Patient Group Pathway Model to Accessing Cancer Clinical Trials

Consensus Meeting Report

Colorectal Cancer Canada

October 2017

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In collaboration with

Coalition Priorité Cancer au Québec
www.coalitioncancer.com

Executive summary

Colorectal Cancer Canada (CCC) believes that access to clinical trials of new drugs, medical technologies and other cancer treatments should be a standard of care for all Canadian patients, regardless of their age, where they live, and their income. For too many patients, the barriers to participation in cancer clinical trials are significant and contribute to unacceptably low enrollment rates. Suboptimal clinical research processes hinder therapeutic advancements for cancer and waste resources invested by sponsors and by all Canadians.

Consensus meeting goals

This consensus meeting was organized to gain agreement among a robust cross-section of stakeholders on a way forward to develop a comprehensive framework for patient group involvement across the cancer clinical research and development continuum in Canada. Such involvement entails 1) inputs at core decision making tables about patients' values, priorities and realities, and 2) improving recruitment, participation and retention by helping patients to overcome challenges in accessing clinical trials.

The consensus meeting was designed to address the following hypothesis:

"Canadian cancer patient groups may offer valuable assistance in increasing patient participation and retention rates in Canadian cancer clinical trials. A patient group pathway model could substantially add value to these efforts. A Canadian Patient Group Pathway Model to Accessing Cancer Clinical Trials may:

- *Promote understanding and awareness of clinical trials to defined patient populations*
- *Provide insight and inform patient values, outcomes and study endpoints that are important and matter to patients*
- *Increase recruitment, participation, and retention rates of participants*
- *Allow for the capturing of Real World Evidence post-trial to inform long term outcomes of the interventions and to be incorporated into high quality patient group submissions being made to authorities such as the pan-Canadian Oncology Drug Review, the Institut national d'excellence en santé et en services sociaux, and the newly formed Cancer Drug Implementation Advisory Committee."*

Meeting outputs

A key output of the meeting was a consensus that the Clinical Trials Transformation Initiative (CTTI) model should form the basis of a Canadianized pathway. Nine consensus questions were submitted to the meeting participants for review and consensus. These were formulated based on the expertise of the Scientific Advisory Committee and on evidence from the scientific literature and grouped under four themes:

Part I: The barriers to accessing cancer clinical trials overall and the barriers to a "Patient Group Pathway Model" in cancer clinical trials

Part II: The role of patient groups in cancer clinical trials

Part III: Best practices and validity of the Clinical Trials Transformation Initiative (CTTI) model for Canada

Part IV: The development of a Canadian Patient Group Pathway Model for cancer clinical trials: patient engagement, awareness, recruitment, retention, ongoing and post-trial communication. Adapting the CTTI model for cancer clinical trials to the Canadian reality.

Consensus was achieved that the Clinical Trials Transformation Initiative (CTTI) model could be Canadianized to form a Canadian Patient Group Pathway to Accessing Cancer Clinical Trials.

The process of developing a Canadian Patient Group Pathway to Accessing Cancer Clinical Trials requires:

- engagement of a broad range of stakeholders;
- adaptation of the CTTI model to the Canadian landscape; and
- consideration of components of other successful models of patient group engagement.

Several aspects of cancer clinical research in Canada are different from those in the United States. Factors raised at the consensus meeting and their implications for the Canadian Patient Group Clinical Trials Pathway Model must be taken into account.

Moving to action

A key component of successful models cited by meeting participants was a collaborative approach involving all stakeholders, including patient groups. Recommendations were offered to all stakeholders to guide the development of a Canadian Patient Group Pathway to Accessing Cancer Clinical Trials. In addition, specific recommendations were addressed to patient groups specifically.

The following will be the next steps to develop and implement the pathway.

Step 1: Disseminate the meeting report

The first step will be to further engage the core base of support (i.e., the Scientific Advisory Committee and meeting invitees) by requesting feedback on the draft meeting report.

The final report, including the guidance recommendations will be:

- issued as a publication of Colorectal Cancer Canada;
- submitted as an abridged version to one or more open-access clinical journals; and
- submitted to online blogs and open-circulation publications.

Step 2: Form a working group

Scientific Advisory Committee members will be invited to form small working group to advance the development and adoption of a Canadian Patient Group Pathway to Accessing Cancer Clinical Trials. The working group's task will be to:

- develop a proposed framework for the Pathway;
- map out a process for adoption and operationalization of the Pathway within the next year;
- create a Charter outlining the needs and expectations of stakeholders, including patient groups, related to their participation in the clinical trials process; and
- advise Colorectal Cancer Canada on training programs needed to enable all cancer patient groups to participate in the Pathway.

Step 3: Engage the broader cancer research community.

The broader research community will be engaged through dissemination of the outputs from the consensus meeting and by outreach at various conferences and research meetings.

Step 4: Engage sponsors of clinical trials to adopt a "Charter" recognizing the importance of including patient groups in the development and execution of cancer clinical trials.

An important step in ensuring that the model is adopted is to have the endorsement of sponsors of trials and to encourage them to adopt policies that require the participation of patient groups in all stages of a cancer clinical trial.

Step 5: Engage trial sponsors to engage in training of patient groups through an independent body to ensure quality research partners.

Adopting the Canadian Patient Group Pathway to Accessing Cancer Clinical Trials, incorporating the concepts of multi-stakeholder collaboration and the inclusion of patient groups as equal partners, is expected to generate significant benefits for all stakeholders.

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Chapter 1 Introduction

Colorectal Cancer Canada believes that access to clinical trials of new drugs, medical technologies and other cancer treatments should be a standard of care for all Canadian patients, regardless of their age, where they live, and their income. For too many patients, the barriers to participation in cancer clinical trials are significant and contribute to unacceptably low enrollment rates, as elaborated in this report. Suboptimal clinical research processes hinder therapeutic advancements for cancer and waste resources invested by sponsors and by all Canadians.

This consensus meeting was organized to gain agreement of a robust cross-section of stakeholders on a way forward to develop a comprehensive framework for patient group involvement across the cancer clinical research and development continuum in Canada, as illustrated in Figure 1 below. Such involvement entails 1) inputs at core decision making tables about patients' values, priorities and realities, and 2) improving recruitment, participation and retention by helping patients to overcome challenges in accessing clinical trials.

Figure 1 Canadian cancer clinical trials process

Growing impact of patient engagement

Patients have, over the past two decades, increasingly provided unique perspectives to all phases of cancer clinical research and development.[1] For example:

- Organizations such as the James Lind Alliance,[2] a non-profit initiative established in the United Kingdom in 2004, address mismatches between patients' priorities and those of clinicians and researchers[3] by bringing together patients, carers and clinicians to ensure that clinical research funders are aware of the issues that matter most to patients and clinicians.
- The Patient-Centered Outcomes Research Institute (PCORI) was created in 2010 in the United States to produce and promote high-integrity comparative effectiveness research that is "guided by patients, caregivers, and the broader healthcare community."[4] Patient engagement is most commonly done at the beginning of research, and this approach has resulted in increased study enrollment rates and has aided researchers in securing funding, designing study protocols and choosing relevant outcomes;[5]
- Patient-reported outcomes (PROs) are now accepted in Europe for drawing regulatory conclusions regarding treatment effects, in the benefit risk balance assessment, or as specific therapeutic claims;[6]
- Patients have been integrated within cancer research units since at least 2005 in the United Kingdom;[7] and
- Experiences in the United States and the United Kingdom have demonstrated that patient group participation has led to improved clinical research outcomes.[1,4,5]

Need for a systematic framework

Despite this progress, inclusion of the patient voice in cancer clinical research remains inconsistent. Research sponsors may not be convinced of the value of this approach, in large part because the evidence base for patient involvement is still evolving and, lacking a standardized approach, its impact is

difficult to measure.[8] From the industry standpoint, there is no accepted framework for systematic patient involvement in medicines research and development, regulatory review, or market access decisions.[9]

Some jurisdictions have attempted to implement systematic frameworks for patient involvement in cancer clinical research. Notably, the Clinical Trials Transformation Initiative (CTTI) in the United States was established in 2007 by Duke University and the Food and Drug Administration (FDA) as a public-private partnership. CTTI now comprises more than 80 organizations from across the clinical trial enterprise working to develop and drive adoption of practices that will increase the quality and efficiency of clinical trials.[10]

Goals of the consensus meeting

This consensus meeting brought together interested parties to agree on the elements of a "Patient Group Pathway Model to Accessing Cancer Clinical Trials" and to outline practical ways in which patient groups can participate in the research and development process. The goal is to help make cancer clinical trials accessible to all patients and their outcomes significant for the advancement of cancer research and treatment.

The consensus meeting was designed to address the following hypothesis:
"Canadian cancer patient groups may offer valuable assistance in increasing patient participation and retention rates in Canadian cancer clinical trials. A patient group pathway model could substantially add value to these efforts. A Canadian Patient Group Pathway Model to Accessing Cancer Clinical Trials may:

1. *Promote understanding and awareness of clinical trials to defined patient populations*
2. *Provide insight and inform patient values, outcomes and study endpoints that are important and matter to patients*
3. *Increase recruitment, participation, and retention rates of participants*
4. *Allow for the capturing of Real World Evidence post-trial to inform long term outcomes of the interventions and to be incorporated into high quality patient group submissions being made to authorities such as the pan-Canadian Oncology Drug Review, the Institut national d'excellence en santé et en services sociaux, and the newly formed Cancer Drug Implementation Advisory Committee."*

Cancer clinical trials in Canada

Value of cancer clinical trials

The Canadian Partnership Against Cancer's *2017 Cancer System Performance Report* describes the positive impacts of clinical research.

> *"Clinical trials are the foundation for the consolidation of effective, high-quality cancer treatments. Trials evaluate the safety and efficacy of emerging treatments, paving the way for improved best practices. Evidence shows that local centres participating in clinical trials are more likely to follow evidence-based treatment guidelines and thus improve patient outcomes than centres that do not host clinical trials. Finally, if the trial or regimen is successful, patients in the treatment group can benefit from a breakthrough treatment.*
>
> *"In synergy, these benefits improve treatment quality at both the individual and system level and can provide better care options for present and future generations. An effective, high-quality*

cancer system ensures the availability of clinical trials for a broad range of cancers and stimulates participation among eligible patients."[11]

Low patient participation in Canadian cancer clinical trials

Despite these significant benefits, participation rates of adult cancer patients in clinical trials in Canada remain significantly low. *The 2017 Cancer System Performance Report* states that, in 2014, less than 7% of adult cancer patients in Canada were enrolled in a clinical trial, compared to fewer than 5% in the United States and 12% in the United Kingdom.[11] Also of concern, an earlier report stated that rates of participation in Canada had plateaued or were decreasing.[12]

By comparison, enrollment rates for pediatric cancer patients ranged from 19% to 57% by province across Canada.[12] Greater participation of this population in clinical research is believed to have contributed to improved health outcomes. In the United States, for example, mortality rates among pediatric cancer patients have been decreasing since the 1970s by approximately 2.6% per year, whereas those for adults did not decrease until the 1990s.[13]

Recent data point to the importance of recruitment and retention of patients. In the United States, it is estimated that:

- 85% of clinical trials fail to retain enough patients to continue;
- 80% fail to finish on time; and
- half of sites enroll one or no patients.

Furthermore, of the overall pharmaceutical clinical trial budget, 40% is spent on recruitment. The fact that 30% of patients drop out of a clinical trial indicates that more could be done to improve retention.[14] These statistics reflect an enormous waste of time and money on behalf of clinical trials sponsors, researchers and the general public. Moreover, they signify that opportunities for potentially life-saving improvements in patient outcomes are being missed, leading to a devastating loss of hope for many cancer patients.

Patient group involvement across the cancer clinical trials continuum

Several studies across geographical regions and therapeutic areas have reported that engaging patients in research improves patient enrollment and decreases drop-out rates.[15,16,17,18,19] In Canada, patient groups increasingly participate in all stages of the cancer clinical trials process (detailed in Appendix 2) with the goal of helping to shape the goals, design, implementation and outcomes of new approaches to cancer treatment.

