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MEETING REPORT

Report on a Delphi process and workshop to improve accrual to cancer clinical trials

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ABSTRACT

Cancer clinical trials (CCTs) are essential for furthering knowledge and developing effective interventions to improve the lives of people living with cancer in Canada. Randomized controlled trials are particularly important for developing evidence-based health care interventions. To produce robust and relevant research conclusions, timely and sufficient accrual to CCTs is essential.

The present report delivers the key recommendations emerging from a workshop meeting, Improve Accrual to Cancer Clinical Trials, that was hosted by the Canadian Cancer Trials Group and funded by the Canadian Institutes of Health Research. The meeting, which took place in Toronto, Ontario, in April 2012 before the Canadian Cancer Trials Group annual spring meeting, brought together key stakeholders from across Canada to explore creative strategies for improving accrual to CCTs. The objectives of the workshop were to provide an opportunity for knowledge exchange with respect to the research evidence and the ethics theory related to CCT accrual and to promote discussion of best practices and policies related to enhancing CCT access and accrual in Canada.

The workshop provided the foundation for establishing new interdisciplinary research collaborations to overcome the identified barriers to CCT participation in Canada. Meeting participants also supported the development of evidence-based policies and practices to make trials more accessible to Canadians living with cancer.

Key Words Cancer clinical trials, trial accrual, ethics, patient autonomy, patient decision-making, knowledge translation, access, barriers

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INTRODUCTION

The Canadian Cancer Trials Group (CCTG—formerly the NCIC Clinical Trials Group) has had a long-standing commitment to clinical trial research in Canada. However, timely accrual is a frequent issue that threatens the success of randomized cancer clinical trials (CCTs) within Canada and within the CCTG[1].

A workshop meeting, Improve Accrual to Cancer Clinical Trials, was held in advance of the CCTG annual spring meeting (27–29 April 2012) in Toronto, Ontario. The meeting brought together CCT researchers and personnel, cancer centre executive representatives, lay patient representatives, and ethicists to share their perspectives about accrual issues associated with CCTs, particularly in the light of recent research findings and ethics theory. The purpose of the workshop was to identify and prioritize factors that affect CCT accrual in Canada; to share new research findings related to perspectives of patients concerning personal, social, and structural barriers to CCT participation; and to clarify how patient autonomy can be enhanced through the removal of barriers to CCTs.

PRE-WORKSHOP DELPHI PROCESS

Before the workshop, a Delphi process was conducted to develop consensus-based priorities for informing strategies to address accrual issues. The Delphi technique is an established consensus-building method[2,3] that is extensively applied in health care, business, and education[4–6].

The technique involves the presentation of a series of structured questionnaires to a panel of experts (that is, individuals who are knowledgeable about the specific topic under consideration) to seek their opinion or judgment on an issue[7]. The responses from each round of questionnaires are iteratively returned to all panel members in a summarized quantitative form, and members are requested to communicate their judgments back to the group. We conducted a two-round Delphi process in advance of the workshop to ensure a focussed discussion

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during the meeting and to generate specific strategies (for example, ethics practices and policies) and research priorities that would address low accrual to CCTs in Canada[1].

Participants: The Expert Panel

Validation of the results from a Delphi process depends largely on the composition of the expert panel. We invited all executive site committee members (n = 184) who were confirmed to attend the CCTG 2012 meeting, as well as an ethicist and 3 researchers with complementary backgrounds in CCTs, to participate in the Delphi process. The invitation to participate in the workshop was accepted by 46 attendees, including the planning team (JAHB, LGB, HR). Participants represented key CCT stakeholder groups from across Canada, including those involved in trial design, administration, recruitment, and participation. Stakeholder backgrounds included CCT researchers (principal investigators and disease site chairs), CCT personnel (research nurses and data managers), CCTG senior faculty, patient advocates, and ethicists. Participants received an e-mail message with a link to a consent form and online questionnaire. In total, 37 participants responded to the round 1 questionnaire, and 34 participants responded to the round 2 questionnaire.

