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INTERNATIONAL REVIEW
OF THE
CANADIAN INSTITUTES OF HEALTH RESEARCH

Expert Review Team Report
for
Institute of Musculoskeletal Health and Arthritis

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

Canada

TABLE OF CONTENTS

Summary

The Expert Review Team (ERT) recognized substantial strengths amongst musculoskeletal research in Canada, particularly in clinical and health services research. We could not comment on the contribution of specific Institute of Musculoskeletal Health and Arthritis (IMHA) initiatives in achieving its strategic goals. The same is probably true for the entirety of musculoskeletal funding by IMHA including the investigator initiated competitive grants. The bibliometric data presented only captures a portion of the scientific impact.

IMHA has a number of successes:

- IMHA has been very successful in being inclusive, transparent, and engaging with the various musculoskeletal and skin disease and oral disease stakeholders in developing their research strategy. IMHA has developed partnerships which have leveraged new funding and/ or targeted investigators or science at different stages of development. Some of this funding would not have happened without IMHA.
- IMHA has also been successful in developing collaborations between different disease focus areas within IMHA and between relevant institutes of CIHR.
- IMHA strategic priorities are supported by the community and represent the major public health concerns in this area.
- The Strategic Training Initiative in Health Research and Catalyst grant programmes have been very successful in driving forward early research support but need to be followed by further support.

There are issues that should be addressed, some unique to IMHA, others relevant to all of CIHR, Canada and/or worldwide:

- Some stakeholders are excluded from the process of strategy setting and the involvement of patients and consumers input is not so strong especially in the non-musculoskeletal core areas. As an example Osteoporosis Canada was only engaged in providing 50% support for a grant but did not seem to have been engaged in setting research priorities for osteoporosis.
- There is a strong case for a greater proportion of CIHR funding for this Institute based on public health need. With limited funds there should be a greater emphasis on major project support and getting key disciplines and groups working together. This appears to be starting.
- There is a disconnect between the priority areas identified by IMHA requests for applications (RFAs) and the majority of the funding which is by open competition: the reviews of which do not take account of IMHA priorities.
- Although potentially self-serving, some investigators felt that some review panels had insufficient representation of either experts in the field or advocates for the research questions.
- Specific RFAs are few in number, may have a long gestation and the peer review process may not fully engage with the strategic wishes of the Institute. If the Institute itself is not centrally involved in the vetting of the RFA grants then its ability to deliver on strategic needs is constrained.

- Proposed randomised controlled trials are reviewed predominantly by methodologists and there needs to be stronger IMHA, as customer, input into the decision making.
- There are real problems in building and sustaining research capacity especially in the clinical sciences. Some of these problems reflect national salary structures for groups of clinicians. There is a need to incentivize some to stay in research or at least not to discourage their involvement. This is a major threat to the future strength of clinical research.
- There is no real plan for commercialisation of discoveries but a feeling there is a responsibility to do so. This is not a trivial task and investment by the Institute in the infrastructure to achieve this may not be successful.

Section 1 – Institute mandate

The CIHR Institute of Musculoskeletal Health and Arthritis supports research to enhance active living, mobility and movement and oral health. More specifically, it supports research that addresses causes, prevention, screening, diagnosis, treatment, support needs and palliation for a wide range of diseases and conditions related to the Institute's six foci: arthritis, bone, skin, muscle, musculoskeletal (MSK) rehabilitation, and oral health. The mission of IMHA is to enable the creation and translation of knowledge to improve MSK, skin and oral health.

The mandate is possibly outside the remit of the ERT to comment on but there was confusion in the ERT as to its origin. The fit of skin and oral health can be made artificially as there are obvious disease similarities in some areas e.g. periodontal disease and rheumatoid arthritis (RA). The ERT felt that the Institute either had to struggle to find cross cutting themes between these foci or felt that all had to be satisfied within a very limited budget.