Formal and informal roles for patients have evolved over the past decade. These are a few examples:

- Health Canada has established a Scientific Advisory Committee on Oncology Therapies, including patient representation, to provide advice on the clinical merits of cancer treatments;[20]
- Pharmaceutical company sponsors of cancer clinical trials reported that they now routinely seek advice from patient groups;
- The Canadian Cancer Trials Group (CCTG) has in place a Lay Representative Committee which is available to provide patient and public inputs in the development and delivery of clinical trials;[21] and
- Canadian health technology assessment processes formally include patient group submissions and/or patient representation. These include the pan-Canadian Oncology Drug Review,[22]

Quebec's Institut national d'excellence en santé et en services sociaux,[23] Ontario's Health Technology Assessment,[24] and British Columbia's Health Technology Review.[25]

The value of patient group involvement in the Canadian clinical trials process has been recognized by major national institutions. For example:

- A committee of the Standing Senate committee on Social Affairs, Science and Technology in 2010 reported that it "was frequently told that collaboration and the establishment of networks between academic institutions, research networks and patient groups were helping to streamline clinical trials and improve patient recruitment from the sponsor's perspective while also improving access to investigational drugs from the perspective of the patient." The committee recommended a National Framework for Coordinating Clinical Trials.[26]
- The Canadian Institutes for Health Research's "Canada's Strategy for Patient-Oriented Research" is a cornerstone of its work. The agency notes that "a growing body of evidence supports the inclusion of patients and the wider public in setting national research agendas and incorporating patient and public preferences and values into health research."[27]
- The Canadian Agency for Drugs and Technologies in Health (CADTH) has seen growth in the number of global clinical trial sponsors requesting advice on clinical trial design, including more patient input. (Boothe K. Public and Patient Engagement in Canadian Drug Assessment: 10 Years of Experience in Ontario and at the CADTH Common Drug Review. Presentation at CADTH 2017 Symposium, April 24, 2017.)

While these advancements recognize the valuable role that patient input plays across the research and development continuum, a comprehensive framework would enable measurement of the impact of patient engagement on the cancer clinical trials process and outcomes.

Consensus development process

Colorectal Cancer Canada decided to address the need for systematic involvement by patient groups in the cancer clinical trials process by organizing, in partnership with the Coalition priorité cancer au Québec, a one-day meeting to foster a partnership among parties sharing this common goal.

Terms of reference

The main output of the meeting was a consensus that the Clinical Trials Transformation Initiative (CTTI) model should form the basis of a Canadianized pathway. Also, a set of recommendations was submitted to guide the subsequent development of a Canadian model.

Stakeholders representing the following organizations and roles, which ultimately will be responsible for applying the model in their work, were invited to attend the meeting:

- Cancer patient groups;
- Clinical trial sponsors (industry, government, academia);
- Research sites (clinical research organizations, principal investigators, clinical trials nurses, cancer centre clinical research unit directors and executive staff members);
- Cancer clinical trials networks, research ethics organizations;
- Regulatory bodies; and
- Health technology assessment and health policy bodies.

Inputs to the consensus process

The consensus development process was informed by two presentations, a panel discussion and dialogue among audience members. Detailed summaries of the following keynote presentations are provided in Appendix 3.

Keynote address: "Interesting patients in clinical trials"

Deborah Collyar of Patient Advocates In Research (PAIR) stressed that interesting patients in participating in clinical trials requires a change in the mindsets of decision makers: patients should be at the centre of research rather than merely its subjects. The research process must address the significant barriers that each person may experience.

Patient groups play a pivotal role. They can be vital to researchers by providing inputs into all phases of research, and to patients by maximizing their health literacy and reducing fear and uncertainty. By bridging the interests of both parties, patient groups can increase participation in clinical trials for the benefit of all.

Key note address: "Patient group pathway model"

Bray Patrick-Lake, now of Duke University, described the history and experience of the Clinical Trials Transformation Initiative[28] (CTTI), which served as a reference for the development of the Canadian model. The CTTI model consists of a set of recommendations for each stakeholder group and tools to educate and assist patient groups to participate in the process.[29]

Panel discussion: "Development of a clinical trials patient group pathway model"

The two presenters engaged with the audience in a facilitated discussion which is summarized in the next section of this report.

Consensus process

A series of nine consensus questions and proposed responses (reproduced in Appendix 5) were developed by the meeting Co-Chairs, based on the expertise of the Scientific Advisory Committee and on evidence from the scientific literature, and were grouped under four themes.

- Part I: The barriers to accessing cancer clinical trials overall and the barriers to a "Patient Group Pathway Model" in cancer clinical trials
- Part II: The role of patient groups in cancer clinical trials
- Part III: Best practices and validity of the Clinical Trials Transformation Initiative (CTTI) model for Canada
- Part IV: The development of a Canadian Patient Group Pathway Model for cancer clinical trials: patient engagement, awareness, recruitment, retention, ongoing and post-trial communication. Adapting the CTTI model for cancer clinical trials to the Canadian reality.

The questions were circulated in advance to attendees together with a background summary document. Following the presentations and panel discussion, each consensus question was discussed in detail in a session moderated by two Co-Chairs and the meeting facilitator. Participants were then invited to propose wording changes to the suggested responses. Attendees voted their acceptance by responding 'yes' or 'no' using electronic polling. Consensus was deemed to have been reached when a majority of 'yes' votes was achieved. A 'yes' response of 90% or more was achieved for each question.

Chapter 2 Towards a Canadian Patient Group Pathway to Accessing Cancer Clinical Trials

Consensus was achieved that the Clinical Trials Transformation Initiative (CTTI) model could be Canadianized to form a Canadian Patient Group Pathway to Accessing Cancer Clinical Trials. Discussions related to the consensus questions are summarized below, supplemented by corroborating evidence from the scientific literature.

Part I: The barriers to accessing cancer clinical trials overall and the barriers to a "Patient Group Pathway Model" for cancer clinical trials

The first step in building the pathway was to consider barriers faced by both patients and patient groups in accessing the cancer clinical trials process, and factors that facilitate their participation. Responses to the two consensus questions under this theme are summarized in Table 1 below, with further detail provided following the table.

Table 1 Patient- and patient group-specific barriers to accessing cancer clinical trials

Types of barriers	Patient-specific	Patient groups
Education/awareness	Lack of patient education on clinical trials and/or misconceptions of and inability to navigate clinical trials in general Lack of awareness of ongoing cancer clinical trials as a possible option	Lack of understanding of and education by patient groups about clinical trials Patient groups are unaware of how they can be involved
Practical issues	Logistical and cost-related concerns: lack of time, lack of resources to support out-of-pocket expenses for travel/parking/childcare, etc. Geographical proximity to cancer clinical trials may be prohibitive	Lack of resources (including people, time, money) to participate in the process
Availability of clinical trials	Too few clinical trials offered in Canada	Long wait times for trials to be activated

Types of barriers	Patient-specific	Patient groups
System support	Uncommitted or uninformed oncologist: • Health care professionals may serve as 'gate keepers', limiting therapeutic options for the patient • Risk aversion of health professionals Potential participants may be concerned about the impact on their care if they choose to advocate for a cancer clinical trial	Silos within sponsor organizations block patient group engagement Sponsors may be unaware or uninterested in working with the patient groups that are engaged Lack of understanding by sponsors and/or investigators as to how to include patient groups
Clinical trial design	Participants may not be eligible based on restrictive inclusion criteria Design of clinical trial may not be acceptable to patients • Placebo arm • The same treatment is more easily available outside of study • Cannot wait for required procedures to be done or for enrollment process Local clinical trial site unavailable	Compliance issues across various stakeholders regarding privacy and confidentiality
Socioeconomic factors	Education: Persons with lower levels of education are less likely to consent Social circumstances: Patients who lack time to attend extra trial-related appointments due to family commitments are less likely to consent Language impediments and cultural issues: Minority populations are less likely to participate due to distrust of health systems and institutions	
Implications on future care	Jurisdictional boundaries: Many clinical trials sites refuse to treat patients who reside in other cities or provinces Government restrictions on future therapies because of exposure to the experimental drug	

Patient-specific barriers

Patients can experience a constellation of barriers to participation in cancer clinical trials depending on their personal situations. Cancer patients are eager to participate in clinical trials but many must overcome significant hurdles to do so. The fact that 70% of American patients are estimated to be inclined or very willing to participate in clinical trials,[30] yet actual participant rates are below 5%, reinforces attendees' views that barriers to trial participation are numerous and often insurmountable. A systematic review of published papers concluded that most patients want to participate in clinical trials but do not because of one or more barriers.[31] Obstacles may pertain to the patient's situation or to how the system of cancer clinical trials is organized.[32]

Education and awareness

Predominant patient-related barriers concern patients' knowledge and the power imbalance in the doctor-patient relationship.[31] Knowing that a clinical trial is available is key to patient participation. A prospective survey showed that the majority of patients who were approached consented to participate in a clinical trial.[33] Other factors include fears surrounding clinical trials, particularly related to cancer diagnosis, clinical trial participation, and fear of the unknown.[34]

Practical issues

Logistical concerns present barriers for some patients. Costs and availability of transportation, parking and childcare can be significant. For example, problems with transportation and distance from the medical centre were cited as top barriers to participation by the 31.1% of lung cancer patients who did not enroll in a clinical trial.[35] The geographical distance from study site can be a major factor and patients from smaller provinces often do not have access to any cancer clinical trials. Programs to address the financial burden have been shown to increase clinical trial participation.[36]

System support

The single most influential factor in enrolling patients in clinical trials has been cited as physician influence.[37] A study of 7,887 patients with lung or colorectal cancer found that most learned about trials from their physicians but only 14.1% had discussed the possibility of clinical trial participation; of these 25.8% participated compared to 3.6% of all patients. Discussions were less frequent among older patients, racial minorities, and those with lower incomes and more comorbidity.[38]

There are several reasons why clinicians may not be supportive or knowledgeable about clinical trials. Physicians are focused on providing high quality standard care which, given the short timeframes in which they operate, may leave them with insufficient time or desire to explain the intricacies of clinical trials to their patients. It is difficult to be aware of the multitude of cancer clinical trials being conducted at a given time. Some physicians may be uncommitted or uninformed, which can create a quandary for patients who are concerned about the impact on their care if they choose to advocate for a cancer clinical trial.

Availability of clinical trials

Attendees reflected that there are too few cancer clinical trials in Canada and it takes far too long to activate them. By the time the trial is accruing patients, it is often stale-dated, with the question no longer being of major interest or importance.

Clinical trial design

Common hindrances for patients include: concerns with the trial setting; a dislike of randomization; general discomfort with the research process; complexity and stringency of the protocol; presence of a placebo or no-treatment group; potential side-effects; being unaware of trial opportunities; the idea that clinical trials are not appropriate for serious diseases; fear that trial involvement would have a negative effect on the relationship with their physician; and their physician's attitudes towards the trial.[39]

Inclusion criteria for cancer clinical trials may be too restrictive to allow many patients to participate. One reason is that studies are designed to show the benefit of new therapies and therefore exclude patients outside a narrow range of disease type and co-morbidities. Often patients have advanced disease and cannot wait for lengthy enrollment and pre-testing procedures. Meeting attendees noted that the processes for getting patients into trials needs to be much faster and more efficient.

Socioeconomic factors

Some populations of patients have been shown to be less likely to participate in clinical studies. Factors include: lower levels of education, family commitments, language impediments and cultural issues. Patients with lower incomes may face prohibitive costs associated with participation (many cancer patients experience a significant loss of income due to their diagnosis). Racial and ethnic minorities face additional barriers and have been shown to respond to approaches that facilitate minority recruitment.[40]

Implications for future care

An unintended consequence of participating in clinical trials is that some participants may be denied access to future treatments because a payer's authorization criteria are too narrow. An example was cited of a patient who, as part of a clinical trial, is given an experimental drug in the same class as a treatment designated as first-line by their drug plan. The patient would be disqualified from receiving any second-line treatments because he or she has not received the listed first-line treatment, although this option would clearly not work in this setting. Involving payers as active participants in the design of research studies would help to avoid these types of situations.

Health system barriers

Discussions during the meeting also included barriers experienced by those working within the health system. Overcoming obstacles and adopting new methods will require stakeholders to understand each other's perspectives and to systematically incorporate changes in their work flows to achieve a more effective and efficient process.

Regulatory and safety requirements

Expanding government and Research Ethics Board requirements and increasing time commitments have contributed to a declining interest among researchers in performing clinical studies. Some of these requirements, designed to increase safety, may be unnecessary if seriously ill cancer patients are willing to assume more risk in return for the chance of benefitting from an experimental treatment.

Resourcing

Resourcing is also a concern. Hospitals' budgets are stretched and they may lack the financial and human resources to facilitate clinical trials. Ministries of Finance and Ministries of Innovation and Science may influence their counterparts in Ministries of Health and should be included as stakeholders.

Jursidictional boundaries

Many clinical trials sites refuse to provide care to patients from other centres, cities, provinces. Meeting participants viewed the health care system as a whole as being heavily weighted to discourage patient travel. For example, oncologists are assessed on referral wait times; if the oncologist sees a patient from another province this results in delays for local patients. Extra resources are not available to facilitate referrals for out-of-province patients, rather oncologists are penalized for doing so. In addition, the patient's province will pay the referral centre an amount restricted by the interprovincial agreement, which often does not cover the costs of treating the patient.

These inequities in access to care could be improved by recognizing the value of interprovincial referrals and by allocating a proportion of clinical trial spaces to patients from other jurisdictions.

Global decisions

Meeting attendees reported that conducting studies in Canada has become cost-prohibitive and that the standard of care offered cancer patients is lower than in other countries. As a result, Canadian subsidiaries are often unable to compete with their global counterparts for research studies.

