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The Canadian Partnership for Tomorrow Project: building a pan-Canadian research platform for disease prevention

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As the proportion of the population over age 65 increases in Western countries, the burden of cancer[1] and other chronic diseases is also increasing. If advances in preventing these diseases are to be realized, better information is needed about their causes and the antecedents of the causes. For example, although it is known that many sporadic cancers are caused by a combination of lifestyle factors, exposure to environmental carcinogens and individual genetic makeup,[2,3] detailed knowledge about the interplay among these factors is lacking.

Much of our current knowledge about the causes of cancer and most relatively rare chronic diseases has come from retrospective case–control studies, in which the characteristics of patients (cases) are compared with those of age- and sex-matched people who do not have the disease (controls). This design has strengths but also a number of weakneses, including potential recall bias and selection bias[4] (Table 1). To address some of these weaknesses, in particular recall bias and the temporal relation between risk factors and outcomes, prospective cohorts are helpful because participants are enrolled before the onset of disease. In studies with a prospective cohort design, large numbers of participants, who generally have not had cancer or any other significant diagnosis, are recruited and followed over a long time, periodically providing updated health and lifestyle information and biologic samples. Layers of data and samples accumulate over time, allowing an exploration of why cancer develops in some people within the cohort but not others.[6] The disadvantages of such a design (Table 1) are cost and time, as it may be a decade or more before major results are obtained. Fortunately, many shorter-term results are also available, such as information on screening attendance and information on the frequency of major risk factors and health states, as well as environmental and individual determinants of these risk factors, all of which are useful for planning various health services. Furthermore, because many diseases can be studied simultaneously, the cost over time per health outcome studied is substantially lower than the cost of case–control studies for a comparable number of participants.

In this paper, we describe the rationale for, challenges associated with and methods being used in a new pan-Canadian cohort for the study of cancer and chronic disease.

Key points

- The Canadian Partnership for Tomorrow Project is a pan-Canadian initiative to learn more about the causes of cancer and other chronic diseases.
- This project will follow 300 000 Canadians on a long-term basis.
- Data collection methods include questionnaires, blood and urine samples, and physical measurements to provide the foundation for hundreds of studies.
- The aim is to understand how environment, lifestyle and genetics contribute to chronic diseases and to use this understanding to inform prevention strategies.

This cohort will, in time, form the foundation for a major research platform for the study of disease causation, both nationally and internationally.

Design

A strategic partnership has been formed to establish a large prospective cohort for the study of the causes of cancer and other chronic diseases in Canada. This partnership, the Canadian Partnership for Tomorrow Project, aims to develop a comprehensive, long-term, pan-Canadian health research platform with sufficient statistical power to examine the complex interplay of genetic and environmental factors that leads to the development of important chronic diseases in the Canadian population.[7] The Canadian Partnership for Tomorrow Project

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comprises a confederation of provincial and regional cohorts (Table 2) in British Columbia, Alberta, Ontario, Quebec and Atlantic Canada (Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland and Labrador). The operational objective is to enrol 250 000 to 300 000 Canadians aged 35–69 years by 2012, and enrolment is already under way. A number of task forces and working groups have been established to address issues related to ethics, privacy, harmonization, information technology, sample processing and definition of environmental exposures of interest (Figure 1).

Participants

Canadian residents are eligible for a provincial or regional component of the project if they reside in the province or region and meet the cohort's age criteria (Table 1). The mechanisms for identifying potential participants vary among jurisdictions and include random selection from population-based data, purchase of mailing lists for specific geographic areas, random-digit dialing and word of mouth.

Project staff contact potential participants by letter with an invitation to join, although volunteers will be accepted in some cases. The sources of contact information vary by region, and the impact of this variation will be monitored regularly to help ensure that the resulting cohort is relatively representative of the Canadian population. All five regional cohort teams have agreed to the core measures, and individual provinces or regions will schedule the acquisition of data, biologic specimens and physical measurements according to the most efficient methods of local practice.

Initially, those who express an interest in participating make an appointment to come to an assessment centre for 90–120 minutes. During this visit, a project staff member explains the study to the participant, who provides written informed consent and completes an epidemiologic questionnaire on lifestyle, health events and other factors. Physical variables are measured, including sitting height, standing height, weight, percentage body fat (by bioelectrical impedance), waist circumference, hip circumference, grip strength, blood pressure and resting heart rate. Bone density by ultrasonography and lung function by spirometry are in the extended variable set, which consists of variables that are collected, in a consistent manner, by two or more regions but are not a required part of the protocol for all regions. Data that may be important for later interpretation of these physical measures are also collected. Eligible participants also provide biologic specimens (primarily blood). As recruitment proceeds, it may prove more cost-effective for the component cohort teams to collect data in a different sequence from that noted above. For example, there might be initial concentration on completion of enrolment questionnaires and collection of biologic specimens, with physical measurements being obtained later.