Data Analysis Process

Descriptive statistics were used to analyze responses from the panel members in each round of the Delphi process. Results were also analyzed collectively to explore whether consensus was achieved throughout each round or only in the second round. The latter analysis helped in determining the reliability of results by paying attention to the process by which consensus was achieved and examining what happened between rounds instead of examining the final results only[8]. Consensus was achieved throughout the process, indicating enhanced reliability.

Round 1 Questionnaire

A list of factors influencing CCT participation (both barriers and facilitators) was developed by the planning team, informed by recent research describing the CCT decision-making processes of cancer patients and the influence of relational autonomy[9]. Relational autonomy acknowledges both the social factors (for example, family relationships) and the structural factors (for example, availability of care) that influence the ability of patients to make independent decisions about treatment and care. Applying relational autonomy theory to the issue of low accrual to CCTs allowed for richer and more comprehensive understandings of the factors influencing the CCT decision-making processes of cancer patients.

The three sections of the round 1 questionnaire addressed personal, social, and structural influences on the relational autonomy of, and CCT decision-making by, cancer patients. The first section asked participants to select the top 5 personal factors influencing CCT participation from a list of 9 factors. The second section asked participants to select the top 3 social factors influencing CCT participation from a list of 6 factors. The third section asked participants to select the top 5 structural factors influencing CCT participation from a list of 10 factors. Participants were able to add additional barriers or facilitators to all three sections.

Results of Round 1

The most common personal barrier to CCT participation identified by workshop participants was information overload about cancer, cancer treatment, and trials (73%). Additional personal barriers described by participants included travel to the study site, lack of patient awareness about the trial, fear of delay in treatment, and out-of-pocket costs. Table I details the top 5 personal factors identified in round 1 of the Delphi process to influence CCT participation.

The most common social factor identified to influence CCT participation was the presentation style (that is, positive and negative presentation) used by physicians and CCT personnel when describing the trial to patients (86.5%). Table II details the top 5 social factors identified in round 1 of the Delphi process.

The structural factor most commonly identified by participants to influence CCT accrual was the stringency

TABLE I Top five personal factors influencing clinical trial accrual, round 1 (n = 37)

Rank	Factor	Participant support (%)
1	Information overload about cancer, cancer treatment, and clinical trials	73.0
2	Fear and uncertainty about receiving an unknown treatment that might or might not work	59.5
3	Distress related to the cancer diagnosis and treatment plan	54.1
4	Understandings or misunderstandings about clinical trials, including placebo, randomization, and care received while on trial	54.1
5	Fears about known toxic side effects and unknown adverse effects that might result from clinical trial participation	48.6

TABLE II Top five social factors influencing clinical trial accrual, round 1 (n = 37)

Rank	Factor	Participant support (%)
1	Presentation of the trial by physician and clinical trial personnel (positive and negative presentation)	86.5
2	Social commitments of the patient (for example, family, work), geographic location, and socioeconomic status	75.7
3	Gate-keeping behaviour by physicians (for example, not offering a trial)	73.0
4	Provision of clinical trial decision-making support (for example, support in synthesizing information, psychological support for decision-making, and promotion of patient autonomy and control over the decision to participate)	59.5
5	Encouragement or discouragement by family members and other support persons	56.8

or demanding nature of the CCT protocols [that is, numerous blood tests, frequent clinic visits (75.7%)]. Additional barriers cited by workshop participants included a lack of money to run trials at centres, difficulty in translating trial information to patients, and trials taking too long or having too many correlative studies (for example, tissue banking). Table III details the 5 most frequent structural barriers or facilitators identified by participants in round 1 of the Delphi process.

Round 2 Questionnaire

The round 2 questionnaire contained the 5 most frequent personal, social, and structural barriers or facilitators to trial participation identified in round 1 of the Delphi process. The planning team removed barriers and facilitators selected by fewer than 25% of panel the members in round 1, because those factors did not represent priority issues.

In round 2, participants were asked to select the 3 most influential personal, social, and structural barriers and facilitators to CCT participation from the list of 5. Participants could identify factors not appearing on the list.

Results of Round 2

The round 2 questionnaire drew 34 responses. The most frequently cited personal barrier was information overload about cancer, cancer treatment, and CCTs (67.6%). The most frequent social barrier or facilitator was the social circumstances of the patient, including social commitments, geographic location, and socioeconomic status (76.5%). The most frequent structural barrier was the stringency or demanding nature of the CCT protocols (85.3%). Table IV details the 3 most influential personal, social, and structural factors influencing CCT accrual that were identified in round 2. Those 9 factors were the focus of discussion at the CCT accrual workshop meeting.