Also, the fact that decisions about cancer clinical trials are often made at the global level makes it difficult for national patient groups to influence study design or to communicate with decision makers. For example, protocols may not be designed to meet the needs of Canadian health technology assessment bodies which require the collection of specific data over and above the clinical information. (Although this is changing with, for example, the recent introduction by the Canadian Agency for Drugs and Technologies in Health (CADTH) of a service to assist sponsors in the design of their studies.[41]) At the same time, Canadian requirements must align with the sponsor's global priorities.

Lack of a standardized approach

The National Comprehensive Cancer Network guidelines in the United States support routine enrollment, stating that "the best management of any cancer patient is in a clinical trial".[42] Yet, patient group representatives reflected that patients are often not informed about clinical trials until their disease is quite advanced.

Impact of new trends on patient engagement

Two emerging trends were identified by meeting attendees as having significant consequences for how patients will engage in cancer clinical research in the future: personalized medicine and information technologies.

Personalized medicine

Conventional clinical trial design is being re-thought in light of personalized, or precision, medicine. Cancer is now viewed as a collection of rare diseases and biomarkers are increasingly used to indicate which targeted therapies are more likely to succeed in specific patients. Meeting attendees suggested that traditional (i.e., randomized, controlled) trials measuring aggregate response rates will be supplanted by those studying individuals' responses. Research questions now need to ask "Who (if anyone) benefits from the new treatment?".

Meeting attendees offered that current clinical trials processes do not work well in the era of precision medicine. For example, mutational testing using traditional biopsy procedures can take weeks to set up

and provide results only for selected mutations. Instead, Next Gen sequencing would assess several different genes for mutation at the same time. If a mutation is found that is appropriate for a clinical trial that is open somewhere in the world, the patient could then be enrolled immediately.

New approaches to cancer clinical research may offer extended opportunities for patient group involvement. Examples are:

- 'Just- in-time trial activation' – pre-selected study sites can enroll patients before the protocol is approved by an Research Ethics Board[43] – has been shown to be successful in raising enrollment rates, especially in trials of new treatments for rare and selective cancers.[44] Other approaches, such as having biomarker testing equipment available at each cancer centre can help facilitate patient access to clinical studies.
- Exactis, a Business-led Network of Centres of Excellence (BL-NCE), recently introduced the 'Personalize My Treatment' initiative in which cancer patients consent to give access to their medical record and their biospecimens from which a molecular profile can be derived.[45] This pan-Canadian patient registry can then be used for the conceptualization, design and conduct of clinical trials and enable the cancer centre to provide other kinds of personalized support.
- The Biobank Resource Centre, a collaboration between the University of British Columbia and the Canadian Tissue Repository Network, developed a 'Permission to Contact (PTC) Platform' which asks patients *"Do you give permission to be contacted for future research opportunities?"* as part of the routine health clinic practice. The Platform streamlines recruitment of participants enabling completion of research studies.[46]

Patient groups can support these new directions by, for example, organizing biobanks and registries of patients who have indicated their interest in participating in clinical trials. They can also provide inputs into the design of new initiatives to attract more patients.

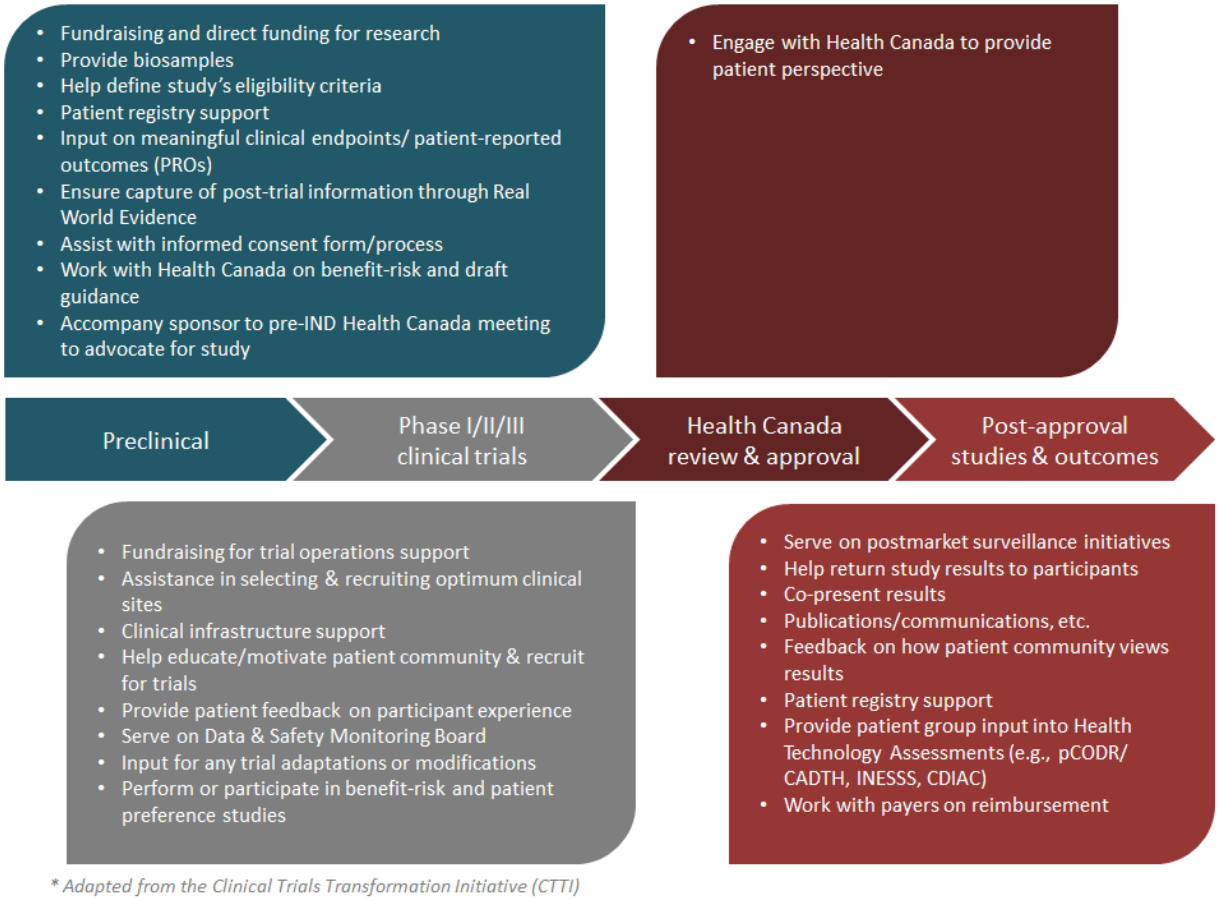
New applications of information technologies

The growing use of information and communications technologies is shaping the way clinical research is conducted. Increasingly, patients are educating themselves about clinical trials before they enroll. Clinical research organizations are developing ready repositories of patients, allowing for faster testing and easier pre-screening. Educational websites are designed that can be accessed 'anywhere, anytime'. Facebook is used for patient referrals and retention strategies, and crowdsourcing techniques are being used for protocol building and surveying online patient communities. This explosion of new technology tools and applications serves to facilitate and create efficiencies.[47] Involved patient groups can help to direct these interactions and safeguard patients' interests.

Part II: The role of patient groups in cancer clinical trials

The role of patient groups was considered by two consensus questions related to their relationship with the clinical trials system and with their patient constituencies. The discussion highlights are summarized in Figure 2 and elaborated below.

Figure 2 Patient group engagement in the clinical trials system



** Adapted from the Clinical Trials Transformation Initiative (CTTI)*

Contributing to clinical research design and implementation

At the clinical trials system level, patient groups can provide strategic inputs to decision makers throughout the research continuum and can provide practical assistance by facilitating patient participation in clinical trials.

Promoting research in Canada

Patient groups can support the research community by helping government ministries, other potential funders and the general public to understand the benefits of clinical research to people, revenues and innovation. They can also support Canada's participation in specific global research programs by being involved in discussions at this level that are aimed at improving Canada's competitiveness, showcasing our unique advantages, and helping to make a business case for the inclusion of Canadian sites. Connecting with global patient networks may enable Canadian cancer patient groups to exert greater influence at this level.

Influencing study design

At the study design phase, patient groups can reflect patients' priorities and preferences with respect to clinical and health economic outcomes. For example, cancer patient groups can learn from the experiences of the HIV/AIDS community where patients in life-threatening circumstances were

successful in convincing regulators that they are willing to accept the risk of experimental therapies. Further, clinical trials were designed with compassionate access arms that allowed access to an experimental drug by people who did not meet the eligibility criteria.

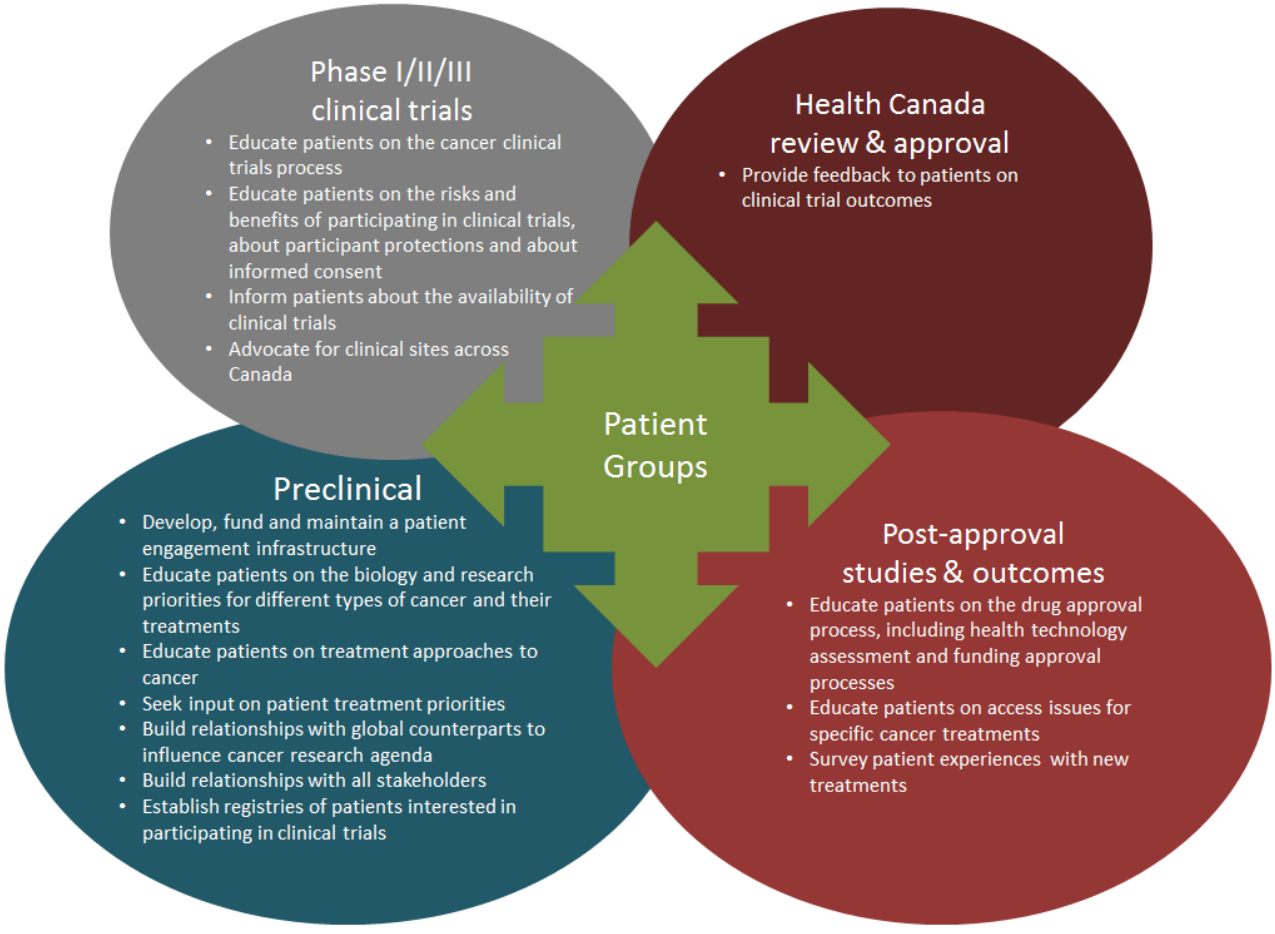
In the United States and Europe, patients are being involved in the initial stages of the clinical trial process and researchers are building patient friendly protocols and grooming study staff to be responsive to the needs of patients as people, not just as study subjects. Open discussions on draft protocols are especially focused on 'real world' endpoints.[48] Technologies are being utilized to gather ideas and feedback on trial designs, informed consent forms and protocols.

Role of patient groups with patients

Patient groups can play a fundamental role in informing patients about the clinical trials process and facilitating access for those interested in participating.