Table 1: Strengths and limitations of case–control and prospective cohort study designs[5]

Strengths	Limitations
Case–control studies	
Relatively quick	Difficult to examine temporality
Relatively inexpensive	Potentially prone to bias (selection and recall)
Can be used to examine multiple factors	
Prospective cohort studies	
Can be used to examine multiple outcomes	Expensive and time-consuming
Allow for prediagnostic specimens	Losses to follow-up over time
Minimal bias in selection, recall and ascertainment of exposure	
Can be used to examine temporal relations between exposure and disease	

Biologic specimens

Specimens of urine and of venous blood (nonfasting; 36–50 mL, depending on the province or region), the latter fractionated into multiple aliquots of plasma, serum, buffy coat and red blood cells, are stored at –80°C in mechanical freezers or in liquid nitrogen in local repositories. Some provinces or regions are collecting spots of whole blood for storage on Whatman FTA cards (Whatman International Limited, Kent, United Kingdom) at room temperature, whereas others are storing whole blood for future extraction of lymphocytes. In addition, spot urine samples and toenail clippings may be collected. Ultimately, we anticipate that specimens stored in local provincial biorepositories will be mirrored within a national biorepository.

Follow-up and outcomes

After enrolment, cohort members will be followed with both active and passive methods for at least 25 years. Active follow-up may include requests for additional questionnaire data, biologic samples or physical measurements. Passive follow-up will involve linking to provincial health care data systems (for example, registries or provincial health services databases) to determine health outcomes and to take full advantage of Canada's integrated health information systems. Because outcomes linkages will be performed at the provincial level, there could be some variation in methods, but as much as possible, the linkages will be conducted in a consistent manner. Such linkages will be subject to the usual quality control processes in place in each provincial cancer registry.

Making Canada's cohort unique

Cohort studies of cancer and other chronic diseases are under way in many countries.[8–10] Cohorts of 200 000 or more participants that are established or being planned are shown in Table 2. The question therefore arises of why Canada should invest in such a cohort. This initiative has three unique aspects.

First, the Canadian Partnership for Tomorrow Project will include a major emphasis on the effects of exogenous or environmental factors on the risk of cancer and chronic disease.

The Partnership is building a prospective platform that will integrate environmental measures and lifestyle risk factors to study their interaction with genetic and epigenetic risk factors. To this end, the Occupation and Environment Expert Advisory Group is providing expertise on the collection of environmental data and samples and is planning to use existing Canadian data resources related to environmental exposures of interest. For example, the collection of a detailed residence history for each participant offers the potential to map possible exposures using postal codes and long-established geographic information systems databases for the locations of fixed sources of carcinogens and mobile sources of potential morbidity, such as air and water pollution.

Second, through linkages to provincial health utilization data, this Canadian cohort study will allow researchers to study chronic diseases other than cancer in relation to health services usage and outcomes data generated by provincial health services programs. This process will be crucial for chronic diseases that are not recorded on disease registries and that may not be noted on death certificates. Linkage with the emerging national tumour-tissue collection program, the Canadian Tumour Repository Network, will result in further valuable data.

Finally, the Canadian Partnership for Tomorrow Project is structured such that each province or region (Table 2), in addition to collecting core information measurements and specimens, will be encouraged to make use of data sources

Table 2: Cohort studies of cancer and chronic disease, including component studies of Canadian Partnership for Tomorrow Project

