostic and therapeutic approaches and by establishing which treatments do more good than harm. Ultimately, this investment and all of its programs should significantly improve health outcomes for Canadians.

REFERENCES

1. Evidence-Based Medicine Working Group. Evidence-Based Medicine: A New Approach to Teaching the Practice of Medicine. *JAMA*. 1992; 268(17):2420-2425.
2. Haynes AB, Weiser TG, Berry WR, Lipsitz SR, Breizat AS, Dellinger EP et al. A surgical safety checklist to reduce morbidity and mortality in a global population. *N Engl J Med*. 2009 March 24; 360 (5): 491-499.
3. Wennberg J, Gittelsohn A. Small area variations in health care delivery. *Science*. 1973 Dec 14;182:1102-1108.
4. Wennberg JE. Dealing with medical practice variations: A proposal for action. *Health Aff*. 1984 Summer;3(2):6-32.
5. Wennberg JE, Elliott SF, Skinner JS. Geography and the debate over Medicare. *Health Aff*. 2002 Feb 13; W97-W114.
6. Fisher ES, Wennberg DE, Stukel TA, Gottlieb DJ, Lucas FL, Pinder EL. The implications of regional variations in Medicare spending. Part 1. The content, quality, and accessibility of care. *Ann of Intern Med*. 2003; 138:273-287.
7. Wennberg DE, Wennberg JE. Addressing variations: Is there hope for the future? *Health Aff*. 2003 Dec 10; W3:614-617.
8. Weinstein JN, Bronner KK, Morgan TS, Wennberg JE. Trends: Trends and geographic variation in major surgery for degenerative diseases of the hip, knee, and spine. *Health Aff*. Web Exclusive. 2004 Oct 7:Var81-Var89.
9. Straus SE, Ball C, Balcombe N, Sheldon J, McAlister FA. Teaching evidence-based medicine skills can change practice in a community hospital. *JGIM* 2005 April;20(4):340-343.
10. Lloyd K, Cella M, Tanenblatt M, Coden A. Analysis of clinical uncertainties by health care professionals and patients: an example from mental health. *West J Med*. 2000 May;172(5):315-319.
11. Kiesler DJ, Auerbach SM. Optimal matches of patient preferences for information, decision-making and interpersonal behaviour: Evidence, models and interventions. *Patient Educ Couns* 2006; 61:319-41.

STRATEGY FOR PATIENT-ORIENTED RESEARCH

12. DuBois A, Rochon J, Lamparter C, Pfisterer J. Pattern of care and impact of participation in clinical studies on the outcome in ovarian cancer. *Int J Gynecol Cancer*. 2005; 15:183-191.
13. Majumber SR, Roe MT, Peterson, ED, Chen AY, Gibler WB, Armstrong PW. Better outcomes for patients treated at hospitals that participate in clinical trials. *Arch Intern Med*. 2008; 168(6):657-662.
14. McKinnon JD, Bendavid N. Congress is buying time for health care savings. *The Wall Street Journal*. 2009 March 28; <http://online.wsj.com/article/SB123820414330062983.html>
15. National Institute for Health Research. Best research for best health. 2007. Available from: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4127152.pdf
16. National Health Service. Delivering health research. National Institute of Health Research progress report 2008-09. http://www.nihr.ac.uk/files/Publications/296542_DeliveringHealthResearchReport_acc3.pdf
17. Weinsaft J W, O'Rourke M F, Nichols WW, Sharma A M, Pischon T, Engeli S, et al. Effect of Ramipril on cardiovascular events in high-risk patients. *N Engl J Med* 2000; 343:64-66, Jul 6, 2000
18. Fergusson D, Glass KC, Hutton B, Shapiro S. Randomized controlled trials of aprotinin in cardiac surgery: could clinical equipoise have stopped the bleeding? *Clinical Trials*. 2005; 2: 218-232.
19. Hébert PC. Transfusion requirements in critical care. *Vox Sang*. 2002 Aug; 83 Suppl 1:387-396.
20. Kwan J, Sandercock PAG. In-hospital care pathways for stroke. *Cochrane Database Systc Rev*. 2004;4. Art. No.: CD002924. DOI: 10.1002/14651858.CD002924.pub2
21. Bailey RC, Moses S, Parker CB, Agot K, Maclean I, Krieger JN, Williams CF, Campbell RT, Ndinya-Achola JO. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. *Lancet*. 2007 Feb 24:369(9562):643-656
22. Murphy KE, Hannah ME, Willan AR, Hewson SA, Ohlsson A, Kelly EN, et al. Multiple courses of antenatal corticosteroids for preterm birth (MACS): a randomised controlled trial. *Lancet*. 2008 Dec 20/27;372:2143-2151.
23. Stevens B, Yamada J, Ohlsson A. The efficacy of sucrose to reduce procedural pain in neonates as assessed by physiologic and behavioural outcomes. *Neonatal Modules of the Cochrane Database of Systematic Reviews*. The Cochrane Collaboration. Eds. Sinclair JC, Brachen MB, Soll RS. Update Software, Oxford. 2002.
24. Pisters KM, Evans WK, Azzoli CG, Kris MG, Smith CA, Desch CE, et al. Cancer Care Ontario and American Society of clinical Oncology adjuvant chemotherapy and adjuvant radiation therapy for