Figure 3 outlines the roles patient groups can play, as identified by meeting participants.

Figure 3 Patient group roles with cancer patients



Education

Education by patient groups can help potential clinical trial participants to overcome misconceptions, enable them to navigate clinical trials (including being aware of ongoing cancer clinical trials) and encourage self-advocacy. At the same time, it is important that the risks, benefits and availability of clinical research are realistically portrayed, including the potential impacts of participation in a clinical trial on access to future therapies.

Outreach

Patient groups can play an important role in reaching out to individual patients to inform them of ongoing or future clinical trials. Tailored outreach initiatives to populations who experience socio-economic barriers can further improve access. Patient groups can also help to remove barriers by serving as information hubs, directing patients to organizations that offer practical help, such as transportation or travel subsidies.

Facilitating patient recruitment, participation and retention

Working with clinical trial sponsors and research organizations, patient groups can inform their constituencies about a specific study, receive feedback from trial participants (or patients considering participation) on their experiences in the study, and communicate the results of the research to patients.

Many patient groups have tangible resources that can be applied to this endeavour. Some maintain registries of patients with, for example, specific genetic mutations who are interested in participating in studies. Others are connected to global research networks which may encourage the inclusion of Canadian study participants. Assets such as these could be replicated by other patient groups.

Part III: Best practices and validity of the Clinical Trials Transformation Initiative (CTTI) model for Canada

The Clinical Trials Transformation Initiative[28] (CTTI) was considered by meeting attendees as a potential reference for the development of a Canadian model of patient group engagement in clinical research. (Please see the Appendix 3 for a summary of the CTTI model.)

Highlights of the Clinical Trials Transformation Initiative (CTTI) model

The goal of CTTI is to identify and communicate practices that may increase the quality and efficiency of clinical trials by involving all sectors, involving the patient voice as central to all endeavours. CTTI provides evidence that can reduce uncertainty in the regulatory process, helps to develop more effective, efficient trials with a greater chance of success, and focuses on real-world impacts.

The initiative operates by identifying key issues for development and attempts to balance stakeholders' interests when recommending change. CTTI's success has depended upon:

- setting clear expectations, goals and roles among stakeholders;
- building trust;
- involving expertise; and
- managing conflicts of interest.

The impacts of patient engagement using the CTTI model include maximizing product lifecycle timelines, reducing clinical trial amendments and improving the patient experience. A recent study calculated that the cumulative impact of a patient engagement activity that avoids a single protocol amendment and improves enrollment, adherence, and retention results in an increase in expected net present value of up to $75 million. This is the equivalent of accelerating product launch by 1½ to 2½ years, depending on the clinical research phase.[49]

Part IV: The development of a Canadian Patient Group Pathway to Accessing Cancer Clinical Trials.

The process of developing a Canadian Patient Group Pathway to Accessing Cancer Clinical Trials requires:

- engagement of a broad range of stakeholders;
- adaptation of the Clinical Trials Transformation Initiative (CTTI) model to the Canadian landscape; and
- consideration of components of other successful models of patient group engagement.

Key stakeholders

The following groups and organizations are vital to be engaged in the development of a Canadian pathway.

- Patients/caregivers/potential study participants
- Cancer patient groups and health charities
- Researchers (including clinicians, cancer centre directors, clinical trial managers/ coordinators)
- Research ethics boards
- Healthcare providers
- Funders of clinical research
- Industry sponsors (including pharmaceutical, biotechnology, medical devices), clinical research organizations, industry associations (such as Innovative Medicines Canada, BIOTECanada, MEDEC)
- Clinical research organizations
- Health Canada
- Clinical trials networks (e.g., Canadian Clinical Trials Coordinating Centre, Canadian Cancer Trials Group, Canadian Cancer Clinical Trials Network, Network of Networks, BioCanRx, Clinical Trials Ontario, Consortium de recherche en oncologie clinique du Québec (Q-CROC), Clinical Trials BC, Exactis)
- Academic research networks (e.g., Strategy for Patient-Oriented Research (SPOR) Support Units)
- Health policy researchers and organizations (e.g., The Canadian Partnership Against Cancer)
- Health technology assessment bodies (such as the pan-Canadian Oncology Drug Review, Canadian Agency for Drugs and Technologies in Health, Institut national d'excellence en santé et en services sociaux)
- Third-party payers (e.g., Canadian Life and Health Insurance Association, individual private insurers, provincial/territorial and federal public insurers)
- Provincial Ministries of Health

- Individuals and organizations providing expertise and data resources (e.g., statisticians, biobanks)

Adapting the CTTI model to the Canadian reality

Several aspects of cancer clinical research are different from those in the United States. Factors raised at the consensus meeting and their implications for the Canadian Patient Group Clinical Trials Pathway Model are summarized in Table 2.

Table 2 Differences between Canadian and U.S. cancer systems and implications for the Patient Group Clinical Trials Pathway Model

Differences	Implications for the Canadian Patient Group Clinical Trials Pathway Model
The concept of patient group engagement in cancer clinical trials is relatively new to Canada for all stakeholders	Time must be invested to build strong relationships with stakeholders across the cancer clinical trials continuum
Pharmaceutical research is designed and implemented at a global level	Stakeholders must work both at the national and global levels to influence the goals and design of research protocols to meet Canadian patients' needs
Less pharmaceutical research is done in Canada	Stakeholders need to work collectively with research decision makers to improve Canada's competitiveness by reducing barriers and promoting Canada's assets
Canadian healthcare system is largely government-funded and operates under provincial jurisdiction	Networks bridging provincial systems of cancer clinical research across Canada will foster a consistent approach
Patient groups are typically not involved in Health Canada meetings	Health Canada has shown openness to meeting with patient groups; early involvement may help to shape a patient-centric cancer clinical trials process
Public sector health technology assessment (HTA) and funding approval bodies at the national and provincial levels play a pivotal role in access to drugs in Canada	If a clinical trial does not examine and measure the outcomes needed for HTA evaluations, the drug will not be funded. Health economists should be involved early in the research process to ensure the appropriate outcomes are measured. As the concepts of real-world evidence and patient-reported outcomes gain prominence with HTA bodies, patient inputs into clinical trial design will help to anticipate these changing requirements.

Recommendations

A key component of successful models cited by meeting participants was a collaborative approach involving all stakeholders, including patient groups. The following recommendations were offered to guide the development of a Canadian Patient Group Pathway to Accessing Cancer Clinical Trials.

Recommendations for all stakeholders

Commit for the long term

Stakeholders must be prepared to invest time and resources into building multilateral relationships to advance mutual goals. The success of relationships should be formally measured over time as a way to understand how each party benefits, to aid in continuous improvement of the relationship, and to demonstrate to others the value of collaboration.

All stakeholders – including sponsors, patient groups, academic investigators, regulators, health economists, payers and clinical trials service providers – must ensure that their representatives are allowed sufficient time and budgets to participate. In turn, delegates must be prepared to demonstrate to their leadership the value of collaborative action.

Create partnerships of equals

All stakeholders, and patient groups especially, must be treated as equal partners, avoiding paternalistic approaches. Multipronged tactics, based on establishing a shared vision, have proven successful. At the system level, each stakeholder organization must take the initiative to think through how to incorporate the patient voice.

Reach out to patient groups

For some stakeholders, knowing how to reach out to patient groups is a first step. A proactive approach is essential, since not all personnel in Canadian subsidiaries are aware of their global clinical development programs and can be called upon at short notice to provide input. Identifying patient groups as early as possible enables a coordinated and informed approach to influencing clinical research design under these circumstances. Patient groups can facilitate this process by preparing registries of organizations. (Please see Appendix 1 for links to key stakeholder organizations.)

Patient groups exist for different reasons (such as patient support, expertise, or fundraising) and it is important that the most appropriate groups are involved. Clinical trial decisions are made globally in many cases and it is important that stakeholders have strong connections to their global counterparts.

Involve all stakeholders

The scope of stakeholders included should encompass the entire clinical trials process. Third party payers, statisticians, health economists, ministries of health, research nurses, bench scientists and clinical research associates are examples of roles that may be overlooked.

Engage early and often

The value of establishing relationships early and having regular meetings was repeatedly reinforced. Stakeholder organizations will inevitably experience staff turnover during the lengthy clinical trial development process and it is important to proactively address this reality by having back-ups available, by fully briefing people who are new to their roles, and by transferring knowledge systematically.

Set the ground rules

Clear standards of relationship management are foundational for productive and long-lasting collaborations. Principles of engagement should be developed which apply across all phases of research and development. Formal mechanisms for disclosure, conflict of interest, data sharing and dispute management can help create safe spaces for dialogue and enable relationships to bear external scrutiny.

A set of standards can be written collectively and published. These could include policies, guiding principles, standards and a 'seal of approval' indicating that an organization agrees to abide by and be held accountable to their commitment. Transparency about how the standards were developed is key to their acceptance.

Navigate differences

Stakeholders must take into account their counterparts' needs when working towards a shared goal. While stakeholders share a common cause, each has a different outlook and goals, and is responsible to a different constituency. Participants should be prepared to share their views and to understand each others' histories, motivations and interests and to respectfully acknowledge areas of disagreement. Lessons can be learned from successful multistakeholder collaborations which have evolved to address therapeutic challenges.[50]

Build trust

Expectations need to be explicit and safe spaces created to engage in candid interactions. The focus should be on providing each participant what they need in order to change behaviours in a secure way.

Trust can be advanced by implementing policies promoting transparency, by providing opportunities for people to get to know one another informally, and by each party establishing a track record of delivering on its commitments. Partners need to educate themselves about the system of clinical research and about ongoing issues. Alliances with other organizations such as academic institutions can help in this regard.

Build expertise

It is essential that all stakeholders build credibility and capacity by educating themselves about the scientific and business aspects of research and development, by building networks nationally and globally.

Overcome internal barriers

Each participating group will face internal barriers to collaboration and must take steps to overcome them.

Pharmaceutical and biotechnology companies, for instance, must convince their global and national leadership that engagement with patient groups and other stakeholders is a wise investment of resources, that their intellectual property and competitive positions are not compromised, that regulators and other stakeholders will not view these relationships negatively, and that the company's efforts to include patient groups and other stakeholders will result in a net gain in terms of product lifecycle value.

For many organizations, breaking down internal silos (such as between clinical and marketing departments, or within large patient groups) is critical. This point was raised frequently in discussions by many participants.

Communicate in all directions

Strong communications are needed in all directions. Stakeholder organizations need effective internal communications so that all involved roles are engaged and up to date. External communications to broader audiences should be coordinated among stakeholders and their respective messages aligned.

Patient groups who are connected to global networks sometimes have access to early information about clinical trials about which their counterparts in industry may be unaware. Messages about, for example, the importance of including health economic outcomes must be delivered to global decision makers in the early planning stages.

Develop supporting systems

Clinical trial sponsors and research sites could play an important role in making available databases of ongoing or upcoming studies, organized by disease site. This approach would facilitate access by patient groups who would, in turn, more easily access potential trial participants.

Start small

A suggested approach to initiating collaborative relationships is to choose an area of focus over which the research sponsor has control. For example, involving patient groups in the design of observational studies can demonstrate the value of this approach to global decision makers. Learnings from initial attempts at involving stakeholders can then be applied to more complex situations. Another 'quick win' is for funders of clinical research to ask that proposals include a statement showing how patient groups will be involved in the study.

Recommendations for patient groups

In addition to the above, the following recommendations are addressed to patient groups specifically.

Build capacity

Patient groups must ensure they have sufficient people, expertise and funding to enable long term long term participation. Years of investment of their limited resources are required to achieve equal participation.

Develop expertise

Expertise can be developed by training in programs such as the European Patients Academy on Therapeutic Innovation (EUPATI), for example, which requires hundreds of hours. Patient groups can look to effective global practices for developing capacity and can set interim goals, such as participating in international scientific meetings.

Build relationships with stakeholders

Success factors for collaboration between researchers and patients include communication and shared leadership strategies.[8]

Embed infrastructure

Patient groups also need to ensure they have the available infrastructure to reach out to individual patients and to support other practical resources such as patient registries and biobanks.

Work collectively

Efficiencies can be achieved by working collectively with patient groups and other stakeholders. This is especially the case with patient groups that serve smaller constituencies, such as patients with rare cancers or specific age cohorts, or whose primary purpose lies outside the treatment research and development sphere.

Pool resources

Online curricula and in-person training can be delivered through cross-country webinars. Patient groups can pool resources to form representative bodies. Two exemplars were suggested, among many excellent models available worldwide. HIV/AIDS groups set up an overarching council of patient groups to address issues and connect with counterparts globally. The Patient Leadership Team, as presented by Deborah Collyar, uses a different approach by focusing on all phases of a specific research endeavour over the long term.