Study name	Type of participants	Target or final (current) no. of participants*	Age, yr, min–max	Country or Canadian region of residence	Current status	Year recruitment started
Under way or planned (outside of Canada)†						
European Prospective Investigation into Cancer and Nutrition	Individuals	520 000	30–70	Sweden, Italy, Netherlands, United Kingdom, Germany, Norway, France, Greece, Spain, Denmark	Follow-up	1993
Multiethnic Cohort Study	Individuals	215 251	45–75	United States	Follow-up	1993
NIH-AARP Diet and Health Study	Individuals	567 169	50–69	United States	Follow-up	1995
Million Women Study	Individuals	1 300 000	50–64	United Kingdom	Follow-up	1997
Norwegian Mother and Child Cohort Study	Families	260 000	NA	Norway	Follow-up	1999
Kadoorie Study of Chronic Disease in China	Individuals	500 000	35–74	China	Follow-up	2004
45 and Up Study	Individuals	250 000	≥ 45	Australia	Follow-up	2006
Cancer Prevention Study, cycle 3	Individuals	500 000	30–65	United States	Recruitment	2007
UK Biobank	Individuals	500 000	40–69	United Kingdom	Recruitment	2007
LifeGene	Families	500 000	≤ 55	Sweden	Development	2010
National Guard Health Affairs Bio-bank		200 000	NA	Saudi Arabia	Development	No information
Canadian Partnership for Tomorrow Project						
BC Generations Project www.bcgenerationsproject.ca	Individuals	40 000 (4722)	40–69	British Columbia	Recruitment	2009
The Tomorrow Project www.cancerboard.ab.ca /tomorrow	Individuals	50 000 (3952)	40–69	Alberta	Recruitment	2009
Ontario Health Study www.ontariohealthstudy.ca	Individuals	150 000 (5887)	35–69	Ontario	Recruitment	2009
CARTaGENE www.cartagene.qc.ca	Individuals	20 000 (5794)	35–69	Quebec	Recruitment	2009
Atlantic Partnership for Tomorrow's Health www.atlanticpath.ca	Individuals	30 000 (6005)	40–69	Atlantic‡	Recruitment	2009

Note: NA = not applicable, NIH–AARP = National Institutes of Health – American Association of Retired Persons.
*Data on current enrolment (as of Mar. 20, 2010) are provided for Canadian Partnership for Tomorrow Project.
†At least 200 000 participants.
‡Nova Scotia, New Brunswick, Prince Edward Island, Newfoundland and Labrador.

unique to its catchment area and thus to extend and augment the national effort.

Key deliverables

The Canadian Partnership for Tomorrow Project is establishing a platform to help support research in cancer, as well as other chronic diseases, in Canada and internationally over the coming decades. This effort is guided by the prevention-related objectives of the Canadian Strategy to Control Cancer,[11] particularly "to reduce the expected number of new cases of cancer among Canadians" and "to lessen the likelihood of Canadians dying from cancer." The Partnership is also motivated by the fact that a common constellation of risk factors leads to the development of cardiovascular disease, diabetes mellitus and other important chronic diseases. The work described in this paper will meet the key research goals presented in Box 1.

Key challenges

To date, needs for funding have been met in three ways: by obtaining major support from the Canadian Partnership Against Cancer, an independent organization funded by the federal government to accelerate action on cancer control in Canada; by reducing costs, which has been achieved by leveraging and harmonizing existing regional cohort initiatives; and by forming strategic partnerships within some provinces to help with data collection and to obtain significant additional funding. Nonetheless, ensuring sustainable long-term funding continues to be a challenge that must be addressed at the national level. Funding for individual research projects that wish to use the data gathered will be the responsibility of the requesting research group.

When the Partnership was formed, harmonization was an important challenge because researchers using the data and biospecimens must be confident that materials collected across Canada are directly comparable. To ensure adequate harmonization, a task force was struck to define the "core" questionnaire items, physical measurements and biospecimens to be collected. The provinces and regions have now agreed upon these core items, along with standard operating procedures for acquiring data and for obtaining, processing and storing specimens.

