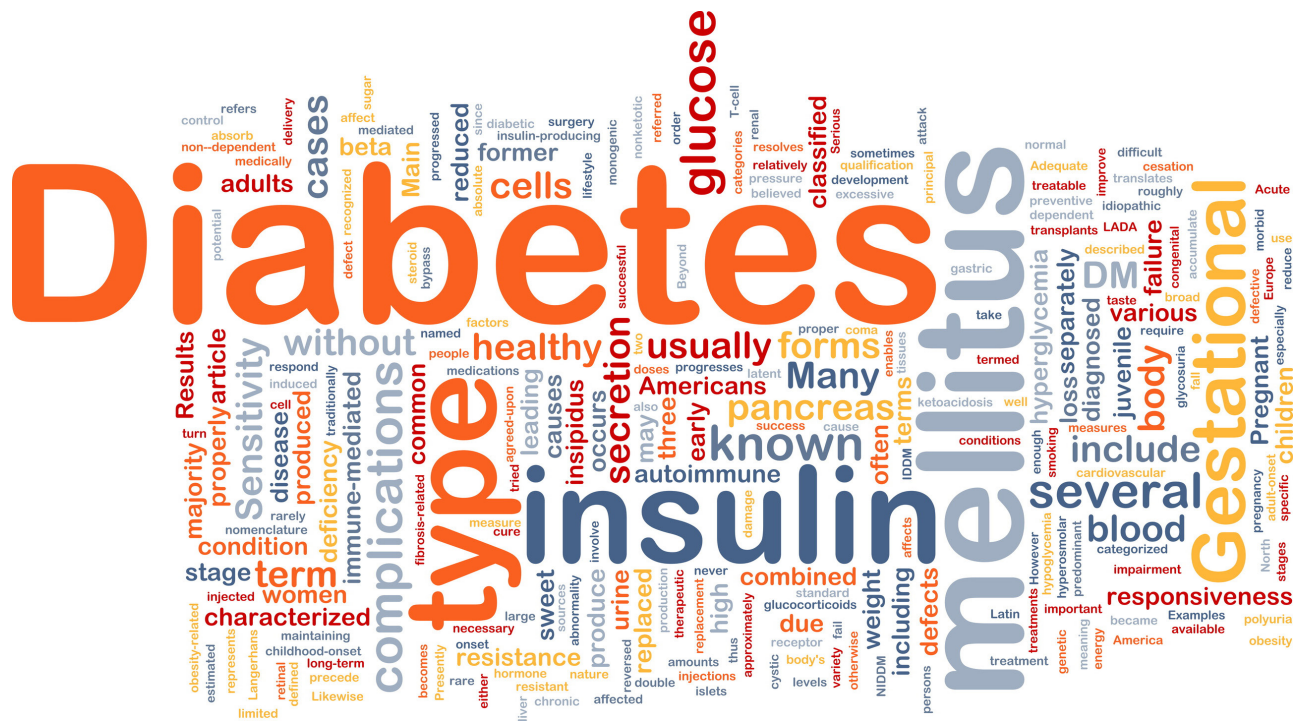

Report from the Diabetes and Related Complications National Research Network Strengthening Workshop

Canadian Institutes of Health Research

Institute of Nutrition, Metabolism and Diabetes

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Key Messages

The 60 Workshop participants, representing the research community, potential funding partners and other stakeholders, reached a consensus that a national research network in diabetes and related complications was desirable, operating as a part of the CIHR Strategy for Patient-Oriented Research (SPOR). There was a preference for a single, comprehensive network, rather than fragmentation of the field through the formulation of several narrowly-focused networks.

The overall roles for the network fell into four broad areas: doing the type of research that cannot be done without a network; achieving outcomes for patients; facilitating health research; and improving competitiveness in Canada for industry funding.

While a thorough discussion of specific research priorities was beyond the scope of the Workshop, the network was advised to set defined goals as a first step, and work back from them to determine the research needed to reach those goals, which should address patient-centred outcomes. Network research activities should be focused appropriately for the amount of funding available. Prevention research and knowledge translation activities should be included.

Indicators of success (after five years of operation) would include evidence that network research had been used to inform policy and practice, including new approaches to prevention and treatment of diabetes and complications; that the network was sustainable because funding partners were convinced they were getting a return on investment; and patients and citizens were involved as full partners, with researchers learning from their needs.

Much work lies ahead in order to prepare a funding application for the network, including: reviewing lessons learned from other networks in Canada and abroad; establishing a thorough and consultative process for defining research priorities; identifying leaders, champions and multiple funding partners; recruiting groups that would collaborate with potential funding partners in drafting a detailed proposal; and ensuring that there remains ongoing support from INMD for application development.

A number of important issues were unresolved or remain controversial. These include: the role, if any, for biomedical research in the network; the extent to which the research agenda will be driven by the agenda of funding partners; and, related to this, how the research agenda should be developed with a balance of perspectives and viewpoints from patients, health care practitioners, decision-makers, industry and researchers themselves. At this point, it remains unclear how existing organizations, like the JDRF Canadian Clinical Trial Network, would interact with this network. There were mixed opinions expressed about what would be realistic health outcomes to anticipate after only five years of network operation. There were also a large number of different perceptions about the term "transformative". Additional clarity about the vision for SPOR Networks in this regard was requested. In addition, greater specificity about the application process for SPOR Networks would prove helpful.

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Summary

Under the auspices of the CIHR Institute of Nutrition, Metabolism and Diabetes (INMD), 60 experts from the research, policy, practice, and charitable sectors met on January 23-24, 2014 to consider the prospects for a national research network in diabetes and related complications, operating as part of the CIHR Strategy for Patient-Oriented Research (SPOR). There are two structural elements planned for SPOR: SUPPORT Units - regional centres providing support to patient-oriented research, including data access, methodological and research services, knowledge translation, clinical trials and capacity development; and SPOR Networks (the topic of this workshop) - national collaborations of patients, health professionals, decision-makers, researchers and other stakeholders, which will generate evidence and innovations to advance practice and policy changes, leading to transformative and measurable improvements in patient health, health care, and service delivery.

The objectives for this workshop were to:

1. Bring together partners with a shared interest in improving care for people with diabetes and complications of diabetes through a coordinated research agenda.