Leverage the resources of other stakeholders

Other stakeholders can assist patient groups to build expertise. For example, BioCanRx, a Network of Centres of Excellence (NCE) joining academic centres from across Canada in the area of immunotherapy development, has put in place a Learning Institute in immunotherapy which pairs patient representatives with researchers.

Reach out to patients

Patient groups must fulfil several roles on behalf of their constituents:

- Make them aware of clinical trials and encourage their participation;
- Provide education on clinical trials and on how to advocate for their own care during their cancer journey;
- Solicit their inputs;
- Set realistic expectations about patient group influence on the clinical research process; and
- Provide practical support, for example hiring a ‘consent coach’ who helps patients understand the informed consent process.

Take the initiative

The experience of both the Clinical Trials Transformation Initiative (CTTI) and the Patient Advocates In Research (PAIR) have shown that patient groups are effective convenors of multistakeholder initiatives. They should not wait to be asked but create an opportunity to do so (as exemplified by the present consensus meeting).

Chapter 3 Moving to action

Bringing forward a proposed Canadian Patient Group Pathway to Accessing Cancer Clinical Trials will require concerted action on the part of all stakeholders. A systematic approach is needed to ensure that the momentum generated continues to drive an agenda for inclusion of patient groups as equal partners in the cancer clinical trials process.

Step 1: Disseminate the meeting report

The first step will be to further engage the core base of support (i.e., the Scientific Advisory Committee and meeting invitees) by requesting feedback on the draft meeting report. The final report, including the guidance recommendations will be:

- issued as a publication of Colorectal Cancer Canada;
- submitted as an abridged version to one or more open-access clinical journals; and
- submitted to online blogs and open-circulation publications.

Step 2: Form a working group

Scientific Advisory Committee members will be invited to form small working group to advance the development and adoption of a Canadian Patient Group Pathway to Accessing Cancer Clinical Trials. The working group's task will be to:

- develop a proposed framework for the Pathway;
- map out a process for adoption and operationalization of the Pathway within the next year;
- create a Charter outlining the needs and expectations of stakeholders, including patient groups, related to their participation in the clinical trials process; and
- advise Colorectal Cancer Canada on training programs needed to enable all cancer patient groups to participate in the Pathway.

Step 3: Engage the broader cancer research community

The broader research community will be engaged through dissemination of the outputs from the consensus meeting and by outreach from meeting attendees. Appendix 1 provides links to key national and regional organizations, as a starting point for this task.

Step 4: Engage sponsors of clinical trials to adopt a "charter" recognizing the importance of including patient groups in the development and carrying out of cancer clinical trials.

An important step in ensuring that the model is adopted is to have the buy in from sponsors of trials and encourage them to adopt policies that require the participation of patient groups in all stages of a cancer clinical trial.

Step 5: Engage trial sponsors to engage in training of Patient Groups through an independent body to ensure quality research partners.

Adopting the Canadian Patient Group Pathway to Accessing Cancer Clinical Trials, incorporating the concepts of multi-stakeholder collaboration and the inclusion of patient groups as equal partners, is expected to generate significant benefits for all stakeholders.

Chapter 4 Conclusions

Expected outcomes and benefits

Adopting the Canadian Patient Group Pathway to Accessing Cancer Clinical Trials, incorporating the concepts of multistakeholder collaboration and the inclusion of patient groups as equal partners, is expected to generate significant benefits for all stakeholders, as summarized in Table 3.

Table 3 Expected benefits of the Canadian Patient Group Pathway to Accessing Cancer Clinical Trials

Stakeholder group	Expected benefits
Cancer patients and patient groups	• Faster access to innovative treatments • Strengthened expertise and involvement at all stages of the research continuum • Productive relationships with networks, including a wide array of stakeholders in Canada and internationally
Clinical trial sponsors (academia and industry)	• Improved cancer research and development strategies • Shorter timelines • Higher success rate for bringing valuable new treatments to market • Better understanding of unmet needs • Eligibility criteria and protocols that reflect patients' experiences • Real-world health economics outcomes • Improved relationships with other stakeholders, such as regulators, academics and health technology assessment bodies, as well as with companies' global headquarters • Canadian organizations will be better positioned to attract cancer research opportunities
Clinical research organizations	• Improved recruitment rates • Fewer protocol amendments • Decreased participant drop-out rates • Shorter timelines • Reduced costs • Smoother interactions with clinical trial sponsors, health care professionals, cancer care institutions and ethics review boards
Health technology assessment and third party payer organizations	• Health technology assessments align with patient values • Third-party payers can make funding decisions based on outcomes of importance to patients
Governments and academic researchers	• More clinical trials in Canada • Greater inflows of funding for cancer research from abroad • Increased utilization of Canada's extensive research infrastructure • Standards of care for cancer patients, currently considered by meeting attendees to be below those of our international peers, will improve, benefitting all Canadians

Leadership and accountability

Colorectal Cancer Canada, with support from the Coalition Priorité Cancer au Québec, has begun to lead the development of an effective and practical Canadian Patient Group Pathway to Accessing Cancer Clinical Trials.

The goal of having the pathway adopted by all stakeholder groups in Canada will require committed leadership from Colorectal Cancer Canada and from its partners to ensure endorsement and action by all sectors. Establishing a working group to assist in developing tools, promoting the pathway, and reaching out to a broad stakeholder network will be essential to its success.

Measuring progress and the achievement of key outcomes will encourage accountability among all partners for achieving the ultimate goal of improved access to new treatments for Canadian cancer patients.

Invitation to participate

Colorectal Cancer Canada invites you to join us in this important endeavour.

Please contact us if you are interested in participating.

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Appendix 1 Key stakeholder organizations

The following links to key stakeholder organizations are intended to assist in communicating the Canadian Patient Group Pathway to Accessing Cancer Clinical Trials and in identifying potential collaborative partners.

National and key regional organizations

Cancer patient groups

Colorectal Cancer Canada
http://www.colorectalcancer.com/

Coalition Priorité de Cancer au Québec
http://coalitioncancer.com/

The Canadian Cancer Action Network includes over 100 member organizations:
http://www.ccanceraction.ca/partners/membership-program/

Pharmaceutical, biotechnology and medical devices companies

Innovative Medicines Canada, the industry association for pharmaceutical companies, list of members:
http://innovativemedicines.ca/about/member-companies/

BioteCanada's list of member biotechnology companies:
http://www.biotech.ca/about/member-listings/

MEDEC membership list of medical technologies companies:
http://www.medec.org/page/MemberList

Health Canada

Health Products and Food Branch (includes the Therapeutic Products Directorate and the Biologics and Genetic Therapies Directorate)
https://www.canada.ca/en/health-canada/corporate/about-health-canada/branches-agencies/health-products-food-branch.html

Academic research organizations

The Canadian Centre for Applied Research in Cancer Control
http://cc-arcc.ca/

Canadian Institutes for Health Research
http://www.cihr-irsc.gc.ca/e/193.html

Clinical trials networks

Canadian Clinical Trials Coordinating Centre
http://www.cctcc.ca/

The Canadian Cancer Clinical Trials Network
http://3ctn.ca/

Network of Networks
http://n2canada.ca/

Canadian Cancer Trials Group
https://www.ctg.queensu.ca/

Canadian Cancer Clinical Trials Network
https://3ctn.ca/

Strategy for Patient-Oriented Research (SPOR) Support Units
http://www.cihr-irsc.gc.ca/e/45859.html

Consortium de recherche en oncologie clinique du Québec (Q-CROC)
https://www.qcroc.ca/

CATALIS
http://www.catalisquebec.com/en/

Clinical Trials Ontario
http://www.ctontario.ca/

BC Clinical Research Infrastructure Network
http://www.bccrin.ca/

Health technology assessment organizations

pan-Canadian Oncology Drug Review (part of the Canadian Agency for Drugs and Technologies in Health)
https://cadth.ca/pcodr

Institut national d'excellence en santé et en services sociaux (Quebec)
https://www.inesss.qc.ca/en.html

Cancer Drug Implementation Advisory Committee (part of the Canadian Association of Provincial Cancer Agencies)
http://www.capca.ca/current-issues/the-pan-canadian-cancer-drug-funding-sustainability-initiative/cancer-drug-implementation-advisory-committee-cdiac

Appendix 2 Cancer clinical trials process overview

The following summary is reproduced from the Canadian Cancer Society's Drug Information website.[51] Please note that this information is updated regularly and readers are encouraged to check the link provided for updates.

Phases of clinical trials

Clinical trials for new treatments are always tested through several steps, called phases. Other types of trials, such as screening and early detection, diagnostic or supportive care studies, do not necessarily have phases. In a treatment trial, each phase is designed to answer specific research questions. A new approach to cancer treatment can only progress to the next phase after it is shown to be safe and effective. This is why it often takes a long time for an experimental treatment to be approved as a cancer treatment. There are up to 5 phases involved in a clinical trial: phases 0, I, II, III and IV.

Preclinical research

Scientists test new ideas in the laboratory first, to see the effects on animals or on human cells, before testing it with humans. It is difficult to know what effect a new treatment will actually have when it is used with humans. The effects may not be the same as they were in the laboratory or animal studies.

Phase 0

Sometimes a phase 0 trial is conducted before a phase I trial. Phase 0 trials use a very small dose of a drug to study the effects in a small group of people (about 10–15). These trials are used to gather information about how the drug is used by and affects the human body. Researchers may need blood tests or biopsies of the tumour. Phase 0 studies are not used to gather information about the safety of the drug or its effectiveness in treating cancer. People who take part in phase 0 studies usually have advanced disease and do not have an effective, known treatment option.

Phase I

Phase I trials look at how safe a treatment is and try to determine the best dose. A phase I trial tries to find out:

- how the new treatment should be given (such as by mouth or injection) and how often
- the safest dosage and the highest dose a person can tolerate (maximum tolerated dose)
    - Participants are divided into groups called cohorts.
    - Each cohort is made up of 2–6 people.
    - The first cohort is given a dose that is thought to be safe (based on the results of animal studies). Then the dose is gradually increased in the other cohorts. This increase in dose is called *dose escalation*.
- what effect the drug or therapy has on the body
- what side effects people taking the drug or treatment experience.

A phase I trial is often the first time a new drug, combination of drugs or therapy is tested on humans, so these trials may involve more risk compared to phase II or III trials. For this reason, phase I trials usually

involve only a small number of people with cancer (about 15–30) who are not getting better with standard treatment. Phase I trials are not always specific to one type of cancer and may be used in people with different types of cancer.

Phase I trials may also test an already-approved drug or therapy to try to improve its effectiveness or see if it can be used in a different way. For example, a phase I trial may test a drug or therapy that is already used for another disease or type of cancer.

Most phase I studies in children are done once phase I of the adult trial has been completed or is near completion. They use the same drug or treatment as the adult trial. However, children are often started on a lower dose than that given to adults.

The dose and schedule that researchers find most effective with tolerable and reversible side effects in a phase I trial is used to determine the dose and schedule of a phase II trial.

Phase II

Phase II trials test whether a drug or other treatment is effective against a specific type of cancer based on the dose and schedule determined to be safe in a phase I trial. Phase II trials may also compare different schedules of giving the treatment. Researchers study a drug or treatment in a relatively small group of people (usually less than 100) with one type of cancer. Most participants in phase II trials have not responded well to standard treatment or do not have a standard treatment available to them.

Phase II trials:

- try to get a better idea of how effective a treatment is for a certain type of cancer
- continue to evaluate how safe the drug is and what effect it has on the body.

Phase III

A phase III trial provides a detailed evaluation of a promising new treatment identified during a phase II trial. It compares the new treatment to the best current standard of cancer treatment. Researchers may test a drug alone or in combination with another drug or form of treatment. Phase III trials usually involve a large number of people (hundreds to thousands) at several different locations. People who participate in phase III trials may not have received any previous treatment.

A phase III trial tries to:

- find out whether the treatment being tested is better, as good as or worse than the standard treatment
    - This includes evaluating quality of life and survival.
- compare side effects of the new treatment and the standard treatment

Phase III trials often depend on a process called *randomization*. This means that participants are selected by chance and put into 1 of 2 groups. An *experimental* group receives the new treatment being tested, while the *control* group receives the standard treatment. Some trials may involve more than 2 groups of participants. Randomization helps make sure the study results are accurate.

If the results of a phase III trial show that the experimental treatment is better than the standard treatment, the experimental treatment may move forward to become the new standard treatment.

Phase IV

Phase IV trials gather more information about the possible risks and benefits of a drug that did not show up in earlier testing. Researchers look into risks and benefits that could be associated with long-term effects after a drug or treatment has been approved for clinical use. In this phase, researchers continue to follow participants who have completed phase III trials. Not all new treatments will enter into phase IV studies.

Approving a new drug or treatment

After clinical trials show that a new drug or treatment for cancer is safe and effective, it is submitted to Health Canada for approval. Once approved, doctors can then recommend this treatment to people with cancer.

It often takes more than 10 years for a new drug or treatment to go from preclinical research, through clinical trials, to the approval process before it is available as a standard treatment to people with cancer.