WORKSHOP PROCESS

Preparatory Sessions

The workshop began with a welcome and introduction to orient the participants and to clarify their expectations of the evening. Included was a review of the workshop objectives and agenda and provision of information about the small-group activity (Table IV).

To provide knowledge context, 4 researchers with experience in CCT-related research (designations and affiliations at the time of the workshop) presented their findings related to CCT accrual:

- Chris O'Callaghan DVM MSc PhD MRCVS, Kingston General Hospital and Department of Public Health Sciences, Queen's University, Kingston, ON (CO.20: Accrual experience from a CCTG trial)
- Jennifer Bell MA PhD(c), W. Maurice Young Centre for Applied Ethics, University of British Columbia, Vancouver, BC (Cancer patient autonomy and decision-making about clinical trials: Barriers and facilitators)
- Sally Thorne PhD RN, School of Nursing, University of British Columbia, Vancouver, BC (Patient perspectives of communication with cancer care providers)
- Andrew Arnold MD, Department of Oncology, McMaster University and Juravinski Cancer Centre, Hamilton, ON (Addressing barriers to participation on cancer trials: The Juravinski Cancer Centre experience)

After the presentations, workshop participants were asked to reflect on and to share their own recruitment challenges with colleagues. Small groups were subsequently formed, and workshop participants reviewed assigned exercises about existing barriers, needed resources, best practices and policies, and research to improve accrual to CCTs in Canada.

Small-Group Brainstorming

The 48 participants were divided into 6 groups. The composition of each group had a purposeful mix of disease site chairs, centre executive representatives, and patient lay representatives, plus a facilitator from the organizing committee. The groups were asked to discuss 1 personal, 1 social, and 1 structural factor (3 in total) from the Delphi round 2 results and to develop a strategy or an intervention to address each factor. To promote diversity in the strategies developed, 2 groups were assigned to discuss each factor, which for the most part were barriers to CCT accrual.

TABLE III Top five structural factors influencing clinical trial accrual, round 1 ($n = 37$)

Rank	Factor	Participant support (%)
1	Clinical trial protocols being too stringent or demanding (that is, blood tests, number of clinic visits)	75.7
2	Stringency of eligibility criteria for clinical trial participation	51.4
3	Complexity and length of consent forms and other clinical trial material	51.4
4	Complexity of trial design, including treatment options and protocols	51.4
5	Access to new cancer treatments not yet accessible outside of clinical trials	45.9

RESULTS

Strategies to Address Personal Barriers and Facilitators

Participants suggested 3 strategies to overcome the highest-ranked barrier: patients feeling overwhelmed with information about cancer, cancer treatment, and clinical trials (Table IV). First, clinicians should separate discussion of the CCT from their discussion of the cancer diagnosis and treatment with patients. Second, clinicians should connect patients to advocacy groups that have experience with CCTs and that can provide support to patients considering enrolment. Finally, information about CCTs could be made available on a public Web site or podcast to promote broader awareness about CCTs in Canada.

With respect to fears that patients express about the side effects and unknown adverse reactions associated with CCT participation, workshop participants suggested 3

TABLE IV Top factors influencing clinical trial accrual, round 2 ($n = 34$)

Factor type	Rank	Factor	Participant support (%)
Personal	1	Information overload about cancer, cancer treatment, and clinical trials	67.6
	2	Fears about known toxic side effects and unknown adverse effects that might result from clinical trial participation	58.8
	3	Fear and uncertainty about receiving an unknown treatment that might or might not work	55.9
Social	1	Social commitments of the patient (for example, family, work), geographic location, and socioeconomic status	76.5
	2	Gate-keeping behaviour by physicians (for example, not offering a trial)	58.8
	3	Presentation of the trial by physicians and clinical trial personnel (positive and negative presentation)	50.0
Structural	1	Clinical trial protocols being too stringent or demanding (that is, blood tests, number of clinic visits)	85.3
	2	Stringency of eligibility criteria for clinical trial participation (tie)	58.8
	2	Complexity and length of consent forms and other clinical trial material (tie)	58.8

ways to potentially overcome this barrier: First, physicians should differentiate between common and rare side effects to promote a better understanding of the probability of such effects by patients. The clinician introducing the trial should also emphasize that patients can withdraw from a CCT at any time and that trial participants are closely monitored for adverse effects. Finally, it was suggested that a research nurse be on call to explain side effects or adverse drug reactions, should they occur.