Much of the research was in areas more suited perhaps to the other institutes such as Aging and the work on physical activity seemed somewhat tangential to the main disease thrust of the Institute. Perhaps the mandate of this Institute needs to be reconsidered, taking into account the other institutes. We are concerned the broad and ill-defined boundaries of this Institute lead to mission creep and lack of clarity in prioritisation.

Section 2 - Status of this area of research in Canada

The number of Canadian clinician-scientists in rheumatology, orthopaedics, dermatology, rehabilitation is small, in oral health even smaller and their distribution uneven across the provinces. Funding is small compared to the enormity of the societal and personal impact of arthritis and related musculoskeletal diseases to Canadians. The committee and leaders in the field confirmed the inability to recruit new investigators and to retain young investigators who have almost or just achieved independence. This is a major threat to the vigor of the clinical sciences in these fields and with the aging of the current generation of scientific leaders suggests a looming crisis.

Despite these trends, Canada is an international force notably in arthritis and musculoskeletal conditions. Using metrics from the IMHA Micro Impact Survey in-house tool, even with the acknowledged difficulties in attribution and classification, the publications and other scholarly activities are impressive, have increased since 2006, and compare favorably with other western nations including the USA and Western Europe.

A subjective assessment from the perspective of what has made a difference to the patients or to Canadians since 2006 would certainly support the conclusion that Canadian researchers have made genuine achievements. Whether IMHA is the force behind this is not answerable with any confidence and immaterial, perhaps.

The major areas of medical research relevant to IMHA's mandate are rheumatology, orthopedics, dermatology, neurology, dentistry, and rehabilitation. Since the 2006 International Review of CIHR, the major advances which have improved patient outcomes or treatment decisions include the dissemination of anti-Tumour Necrosis Factor (TNF) therapy and other biologics in the management of RA and ankylosing spondylitis; the demonstration that rituximab is efficacious in anti-neutrophil cytoplasmic antibody (ANCA)-associated disease and renal vasculitis; studies that show that anti-TNF therapy is not be efficacious in some forms of systemic vasculitis; that anti-B-lymphocyte stimulator (BLyss) and rituximab are not effective in lupus subsets; and the recognition that early aggressive treatment may change the natural history of RA. There have been fewer substantive advances in common musculoskeletal problems such as osteoarthritis and regional pain syndromes such a low back pain.

Canadian scientists have made important contributions by confirming the findings in RA and have led the efforts to identify shortfalls in the delivery of known effective interventions and addressing these gaps in RA; defining the appropriate role for the use of expensive biologics in RA; discovering new determinants of outcomes in joint replacement, developing and testing new systems of care for persons rehabilitating after total joint arthroplasty; developing methods for the early recognition of knee osteoarthritis and its risk factors; understanding how people decide treatment options in early RA; clinical outcome measures for new for systemic lupus erythematosus; documenting the gaps in musculoskeletal disease and arthritis care in First Nations peoples and in the provision of oral health care, for example. Canadian research has focused on common musculoskeletal problems such as osteoarthritis and regional pain syndromes such a low back pain and is welcomed. All of these are examples of knowledge that has a direct impact on people.

Overall impression of the Canadian research landscape in this area

Canada is amongst the world leaders in many areas of the IMHA mandate as listed above. Some of this is historic for example Gladman's research on psoriatic arthritis in Toronto and Tugwell's international leadership in evidence based rheumatology. Clinical epidemiology and outcomes research are also major areas of international strength with work from several groups. The overall achievements are more significant despite its small, rapidly changing, and shrinking cadre of clinician scientists, particularly at its junior levels.

In clinical research, Canadian musculoskeletal researchers, both in breadth and strength are equal to anywhere else in the world. The future challenge is to maintain this with a decline in resources. The IMHA budget has been essentially flat since 2006. Factoring in an average inflation rate of 3.2% and coupled with the trend towards increasing costs and complexity of doing clinical research, the total support to the community is smaller. The end of the Canadian Arthritis Network funding in 2012 will make the funding situation worse.

