

DECEMBER 2005

EXECUTIVE SUMMARY
THE CANADIAN LONGITUDINAL STUDY ON AGING

1.0 Introduction

Canada, like most other industrialized nations, is facing a shift in the age distribution of its population, and this trend is predicted to continue. Nationally, the proportion of the population aged 65 years and over has grown from less than 8% in 1951 to more than 12% in 2000. The aging process entails multifaceted changes during an individual's lifetime (from the cellular level, to individual psychological and behavioural factors, through to the broad social contexts), but a clear picture of the combined effects of these changes has not emerged. To advance our understanding of the pathways leading to adverse events or favourable outcomes and to meet the needs of today and tomorrow's seniors, there is an urgent need to invest in ongoing research. The dynamic process of aging can only be appropriately examined through longitudinal studies that capture the changing individual within a changing social context and incorporate multiple levels of inquiry: the cell, the individual and society. It is upon this background that the planning for the Canadian Longitudinal Study on Aging (CLSA) was initiated.

In the fall of 2001, the Canadian Institutes of Health Research (CIHR) Institute of Aging hosted an invitational research symposium, *From Cell to Society*. At this meeting, more than 80 researchers from 50 institutions from the basic sciences, social sciences and clinical disciplines agreed on the need for an innovative longitudinal study to support a research program in successful aging in Canada. A Request For Applications (RFA) to develop the protocol for this study, known as the Canadian Longitudinal Study on Aging (CLSA), was officially launched at that meeting.

The objectives of the RFA were to develop a protocol for a longitudinal study to address the following general objectives:

- To determine how the inter relationship among the following factors contribute to the process of aging over time:
 - Genetic and biochemical factors;
 - Health behaviours (including exercise and nutrition);
 - Physical, psychological and cognitive abilities;
 - Social, economic and cultural factors;
 - Health and community services; and,
 - Disease and disability processes;
- To identify factors that will inform intervention strategies to promote successful aging;
- To inform evidence-based practice, healthcare delivery and public policy.

A principal investigator triumvirate from three major Canadian institutions responded to the RFA and led a team of more than 200 investigators from across Canada in the development of a proposal to conduct the protocol development phase: Drs. Susan Kirkland (Dalhousie University), Parminder Raina (McMaster University) and Christina Wolfson (McGill University). This proposal was accepted and the team worked for two years on the development of the protocol for the CLSA. The main features of the protocol are summarized in the following pages.

1.1 Aims of the CLSA

The overall aim of the CLSA is to examine aging as a dynamic process. Through the CLSA we will investigate the interrelationships among intrinsic and extrinsic factors influencing health from mid-life to older age. This will allow us to capture transitions, trajectories and profiles of aging, elucidate the concept of successful aging, and identify modifiable factors that could be used to develop interventions to improve the health of older populations. Once in place, the CLSA will also provide infrastructure and enhance capacity for sustained high quality longitudinal research on aging in Canada.

1.2 Contribution of the CLSA to the study of aging

In recent years, our ability to study the complexity of aging has been enhanced through biological and technological advances, such as the sequencing of the human genome. In this era of longitudinal research, we are thus able to move beyond a simple *description* of change over time to actually studying the dynamic *determinants* of change within and between individuals over time.

Although there is a growing body of research on the *aged*, there is a need for studies that examine the *aging process* incorporating the adult development and life-course perspectives. In the adult development and life-course literature, the concept of life pathways plays a central role. The outcomes include successful aging and transitions into and out of critical and sensitive periods (e.g., changes in family structure and changes in work and retirement). As individuals move along life pathways, they may modify their roles, personal ties and social relationships to meet the demands of their changing physical, psychological, social and biological environments, and employ novel strategies and/or technologies to respond to these changes. Thus, the life-course and adult development perspectives facilitate the identification of adaptive mechanisms that aging adults create and use.

The CLSA is a longitudinal study that will not only examine the complexity of the aging process by examining interrelationships among biological and psychosocial environmental factors but will also incorporate the perspective of life pathways. The CLSA is unique in that it will emphasize successful aging in contrast to most previous studies that have focused exclusively on disease and disability processes.