Appendix 3 Summary of presentations

Deborah Collyar: How to interest patients in clinical trials

Keynote speaker Deborah Collyar of Patient Advocates In Research (PAIR), an organization in the United States dedicated to engaging patients in clinical trials, stressed that interesting patients in participating in clinical trials requires a change in the mindsets of decision makers: patients should be at the centre of research rather than merely its subjects. The research process must address the significant barriers that each person may experience.

Building trust is key to success and can be achieved by involving patients over the long term, not just to fill an enrollment target. By involving patient groups in key decisions at the outset of developing a research program, their perspectives and concerns may be built into the study design which will allow them to support aspects of the research during clinical, ethical, regulatory and health economics reviews and to promote the published results with patients.

Changing language is one immediate way in which a patient-centric approach can be reinforced, for example by saying: "The treatment failed the patient" rather than "The patient failed the treatment". Similarly, new technologies should be adopted not for their own sake but only if they serve the needs of patients, such as providing more useful answers, delivering better ways to endure treatment or lowering costs.

Patient groups play a pivotal role. They can be vital to researchers by providing inputs into all phases of research, and to patients by maximizing their health literacy and reducing fear and uncertainty. By bridging the interests of both parties, patient groups can increase participation in clinical trials for the benefit of all. Roles of patient groups include: concept and protocol design and review, recruitment, meetings with regulators and ethics review boards, encouraging patient constituencies to participate, and preparing plain language documents. Patient values reflected in this way are becoming increasingly important as concepts such as patient-reported outcomes (PROs) gain prominence.

While patient groups have made extensive inroads in influencing clinical research, it has yet to become standard practice. Positive results from patient group involvement have been reported by organizations such as the National Cancer Institute's Specialized Programs of Research Excellence (SPORE),[52] the European Medicines Agency (EMA),[53] and the Multi-Regional Clinical Trials Center (MRCT) at Harvard University.[54] Outstanding issues include setting appropriate boundaries for relationships between patient groups and other stakeholders, and improving communications among patient groups.

Bray Patrick-Lake: Patient group pathway model

Bray Patrick-Lake, now of Duke University, described the history and experience of the Clinical Trials Transformation Initiative[28] (CTTI), which served as a reference for the development of the Canadian model.

History

The Clinical Trials Transformation Initiative (CTTI) is a public-private partnership of over 80 members that strive to identify and drive adoption of practices that will increase the quality and efficiency of

clinical trials. CTTI was established in 2007 through a partnership between the Food and Drug Administration and Duke University and is administered through the Duke Translational Medicine Institute. CTTI's approach includes conducting projects to better understand the range of current practices, assess alternative approaches, understand barriers to change, and propose recommendations for improvement.[10]

CTTI recommendations

The following CTTI recommendations[55] are best practices for effective engagement with patient groups around clinical trials. These were developed as a result of a qualitative survey and semi-structured interviews involving stakeholders from industry sponsors, academic investigators, and patient groups. The recommendations also incorporate feedback and experience from participants at the 2015 Expert Meeting representing a diverse group of stakeholders including patient groups, industry sponsors, academic investigators, and government and regulatory agencies.

I. Recommendations for All Stakeholders

- Engage the patients' "voice" by establishing partnerships from the beginning of the research and development program to improve trial design and execution.
- From the start, clearly define the expectations, roles, and responsibilities of all partners, including the resources being committed, data being shared, and objectives of the program.
- Build the trust required for successful partnerships by being transparent and trustworthy, following through on commitments, and honoring confidentiality.
- Involve the expertise of multiple partners for a broader perspective to mitigate risk and enrich pipeline development.
- Manage real or perceived conflicts of interest by establishing policies that require full disclosure, transparency, and accountability.

II. Recommendations for Research Sponsors—Industry and Academia

- Integrate into your ongoing research and portfolio planning an assessment of PG expertise, assets, and value to your program.
- Match patient group expertise and assets to the specific needs and phases of your research and development program.
- Ensure that patient groups are essential partners throughout the research and development process and not token voices.
- For consistency, establish guiding principles and clear lines of communication to facilitate a fit-for-purpose process for collaborating with patient groups.
- Measure the impact of patient group engagement.
- Establish ongoing relationships with patient groups and communicate openly with them on a regular basis.

III. Recommendations for Patient Groups

- Proactively identify, engage, and bring the patients' voice to stakeholders relevant to your research and development interests.
- Promote your value as an essential partner by maximizing and articulating your expertise and assets.
- Deliver your expertise and assets to sponsors throughout the entire research and development process.

- Select sponsors who have a product or program with significant promise for your constituents and who are committed to engaging in a meaningful way.
- Manage real or perceived conflicts of interest by establishing policies that require full disclosure, transparency, and accountability.

CTTI Tools

CTTI has developed tools to assist patient groups prepare for their role in clinical trials:

- Tool 1. Patient Group Organizational Expertise and Assets Evaluation Tool
- Tool 2. Assessment of Patient Group Internal Aspects: Focus
- Tool 3. Assessment of Patient Group External Relationships: Other Patient Groups

Appendix 4 Agenda, organizers, Scientific Advisory Committee and participants

Agenda

Colorectal Cancer Association of Canada

PATIENT GROUP PATHWAY MODEL TO ACCESSING CANCER CLINICAL TRIALS

TUESDAY, JUNE 13TH, 2017, LOEW'S HOTEL VOGUE, MONTREAL

CONSENSUS MEETING AGENDA

7:00 A.M.	**BREAKFAST**		
8:00 A.M.	**MEETING START**	WELCOME FROM CCAC PRESIDENT: **BARRY D. STEIN**	FILOMENA SERVIDIO-ITALIANO
8:10 A.M.	**INTRODUCTIONS**	SCIENTIFIC ADVISORY COMMITTEE & COCHAIRS: • GERRY BATIST • STEPHANIE MICHAUD • DAWN RICHARDS	FILOMENA
8:20 A.M.	**MEETING OBJECTIVES**	DELINEATION OF MEETING OBJECTIVES: • IDENTIFY AND AGREE TO THE ROLE OF PATIENT GROUPS ("PGs") IN CANADIAN CANCER CLINICAL TRIALS ("CCTs"): WHERE ARE WE NOW; SNAPSHOT OF WHAT IS BEING DONE INTERNATIONALLY (US & EU) • IDENTIFY THE FACILITATORS & BARRIERS RELATED TO CANADIAN CANCER CLINICAL TRIALS ("CCTs") • DEVELOP THE PATIENT GROUP PATHWAY MODEL ("PG-PM") IN CANCER CLINICAL TRIALS BY ADAPTING THE CLINICAL TRIALS TRANSFORMATION INITIATIVE ("CTTI") TO THE CANADIAN REALITY WHAT DO WE HOPE TO ACCOMPLISH? • FOR PATIENTS • FOR PATIENT GROUPS • FOR OTHER STAKEHOLDERS	MEETING FACILITATOR: ANNE MARIE WRIGHT
8:30 A.M.	**KEYNOTE SPEAKER: HOW TO INTEREST PATIENTS IN CLINICAL TRIALS**	PRESENTATION HIGHLIGHTS INCLUDE: • HOW PATIENTS PERCEIVE CLINICAL TRIALS • HOW TO COLLABORATE TO 'FIX' CLINICAL TRIALS FOR PATIENTS • PROVIDING SOME REAL-WORLD EXAMPLES	DEBORAH COLLYAR (PAIR)

9:30 A.M.	**BARRIERS & FACILITATORS TO ACCESSING CANCER CLINICAL TRIALS**	IDENTIFYING PATIENT-SPECIFIC ***BARRIERS*** IN THE CANADIAN CLINICAL TRIALS PATIENT RECRUITMENT PROCESS:
		• PATIENT & PATIENT GROUP LANDSCAPE
		  ○ KNOWLEDGE & EDUCATION RE: CLINICAL TRIALS
		  ○ PATIENT GROUP INPUT (TRIAL DESIGN, CONSENT)
		• BUSINESS/ORGANIZATIONAL LANDSCAPE
		  ○ CRO/PRINCIPAL INVESTIGATOR/SPONSOR INPUT
		• REGULATORY/ETHICS LANDSCAPE
		  ○ REGULATORY & EQUITY ISSUES
		IDENTIFYING PATIENT-SPECIFIC ***FACILITATORS*** IN THE CANADIAN CLINICAL TRIALS PATIENT RECRUITMENT PROCESS:
		• STRATEGIES THAT HAVE PROVEN EFFECTIVE AT PATIENT RECRUITMENT IN THE CANADIAN CLINICAL TRIALS PROCESS
		  ○ PATIENT GROUP ENGAGEMENT?
		  ○ CRO/P.I./SPONSOR?
			ANNE MARIE WRIGHT

10:30 A.M.	**HEALTH BREAK**		
10:45 A.M.	**PATIENT GROUP PATHWAY MODEL**	WHAT IS A PATIENT GROUP PATHWAY MODEL AND WHAT DOES IT LOOK LIKE? • REVIEW CLINICAL TRIALS TRANSFORMATION INITIATIVE ("CTTI") MODEL • STRENGTHS/SUCCESSES OF THE "PATIENT GROUPS & CLINICAL TRIALS" ("PGCT") PROJECT	BRAY PATRICK-LAKE (DUKE'S UNIVERSITY)
12:00 P.M.	**LUNCH**		
1:00 P.M.	**DEVELOPMENT OF A CLINICAL TRIALS PATIENT GROUP PATHWAY MODEL**	DEVELOPMENT OF A CANADIAN CLINICAL TRIALS PATIENT GROUP PATHWAY MODEL: • HOW TO UTILIZE THE CTTI MODEL IN THE CANADIAN CONTEXT/LANDSCAPE	ANNE MARIE WRIGHT, BRAY PATRICK LAKE, DEBORAH COLLYAR
3:00 P.M.	**HEALTH BREAK**		
3:15 P.M.	**CONSENSUS DOCUMENT**	DEVELOPMENT OF CONSENSUS DOCUMENT: • PROVIDE OVERVIEW OF CONSENSUS QUESTIONS TO SERVE AS BASIS FOR THE PATIENT GROUP PATHWAY MODEL • VOTE ON CONSENSUS QUESTIONS	ANNE MARIE WRIGHT, DAWN RICHARDS, STEPHANIE MICHAUD
4:45 P.M.	**MEETING WRAP UP**	REITERATE DELIVERABLES/FOLLOW UPS	ANNE MARIE
5:00 P.M.	**THANK YOU!**		BARRY STEIN

Meeting Co-Chairs

Stéphanie Michaud, President and CEO of BioCanRx.

Dawn Richards, Founder, Five02 Labs Inc. and Associate Director of Patient and Public Engagement at Clinical Trials Ontario.

Dr. Gerald Batist, Professor of Oncology and Helen & Sam Steinberg Family Career Scientist, Jewish General Hospital, Montreal.

Scientific Advisory Committee

Karen Arts is the Executive Director for the new Canadian Cancer Clinical Trials Network (3CTN). With thirty-eight years of professional experience, the focus of Karen's work at 3CTN is to collaborate with all Canadian stakeholders in clinical research to achieve enhancements and efficiencies in their infrastructure and processes to enhance the conduct of clinical trials. She is also one of the founding members and chair of the board of directors of the Network of Networks (N2), a not-for-profit organization which aims to enhance Canada's clinical research capability and capacity. Karen holds Masters and Bachelor of Science degrees in Nursing and is certified in several areas, including Oncology, Clinical Research, Nursing Management and Administration, Palliative Care, Obstetrics and Gynecology.

Vatché Bartekian is the President of Vantage BioTrials, a family-owned niche Canadian Clinical Research Organization (CRO), which he founded in 2007. His experience working with big pharma and CROs in monitoring, clinical operations and project management roles has established him as a trusted expert and partner to numerous clients over his many years of passionate service with patients continuously in mind. His goal has always been straight-forward: enable speed, safety and effectiveness of therapies for those who need it most urgently, bringing them to market sooner rather than later.

Dr. Gerald Batist is the former Chairman of the Department of Oncology at McGill University, Director of the McGill Centre for Translational Research in Cancer, and Acting Director of the Lady Davis Institute. A major award from the Canadian Foundation for Innovation led to the expansion of the Centre and its integration into the Segal Cancer Centre at the Jewish General Hospital, which he also directs. Dr. Batist is a clinician-scientist, trained in medical oncology and molecular pharmacology. His work, both in his lab and clinical research, focuses on therapeutic resistance. This includes large consortia of biopsy-based clinical trials. In 2014, he co-led a successful application that resulted in the establishment of the Canadian National Centre of Excellence in Personalized Medicine, Exactis Innovations. The core feature is a program to build a massive bio bank and database linked to a prospective longitudinal registry of cancer patients followed throughout the trajectory of their illness, a project called 'Personalize My Treatment'. In 2016, Dr. Batist was appointed Member of the Order of Canada and Knight of the National Order of Quebec.