To overcome the final personal barrier related to fear and uncertainty about receiving an unknown treatment that might not work, workshop participants advised that clinicians should promote trust by explaining the ethics approval process, including the scrutiny that CCTs undergo by research ethics boards, and the rigour with which CCTs are developed. Patients also have to be reassured, based on the concept of clinical equipoise, that they will not be disadvantaged in their care because of participation in a CCT. Finally, the patient's fear and uncertainty can be reduced by having an educator independent from the CCT explain the various types of trials and the differences in goals for phase I, II, and III trials.

All the suggested strategies to overcome personal barriers involved modifying how CCTs are introduced to patients. In addition, the participants emphasized the need to find the appropriate trial for each patient and the proper time to introduce a trial (that is, not during initial consultations about diagnosis and treatment). Patients considering taking part in a CCT could also benefit from speaking with a cancer survivor who has faced a similar decision in the past. Developing education sessions about CCTs or including CCT decision-making as part of patient navigation could also be beneficial.

Using the media to promote public awareness of clinical trials might also address some of the fear and uncertainty experienced by patients related to taking part in trials. For example, the Canadian Cancer Society could launch a social media campaign to create public awareness about CCTs and to normalize the expectations of cancer patients regarding being asked to participate in a CCT. The CCTG or the Society for Clinical Trials could develop patient education materials that could be used by health professionals to educate the public about clinical trials and to demystify some of the uncertainty about taking part in trials. With the first week in May being Clinical Trials Awareness Week in Canada, promotional events could occur at local cancer agencies to educate the public about CCTs and to emphasize the important role that patients can play in contributing to the understanding of cancer and its treatment.

Personal barriers to CCT participation might also be mitigated by the presence of national or regional CCT Web sites, which could provide the public with current information about trials. The development of knowledge translation public events to share information about trials would also educate patients about the role of clinical trials in research and medical care and encourage dialogue between patients and researchers about clinical trials.

As noted by workshop participants, an important personal barrier that is not always acknowledged and that could be resistant to change is the lack of interest in CCTs and participation in research on the part of some patients.

Strategies to Address Social Barriers and Facilitators

To overcome the barrier to CCT accrual posed by social commitments on the part of some patients, workshop participants suggested that researchers partner with industry to provide more funding to reimburse travel costs incurred by patients participating in CCTs. Participants also suggested that driving services for patients be expanded in rural areas to support those attending study visits. To further support the involvement of rural patients in CCTs, study nurses could travel to the home communities of participants to administer CCT interventions and to collect data. Lastly, patients with significant family commitments (young children at home, for example) might require help from social support programs (such as an offer by community or cancer centres of low-cost child care) to support their participation in CCTs.

The social barrier of gate-keeping behaviour on the part of physicians was perceived by workshop participants to be related mainly to the physician's lack of awareness of available trials, lack of resources (for example, time), and assumptions about the ability of patients to engage in

CCTs. To address those issues, participants recommended that information about ongoing trials, including eligibility criteria and accrual time periods, be provided at weekly or monthly professional education sessions, such as interdisciplinary rounds. With busy clinic schedules and limited time, participants mentioned that many physicians simply forget to discuss CCTs with patients. Two strategies to overcome that barrier were suggested:

- Have clinical research associates screen patient charts and flag eligible patients that physicians could then approach for a discussion of CCTs.
- Create a standardized script that could be used by physicians to introduce a trial to eligible individuals. Having a script might not only increase trial accrual, but also reduce the potential for bias in the way that the CCT is described by physicians.