Our operational definition of successful aging includes not only physical, psychological and social functioning but also the concepts of adaptation, context and the perception of the individual themselves. The full spectrum of aging trajectories is of interest, acknowledging that not all outcomes are negative and that many individuals feel that they can and do age well even when faced with decline and adverse circumstances. What remains unclear, however, is the balance between the elements of function and well-being in relation to successful aging. The CLSA will provide the opportunity to examine this over time and will provide needed data to clarify our understanding of what it means to age successfully. Ultimately, we hope to identify the factors that have the greatest impact on successful aging and to better understand how they exert their effects.

2.0 Overarching research questions

Based on a conceptual framework the following overarching research questions guide the overall structure of the CLSA and reflect the major concepts that the CLSA will address over the life of the study.

1. What changes occur in physical, psychological and social function and perceived well-being over time and across ages?
2. What are the determinants of changes in physical, psychological and social function and perceived well-being over time and across ages?
3. What are the adaptive responses to changes in physical, psychological and social function and perceived well-being over time and across ages?
4. How do changes in physical, psychological and social function, perceived well-being and adaptations determine successful aging?

3.0 Study content

The areas of focus for the CLSA are broadly classified according to whether they relate to physical functioning, psychological functioning, or social functioning. Topic areas that do not fall under functioning and those that cover more than one theme, such as genetics and biomarkers, quality of life, lifestyle behaviours and health services, are grouped under the category of “inter-theme” content. Together, these constructs form the content of the CLSA.

3.1 Physical functioning

Physical functioning reflects the cumulative experience of age-associated physiological decline, as well as the experience of living with acute disease, chronic conditions and disability over time, and the many factors that contribute to their development. The CLSA presents an opportunity to understand physical functioning in a broader context than the study of individual diseases provides. Thus, key (and interrelated) elements to be considered within the scope of physical functioning include limitations in activities of daily living, participation, disability, injuries, co-morbidity and frailty. Over the course of the CLSA, we will also examine the occurrence of, and mortality from, major diseases. Even in a study of this magnitude, however, it will be difficult to accumulate large numbers of individuals with any one disease. Nevertheless, as long as the appropriate precursors are captured during the course of the study, many disease outcomes can be examined. For example, given the existence of cancer registries in every Canadian province, linkage with these data will allow us to study the development of cancers prospectively. The CLSA offers an opportunity to better understand the risk factors as well as the natural history of numerous diseases that lead to the loss of physical functioning and autonomy in aging individuals.

3.2 Psychological functioning

Psychological functioning is required to maintain autonomy, engage in society and perform everyday activities. Large-scale longitudinal studies in psychology have been conducted within the area of adult development and aging, however, most have focused on specific psychological processes, such as memory and intelligence, or have taken place within the context of specific diseases or disorders, such as dementia or heart health. The CLSA will expand this research by

examining a number of psychological constructs as antecedents or mediators of specific as well as global aspects of health and health-related outcomes. The study of self, personality and social cognition across the lifespan will capture not only individual differences in biological patterns of perception, information processing, emotions and motivation, but will also capture bodies of knowledge (e.g., wisdom, beliefs, and attitudes) and regulatory functions and behaviours (e.g., skills, adaptive and maladaptive behaviours and coping) regarding the world and the self. Psychological constructs will be examined in key areas in the CLSA: cognitive functioning, values and meaning, everyday competence, adaptive functioning and coping, personality, emotion and psychopathology, and psychological distress.

3.3 Social functioning

Social functioning emphasizes issues of sustained engagement with life, the essential characteristic being the interaction between the individual and the social environment. Exchanges between individuals, the community, and society all contribute to social functioning. Such exchanges are facilitated through family and social ties, employment and retirement, and are influenced by access to structural supports such as housing, transportation, community resources and health services. The contribution of the CLSA will result from the collection of data on both continuity and change in social functioning over time, and the ability to track the reciprocal and interactive effects of social networks, social support, paid and unpaid work, and the environment as well as their interrelationships with physical and psychological functioning. Social constructs will be examined in four key topic areas in the CLSA: social networks and social support, work to retirement, structural inequalities, and matters of place and mobility.

3.4 Inter-theme content

Inter-theme topics include lifestyle factors (smoking, alcohol consumption, nutrition, and physical activity); health services utilization (institutional care, continuity of care, home care, medication use, assistive devices/technologies), genetics and biological markers, quality of life, spirituality, and pain.

