CANADIAN DEMAND FOR HIGHLY QUALIFIED PERSONNEL FOR THERAPEUTIC EVALUATION: AN OPPORTUNITY FOR ACADEMIC INSTITUTIONS

Stuart M MacLeod[1]; Judith A Soon[2,3]; Sunaina Sharma[4]; Matthew O Wiens[2,3]

[1]Child and Family Research Institute, Department of Pediatrics, University of British Columbia, Vancouver, British Columbia, Canada; [2]School of Population and Public Health, University of British Columbia, Vancouver, British Columbia, Canada; [3]Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, British Columbia, Canada; [4] Patients in Action Together Society, Vancouver, British Columbia, Canada

Corresponding Author: *smacleod@cfri.ca*

ABSTRACT

Achievement of optimal therapeutics requires individuals with analytic skills appropriate to the balancing of enterprise, innovation and the need for rigorous scientific validation. A synergistic convergence of discovery research, clinical investigation, evaluative, regulatory and implementation sciences will be essential. None of the needed research capacities are likely to prove obtainable on demand. On the contrary, they require accurate projection of future needs and careful planning of post-secondary training programs.

A survey conducted for Health Canada in 2010 revealed significant shortfalls in research skills available outside government and industry. This commentary argues that such an environment represents an outstanding opportunity for the academic community to demonstrate that it is eager to meet the needs of the Canadian public. University leaders should be assertive about their commitment to the ideals of patient oriented research and all governments should be clear about deliverables anticipated in return for consistent post-secondary funding.

Key Words: *Human resources, clinical evaluation, drug safety, drug efficacy/effectiveness, pharmacoepidemiology*

Background

Canada's achievements in health sciences research over recent decades have been considerable and are acknowledged as representing a leading edge of Canadian science and technology.[1] The federal government has invested heavily in infrastructure for health sciences research through the Networks of Centres of Excellence program and the Canada Foundation for Innovation, as well as through maintenance of stable funding through the Canadian Institutes of Health Research (CIHR). Despite these investments, Canada has been faulted for its relatively poor track record in innovative science and Canadian industry, in particular, has been urged to increase its investment in discovery research.[2]

In 2010 a blue chip panel chaired by Paul Lucas, the president of Glaxo Canada, and John Manley, president of the Canadian Council of Chief Executives, produced a 10-point program recommending steps that would bring about improvement of Canada's innovation environment. These points included a compelling argument for strengthened relationships between industry and Canada's academic centres.[3] The report was followed in 2011 by an analysis of innovation performance commissioned by the federal government and provided by a task force chaired by Tom Jenkins. The focus was on a review of federal support for research and development and again urged greater engagement by the private sector.[4]

The conclusions of 2010 and 2011 have resulted in considerable achievement; however, as emphasized most recently in the budget of February 2014, it remains the opinion of the federal government that more can be done. The latest Canadian budget introduced the promise of a Canada Research Excellence Fund designed to provide $1.5billion in incentives over the next decade to Canadian post-secondary institutions aimed at improving Canada's future in science and technology.[5] It would be timely to consider how these funds may be optimally deployed.

Health sciences research

Despite high international achievement relative to population, in the environment of health sciences and health care,[1] Canada's performance may be seen in some ways as erratic. The root cause of inconsistency may lie in the fluctuating targets put forward by the CIHR or in the emphasis on infrastructure at the expense of adequate operating funds for both discovery and clinical research that has characterized the Canadian environment over the past two decades. The CIHR budget has not increased in constant dollars since 2006, although redirected funds have been allocated for some novel specific targets. Canada continues to rank highly in bibliometric analysis but little of the evident research productivity has translated readily into enhanced health service delivery, therapeutic innovation or improved health outcomes. Recent efforts of CIHR to develop a strategy for patient oriented research are laudable but have so far been marked by remarkably slow progress.[6]