2. Scope out the boundaries of a Canadian Diabetes and Related Complications Network and Clinical Care Research Agenda.

3. Develop an action plan for strengthening a proposal for the Network.

4. Identify and align potential funders to support the Network.

Dr. Philip Sherman, Scientific Director of INMD, noted that these were ambitious objectives, and that this workshop was the first step, not the last word. He also stated that INMD had funding available to support the 50% CIHR contribution to the overall funding of a SPOR network, so this workshop was a step towards a definite goal.

The workshop featured a combination of short presentations and small group discussions, followed by plenary reporting sessions. The keynote presentation was on the work of the UK Diabetes Research Network, given by its Director, Dr. Desmond Johnston. He succeeded in inspiring the workshop participants with a vision of what a diabetes network could achieve for patients. While the emphasis of the UK Diabetes Research Network is on clinical trials, it also conducted technology assessments, studies in prevention and epidemiology, population genetics, pharmacogenetics, health services research, and health economics relevant to all types of diabetes and related complications. Over 40,000 patients have been involved in interventional studies and over 140,000 in observational studies. 145 studies are in progress, 18 of them funded by industry.

The goals and requirements of SPOR were outlined and discussed in detail. Critical attributes of a SPOR Network include meaningful patient involvement to ensure that the research agenda generates outcomes important to patients; engagement with decision-makers and clinicians to ensure integration of research findings into practice and policy; 1:1 matched funding between CIHR and funding partners; and an emphasis on tangible results, with accountability for achieving milestones and deliverables. Networks also have to be “transformative”, precipitating subsequent debate about exactly what that meant.

To help participants envision roles for a network, there were several presentations describing other networks, including the Diabetes Trial Net supported by the US National Institute of Diabetes and Digestive and Kidney Diseases, and the Canadian chronic kidney disease pre-dialysis research network, which is under development. Another presentation described the various types and uses of outcomes studies.

The possible scope of a network was addressed in presentations on the complications of diabetes, with diabetic neuropathies and cardiovascular complications as examples. The economic costs of complications and co-morbidities were also presented, along with arguments for a research agenda balanced between treatment and prevention, and inclusion of health services and policy research.

The final presentations addressed the benefits and risks of partnerships. Dr. Jan Hux of the Canadian Diabetes Association emphasized the research culture change required to succeed in the era of multidisciplinary, multi-partner collaboration. Dr Robert Goldstein of the JDRF described the new southern Ontario type 1 diabetes Canadian Clinical Trial Network, which JDRF seeks to expand nationally. Catharine Whiteside, Dean of Medicine, University of Toronto, related her experience in developing proposals for large, multi-partner research collaborations, emphasizing the necessity for a compelling academic business plan. In the discussion session, Dr. Braden Manns, University of Calgary, spoke about a process of patient engagement used to set research priorities for people with kidney failure on dialysis. Using the model of the UK's James Lind Alliance, a workshop was held to determine the 10 most important questions in the area, based on responses to a national survey of patients, caregivers, and clinicians.

Two small-group discussion sessions were scheduled between the series of plenary presentations. In the first session, participants were asked to consider the question: what can a network do for diabetes and related complications research? Responses from the five groups can be synthesized under four main roles and functions:

1. **Supporting a new type of research that could not be done without a Network.** While this may seem obvious, it is a critical point, especially for a network that has to be "transformational". Multiple research approaches are necessary to alleviate the burden of diabetes and its complications, and it is important to identify those that can be addressed only by a SPOR network, rather than through other forms of support.

2. **Achieving outcomes for patients.** This is an absolute requirement for a SPOR network, and a number of activities that can support this role, including knowledge exchange, development of best practices, and meaningful patient engagement in the choice of research priorities.

3. **Facilitating research**, by removing barriers and by sharing of information and best practices. This can be achieved, for example, by standardizing industry contracts and harmonizing research ethics approvals across institutions that are involved in multicentre trials.

4. **Improving Canadian competitiveness** for industry funding and clinical trials, as well as the international stature of Canadian research. This is a consequence of the first three roles.

The second small group discussion, held after participants had a chance to digest insights about structure and function of a network, considered the following questions:

1. Considering the whole possible range of research issues, what are the priorities for the network?
2. What would a successful network look like in five years?
3. What would be the next steps in building a network to achieve that success?

A variety of views emerged, some contradictory, but the main themes with a degree of consensus are listed below, followed by issues that were unresolved.

Research Priorities and Network Scope

- One comprehensive network is better than many
- Choose a limited number of priorities: funding is limited
- Include prevention research
- Include knowledge translation
- Engage patients in determining research priorities and in all aspects of the network
- Define goals and added-value of network first, then work back to needed research

Success (in five years)

- Specific and measurable targets for performance and outcomes of the network in meeting them
- Self-sufficiency, because the network provides a return on investments through improved health and/or reduced health care costs
- Quick wins, including network data used in policy making, in the development of new therapies
- Quantitative and qualitative indicators of research activities and outputs
- Patients and citizens involved as full partners, and researchers are learning from patient needs
- New partners, (e.g. from the food and insurance industries) are on board
- There is strong public engagement in the network

Next Steps

- Learn from similar networks, and strategies for integrating diabetes research internationally
- Identify champions (including high-profile public figures) who can advance the network concept and funding: establish strong leadership and management: hire a project coordinator experienced in building coalitions
- Begin a formal and rigorous patient engagement process to identify research priorities
- In collaboration with partners, recruit working groups to write a concept paper, then a research proposal and academic business plan to develop a coherent, focused vision for the network
- Acquire multiple funding partners to ensure diversity of research
- Ensure continued INMD support for the development of a network proposal

Unresolved questions

- Is there a place for biomedical research in the network?
- To what extent will the agenda be driven by the priorities of funding partners?
- How to balance patient input into the network research agenda with other viewpoints, including those of practitioners, decision-makers, industry, and researchers themselves

- How to interact with and incorporate existing and developing research platforms into a single diabetes-wide national network
- What are realistic 5-year goals? Are transformative health outcomes realistic in this short time?
- What is meant by "transformative"? We need specificity on this and other applications

In concluding, Dr. Philip Sherman remarked on the "buzz" in the room, indicating that this research community and its partners were indeed interested in developing a network proposal. This workshop was the start of a multi-step process: writing a business plan to include the short-, medium- and long-term deliverables; defining research priorities; identifying leadership; engaging partners and patients, in particular, those from vulnerable populations. He underlined that we are working towards a network that will be transformative in terms of improved health outcomes for Canadians. Though INMD cannot write the proposal, he assured workshop participants that the institute will help to move forward the discussions and next stages of network development.