Sarita Benchimol is a Sciences graduate from Concordia (BSc.) and l'Université de Montréal (MSc.). She has acquired close to 40 years of experience in a variety of aspects of cancer research, both at the academic and the industrial spheres. More precisely, she has made significant contributions in the field of colon cancer research and the evolution of the major marker, CEA. She is main author and co-author on several key publications in this domain. She presently holds the position of Facilitator for the Rossy Cancer Network. In this capacity, she has the opportunity to contribute to the much needed improvements in the area of services and care for cancer patients. Ms. Benchimol was closely involved

with the founding of the Colorectal Cancer Canada and continues to be an administrator and a Board member.

Franca Cantini is the President of Groupe Cantini Inc., founded in 2016, prior to which she served for 15 years as the Chief of the Research Ethics Office at the Jewish General Hospital. Over the past 20 years, she has contributed to the field of research ethics and regulatory affairs at an academic, governmental and health ministry network level. This experience has also allowed her to fully appreciate and understand the multitude of aspects inherent in clinical research. Mrs. Cantini received her Master's degree in Science of Nursing/Research Ethics at the University of Montreal.

Deborah Collyar formed 'Patient Advocates in Research' (PAIR) in 1996 after getting involved in translational and clinical research efforts through the U.S. National Cancer Institute. PAIR is an informal international communication network of patient advocates from other advocacy organizations. In addition, she helped develop patient advocacy committees throughout the cancer clinical trial groups that are part of the National Cancer Institutes Clinical Trial Network. She also created the Patient Advocate Research Team (PART) program in connection with the National Cancer Institute's translational Specialized Programs of Research Excellence (SPORE) program.

Dr. Martin Gagnon. As Chief Operating Officer of Exactis Innovation, Martin brings strategic and operational expertise having secured more than $90M in research financing over the past ten years. Previously, he co-founded Chlorion Pharma, a neuroscience-focused biotechnology company. Martin obtained a PhD in pharmacology and therapeutics from McGill University.

Dr. Thérèse Gagnon-Kugler is the President and CEO of le Consortium de recherche en oncologie clinique du Québec (Q-CROC) and co-founder of Exactis Innovation. She strongly believes in the power of networks: she serves on the boards of N2, Canada's Alliance for Excellence in Clinical Research, and of the Coalition Priorité Cancer au Québec, a patient advocacy group. She also actively serves on expert advisory committees for other Canadian clinical research initiatives. Thérèse received her PhD in molecular and cellular biology from Laval University in 2007.

Dr. Carmen Loiselle is a Professor in the Department of Oncology and the Ingram School of Nursing at McGill University. Her research focuses on how to best support individuals affected by cancer, through e-health and m-health, while they navigate the health care system. She is the recipient of numerous grants and awards and has published more than 120 scientific papers.

Susan Marlin is the President and CEO of Clinical Trials Ontario, a provincial organization committed to improving the environment for clinical trials, where she has led the establishment of a province-side streamlined research ethics review system. Previously, Susan served as the Associate Vice-Principal of Research at Queen's University and worked for many years with the Canadian Clinical Trials Group.

Stéphanie Michaud is the President and CEO of BioCanRx, a not-for-profit that seeks to accelerate the delivery of innovative immunotherapies from the bench to the bedside. In this position, Stéphanie is responsible for running all facets of the organization. She brings over 20 years of public, government and private sector experience in research and science and technology innovation policy. She strives to create partnerships between government, not-for-profits, academia and industry to maximize the impact of research funded by the BioCanRx, Stéphanie was Deputy Director of the flagship Government of Canada Network Centres of Excellence program. In addition to responsibility for its performance, management and delivery, she led the implementation of high profile bilateral international initiatives

and provided strategic advice to government and stakeholders. She is a strong contributor to science and technology policy, most notably in intellectual property. Dr. Michaud earned a PhD degree in Organic Chemistry from McGill University. She is involved with a number of not-for-profit organizations including Director of the Board of the Stem Cell Network.

Dr. Wilson H. Miller, Jr. is the James McGill Professor in the Departments of Oncology and Medicine at McGill University, Clinical Lead of the Rossy Cancer Network, and Director of the Clinical Research Unit at Jewish General Hospital. His research investigates molecular mechanisms underlying leukemia, breast cancer, and melanoma, with a focus on the development of novel targeted therapies.

Teresa Norris is the Founder and President of the registered charity, HPV Awareness. She regularly speaks internationally in public media and academic forums on sexual health. She works daily with leaders to improve decisions and solutions around cervical cancer screening policies at the provincial, federal and global levels.

Elizabeth (Bray) Patrick-Lake supports efforts to actively engage participant partners in Duke University's research programs, as well as patient advocacy organizations and other stakeholders in Clinical Trials Transformation Initiative (CTTI) efforts to improve clinical trials. She implements strategies to enhance awareness of Duke's Clinical and Translational Science Awards and CTTI's work, particularly with patient advocates, and extend its impact by working in partnership with the patient advocacy community on research design and conduct and improvement of the clinical trial enterprise.

Dawn Richards is the Founder of Five02 Labs Inc., and Associate Director of Patient and Public Engagement at Clinical Trials Ontario. With a PhD (Analytical Chemistry) from the University of Alberta, and experience in a variety of roles during the past 15 years, it is her diagnosis with rheumatoid arthritis ten years ago that instigated a journey to combine her passion for science with making the most of her diagnosis. In her role at Clinical Trials Ontario, Dawn is charged with executing on the organization's strategic pillar of patient and public engagement. As a patient advocate and volunteer, Dawn is Vice President of the Canadian Arthritis Patient Alliance, a Research Ambassador for the Institute of Musculoskeletal Health and Arthritis (of the Canadian Institutes for Health Research), and a member of the British Medical Journal's Patient Panel Reviewers, and was the first Patient Advisor of the Canadian Medical Association's Wait Time Alliance. She advocates for arthritis awareness, access to treatment, the inclusion of patients in decision-making and as research collaborators, and the importance of research.

Dr. Caroline Rousseau has over 10 years of broad clinical research experience in oncology & hematology. After completing a PhD in Experimental Medicine, she joined the Clinical Research Unit at the Jewish General Hospital, then Q-CROC, and Exactis Innovation. In 2015, Caroline joined the Rossy Cancer Network where she currently oversees health care services quality improvement efforts.

Dr. Mitali Banerjee Ruths graduated from Baylor College of Medicine then did her pediatrics internship at Texas Children's Hospital. She now works as a Clinical Liaison at the McGill Rossy Cancer Network's Leading-Edge Treatment Program.

Dr. Marc Steben. As a family practitioner Dr. Steben is at the Sexually Transmitted Infections (STI) unit of the Institut national de santé publique du Québec (INSPQ). He is a professor at the School of Public Health at the Université de Montréal. He is the medical director of Clinique A. He has chaired the 26th International Papillomavirus Society meeting in July 2010. He is Chair of the Canadian Network on HPV

Prevention. He is on the board of the International Society for the Study of Vulvovaginal Disease, International Papillomavirus Society and American STD Association.

Dr. David Stewart returned from MD Anderson Cancer Center (Houston) in 2011 to become the Head of Medical Oncology at the University of Ottawa. His research has included therapy of lung cancer, drug resistance mechanisms, and factors driving up costs of new anticancer drugs while slowing access to effective new therapies.

Eva Villalba is the Development Director of the Palliative Home-Care Society Foundation, as well as Executive Advisor: Strategic development, partnerships & philanthropy for the Palliative Home-Care Society of Greater Montreal. She has been involved in cancer patient advocacy and non-profits since 2008. Previously the Vice-President of the Coalition Priorité Cancer ay Québec from 2012-2016 and a current board member, she is also currently the President of the Regroupement au service des organismes et groupes d'entraide communautaire en oncologie du Québec. She specializes in strategic partnerships and fundraising, and is an active member of the Association of Fundraising Professionals.

Meeting organizers

Colorectal Cancer Canada

Barry D. Stein is an Attorney and member of the Barreau du Quebec since 1981. An accomplished lawyer and president of the Colorectal Cancer Canada, he actively represents the interests of cancer patients and speaks regularly to medical professionals, industry, government and patient groups across Canada and internationally. Barry is a survivor of metastatic colorectal cancer diagnosed in 1995 and was obliged to seek health care outside of Canada to fight his disease. His judgment, obtained in the Superior Court of Quebec, serves as a leading precedent for the reimbursement of out of country health care.

Filomena Servidio-Italiano is the Director of Education and Clinical Information for the Colorectal Cancer Canada. She oversees the national patient and caregiver support programs, educational initiatives and management of clinical information. Her undergraduate and graduate work lie in the biological sciences and educational studies. As a caregiver to her father who was afflicted with metastatic cancer, her journey has served as the impetus for the development of the CCC's Colorectal Cancer Resources & Action Network group model. Her previous experience in education has permitted the expansion of the CCC's educational initiatives for both the general public and health care professionals.

Key experts

Susan Turner became President of Turner & Associates Inc. in 2004 following a successful career in the pharmaceutical industry. The company is focused on two areas: cancer and Indigenous health. In the area of cancer, a large part of Susan's work is directed towards access to drugs and other cancer services, with a broad approach of engaging multiple stakeholders to seek solutions. She has produced several investigative reports, developed policy recommendations, organized symposia and facilitated national working groups in this area.

Anne Marie Wright is the President of her own consulting firm, Elements Strategy Inc., providing services to the healthcare industry where transformation through patient focused innovation is critical to success. Patient strategy development and the business and organizational planning required to

support patient focused plans and initiatives is a core expertise. Previous to this, she had a distinguished career working as a senior executive, primarily in the healthcare industry. Educated in business management at Queen's University, she has continued her education through Queen's Executive Development programs, the Niagara Centre for Creative Leadership and the Ashridge School of Management in London, England.

Participants

First Name	Last name	Organization
Health system agencies		
Amy	Sood	CADTH
Sara	Urowitz	CPAC
Patient groups		
Louise	Binder	Canadian Cancer Survivor Network (CCSN)
Dale	Boidman	Bladder Cancer Canada
John-Peter	Bradford	Life Saving Therapies Network
Michelle	Capobianco	Pancreatic Cancer Canada
Niya	Chari	Canadian Breast Cancer Network (CBCN)
Colin	Cooke	Life Saving Therapies Network
Aldo	Del Col	Myeloma Canada
Véronique	Dion	Colorectal Cancer Canada (CCC)
Maxime	Dumais	Quebec Breast Cancer Foundation
Patricia	Gilmore	Lymphoma Canada
Shawna	Ginsberg	Rethink Breast Cancer
Sabrina	Hanna	Save Your Skin
Cathie	Jackson	Colorectal Cancer Canada (CCC)
Jennifer	Laliberté	Ovarian Cancer Canada
Barbara	Lapointe	Bladder Cancer Canada
Deborah	Maskens	Kidney Cancer Canada
Judy	Needham	Canadian Cancer Trials Group (CCTG)
Sonia	Pannu	Colorectal Cancer Canada (CCC)
Frank	Pitman	Colorectal Cancer Canada (CCC)
Filomena	Servidio-Italiano	Colorectal Cancer Canada (CCC)
Cheryl-Anne	Simoneau	Chronic Myelogenous Leukemia Society (CML Society)
Maureen	Smith	Canadian Organization for Rare Disorders
Barry	Stein	Colorectal Cancer Canada (CCC)
Patrick	Sullivan	Team Finn
Pharmaceutical companies		
Donald	Allard	Bristol-Myers Squibb
Justin	Buck	Bayer
Russell	Clarke	Hoffman La Roche
Emanuela	De Franco	Novartis
Brad	Gillesby	Amgen

First Name	Last name	Organization
Chantal	Lacasse	AbbVie
Josée	Lajoie	BMS
Kelly	McKee	Eli Lilly
Vincent	Raymond	Pfizer
Caroline	Richard	Novartis
Anne-Marie	Rivard	Roche
Sophie	Rochon	Johnson & Johnson
Sabrina	Tremblay	Bristol-Myers Squibb
Isabella	Voccia	Boehringer-Ingelheim
Catherine	Wheeler	AstraZeneca
Research sites		
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Diane	Sylvestre	Q-CROC/Research Site
Eva	Villalba	Coalition priorité cancer au Québec
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Appendix 5 Consensus questions

1. Proposed consensus questions:

Part I: The Barriers to Accessing "Cancer Clinical Trials" (CCTs) Overall and the Barriers to the "Patient Group-Pathway Model" (PG-PM) in CCTs

1. What are the participant-specific barriers related to CCTs?

a. Lack of participant education on CTs/misconceptions of and inability to navigate CTs in general; lack of awareness of ongoing CCTs as a possible option; demystification of clinical trials process required

b. Logistical and cost-related concerns: i.e. lack of time, lack of resources to support out of pocket expenses for travel/parking/childcare, etc.