Throughout the recent period of enormous investment in health sciences and technology the federal government and its granting agencies have placed consistent emphasis on the critical importance of ensuring availability of highly qualified research personnel to serve the needs of future generations. Success in translation of basic, clinical and population health research requires individuals with analytic skills appropriate to the balancing of enterprise, innovation and the need for rigorous scientific evaluation. What is called for is a synergistic convergence of discovery research, clinical investigation, evaluative and regulatory science and implementation sciences coupled to a robust knowledge mobilization program. None of the needed research capacities are likely to prove obtainable on demand. On the contrary, they require careful projection and planning of post-secondary educational programs. A good example of the approach required can be found in the recent CIHR efforts to foster patient oriented research. In 2013, the Strategy for Patient-Oriented Research (SPOR) national steering committee created an external advisory committee with a mandate to address a perceived deficiency of both clinician and non-clinician patient oriented researchers. The opinion was expressed at the time that Canada's academic health science centres lacked adequate human resources to promote the integration of research into clinical practice and health care decision making. The external advisory committee reported in December 2013 with several valuable recommendations concerning training and career development in patient oriented research within Canadian academic centres.[7] While the report of the advisory committee has broad general ramifications, the present commentary is particularly focused on one area that is an essential element in any effort directed at improved patient care and that is therapeutic innovation and evaluation.

The requirement for the balanced approach described above is nowhere more strikingly illustrated than in the field of therapeutics. It may be taken as a given that Canadians require a steady flow of validated, innovative therapies that may be expected to improve health outcomes. Importantly, however, the final goal cannot be achieved without an adequate human resource base to support clinical investigation, implementation, evaluation and regulatory sciences, and a parallel investment in knowledge transfer.[8,9] Guaranteed availability of such capacity within the Canadian health system will depend on the ability of all levels of government, academic institutions and health professional and scientific organizations to accurately gauge human resource requirements in a rapidly evolving environment.

In recent decades accurate prediction has been complicated by the rapid evolution of biological knowledge with the result that hundreds

of new therapeutic and diagnostic products are brought under scrutiny each year. At the same time, the therapeutic milieu is changing with major emphasis placed on the importance of personalized medicine and tailoring of treatment to an individual's genomic makeup.[10-12] By careful application of growing scientific knowledge about genomic differences among individuals, it is now possible to achieve safer and more effective therapy for many conditions previously considered untreatable or only partially treatable.

With encouragement from the federal Ministry of Health, beginning in October 2012, Health Canada has also assigned particular priority to validation of treatments for rare conditions and an orphan drug framework has been advanced to facilitate such development.[13] In December 2013, a further new focus on drug safety was announced by Health Canada and Bill-C17, the "Protecting Canadians from Unsafe Drugs Act", was given first reading, presenting amendments to the current Food and Drug Act.[14]

The aim of Bill-C17 (designated as 'Vanessa's Law') is to strengthen the oversight of therapeutic products throughout their life cycle. Under the proposed amendments Health Canada will be given power to require information, tests or studies that will improve the safe and effective use of therapeutic products. The regulatory agency will also be granted power to require a label change. Bill C-17 has received third reading on June 16, 2014.[14]

Several of the important policy issues surrounding therapeutic evaluation have been explored in great depth by the Standing Senate Committee on Social Affairs, Science and Technology and three reports have been issued in November 2012, March 2013 and January 2014.[15-17] These reports, taken together signal a strong continuing interest on the part of the Canadian government in improving the environment for future therapeutic evaluation. The reports deal in turn with clinical trial infrastructure, post approval monitoring of safety and effectiveness of prescription pharmaceuticals, and off label use of drugs.

Many of these developments have been characterized by Health Canada and others as a life cycle approach to the evaluation of new therapies. Such an approach is intended to encourage the early introduction of innovative therapies with the parallel responsibility for continuing development of the evidence base concerning safety and efficacy of the new treatment.[14,18] Such an evolution in thinking will necessitate modernization of the entire regulatory environment and will require access on an unprecedented scale to highly qualified scientists well versed in all aspects of evaluation. Achievement of this lofty goal will demand expertise in patient oriented clinical research methods that will underpin generation of a robust evidence base driving innovative therapy.