STRATEGY FOR PATIENT-ORIENTED RESEARCH

stages I-IIIa resectable non small-cell lung cancer guideline. *J Clin Oncol*. 2007 Dec 1; 25(34):5506-5518.

25. Ellard SL, Clemons M, Gelmon KA, Norris B, Kennecke H, Chia S, et al. Randomized Phase II study comparing two schedules of Everolimus in patients with recurrent/metastatic breast Cancer: NCIC Clinical Trials Group IND.163. *JCO* Sep 20 2009: 4536-4541.
26. Anis A, Nosyk B, Sun H, Guf DP, Banasback N, Li X, et al. Quality of life of patients with advanced HIV/AIDS: measuring the impact of both AIDS-defining events and non-AIDS serious adverse events. *J Acquir Immune Defic Syndr* 2009 August; 51(5):631-639.
27. Douketis J, Cook D, Meade M, Guyatt G, Geerts W, Skrobik Y, et al. Prophylaxis against deep vein thrombosis in critically ill patients with severe renal insufficiency with the low-molecular-weight heparin dalteparin: an assessment of safety and pharmacodynamics: the DIRECT study. *Arch Intern Med* 2008 Sept 8; 168(16):1805-12.
28. Lawlor MS. Biotechnology and Government Funding: Economic Motivation and Policy Models. Science and Cents: Exploring the Economics of Biotechnology Conference. (Ed. JV Duka and MK Yücel). Federal Reserve Bank of Dallas. 2002 April 19; 132-146.
29. Collet JP, Fraser W, Johnston C, Lacroix J, Paradis G, Valiquette L et al. Clinical research report. Document submitted to the Board of Directors of the Fonds de la recherche en santé du Québec. 2005 March 11.
30. Brimacombe GG, Gruenewoldt EC. Moving at the speed of discovery [electronic resource]: From bench to bedside to business. 2007. Available from:
http://www.acao.org/docs/pdf_2007_nov_matsd_progresser_en.pdf
31. Prud'homme Généreux A, Cairns J. Summary report: CIHR/CFI Clinical Research Centres/Networks Workshop. Canadian Institutes of Health Research, January 21, 2005. Available from: <http://www.cihr-irsc.gc.ca/e/documents/ClinResInfrastructureWorkshop-1Nov05-v2.pdf>
32. Rouleau J. Clinical research in Canada: A proposed action plan. 2008.
33. Silverman M. A roadmap to ensure Canadian leadership in clinical and translational research. Canadian Institutes of Health Research Clinical Research Initiative. 2004. Available from:
<http://www.cihr-irsc.gc.ca/e/22113.html>
34. Syntegrity Group. Canadian Institutes of Health Research: Clinical research syntegegration – July 2008. Version 1.0.