Narrative Report

Setting the Scene

In welcoming the approximately 60 Workshop participants, Dr. Philip Sherman, Scientific Director of the CIHR Institute of Nutrition, Metabolism and Diabetes (INMD), noted that an earlier call for Expressions of Interest (EOI) for the CIHR Strategy for Patient-Oriented Research (SPOR) Networks had generated over 100 EOIs. While impressive that so many research communities wanted to be a part of the SPOR initiative, it will be necessary to consolidate and integrate many of the communities of interest into a more realistic number of networks, and he hoped that this workshop would be the start of such a planning process for researchers, potential funding partners, and other stakeholders involved in diabetes and its related complications. He pointed out that the SPOR Steering Committee regards chronic disease as a priority area, and had particularly highlighted the need for action in the area of diabetes.

Dr. Sherman urged participants to "think big" about a broad-based translational network that would have an impact on patient outcomes. He suggested that it encompass both primary prevention of diabetes and secondary prevention of complications, that it engage patients, healthcare providers, diabetes educators, policy-makers and funding partners in meaningful ways, noting that 50% of the funding for SPOR networks must be provided by partners. Clear oversight and good governance of the network is also essential. The network should be multidisciplinary, and it should be national in scope. He recognized that it will be challenging to strike the right balance between inclusivity and specificity of focus, and to map out the topic boundaries of the network: this will be influenced not only by the scientific and health care issues but also by the objectives of potential partner organizations. He outlined the objectives for the workshop:

1. To bring together partners with a shared interest in improving care for people with diabetes and complications of diabetes through a coordinated research agenda.

2. To scope out the boundaries of a Canadian Diabetes and Related Complications Network and Clinical Care Research Agenda.

3. To develop an action plan for strengthening a proposal for the Network.

4. To identify and align potential funders to support the Network.

These are ambitious objectives, and this workshop represents the first step, not the last word. Dr. Sherman concluded by stating that INMD has funding available to support the CIHR contribution to overall funding of a SPOR network, so this workshop is an initial step towards a tangible goal.

What a Network Can Do

Stephanie Atkinson, Chair of the INMD Institute Advisory Board, joined in thanking the participants, particularly the representatives of potential funding partner organizations, for taking time to attend the workshop. She then introduced the opening plenary speaker, to stimulate thinking about what a national diabetes research network can accomplish.

The Diabetes Research Network in England
Desmond Johnston
Director, UK Diabetes Research Network, Faculty of Medicine, Imperial College, London

A series of landmark reports in the UK had all arrived at similar conclusions: there was insufficient translation of research findings into improvements in health and healthcare, clinical research was in decline, the research effort was neither strategic nor coordinated, it failed to recognize the needs of patients and the public broadly, it did not harness the resources of the single National Health Service (NHS) and did not recognize the needs of partners in industry. The response was to establish the National Institute for Health Research (NIHR) with a mandate to coordinate and support patient-oriented research, complementing investments of the UK Medical Research Council and the Wellcome Trust in biomedical research. The NHS also has a research mandate written into its constitution, and all NHS organizations are required "to play their full part in supporting research".

In order to improve clinical research, the NIHR created a managed set of clinical research networks (using an established cancer network as a model), intended to support optimal approaches to disease prevention, diagnosis and treatment, with an emphasis on clinical trials. The Diabetes Research Network (DRN) was one of several established, others including Stroke, Mental Health, and Medicines for Children. The "managed" aspect of the Networks was emphasized, and in the case of the DRN, patient recruitment is heavily monitored.

The DRN consists of eight local sub-networks, facilitated, coordinated, and monitored from the centre at Imperial College. While there is an emphasis on clinical trials of new treatments, all forms of clinical research are supported, including technology assessments, prevention and epidemiological studies, population genetics, pharmacogenetics, health services research, and health economics. Topics studied include all types of diabetes and related complications.

Over 40,000 patients are involved in interventional studies ongoing in 2014, and over 140,000 in observational studies. There are 145 studies in progress, 18 of which are funded by industry. There were examples of studies as a response to new regulatory issues, and others to new medical and scientific issues. In collaboration with Diabetes UK and the Juvenile Diabetes Research Foundation (JDRF), the ADDRESS-2 project is recruiting persons recently diagnosed with type 1 diabetes to create a national resource of individuals who can be approached for future research studies. Thanks to the active monitoring by the coordinating centre, patient recruitment in DRN-sponsored studies is on time and on target. The Network also allows for unparalleled recruitment of patients into studies as soon as possible after diagnosis. Patient and public engagement in the work of the network and its decision-making occurs at every level.

DRN funding (~$7M/year) supports the coordinating centre and similar infrastructure in local sub-networks, and provides some compensation for clinical researchers: it does not support the operating costs of individual studies, which are funded from a variety of peer-reviewed sources and from industry. A clinical studies advisory group provides direction on the DRN research priorities. One highly successful innovation has been the provision of small grants allowing "writing groups" from parts of the country to work on writing

research funding applications: this expedient has doubled the success rate for receiving competitive grants by investigators in the DRN.

Dr. Atkinson thanked Dr. Johnston for his inspirational presentation and invited questions, of which there were many. Asked about difficulties in breaking down institutional barriers, such as multiple ethics review board committees, Dr. Johnston replied that the first challenge was replacing a culture of competition with one of cooperation between research centres. It took two to three years for the benefits of collaboration to become clear. Dealing with regulatory issues was difficult, but the NIHR had the clout to require hospitals to deal with ethics approvals in a reasonable time frame, and to monitor their performance. Another question focused on the setting of research priorities in the DRN: was this top-down, or bottom up? The answer was both: although the clinical studies advisory group determines priority areas (including issues of significance to patients), researchers individually or together can propose topics for development through a writing group grant.

Strategy for Patient-Oriented Research: the Canadian vision
Jane Aubin
Chief Scientific Officer, CIHR

Health research in Canada was at a similar stage to that in the UK prior to the establishment of the NIHR, as described by Dr. Johnston. We were good at fundamental research, but not as good as we should be in translating it. Patient engagement was minimal or token, and our research agendas rarely informed by what was important to patients. CIHR has launched SPOR to improve this situation, with the following objectives:

- to improve the health of Canadians by bringing evidence to bear on health care choices, and to accelerate the translation of knowledge from discovery to application.
- to improve the efficiency of health research and the outcomes from it, which will bring economic benefits, including increased investments by the pharmaceutical industry in research in Canada.
- to encourage cooperation between levels of government and among all stakeholders with an interest in the health of Canadians in order to achieve better health outcomes.