A case study: highly qualified personnel for evaluation of innovative therapeutic products

As the context described above evolved it was recognized by Health Canada that it would be important to determine the number of individuals available outside government and the private sector who would be prepared to contribute to the challenging evaluative research process that will be necessitated. It is clear that regulatory decision making in future must be informed by the strongest possible evaluative science. Accordingly, in 2009, Health Canada's Office of Legislative Modernization and Renewal contracted with the Child & Family Research Institute (BC Children's Hospital, Vancouver) to prepare an asset map of human resources available to support the changing environment for the regulation of therapeutic products in Canada.[19,20] A second part of the contracted study related to assessment of post-market drug evaluation research training capacity in Canada and an environmental scan relevant to that question was conducted and is reported elsewhere in this issue. (Wiens MO, et al *J Popul Ther Clin Pharmacol Vol 21(3):e370-78*)

The human resource question was addressed through more than 750 surveys sent to individuals outside government and the private sector known to be involved to some degree with post-market drug surveillance of safety and effectiveness. Individuals were identified on the basis of their use of clinical, epidemiological, economic and outcomes research methodology. The researchers contacted were identified through

universities, research hospitals, health care organizations and funding agencies as well as through contacts within health professional, health care and research organizations. Finally, external scientific data research managers in three Health Canada directorates involved in post-market drug evaluation were invited to forward the survey to key researchers known to them. The survey methodology was approved by research ethics boards at Health Canada and the University of British Columbia and the survey instrument was sent to identified potential participants in French or English as appropriate to language of choice. A total of 354 valid responses were obtained. While this represents a response rate slightly below 50%, it should nonetheless be considered valid since many potential respondents turned out to be ineligible as they were not actively engaged in post-market therapeutic evaluation.

The responses came in almost equal proportion from three sources, research scientists in basic or population health sciences, health science faculty members, and clinicians/clinician scientists. Of the evaluable responses, 146 came from informants with an MD with or without a graduate degree, 107 came from holders of a PhD or equivalent degree and 54 from pharmacists with or without a graduate degree. The age range of respondents was appropriate, with more than 65% falling between the ages of 35 and 55.[19]

Table 1 shows the top 16 areas of clinical expertise identified by respondents who were asked to designate up to five domains. Only 286 individuals identified areas of clinical expertise; the remaining 68 respondents possessed more general skills relevant to evaluation science or post-market surveillance that could not be described as 'clinical'.

Table 2 indicates the top areas of research expertise self-identified by participants. Researchers were asked to select up to five areas of expertise and 346 of 354 respondents provided answers suggesting that the survey had reached the intended audience of experts with interests closely aligned to those deemed important for post-market drug evaluation research.

Table 3 indicates the expertise available among participants in relevant research involving special populations. The availability of expertise is distributed in a pattern that might be anticipated with the possible exception of Aboriginal peoples health where only 31 qualified investigators self-identified.

TABLE 1 Top 16 areas of clinical expertise

Clinical Expertise	Responses*(%)	Clinical Expertise	Responses (%)
pharmacology	99 (34.6)	musculoskeletal	26 (9.1)
internal medicine	66 (23.1)	critical care	22 (7.7)
cardiology	52 (18.2)	pediatrics	24 (6.8)
infectious disease	41 (14.3)	rheumatology	18 (6.3)
mental health	36 (12.6)	neurology	18 (6.3)
cancer	35 (12.2)	pulmonology	17 (5.9)
endocrine/metabolism	33 (11.5)	gastroenterology	15 (5.2)
geriatrics/gerontology	29 (10.1)	obstetrics/gynecology	13 (4.5)

* n=286; as researchers may select up to five areas of expertise, the percentages do not add up to 100%.

TABLE 2 Top areas of research expertise

Clinical Expertise	Responses*(%)	Clinical Expertise	Responses (%)
epidemiology[1]	119 (34.4)	biostatistics[2]	37 (10.7)
pharmacoepidemiology[3]	96 (27.7)	pharmacokinetics	30 (8.7)
health policy research	95 (27.5)	decision analytic modeling	27 (7.8)
clinical trial design	91 (26.3)	health informatics	24 (6.9)
systematic reviews	80 (23.1)	patient decision aids	22 (6.4)
active comparator clinical trials	69 (19.9)	qualitative methodology	20 (5.8)
adherence to drug therapy	65 (18.8)	toxicology	15 (4.3)
health economics[4]	64 (18.5)	pharmacogenetics[6]	15 (4.3)
health technology assessment	64 (18.5)	pharmacogenomics[6]	11 (3.2)
adverse drug reaction monitoring[5]	62 (17.9)	risk management[5]	11 (3.2)
patient safety[5]	54 (15.6)	risk minimization interventions[5]	9 (2.6)
clinical pharmacy practice	54 (15.6)	bioethics	8 (2.3)
population data management	53 (15.3)	other	69 (19.9)
meta-analyses	40 (11.6)		