c. Geographical proximity to CCTs is prohibitive

d. Uninterested/unsupportive oncologist; HCP may serve as a "gate keeper" rendering participants at the mercy of the HCP; risk aversion: participants may be concerned about the impact on their care if they choose to advocate for a CCT

e. Participants' disease status may be prohibitive due to not meeting inclusion criteria

f. Socio-economic status: Level of education (more formally educated tend to consent)/social circumstances (participants who lack time to attend extra trial-related appointments due to family commitments less likely to consent)/language impediments & cultural issues (minority populations less likely to participate due to distrust of existing systems)

2. What are the barriers to having PGs participate in the pathway to CCTs?

a. Understanding of/education about clinical trials

b. Unaware of how they can be involved

c. Lack of resources to participate (including people, time, money)

d. Lack of understanding/awareness of sponsors/investigators to include PGs in the pathway (PGs have inherent value/benefits in terms of promoting awareness of CCTs to their respective patient populations)

Part II: The Role of Patient Groups in Cancer Clinical Trials (CCTs)

3. What is the role of the PG in CCT protocol design (including the developing, tracking and dissemination of patient values) and research collaboration?

a. Provide the participant perspective about the protocol and informed consent form

b. Provide insight in to patient values/outcomes/study endpoints that are important to patients

c. Participate in meetings with the regulatory agencies

d. Engage early with researchers and clinicians (?) and continue to stay engaged

4. What role can PGs play in patient awareness, engagement, recruitment, promotion, retention, ongoing and post-trial patient communication in CCTs?

a. Provide information to patients/caregivers in lay language about ongoing CTs and the 'mechanics of CTs'

b. Provide information on informed consent

c. Ensure capture of post-trial information through Real World Evidence ("RWE")

d. Engage with regulators to provide patient perspective at federal level

e. Provide patient group input into Health Technology Assessments (pCODR/CADTH)

f. Work with sponsors to develop materials that are written in easily understood lay language

g. Develop registries of potential participants

h. Implement/develop transparent communication of clinical trial outcomes/results

Part III: The CTTI Patient Group Pathway Model (PG-PM) to CCTs

5. What best practices are detailed within the CTTI model?

a. Engage the patient voice by establishing partnerships from the beginning of the research and development program to improve trial design and execution (and ensure they are not token voices).

b. From the start, clearly define the expectations, roles, and responsibilities of all partners, including the resources being committed, data being shared, and objectives of the collaborative program.

c. PG input may be taken into account when determining the objectives of a clinical program or development of a protocol, research sponsors must balance that input with scientific understanding as well as business and regulatory needs.

d. Build the trust required for successful partnerships by being transparent and trustworthy, following through on commitments, and honoring confidentiality.

e. Involve the expertise of multiple partners for a broader perspective to mitigate risk and enrich pipeline development.

f. Manage real or perceived conflicts of interest by establishing policies that require full disclosure, transparency, and accountability.

g. It is important to clarify which kind of interactions with PGs are permissible and which ones might violate FDA regulations or fraud, abuse, and other regulations.

h. Measure the impact of PG engagement.

i. Establish ongoing relationships with PGs and communicate openly with them on a regular basis.

j. Proactively identify, engage, and bring the patients' voice to stakeholders relevant to the R&D interests.

6. Is the CTTI PG-PM model valid and amenable for adoption in Canada?

a. Yes, for the following reasons:

b. No, for the following reasons:

c. Perhaps, with the following considerations:

Part IV: The Development of a PG-PM for CCTs: Patient engagement, awareness, recruitment, retention, ongoing and post-trial communication. Adapting the CTTI PG-PM for CCTs to the Canadian reality.

7. Identify the key stakeholders to be engaged in the promotion of the PG-PM for CCTs. What would be their respective roles? a. Patients/Caregivers/Potential participants

b. Cancer Patient Groups/Health Charities

c. Researchers, including clinicians

d. Research Ethics Boards

e. Healthcare Providers

f. Industry (pharmaceutical, biotech, medical device, CROs, industry associations like Innovative Medicines Canada, BIOTECanada, etc)

g. pCODR/CADTH

h. Health Canada

i. Academic Centres (i.e. Cancer Centre Directors, Clinical Trial Managers/Coordinators)

j. Other organizations interested in the clinical trials/patient oriented research space (e.g. Canadian Clinical Trials Coordinating Centre, Clinical Trials Ontario, Q-CROC, Network of Networks, BC Clinical Research Infrastructure Network, Canadian Cancer Clinical Trials Group, Canadian Cancer Clinical Trials Network, SPOR Support Units, DGC, Hope and Cope, CanSupport, CPAC, etc.)

8. What differences in the Canadian landscape need to be taken into consideration before adopting/adapting the CTTI PG-PM for CCTs?

a. Canadian healthcare system operates differently (under provincial jurisdiction) than that of the U.S. The concept of PG-PM in CCTs would be relatively new to Canada for all stakeholders – there is a need to be thoughtful and consider everyone's perspective with any model developed.

b. With respect to the pharmaceutical industry:

i. less research/development is done in Canada compared to other countries

ii. sometimes clinical trials are designed by the global headquarters, not the Canadian affiliates

c. Health Canada vs. the FDA: PGs are typically not involved in HC meetings to provide patient testimonials, which is a common practice with the FDA in the U.S.

9. Are there component parts of other existing PG-PMs that may contribute to the development of a Canadian PG-PM to CCTs?

a. Educational modules about the research & development spectrum (e.g. EUPATI - https://www.eupati.eu/) for patients and patient organizations (for consistent messaging)

b. Industry working collaboratively in this capacity to help drive this agenda

c. Relevant work carried out by SPORE should be included

2. Agreed consensus questions

The original consensus questions were modified by participants to reflect Canadian realities of cancer clinical research. The modified consensus questions were used to develop the Canadian Patient Group Pathway Model to Accessing Cancer Clinical Trials, outlined in Appendix 4.

Part I: The barriers to accessing cancer clinical trials overall and the barriers to the Patient Group Pathway Model in cancer clinical trials

1. What are the participant-specific barriers related to cancer clinical trials?

- Lack of participant education on clinical trials/misconceptions of and inability to navigate clinical trials in general; lack of awareness of ongoing cancer clinical trials as a possible option; demystification of clinical trials process required
- Logistical and cost-related concerns: i.e. lack of time, lack of resources to support out of pocket expenses for travel/parking/childcare, etc.
- Geographical proximity to cancer clinical trials is prohibitive
- Uncommitted or uninformed oncologist:
    - Health care professionals may serve as 'gate keepers' limiting therapeutic options for the patient
    - Risk aversion
    - Potential participants may be concerned about the impact on their care if they choose to advocate for a cancer clinical trial
- Participants may not be eligible based on inclusion criteria
- Social determinants of health: Level of education (more formally educated tend to consent)/social circumstances (participants who lack time to attend extra trial-related appointments due to family commitments less likely to consent)/language impediments & cultural issues (minority populations less likely to participate due to distrust of existing systems)
- Provincial boundaries and government restrictions on future therapies
- Unavailability of clinical trial site
- Design of clinical trial may not be acceptable to patients
    - Placebo arm
    - Same treatment more easily available off-study
    - Cannot wait for required procedures to be done

2. What are the barriers to having patient groups participate in the pathway to cancer clinical trials?

- Understanding of/education by patient groups about clinical trials
- Patient groups unaware of how they can be involved
- Silos within sponsors organizations prevent patient group engagement
- Sponsors may be unaware/uninterested in working/partnering with patient groups that are engaged
- Lack of resources to participate (including people, time, money)
- Lack of understanding by sponsors/investigators as to how to include patient groups
- Compliance issues across various stakeholders regarding privacy/confidentiality

PART II: The role of patient groups in cancer clinical trials

3. What is the role of the patient group in cancer clinical trial protocol design (including the developing, tracking and dissemination of patient values) and research collaboration?

- Provide the participant perspective about the protocol and informed consent form
- Provide insight in to patient values and preferences
- Provide insight into patient relevant outcomes and appropriate study endpoints
- Participate in meetings with the regulatory and health technology assessment agencies
- Engage early with researchers, clinicians, healthcare providers and research teams and continue to stay engaged

4. What role can patient groups play in patient awareness, engagement, recruitment, promotion, retention, ongoing and post-trial patient communication in cancer clinical trials?

- Provide information to patients/caregivers in lay language about ongoing clinical trials and the mechanics of clinical trials
- Provide information to patients/caregivers about the value of clinical trials in general
- Provide patient perspectives on participation in clinical trials to healthcare providers
- Provide information on patient-reported outcomes to healthcare professionals and patients
- Provide information on informed consent
- Ensure capture of post-trial information through real world evidence
- Engage with regulators to provide patient perspective at federal level
- Provide patient group input into health technology assessments (pCODR/CADTH/INESSS)
- Work with sponsors to develop trials specific materials that are written in easily understood lay language
- Develop registries of potential participants
- Implement/develop transparent communication of clinical trial outcomes/results

Part III: The CTTI Patient Group Pathway Model for cancer clinical trials

5. What best practices are detailed within the CTTI model?

- Engage the patient voice by establishing partnerships from the beginning of the research and development program to improve trial design and execution (and ensure they are not token voices).
- From the start, clearly define the expectations, roles, and responsibilities of all partners, including the resources being committed, data being shared, and objectives of the collaborative program.
- Patient group input may be taken into account when determining the objectives of a clinical program or development of a protocol, research sponsors must balance that input with scientific understanding as well as business and regulatory needs.
- Build the trust required for successful partnerships by being transparent and trustworthy, following through on commitments, and honoring confidentiality.
- Involve the expertise of multiple partners for a broader perspective to mitigate risk and enrich pipeline development.
- Manage real or perceived conflicts of interest by establishing policies that require full disclosure, transparency, and accountability.

- It is important to clarify which kind of interactions with patient groups are permissible and which ones might violate Health Canada/health technology assessment regulations or fraud, abuse, and other regulations.
- Measure the impact of patient group engagement.
- Establish ongoing relationships with patient groups and communicate openly with them on a regular basis.
- Proactively identify, engage, and bring the patients' voice to stakeholders relevant to the research and development interests.

6. Is the CTTI Patient Group Pathway Model valid and amenable for adoption in Canada?

- Yes, for the following reasons:
  - Adaptable to the Canadian landscape
  - Represents best practices
  - Demonstrable outcomes

Part IV: The development of a Patient Group Pathway Model for cancer clinical trials: patient engagement, awareness, recruitment, retention, ongoing and post-trial communication. Adapting the CTTI Patient Group Pathway Model for cancer clinical trials to the Canadian reality.

7. Identify the key stakeholders to be engaged in the promotion of the Patient Group Pathway Model for cancer clinical trials.

- Patients/caregivers/potential participants
- Cancer patient groups/health charities
- Researchers, including clinicians
- Research ethics boards
- Healthcare Providers
- Industry (pharmaceutical, biotechnology, medical device, clinical research organizations, industry associations like Innovative Medicines Canada, BIOTECanada, etc.)
- pCODR/CADTH/INESSS
- Health Canada
- Academic Centres (i.e. cancer centre directors, clinical trial managers/coordinators)
- Other organizations interested in the clinical trials/patient oriented research space (e.g. Canadian Clinical Trials Coordinating Centre, Clinical Trials Ontario, Q-CROC, Network of Networks, BC Clinical Research Infrastructure Network, Canadian Cancer Trials Group, Canadian Cancer Clinical Trials Network, SPOR, Support Units, DGC, Hope and Cope, CanSupport, CPAC, Exactis, Wellspring, Gilda's Club, etc.)
- Health policy research
- Provincial ministries of health
- Third-party payers
- Funders of clinical research
- Expertise and data resources

8. What differences in the Canadian landscape need to be taken into consideration before adopting/adapting the CTTI Patient Group Pathway Model for cancer clinical trials?

- Canadian healthcare system operates differently (under provincial jurisdiction) than that of the United States. The concept of Patient Group Pathway Model in cancer clinical trials would be

relatively new to Canada for all stakeholders – there is a need to be thoughtful and consider everyone's perspective with any model developed.

- With respect to the pharmaceutical industry:
    - Less research/development is done in Canada compared to other countries
    - Sometimes clinical trials are designed by the global headquarters, not the Canadian affiliates
    - Health Canada vs. the Food and Drug Administration (FDA): Patient groups are typically not involved in Health Canada meetings to provide patient testimonials, which is a common practice with the FDA

9. Are there component parts of other existing Patient Group Pathway Models that may contribute to the development of a Canadian Patient Group Pathway Model to cancer clinical trials?

a. Education about the research & development spectrum (e.g. EUPATI) for patients and patient organizations
b. To consider: Accreditation of patient groups
c. Stakeholders working collaboratively in this capacity to help drive this agenda
d. Relevant work carried out by the Strategy for Patient-Oriented Research (SPOR) should be included
e. Other existing models in Canada, for example the Canadian Cancer Trials Group (CCTG)