Asked about what CIHR was doing to attract more industry funding to Canada, and to reduce the delays in research caused by multiple and prolonged ethics reviews and other regulatory issues, Dr. Aubin mentioned meetings being held between CIHR institute Scientific Directors and representatives of international "big pharma", and pointed to the Action Plan emerging from the 2011 Clinical Trials Summit sponsored jointly by CIHR, Rx&D, and the Association of Canadian Academic Healthcare Organizations. One of the key actions arising has been the creation of a Canadian Clinical Trials Coordination Centre - with a Director recently recruited, and it is planned to begin operations shortly.

Requirements of a SPOR Network
Jeff Latimer
Director, Platforms and Major Initiatives, CIHR

The fundamental principles of the SPOR initiative include meaningful patient involvement to ensure both the research questions and the results arising are relevant; engagement with decision-makers and clinicians to ensure integration of research findings into practice and policy; 1:1 matched funding with provincial governments and other funding partners; and an emphasis on results, with accountability for achieving milestones and deliverables.

The two major structural elements of SPOR are:

1. **SUPPORT Units:** provincial and/or regional centres providing support and expertise to those engaged in patient-oriented research, including a focus on data access, methodological and research services, knowledge translation, clinical trials and capacity development.

2. **SPOR Networks:** national collaborations of patients, health professionals, decision makers, health researchers and other stakeholders to generate evidence and innovations to advance practice and policy changes, leading to transformative and measurable improvements in patient health, health care, and service delivery.

There are two SPOR networks currently in development: Transformational Research in Adolescent Mental Health (TRAM), and Primary and Integrated Health Care Innovations. The national SPOR Steering Committee has recommended that additional networks in chronic conditions and diseases be selected through an open and transparent process.

The SPOR initiative is also concerned with training, capacity building, patient engagement and improving the environment for clinical trials - Dr. Latimer gave updates on the status of each function. He concluded by emphasizing the key benefits of SPOR:

- **Improved health for Canadians** by ensuring that the best research evidence moves into practice, enhancing the health care experience for patients and improving health outcomes for Canadians
- **Economic benefits** by optimizing spending on health care systems, reinvesting resources where the evidence shows that these can have greatest impact, and attracting private investments in evaluative research
- **Driving innovation** in patient-centred care in areas like e-health, implementation science and clinical practice
- **Linking provinces and territories** by providing jurisdictions with opportunities to learn from each other, translating best practices in patient-centred care across Canada, and benefitting all Canadians
- **Reversing the decline in private sector clinical research** by creating an environment that makes it easier to pursue clinical research in Canada

Following Dr Latimer's presentation, there was an extensive question-and-answer session.

Q: Were SPOR networks for clinical trials only?

A: No, SPOR seeks to address the translational gap between discovery and the development of effective health interventions (sometimes designated as "T1"), as well as the gap between innovations in health care and their widespread adoption ("T2").

Q: Will the interests of the funding partner drive the research agenda?

A: Obviously, funding partners are going to support research that aligns with their interests. While for the first SPOR network (TRAM), the funding partner was attracted by CIHR, in most cases it will be the researchers involved in a network that will seek out and attract the most relevant partners. A consortium of multiple partners is likely going to be required to support many networks, and Scientific Directors can play a brokering role in establishing such consortia. While partners will have a voice in the setting of research priorities for a network, they must agree to respect the results of the peer-review process.

Q: Should researchers interested in establishing a SPOR network be cultivating funding partners now?

A: Partners must be involved in shaping the application at its earliest stages.

Q: Will networks support Phase 1 or Phase 2 clinical trials? What are the boundaries of network activities and their relationship with industry?

A: There are no hard definitions, but it is critical that patients and citizens are involved in decision-making at all stages of network development and operations. It is preferable that there is an open, pre-competitive relationship with industry. Networks should also include population health approaches to improving health and healthcare.

Q: How will the networks be selected for funding?

A: An open, competitive process is intended, where a diabetes network would likely compete against other network proposals. A single, collective network on diabetes and related complications might well prove more competitive than a fragmented multi-network approach, which might divide the community rather than uniting it. Nevertheless, the key to all SPOR Networks is to be transformational in nature.

Q: Will all the Networks be the same size, and receive the same funding?

A: There may be some variation, but this question is not settled. Assume they will have similar levels of funding.

Q: Will the SUPPORT units provide resources to help the Networks?

A: These units will be provincially-driven, and while they will furnish platforms and infrastructure to which the networks will have access, they will not be funding research projects or supporting network coordination.

Insights and Experience Relevant to a Clinical and Translational Network

Network Models and Priority Setting at NIDDK

Judy Fradkin

Director, Division of Diabetes, Endocrinology and Metabolic Diseases, National Institute of Diabetes and Digestive and Kidney Diseases, NIH

Dr. Fradkin described how diabetes research planning in the United States is determined collaboratively by several NIH institutes, the CDC, and diabetes charities and informed by scientific input from external experts. NIH supports a "Diabetes Trial Net" similar to that in the UK, which has conducted a series of multi-centre trials testing interventions to prevent and slow loss of beta-cell function in recently diagnosed type 1 diabetes patients. Generally, these trials are of the type that would not be supported by industry. However, industry sometimes provides in-kind support for these types of trials. She emphasized the value of long-term follow-up in these trials; for example, the Diabetes Control and Complications Trial (DCCT) and the follow-up study, Epidemiology of Diabetes Interventions and Complications (EDIC) Trial demonstrated the benefits of intensive control of blood glucose, and the Diabetes Prevention Program Outcomes Study (DPPOS) showed the long-term benefits of an intensive lifestyle (diet and exercise) intervention in high-risk individuals. This evidence has resulted in this intervention now being delivered widely across the USA, through the YMCA.

She noted that many of the elements planned for SPOR exist in the USA, including Clinical Research Networks, and Diabetes Research Centres, analogous to the SPOR SUPPORT units. There is also an emphasis on developing research capacity since many investigators in the network are approaching retirement age so there are real concerns about recruiting and developing the next generation. Finally, she pointed to the Patient-Centered Outcomes Research Institute (PCORI) as the agency in the United States that supports studies addressing questions important to patients, and involves patients and healthcare providers at all stages of the research process.