* n=346; as researchers may select up to five areas of expertise, the percentages do not add up to 100%. [1–6]These areas of research expertise reflect the core areas evaluated in the Educational Inventory (Wiens MO et al, *J Popul Ther Clin Pharmacol Vol 21(3):e370-78*)

TABLE 3 Top areas of research addressing needs of special populations

Expertise in special populations	Responses* (%)
senior's health	111 (44.9)
women's health	78 (31.6)
child and youth health	72 (29.1)
marginalized populations	57 (23.1)
aboriginal health	31 (12.6)
other	62 (25.1)

* n=247; as researchers may select up to five areas of expertise, the percentages do not add up to 100%.

These results suggest that many of the issues raised by the Standing Committee on Social Affairs, Science and Technology in its report of November 2012[12] might be addressed if agreement is reached on an appropriate evaluation framework and modified regulatory system; however, the available research complement will not likely be able to cope with demand for a wide range of innovative methodologies, especially those required for evaluation during the post-market period. Major investment will be called for in training programs for highly qualified personnel and needs are certain to be amplified as we enter the era of increasingly personalized therapy. Those seeking further details of the human resources survey can access the full report through the Health Canada website.[19]

The results of this survey generally confirm a pending alarming shortage of highly qualified research personnel representing a potential impediment to Canada's future progress in therapeutic innovation. Without the creation of new training opportunities it will not be possible to meet the demands in clinical trials investigation, population health, implementation, evaluative and regulatory science, or related fields of knowledge translation. Fewer than half of the individuals identified in the described survey as possessing some of the required research skills have completed a full range of training required for comprehensive participation in regulatory decision making and clinical implementation science. The described shortfall in human capacity leaves Canada vulnerable.

Furthermore, the survey indicated several areas of particular future concern, including the evaluation of therapies for infants and children, pregnant and lactating women, patients with rare disorders, the frail elderly and those in marginalized or underserved populations. As the emphasis placed on the needs of these populations is growing rapidly, it can be anticipated that the demand for relevant scientific input will be correspondingly magnified.

An opportunity to be seized

Universities everywhere are being called upon to justify their share of both public and private funding and to prove their social value. The health science research demands predicted above are almost certain to be part of the pressure applied to Canadian universities with health science faculties and large investments in health research. Over the past three decades there have been major shifts in the research profile of health science faculties, with increasing emphasis on clinical, population health and health policy research, with the adjustment being led in particular by the CIHR. Nonetheless, Canada's post-secondary institutions continue to show, in most cases, greater interest in discovery research than in practical applied sciences that may contribute sooner and more directly to improved outcomes. The basic research activities of most Canadian universities are too frequently applied to a relatively limited part of the human disease spectrum.

It is time for university leaders to reconsider their commitment to the ideals of the academic health science centre[21] and for federal and provincial governments to be clear about the deliverables anticipated in return for consistent funding. In an ideal world the academy may be expected to strengthen its performance by being attentive to the needs of the community in which it resides.

At the risk of over-generalization it may be said that the glass in Canada appears half full. Despite the call from all levels of government for a greater emphasis on pragmatic health research and the commitment of CIHR to a strategy for patient-oriented research, it has proven difficult to dissuade institutions from perpetuation of the disproportionate emphasis on discovery science. The discussion presented in this commentary underscores the importance of bringing Canadian academic leaders to a recognition of the continuum of research necessary to support innovation. Unless our human resource base in evaluation and implementation science is improved we are unlikely to achieve the often quoted triple aim of the health system: better health outcomes, better health services, better value for resources expended.

The starting point for progress in this important mission is the expansion of training capacity in relevant disciplines and the allocation of resources to creation and strengthening of necessary programs. Nowhere are the opportunities more abundant than in the field of therapeutic evaluation.

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