Section 3 - Transformative Impacts of the Institute

In a geographically dispersed population of over 33 million with a universal health care system funded provincially, and strong collaborative and group decision-making ethos, Canada has a research program which seeks to incorporate and balance societal concerns on what research is needed or opportune in how it uses a limited research budget. The unique feature of the enterprise is that the Institute, IMHA, devises strategies with wide consultation and the science is judged separately.

IMHA, as reported by nearly all those interviewed by the ERT, has served admirably and effectively in its role as a convener, facilitator of research priority setting conferences with wide participation and patients. It has been effective in introducing diverse scientists and partners to each other and to identify the resources needed. IMHA has responded to important new scientific opportunities or addressed important gaps in research. These have often leveraged other sources of funding as well. Thus, as a vehicle for encouraging participation and inclusivity, IMHA has been very successful and its efforts appreciated by academic, clinical, and consumer communities.

The Institute has also succeeded in transforming the working relationships between institutions and within institutions. There is a growing sense that collaborative research is needed to advance and the Institute has fostered this. A small amount of funding has achieved transformative gains in Canadian health care. Thus the research on dental disparities led to $145 increase in targeted dental care. The work on physical activity has led to national guidelines.

Overall impression – to what extent has this Institute been transformative?

Our judgment is that the Institute has been an important asset and has elevated research in these important clinical areas. Without such a dedicated Institute the ERT would be seriously concerned that the gains made would be lost and not built upon.

The intent of IMHA RFAs could be transformative but the ERT was concerned that this potential can be undermined when such submissions are reviewed in the current system where the strategic goals are not understood nor populated with content experts in the field.

It is difficult based on the limited data available to assess the independent impact of the IMHA strategic initiatives as compared to the impact of CIHR as a whole given the understandable priority and funding to the investigator-initiated portfolio.

Section 4 - Outcomes

The most important and (subjective evidence supporting) identifiable outcomes has been the development of a community across the country who have raised the profile of research in this area, engaged with stakeholders to identify the research priorities and brought in partner organizations, agencies and others to maximize the resources and indeed interest in these disease areas. The ERT believes without this energy and activity these accomplishments would not have occurred. These activities focused on identifying important public health priorities and/or scientific opportunities. There are quantifiable (and presumably verifiable) data on the additional funding and partnerships that these activities generated.

Outside musculoskeletal diseases the Institute has brought together scientists and clinicians for enhanced (from a low base) of research and capacity building in skin diseases and has achieved a modest (though growing) success.

Similarly the work on the gap in oral health services for citizens of lower socio-economic status has also brought about change in the funding and awareness of these issues to the relevant sections of Canadian society.

The research networks in osteoarthritis have been transformative in building capacity and new activity in this disease and there have been some gains in terms of assessment of disease outcome.

Overall, transformative is a strong word but these activities have contributed to new knowledge in these disorders and identified major gaps in arthritis care, oral health care, First Nations peoples' care.

IMHA was, we believe, the first CIHR institute to develop formal guidelines, funding requirements, and educational programs for the ethical conduct of research.

Overall impression – to what extent has this Institute been successful in achieving outcomes?

IMHA has been successful in bringing together diverse communities and has achieved a sense of cohesion in a very broad area. It has raised awareness of research in areas that otherwise would have been missed or would not have been so active. It has encouraged inter- and intra-disciplinary work. Its strategically focused activities have achieved worthwhile outcomes, whose individual impact is acknowledged. A global assessment of the impact of the research on clinical outcome in the major disease foci is more difficult to evaluate.

Section 5 - Achieving the Institute mandate

The Institute has responsibility for 6 'Focus Areas' including two: skin and oral health that are not normally considered within the remit of musculoskeletal research structure. There are difficulties in areas with limited capacity such as academic dermatology, dentistry and orthopedics. However, the ERT believes that within its capacity to direct funding, IMHA has allocated an appropriate proportion of activity divided between these areas. The view of the ERT and of many interviewed is that the enormous burden of morbidity and health service expenditure in arthritis and musculoskeletal diseases is not reflected by the relatively small resources committed by CIHR to its program.