Using data from outcomes trials and epidemiologic studies to inform mechanistic research and improve care

Hertzel Gerstein

Population Health Research Institute Chair in Diabetes, McMaster University

Taking as his thesis that "outcome studies are intrinsically network-building studies", Dr. Gerstein emphasized that "outcomes" are events important to the patient (e.g. death, renal failure, pain), not events important to the researcher (e.g. publications). He noted that outcome studies also collect multiple anatomical and pathophysiological measures in large numbers of well-phenotyped subjects followed for clinically relevant periods of time, and that this information tends to be under-exploited.

He distinguished between clinical trials, which are essentially hypothesis-testing experiments, and epidemiological studies, which are more like an observatory, gathering data in order to generate hypotheses. He made a plea for the collection of as much data as possible from patients involved in outcome studies, even if some of these data are not directly relevant to

the specific aims of the study. In some cases, such secondary data eventually generates as much useful information as the primary data. One example provided was the ORIGIN trial, funded by industry and intended to reduce the risk of cardiovascular morbidity and mortality. Blood samples collected from 8,000 subjects are now proving extremely useful in a separately funded study assessing biomarkers of cardiovascular disease. He asked CIHR to be receptive to proposals that leverage outcomes study data already collected by performing statistical, genetic and other secondary analyses.

Dr. Gerstein concluded by underlining that outcomes studies provide the evidence base for clinical care, and are an ideal vehicle around which to build collaborative trans-disciplinary national research network. They should also be exploited for discovery and testing of new models of pathophysiology and therapy.

Developing a Canadian chronic kidney disease pre-dialysis research network
Norman Rosenblum
Professor of Paediatrics, University of Toronto

Dr. Rosenblum explained why a national strategy for dealing with chronic kidney disease (CKD) is necessary: to take advantage of major research opportunities; to harness best practices from across jurisdictions, to connect productively with other relevant national initiatives, and to provide a focal point for researchers, practitioners, patients and their families, and policy-makers. He noted that CKD is the major cause of morbidity and death in diabetes patients.

He explained how kidney researchers are identifying scientific priorities for such a network. They have conducted a web-based consultation, sought the views of patients and caregivers, reviewed the literature to identify current clinical research fronts as well as gaps in research and patient care, and held a stakeholder workshop. Gaps that were identified at the workshop defined fundamental issues: who is at risk? Who will progress to CKD and at what pace? What treatment works and why? How do we connect patients to the most effective treatments? How do we get best practices into routine use? The resulting priorities focused on:

- platforms to connect experts, rapidly identify research needs, and implement best practices;
- assessment of evidence linking current practice to outcomes;
- development of innovative interventions to prevent the onset and slow the progression of kidney disease;
- identification of high-risk populations and matching them with effective care;
- Improving the quality of life for CKD patients;
- Assessing and improving models of care.

Next steps in the formation of a national network will be to form a working group that will engage the research community to write a funding proposal, to collaborate with potential funding partners, and to establish an operational and governance structure.

He concluded by noting that all CKD network objectives are highly relevant to diabetes, and he was convinced that the two networks could and should work together; for example, with mutual and shared research and trials infrastructure.

What can a network do for diabetes and related complications research? A small group discussion

Participants were asked how they would answer this question. To encourage all viewpoints, they divided into five small groups, who agreed to report back to the entire workshop on the group's most important three roles or functions for a SPOR network. These roles and functions are represented in the diagram presented on the next page, under four major headings:

1. **Doing the type of research that cannot be done without a Network.** While this seems obvious, it is a critical point, especially for a network that must be "transformational". Multiple research approaches are necessary to alleviate the burden of diabetes and its complications, and it is important to identify those that can be addressed only by a SPOR network approach.

2. **Achieving outcomes for patients.** As an absolute requirement for a SPOR network, there are a number of activities that can support this role, including knowledge exchange and meaningful patient engagement in the choice of research priorities.

3. **Facilitating research** by removing barriers and sharing information.

4. **Improving Canadian competitiveness** for industry funding and support of clinical trials.

Scope of the Network: Diabetes and its Complications

Diabetic Neuropathies: the Cinderella of Neurological Diseases

Paul Fernyhough

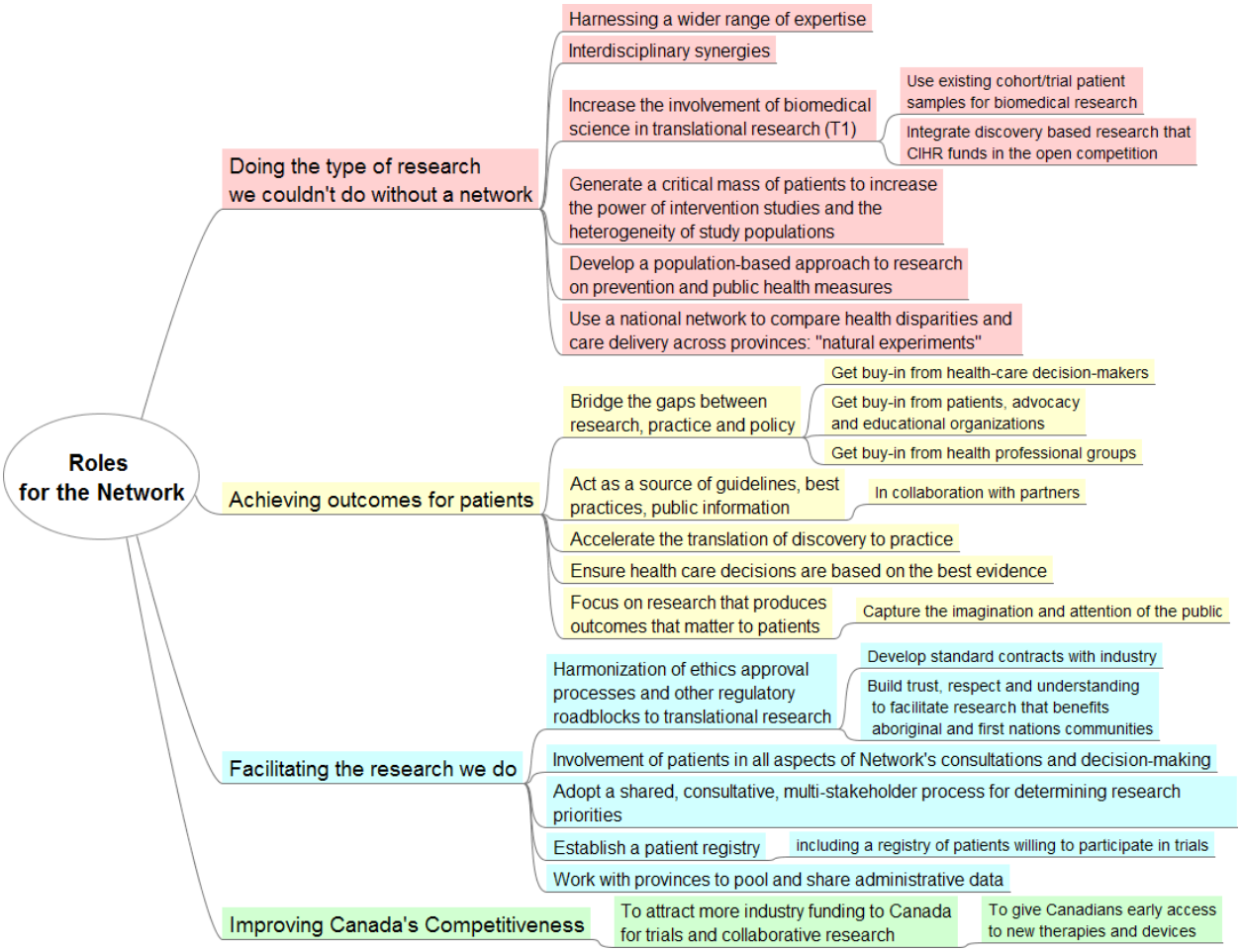
Professor, St.Boniface Hospital Research Centre, Faculty of Medicine, University of Manitoba