STRATEGY FOR PATIENT-ORIENTED RESEARCH

35. SHI Consulting. Clinical trial coordinating centre business case. Report for the CT CTNet Working Group. 2008.
36. Frontera WR, Fuhrer MJ, Jette AM, Chan L, Cooper RA, Duncan PW, et al. Rehabilitation medicine summit: building research capacity. Executive Summary. J Neuroeng Rehabil [serial on the internet] 2006 [cited 2008 Dec 12] 3:1. Available from: <http://www.jneuroengrehab.com/content/3/1/1>
37. DeHaven MJ, Wilson GR, O'Connor-Kettlestrings, P. Creating a research culture: What we can learn from residencies that are successful in research. Educational Research and Methods. 1998; 30(7):501-7.
38. Kekki P. Promoting clinical research in general practice. Educ Health (Abingdon). 2005; 18(2):283-89.
39. Cooke J. A framework to evaluate research capacity building in health care. BMC Family Practice [serial online]. 2005 [cited 2008 Dec 12] 6:44. Available from <http://www.biomedcentral.com/1471-2296-6-44>
40. Vratny A, Shriver D. A conceptual model for growing evidence-based practice. Nurs Adm Q. 2007; 31(2):162-70.
41. Araki Y, Scott SE, Lear S. Challenges of telehealth research in clinical settings. J Telemed Telecare. 2007; 13:425-26.
42. Nuyens Y. No development without research: A challenge for capacity strengthening. Global Forum for Health Research. 2005. Available from: http://www.globalforumhealth.org/filesupld/RCS/RCS_Nuyens.pdf
43. World Health Organization. World Report on Knowledge for Better Health. 2004. Available from: http://www.who.int/rpc/meetings/en/world_report_on_knowledge_for_better_health2.pdf
44. National Physician Survey. National physician survey 2007. Available from: http://www.nationalphysiciansurvey.ca/nps/2007_Survey/2007nps-e.asp
45. Grimes DA, Hubacher D, Nanda K, Schulz KF, Moher D, Altman DG. The Good Clinical Practice guideline: a bronze standard for clinical research. Lancet. 2005; 366:172-74.
46. McMahon AD, Conway DI, MacDonald TM, McInnes GT. The unintended consequences of clinical trials regulations. PLoS Med. 2009; 6(11): e1000131. doi:10.1371/journal.pmed.1000131
47. Patented Medicine Prices Review Board. Annual Report. 2007. Available from: <http://www.pmprb-cepmb.gc.ca/CMFiles/PMPRB-AR07-english42LFLK-6182008-8285.pdf>

STRATEGY FOR PATIENT-ORIENTED RESEARCH

48. IMD. World competitiveness yearbook, 2005. 2005. <http://www.ic.gc.ca/eic/site/lsi-isv.nsf/eng/li00278.html>
49. Thiers FA, Sinsky AJ, Berndt ER. Trends in the globalization of clinical trials. *Nature Reviews Drug Discovery* **7**, 13-14 (January 2008) doi:10.1038/nrd2441 News Analysis
50. National Center for Research Resources. Strategic plan 2009-2013. NIH Publication No. 08-6439. National Center for Research Resources, National Institutes of Health. 2008. Available from: http://www.ncrr.nih.gov/strategic_plan/
51. United Kingdom Clinical Research Collaboration. UK Clinical Research Collaboration progress report, 2006-2008. 2008 (United Kingdom). Available from: http://www.ukcrc.org/PDF/UKCRC_PR_06-08.pdf
52. European Strategy Forum on Research Infrastructures. European Roadmap for Research Infrastructures: Roadmap 2006. Luxembourg: Office for Official Publications of the European Communities. 2006. Available from: ftp://ftp.cordis.europa.eu/pub/esfri/docs/esfri-roadmap-report-26092006_en.pdf
53. European Strategy Forum on Research Infrastructures. European roadmap for research infrastructures: Roadmap 2008. Luxembourg: Office for Official Publications of the European Communities. 2008. Available from: ftp://ftp.cordis.europa.eu/pub/esfri/docs/esfri_roadmap_update_2008.pdf
54. Department of Innovation, Industry, Science and Research, Australian Government. Strategic roadmap for Australian research infrastructure. 2008. Available from: <http://www.innovation.gov.au/ScienceAndResearch/Documents/Strategic%20Roadmap%20Aug%202008.pdf>
55. National Health and Medical Research Council. Clinical research in Australia. Report of the NHMRC Clinical Research Working Group. 2001 (Australia). http://www.nhmrc.gov.au/about/committees/previous/srdc/_files/chalmers.pdf
56. Research for Patient Benefit Working Party. Final Report. Department of Health, United Kingdom. 2004. Available from: http://www.dh.gov.uk/en/Researchanddevelopment/A-Z/DH_4082668
57. Cooksey D. A review of UK health research funding. 2006 (United Kingdom). Available from: http://www.hm-treasury.gov.uk/d/pbr06_cooksey_final_report_636.pdf
58. Stiell I. Ottawa ankle rules. *Can Fam Physician* 1996;42:478-480

STRATEGY FOR PATIENT-ORIENTED RESEARCH

59. Grimshaw JM, Thomas RE, MacLennan G, Fraser C, Ramsay CR, Vale L, et al. Effectiveness and efficiency of guideline dissemination and implementation strategies. *Intl J of Technology Assessment in Healthcare*. 2005; 21(1): 149