The mandate is very broad in these areas covering 'causes, prevention, screening, diagnosis, treatment, support need and palliation' and clearly, with such a large list of areas, it is impossible to cover all these. The strategic priorities have been on tissue regeneration, maintaining physical mobility and reducing pain. These priorities are sensible and supportable but are very broad and indeed cover the major health consequences of most of the diseases in the 6 focal areas. The reality is that the research which is strategically supported does not necessarily reflect these priorities. As an example, the research into deprivation and oral disease has changed health care in Canada but is not financed by the public sector.

There is not perhaps a clear enunciation of the role of basic biomedical research compared with the other 3 pillars of research. We are advised that the open competition grants supported are likely to be weighted towards the biomedical whereas the strategic grants are more likely late translational. There seems to be a gap in early translation and also generally in strategically finding where the biomedical research fits in with the remainder of the program.

Overall impression – to what extent has this Institute achieved its mandate?

The overall impression is that the demands on IMHA are substantial in terms of delivering on a very ambitious mandate over 6 fairly diverse areas. The spectrum of interest is phenomenal ranging from bone biology to understanding how to achieve greater physical activity in patients with cancer. There needs to be a greater sense of what

can be achieved, in a smaller number of areas. What is encouraging is that there is a focus on areas which 'cross cut' between the different areas and between different institutes and this is both resource efficient and will enhance quality. There is clear overlap between the mandate of this Institute and others within CIHR such as Aging and this needs to be tackled more directly. Similarly behavioral research to encourage greater physical activity may not easily or appropriately sit within IMHA.

Section 6 - ERT Observations & Recommendations

As a force for bringing together diverse groups IMHA has been very successful and showed important and novel leadership. Consensus conferences and expert workshops of themselves do not deliver a research agenda but have shaped consensus research agendas and received 'buy in' from the research community and most stakeholders.

IMHA has also been very successful in engaging with relevant partners. This is important as without collaboration there is a limit to what can be achieved. There needs to be more attention given to engaging with the orthopedic community, despite the limited academic orthopedic resource. Further there needs to be a clearer role for industry, including the orthopedic devices industry, in working with academia in research and development in areas of mutual interest.

The osteoarthritis program has also brought together a number of key groups and networked them to tackle key issues in the disease. Indeed, in outcomes research in osteoarthritis, there is international level activity here admittedly in a growing field of endeavor. The oral health agenda would not be covered were it not for the activities of the Institute and similarly the Institute has been instrumental in at least raising skin disease as a target for research, again constrained by lack of clinical research capacity.

Overall impression of the performance of this Institute

This Institute faces a number of issues shared with several other CIHR institutes. It has established itself as a unifying force, supported by the country, in the diverse disease areas under its remit and with this has levered greater research activity and resources. Its strategic focus is clear and broadly supported despite the breadth of the demands by its mandate. It could achieve more strategically with a more joined up relationship between the strategic initiatives and the larger amount of CIHR funding that is awarded to investigator initiated projects. We were impressed by the collegial leadership, its flexibility, and its realistic sense of what can and cannot be achieved.

Recommendations

The ERT has a number of recommendations:

- The IMHA budget is neither sufficient to its mission nor commensurate with the public health importance of the acute and chronic disorders within its mandate. Given its relative small budget, focus is essential least expectations are raised but the resources are inadequate to the task; a situation that can please no one.