Diabetic neuropathies are the most common form of neurodegenerative disorder, affecting 50% of those with diabetes, causing a dramatic decrease in quality-of-life, and often leading to limb amputation with associated high morbidity. Up to 30% of those with neuropathy also experience severe and persistent pain. Other manifestations include autonomic neuropathy, which doubles the risk of myocardial infarction and can cause erectile dysfunction. Despite direct costs of over $1B a year in Canada, for treatment of pain, ulcers and amputations, diabetic neuropathy remains a neglected area of research. The diabetic foot is a common and troublesome presentation, since its management lies at the interface of several disciplines, including endocrinology, wound healing, infectious diseases, neurology, vascular surgery and podiatry. There is a need to harmonize and adopt best practices for foot care, but no forum for the meeting of disciplines exists at present: perhaps this could be a function for the network.

Dr. Fernyhough also felt that the SPOR network could act as an inducement for basic scientists to study the pain and autonomic dysfunction of diabetic neuropathies, lead to the establishment of a tissue bank, and a clinical trials network where new types of drugs and other interventions could be tested.

Possible Roles for the Network

The diagram below is synthesized from verbal reports of small groups, plus notes taken during each small group discussion. To keep the diagram simple, links between roles have been omitted (e.g. involvement of patients will ensure that the research agenda focuses on outcomes that matter to patients: there are many more examples of reinforcing linkages).



Cardiovascular Complications of Diabetes
Jean-Pierre Després
Quebec Heart and Lung Institute, Department of Kinesiology, Faculty of Medicine, Université Laval

Diabetes has a major impact on cardiovascular mortality; for example, diabetic individuals who also have one additional risk factor (e.g. smoking, high cholesterol or high blood pressure) have a mortality rate due to cardiovascular events five times higher than non-diabetics with the same risk factor. However, intensive interventions with multiple drugs and behavior modification in type 2 diabetics can result in >50% reduction in relative risk, indicating that much of this excess mortality is preventable. Although it is clear that simple interventions, such as exercise and the Mediterranean diet have beneficial effects, only about one-sixth of type 2 diabetic patients receive advice about physical activity from their family physicians, and only one-third get advice on improving their diet.

There is a huge gap between the attention paid to individual patients and the focus on health of the population as a whole, and between what we know and what we do. The traditional clinical setting is not designed to address lifestyle risk factors of obesity, nutrition, sedentary behavior, and physical activity. Dr. Després advised that the network should study diabetic individuals not in isolation, but in the context of their complete physical and psychosocial ecosystems.

Economic Costs Associated with Co-morbidities and Complications
Jeffrey Johnson
Scientific Director, Obesity, Diabetes and Nutrition Strategic Clinical network, Alberta Health Services and University of Alberta

Dr. Johnson is also Chair of the Alliance for Canadian Health Outcomes Research in Diabetes (ACHORD) a team of researchers in the clinical, health services and population health sectors which focuses on policy-relevant research related to diabetes health outcomes. In distinguishing between the direct costs of disease (health care system costs and patient out-of-pocket costs) and the indirect costs (costs of lost productivity), he pointed out that it is difficult to determine the indirect costs of any health condition: published figures should be regarded with caution, as many of them are derived for advocacy purposes.

In general, costs to the health care system of a patient with diabetes are about 7x higher than the average patient cost in the year of diagnosis and 4-5x every year thereafter. About half of these costs are for hospitalizations due to the complications of diabetes, so it is essential that a national network include diabetes-related complications. There are also multiple co-morbidities associated with diabetes, including cardiovascular complications, mental health issues, and cancers. One advantage of a national network is that, if access to administrative data is possible, it would allow for a cross-provincial comparison of costs and outcomes.

Since type 2 diabetes is highly preventable and prevention is highly cost-effective, network resources and attention should consider both management of diabetes and its prevention.

How to provide better incentives for healthy behaviour through public policy interventions could also be a priority. These and other important health services and policy research questions should be considered in the scope of the network.

What is the Scope of a Potential Network? A Small Group Discussion

Having listened to these three presentations on complications and costs, participants agreed to discuss this question, and then report back to the whole workshop, providing answers to the following questions:

1. Considering the whole possible range of research issues, what should be priorities for the network?
2. What would a successful network look like (in five year's time)?
3. What would be the next steps in building the network to achieve that success?

The responses from the five groups are listed below. The various items are derived from the verbal reports of each group, as well as notes of the discussion, taken by INMD staff assigned to each group. Similar ideas originating from more than one group have been integrated and paraphrased.