Regulations and codes concerning confidentiality, privacy,

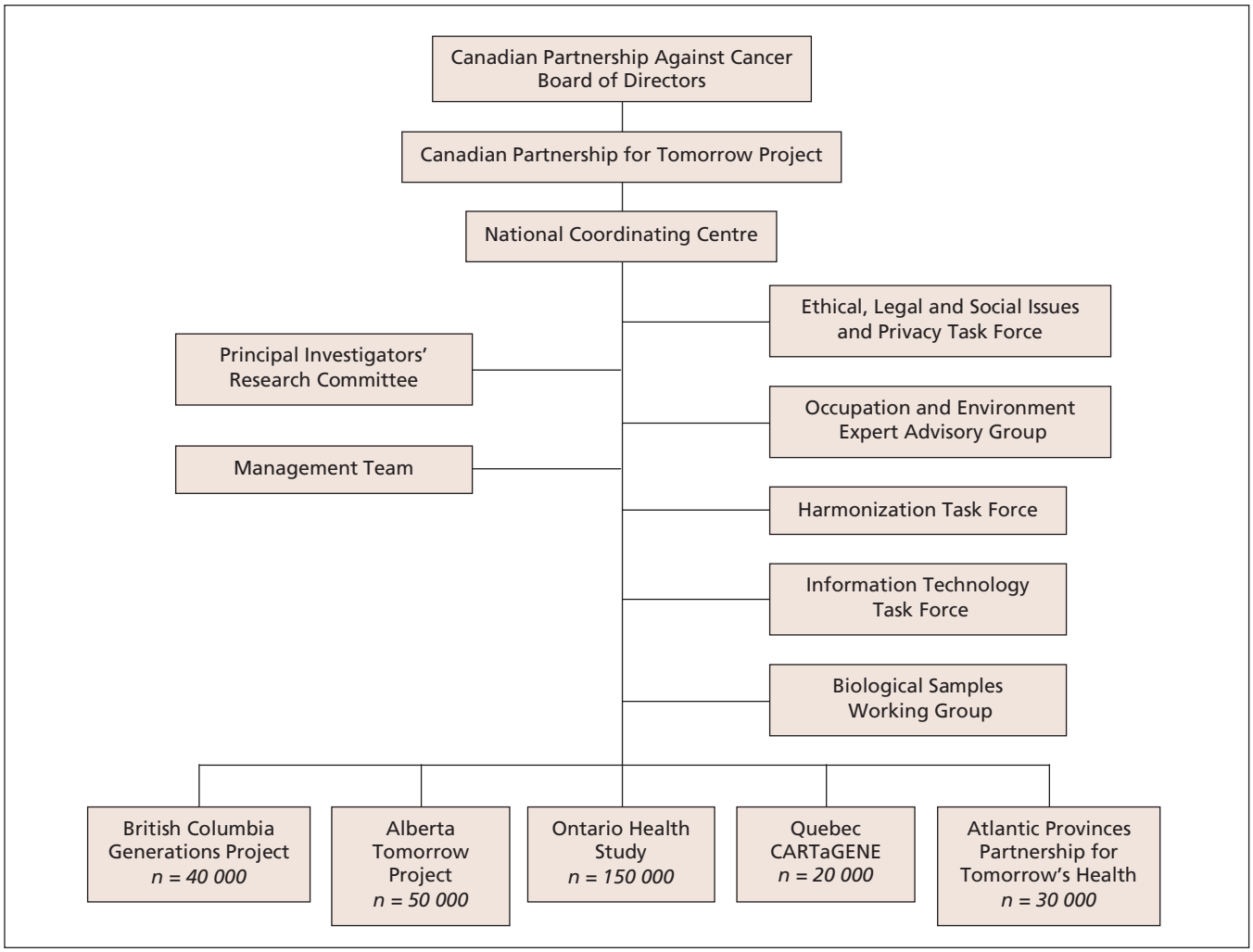

Figure 1: Overview of the Canadian Partnership for Tomorrow Project.

Box 1: Key deliverables of the Canadian Partnership for Tomorrow Project

For research:

- A "population laboratory" for leading-edge, population-based basic and translational research related to cancer and chronic diseases within Canada.
- A bank of biologic specimens and related personal exposure data that can be linked with provincial data on health care utilization.
- A resource and legacy for future generations of Canadians that will continue to yield valuable information about health and risks of disease.

For policy, prevention and care:

- A platform that enables improvement in the control of cancer and the incidence of chronic disease through identification of new risk factors that may be modified through preventive interventions.
- A platform that enables reduction in disease-related mortality through detection of new prognostic factors and markers of early disease.
- An observatory for tracking the results of "natural experiments" occurring over time related to interprovincial variations in the introduction of new technologies, new programs for preventing disease or methods of health care delivery.
- A mechanism for predicting future needs for care, through the tracking of factors that are likely to predict future incidence of disease and related mortality, and the associated costs.
- A platform for investigating the policy issues associated with population studies.
- A mechanism for monitoring uptake of screening and prevention initiatives by the Canadian population and the impact of these initiatives.

research ethics, and legal and social issues differ across the country and are for the most part in the domain of provincial governments. To ensure that legislation, regulations and practices are observed and respected, while optimizing scientific benefit from the cohorts, an Ethical, Legal and Social Issues and Privacy Task Force was struck. This task force has ensured that patient information and consent forms are uniform across the country and that procedures for collecting, storing and accessing data and specimens meet the highest standards of privacy and confidentiality. This task force is now developing policies for data access and prioritization.

Epidemiologic information and specimen annotation must be compatible across Canada if the research platform is to function efficiently. The Information Technology Task Force has designed software for the acquisition of data, physical measurements and specimens, and this software has been harmonized across provinces to ensure uniform quality of recorded data while protecting the confidentiality of participants. All "content-related" information (questionnaire responses, measurements and specimens) is de-identified at the time of acquisition, and the "administrative" information is securely maintained so that re-contact with participants and data linkage to provincial health databases are possible.

In conclusion, harmonization of data and practices forms the keystone of this unique Canadian cohort. Cooperation among regions has allowed consistency across core variables, as well as variation across scientific interests. Data from the cohort will enable a wide range of research and will be accessible to and used by investigators from diverse disciplines.

This article has been peer reviewed.

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