- In addition to bibliometric analysis, the value added to the nation's health and to care which is substantial needs better documentation. The Institute needs to develop (this is beginning to happen) a more robust information system so it can understand what is being funded in its 'space' and how this achieves its strategic goals.
- Signs that clinician scientists are endangered are everywhere and world wide. This is particularly true in arthritis and musculoskeletal disease in Canada. After a mild resurgence a decade or so ago, it has experienced a number of set backs which impede recruitment and retention, even after significant investments in individuals' career development. CIHR cannot solve this alone but its emerging role as good faith agent and convenor/facilitator should make it a logical leader in documenting the problem and devising creative strategies to overcome this. Some ideas that might be considered include:
    - Increasing salary support. With partners, the Institute needs to consider how it can incentivize PhDs, physicians and allied professionals to pursue research.
    - Support the lengthened career development to achieve scientific independence recognizing the protracted time needed to develop independent investigators.
    - Assist institutions in developing biometry and information technology core support for investigators.
    - Matching funds to endow clinical science infrastructure.
    - Incentives for units to merge within and across regions to maintain critical mass and expand opportunities.
    - Expand professorship chairs program strategically to the Associate or Assistant Professor levels depending on where the specific needs are
    - Proactively document and analyze research manpower by birth cohorts in research planning.
    - Exploit the universal health care and provincial healthcare databases and proactively assist investigators-both in academia and the private sector- to make use of them.
- There needs to be an Institute approach to consider the role of basic biomedical science in achieving its strategic goals, considering how to develop areas of discovery that are appropriate and ensuring a better fit with the later translational work.
    - Unless the Institute can contribute more directly to ensure that the open competitive research awarded is tackling the major questions of the Institute's mandate then its overall success is likely to be small. Funding a small number of projects based on a panels judgment of 'scientific excellence' alone will not suffice. The Institute needs to be more involved in the peer review process of the work submitted under its jurisdiction. The firewall structure may prevent conflicts of interest but does not allow for strategic input into decision making.
- Pro-active assistance for proposals which address questions of major interest might be considered. Methodological issues that can be overcome should not be used as a barrier to moving forward on key questions.

- The Institute should continue its tackling of the big questions that could achieve a sea of change even if this in the short term limits their coverage of its entire mandate.

Appendix 1 - Expert Review Team

Chair - Professor Alan J Silman
Medical Director
Arthritis Research UK

Expert Reviewer – Dr. Matthew H. Liang
Professor of Medicine, Harvard Medical School
Professor of Health Policy and Management, Harvard School of Public Health
Boston MA, USA

International Review Panel – Professor Victor Dzau
Chancellor for Health Affairs, Duke University
President and CEO, Duke University Health System
James B. Duke Professor of Medicine
Durham, NC USA

Appendix 2 - Key Informants

Session 1 – Review of Institute

1. **Dr. Jane Aubin, IMHA Scientific Director**

2. **Dr. Phillip Gardiner, Chair – Institute Advisory Board**
   Director, Health, Leisure and Human Performance Research Institute
   Associate Dean of Research, Faculty of Kinesiology & Recreation Management
   Professor, Faculty of Medicine, Department of Physiology
   University of Manitoba

3. **Dr. Jeff Dixon**
   Professor, Department of Physiology and Pharmacology
   University of Western Ontario

4. **Dr. Monique Gignac**
   Co-Scientific Director, Canadian Arthritis Network
   Associate Professor, Faculty of Medicine, Dalla Lana School of Public Health,
   Social and Behavioral Health Sciences Division
   University of Toronto

Session 2 – Consultation with researchers

1. **Dr. Hani el-Gabalawy**
   Rheumatology Research Chair and Professor, Faculty of Medicine
   University of Manitoba

2. **Dr. Jan Dutz**
   Associate Professor, Faculty of Medicine, Division of Dermatology and Skin Science
   University of British Columbia

3. **Dr. Gilles Lavigne**
   Professor, Faculty of Dentistry
   Université de Montréal

Session 3 – Roundtable with stakeholders

1. **Dr. Peter Tugwell**
   Director, Centre for Global Health, Institute of Population Health
   Professor, Medicine, and Epidemiology & Community Medicine
   University of Ottawa

2. **Mr. Steve McNair**
   President and CEO, Arthritis Society of Canada

3. **Dr. John O Keefe**
   Editor-in-Chief, Journal of the Canadian Dental Association

4. **Dr. Famida Jiwa**
   President and CEO
   Osteoporosis Canada