Research Priorities and Network Scope

- A single comprehensive network is more likely to be successful than multiple fragmented networks
- Choose a limited number of priority research themes, rather than spreading limited resources too thinly
- Include prevention
- Include integrated knowledge translation
- Address patient-centred outcomes, which we know will be different from those of researchers (some participants noted that a network driven by the needs of patients would likely be symptom-oriented, and wondered if that was the optimal way to organize the scientific work)
- Should there be a focus on research priorities or health-care priorities (or both)?
- Focus on projects that integrate the maximum number of health research pillars
- How does, and should, biomedical research fit into a SPOR network that includes T1?
- Establish an over-arching outcomes goal for the network, and then work back to define the research priorities needed to achieve this goal
- Where partner funds are coming from may well influence the design of a research agenda, so that will appeal to the partners
- Some participants felt that the question of scope could not be answered yet, because more thought is needed about the value-added of a network. A more thorough and validated process could be used to determine research priorities of the network. The model used by the James Lind Alliance in the UK was suggested as one example to bring patients, caregivers and clinicians together to identify and prioritize the top 10 unanswered questions that they agree are most important.

Specific Suggestions

- Create a network that involves adult patients with type 2 diabetes to complement the JDRF Canadian Clinical Trial Network that is focused on type 1 diabetes.
- Think of new paradigms in managing type 2 diabetes, using innovative therapies early

in the course of the illness.

- Funding for the network (assumed to be $5M/year) isn't an enormous amount when divided between multiple centres and several studies. Accordingly, areas of greatest impact need to be identified and prioritized.
- New approaches in matching type 2 diabetics to optimum management strategies, and to improve compliance.
- Earlier identification and management of pre-type 2 diabetes.
- Innovative new technologies (e.g. artificial pancreas, and use of information and communications technology) for better management of diabetes including among those residing in rural and remote communities.

Success (at five years)

- The network is sustainable and building momentum: the value of the network is evident to funding partners and to stakeholders. Additional stakeholders are seeking participation.
- The network is self-sufficient without CIHR funding, because it has demonstrated to funding partners that there is a return on investments through improved health and reduced care costs.
- The network has an open, inclusive, and adaptable style of leadership.
- There are specific and measurable targets for performance and outcomes, such as a reduction in X by Y% (e.g. average hospital length of stay for dealing with a complication is reduced by 15%). Quantitative outcomes targets were discussed extensively, with a number of participants asserting that significant clinical outcomes would take a long time to attain, and that it is unrealistic to expect major health impacts in a time frame of five years.
- The indicators of research activities and outputs are all positive; e.g. increased international collaborations, more industry trials in progress, more new or repurposed drugs to treat complications are under evaluation in network trials, more primary care healthcare providers are involved in trials, and a growing number of patients are available to or enrolled in trials
- Patients and citizens are involved as full partners, and researchers are learning from patient needs.
- New partners (e.g. from the food and insurance industries) are on board.
- The network has some success with "quick wins", and is engaged in studies to find new therapeutic approaches and new drugs.
- There is an improved understanding of why some patients respond and others do not to certain preventive and therapeutic approaches.
- There is agreement on a research strategy to reduce cardiovascular complications of diabetes, and evidence of progress.
- There is strong public engagement in the network.
- Network data and outcomes are used in policy making decisions.
- The network has achieved operational efficiencies, making Canada a more attractive place to do clinical research.

Next steps

- Learn from other similar networks in Canada and abroad, including clinical trials networks.

- Review existing and old strategies for organizing diabetes research in Canada and elsewhere: what has worked, and what didn't?
- Identify champions (including high-profile public figures) who can advance the network concept and help to recruit funding partners.
- Establish strong leadership and management.
- Identify a project coordinator who is well experienced in building coalitions.
- Establish one or more working groups to develop a concept paper and business plan
- Engage potential partners early in the process of developing a network.
- Collaborate with partners to develop a coherent, focused vision for the role of the network.
- Develop a variety of options, and discuss them with potential partners.
- Acquire multiple funding partners to ensure a diversity of research (i.e. avoid a research agenda being directed towards the interests of a single funder).
- Ensure continued INMD support for the development of a network proposal.

Other recurring themes arising in group discussions

Patient and Citizen Engagement

- Research priorities have to be based on shared needs and objectives.
- Patients must be engaged and in control of their own care; this may be assisted by employing e-health technologies.
- Patients should be involved both in priority-setting and the roll-out of network research, by going beyond patient advocates to becoming patient partners.
- With patients more fully engaged and committed to the network, different types of expertise and skills could be acquired (e.g. in areas such as management and communications). We would also gain enthusiastic supporters who could then cultivate new partners, and help to disseminate new information about diabetes management into the community.

What is meant by being "transformative"?

- Use of a network to do something that a single researcher cannot do isn't necessarily transformative.
- Having patients as full partners - now that would be transformative.
- Transformative means being entirely focused on outcomes in everything the network does.
- Getting provinces to put new funding into a network that delivers outcomes would be transformative.
- Engaging industries that have not traditionally supported health research (e.g. food and insurance) as partners would be transformative. In fact, any large employer should be interested in collaborating in programs that take network and other research findings and build it into incentives for increasing the health and productivity of employees.

An open discussion that followed the small group reports centred around challenges of patient engagement, there being a consensus that the network did need to focus on community interests rather than researcher interests. It was also agreed that a proposal developed in collaboration with patients and showing their clear and essential involvement in all aspects of

the network would prove more competitive for CIHR funding support. There are recognized methodologies for patient engagement strategies on prioritizing health research agendas.

Opportunities for Partnerships: Benefits and Risks

The early involvement of partners in the development of a network emerged as a constant theme in the workshop presentations and discussions. Representatives of two potential partner organizations gave their perspectives, and the final speaker provided reflections on factors contributing to successful applications for funding of complex, multi-partner research initiatives.

Jan Hux, Canadian Diabetes Association
Chief Scientific Adviser

Dr. Hux pointed out that times are changing: most of the researchers in the room had begun their investigative careers in a research culture that rewarded the independent investigator and, conversely, did not always reward collaboration. This resulted in multiple "solo" efforts and added to costs of duplication of infrastructure, as well as the lack of a common language and understanding that bridges the four pillars of health research.

Now, however, funding agencies are increasingly rewarding multidisciplinarity and collaboration as the best way forward in resolving complex health problems. This approach requires mutual respect, generosity, and an open flow of information among researchers. A team with diversity of contributions, but unity of purpose, can achieve synergies and accomplish what individuals labouring alone cannot. There is still a need to ensure that collective and successful investment of shared effort yields commensurate recognition for all those involved.