Participants did discuss the possibility that some physicians might make assumptions about a patient's inability to participate in a trial based on income, language ability, immigration status, and cultural and historical characteristics. That barrier could be addressed by raising awareness among physicians about the importance of justice and equitable access to CCTs for all patients. Such education could occur within clinical settings, but could also be embedded in undergraduate and postgraduate education programs, which would provide training and mentorship about CCTs to new physicians so as to encourage accrual across clinical settings and patient populations.

Other strategies recommended to address gate-keeping behaviour by physicians and the limited time available to discuss CCTs included using patient navigators to help guide patients through the decision-making process after being introduced to a trial. Clinical trial nurses could also be present at new-patient orientation sessions to provide generic information about clinical trials and to discuss trials currently accruing in the clinical setting. Raising awareness among patients about available CCTs will empower them to take an active role in asking their physician about potential research opportunities and their eligibility.

Participants also raised concerns about CCT personnel, including physicians, being overly positive or negative in their presentation of trials to patients. Additional training, including role-playing, might be required to ensure that CCT personnel offer information about CCTs in a neutral manner.

Strategies to Address Structural Barriers and Facilitators

With regard to the structural barrier of CCT protocols being too stringent or demanding, workshop participants engaged in a discussion about whether trials have become too complex. With an ever-increasing number of substudies and correlative studies being attached to CCTs (requiring additional money, resources, and time), patients and cancer centres alike might feel discouraged from participating in trials. Complex trials are particularly difficult for smaller rural centres, with accrual subsequently being limited to large urban centres. In planning CCTs, a balance between feasibility, accessibility, and scientific opportunity is needed. If accrual to CCTs remains problematic, simpler trial designs might have to be encouraged.

Further to the issue of simplicity, stringent eligibility criteria and complex consent material have complicated accrual in many clinical settings. Workshop participants suggested the establishment of multidisciplinary working groups to share and create best practices in trial design and consent procedures to help reduce the complexity of CCTs and to improve accrual rates. Consent forms were seen as being particularly problematic, and participants agreed that the forms should be simpler and shorter, and include only essential information without compromising meaning. For patients who prefer more information, a detailed consent form, linked to the basic consent form, could be provided online, or additional information could be presented in an appendix to ease the consent process. In addition, the process of gaining consent could be facilitated by making a decision aid available or could be simplified through the use of electronic forms with interactive features that provide more information.

Although not identified as a top structural barrier through the Delphi process, much discussion occurred at the workshop about the importance of research being promoted at the institutional level. Elevating CCTs to become part of a clinical organization's mandate would ensure that all health care professionals and CCT staff have the time and resources needed to engage all eligible patients in conversations about CCTs. Accruing to CCTs would also be viewed as an important marker of success for the organization and would be encouraged among all clinicians. Integrated care teams would be developed that include researchers, who could raise awareness about available CCTs and support clinicians in recruiting eligible patients. The need for integrated infrastructure and personnel support for CCT centres was also recognized in a report published by the Canadian Cancer Research Alliance[1]. In response to that report, the Canadian Cancer Clinical Trials Network (3CTN, http://3ctn.ca/) was established in 2013 to provide support and coordination for a network of cancer centre teams and hospitals to help increase their capacity to conduct academic CCTs.

FUTURE DIRECTIONS

A number of strategies and resources are required to overcome the identified barriers to CCT accrual in Canada. There is a need to create knowledge in the public domain about clinical trials, such as through media campaigns or a national education strategy. Patients need more time and space for discussions about CCTs to alleviate fears about untested treatments, and it is imperative that the ethics principle of justice and equitable access be promoted so that clinicians offer clinical trials to all eligible patients. Further research into various consent formats, levels, and types of trial information and how those factors affect patient experience, patient satisfaction, and accrual rates is needed. Finally, it would be useful to establish a National Cancer Research Network to develop best-practice standards for CCT accrual, to promote a national CCT database, and to explore the idea of a centralized ethics review process.

The Improve Accrual to Cancer Clinical Trials workshop provided an important forum for the dissemination of current research about accrual to CCTs and an opportunity

for key stakeholders in Canada to discuss ways in which to address existing personal, social, and structural barriers to accrual. The recommendations developed during the meeting offer the Canadian CCT community direction about how to improve accrual to CCTs and to promote patient autonomy in the CCT decision-making process.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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