Research funding agencies are also looking increasingly to partnerships as a way to achieve mutual goals, and are moving from competition to collaboration. Leveraged dollars are attractive to donors, and by partnering they hope to earmark untargeted research dollars for their cause.

Robert Goldstein, JDRF
Senior Scientific Adviser

The JDRF Canadian Clinical Trial Network (CCTN) was established with $14M from JDRF and $20M from the Federal Economic Development Agency for Southern Ontario. The goals of JDRF CCTN are:

- To create an improved, nationwide infrastructure for diabetes clinical trials in Canada, in order to enable greater clinical trial capacity;
- To conduct advanced clinical trials of leading-edge treatments and technologies for type 1 diabetes;
- To provide Canadians with type 1 diabetes access to the latest diabetes breakthroughs via participating in clinical trials; and
- To create new partnerships between academic researchers, non-profit organizations, industry, and government to accelerate preventions, better treatments, and a cure for type 1 diabetes and its complications.

Although the CCTN originated in southern Ontario, JDRF intends to expand its network from coast-to-coast. Dr. Goldstein noted that during the establishment of that network, participants asked many of the same questions being asked in this workshop, and the network has already achieved many of the requirements of a SPOR network. Industry finds the CCTN attractive, and JDRF has a lot to offer to a SPOR network related to diabetes and its complications.

In thinking about how JDRF might be involved in partnering within a SPOR network, he emphasized that JDRF could not write a blank cheque: it would want to select specific research projects relevant to its mission of "Cure, treat, prevent". For example, JDRF would not be interested in supporting projects focused on neuropathies or cardiovascular complications.

Opportunities for Partnerships: Benefits and Risks

Catharine Whiteside

Dean, Faculty of Medicine, University of Toronto

After describing the complex partnership environment in which she worked (the university plus nine independent hospitals), Dr. Whiteside presented two case studies to illustrate what was necessary for a network proposal to achieve success. Key factors identified include:

- A water-tight academic business plan, which provides a clear statement of the problem, explains how the proposal will address the problem, a description of the deliverables and their impact, and clear milestones along the way. A critical and credible financial analysis and an effective governance and management structure are also essential elements of such a business plan.
- Passionate and dedicated leaders, who can market the value of the network and understand the advantages of stakeholder engagement, are essential. They are creative, tenacious, solutions-oriented and are both servants to and leaders of their network members.
- Adequate resources, including the prospect of access to incremental resources as an incentive for collaboration, and the opportunity for further resources if stated outcomes are achieved.

In one case, a network proposal was strong scientifically, but the accompanying financial analysis was weak and progress milestones were vague. As a result, it has not been funded. In a second case, it had taken two years to develop a sound business plan, but this served to attract first internal and then external investment; ultimately, this second initiative is succeeding and meeting intended milestones.

There are some fundamental truths about successful health networks in Canada:

- Canadian researchers and health care providers are well-positioned to translate discovery into practice
- No single institution has the resources necessary to provide solutions to complex chronic diseases
- Funding from multiple sources, including industry, is necessary
- Collaboration with international consortia is required: partner with the best in the world.
- Professional management is critical, along with

- → Effective internal communication strategies;
- → Professional fund-raising;
- → Strategic marketing of the network's outcomes, impacts, and return on investments.

In the question period, there were several requests for more information about an academic business plan. Dr. Whiteside reiterated that it had to contain a clear problem statement, a clear solution, and provide a set of specific deliverables, linked to a budget. It is not a traditional research grant proposal. The advantage of writing such a business plan is that once completed, it can be converted into a research proposal, an appeal to funding partners, and multiple other uses. It should be about 20 pages long providing a readable narrative that is understandable by a wide range of interested readers.

Dr. Braden Manns, University of Calgary, spoke about a process of patient engagement that was used to set research priorities for people with kidney failure on dialysis. The process was modeled on an approach established by the James Lind Alliance in the UK. A Workshop was held with the goal of determining the top 10 most important unanswered questions in the area of kidney failure and dialysis, based on a short list of 30 research uncertainties generated from a list of nearly 2,000 responses received in a national survey of patients, caregivers, and clinicians. Dr. Andreas Laupacis from St. Michael's Hospital in Toronto forged a collaboration with the Kidney Foundation of Canada (KFOC), the Interdisciplinary Chronic Disease Collaboration, and the Canadian Kidney Knowledge Translation and Generation Network (CANN-NET), to lead this project.

Next Steps

Dr. Philip Sherman thanked the presenters and the participants for their contributions to the Workshop and remarked on the "buzz" in the room, which told him that this strong Canadian research community is indeed interested in developing a network proposal.

He recognised that this workshop is the start of the process and that there are many steps to be completed, including: writing a business plan to include the short-, medium- and long-term deliverables; defining research priorities; identifying leadership; engaging partners and patients, particularly those who represent vulnerable populations.

He intended that the voluntary health organizations would help with the first steps in patient engagement through their existing communities.

He appreciated the joint work towards developing a national network that will be transformative in terms of improved health outcomes for Canadians. Although INMD cannot write the research proposal, he assured the participants that it will provide support to move forward discussions begun at this Workshop.

Workshop Participants

Speakers

Jane Aubin	Canadian Institutes of Health Research
Mark Bisby (Facilitator)	Independent Consultant and Advisor
Jean-Pierre Després	Université Laval
Paul Fernyhough	University of Manitoba
Judith Fradkin	National Institute of Diabetes and Digestive and Kidney Diseases (US)
Hertzel Gerstein	McMaster University
Robert Goldstein	JDRF
Jan Hux	Canadian Diabetes Association
Jeffrey Johnson	University of Alberta
Desmond Johnston	Imperial College London (UK)
Jeff Latimer	Canadian Institutes of Health Research
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Catharine Whiteside	University of Toronto

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Gillian Booth	University of Toronto
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Mauricio Ede	Merck Canada
George Fantus	University of Toronto
Laurie Gibbons	Public Health Agency of Canada
Susanne Gray	Certified Diabetes Educator
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Karen Shelstad	The Lawson Foundation
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Hani El-Gabalawy	Institute of Musculoskeletal Health and Arthritis
Elisabeth Fowler	Institute of Human Development, Child & Youth Health
Malcolm King	Institute of Aboriginal Peoples' Health
Jean Rouleau	Institute of Circulatory and Respiratory Health
Liz Sterling	Institute of Musculoskeletal Health and Arthritis
Robyn Tamblyn	Institute of Health Services and Policy Research

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