In addition to the individual physical, psychological, and social factors, morphological, cellular, biochemical and molecular factors also play an important role in aging. Genetic factors that regulate longevity are thought to be those that control survival processes such as DNA repair and antioxidant defence, mechanisms that are implicated in disease processes. The role of apoptosis, or cell death, as a mechanism to eliminate damaged cells, cellular senescence in suppressing cell division, and the mechanisms of telomere loss provide complex and interweaving links with both cancer and aging. Combined with population-based research on the genetics of human longevity, the interplay of biology with other domains of aging constitutes a major strength of the CLSA.

3.5 Contextual data

An important contribution of the CLSA will be the ability to combine individual-level factors with contextual and environmental indicators. Indicators for social cohesion will include such measures as voter turnout, recycling rates, volunteer organizations per capita, newspaper readership, charitable donations and feelings of safety. Indicators of neighbourhood quality will include general economic base and status, neighbourhood type, amenities for older people, rental costs, vacancy rates, shopping facilities, crime rates and vandalism. Indicators of environmental quality will include green space per capita, air and water quality and climate.

4.0 Study design and methodology

The CLSA will be a population-based 20-year prospective cohort study. The study will recruit 50,000 men and women aged 40 years and over at baseline. Of the 50,000 participants 30,000 will be selected to undergo in-depth assessment requiring visits to CLSA data collection sites. All 50,000 participants will also provide information through interviews (telephone administered and/or in person).

The inclusion of study subjects as young as 40 years of age is motivated by the desire to capture mid-life experiences prospectively, since important changes known to influence outcomes later in life are likely to occur during this period. The lower age limit will also permit inclusion of individuals who are part of the baby boomer cohort (i.e., those born between 1946 and 1964) who will be 44 to 62 years of age in 2008, the year of the proposed launch of the CLSA. The youngest birth cohort overlaps the baby boomer cohort; the middle age group represents those entering into the senior years who are making the transition into retirement or who are already retired; and the oldest age group comprises those who have already reached old age. One of the interests in studying this latter group prospectively is in the follow-up of the oldest old into the final years of life.

Study subjects selected to undergo in-depth assessment will be asked to provide information through questionnaires, clinical examinations and biological testing. Owing to the technical demands for this type of data collection (e.g., in-person examination, biological sample storage and shipping facilities) these participants will be recruited from areas surrounding six major academic centres in six regions of Canada.

While all 50,000 CLSA participants will provide data through interviews, those undergoing in-depth assessment will undergo these interviews through a combination of telephone assisted interviews and in person interviews as part of the assessment at the CLSA data collection sites. The 20,000 who will not be asked to undergo in-depth assessment will participate in the CLSA primarily through computer-assisted telephone interviews (CATI). The sampling strategy for these participants will be broadly based geographically as there is no need to ensure accessibility to a data collection site for in person assessment. There will be a common component of questions asked of all 50,000 participants at each wave of data collection.

The original proposal for sampling was to use the 2008 cycle of the Canadian Community Health Survey as the recruitment vehicle for CLSA participants. The CCHS uses the Labour Force Survey area frame (LFS) as its sampling frame. However, the results of a feasibility study conducted over the past year as part of the pilot work for the CCHS revealed that this strategy would not be optimal and thus other options for the sampling frame are being examined as part of the CLSA developmental work.

4.1 Inclusion and exclusion criteria

While the goal of the CLSA is to examine successful aging in the Canadian population as a whole, there will be exclusion criteria at baseline based on practical aspects of study design, resources and availability of a sampling frame.

Individuals living in long-term care institutions at baseline will be excluded, as will those with moderate to severe cognitive impairment. Participants in the CLSA, who become

institutionalized during the course of the study, however, would continue to be followed either through personal interview or interviews with proxies. CLSA participants who develop cognitive impairment of the course of the study will also continue to be followed and a developmental study is currently underway to examine the possible role of research advance directives and the use of substitute decision makers for such individuals in the CLSA.

4.2 Special populations

The possibility of over sampling special populations, including aboriginal and ethnic populations, was explored but was determined not to be a viable strategy to pursue at the outset of the CLSA. Information on individuals from these groups will, however, be captured to the extent that they are selected through the proposed sampling strategy. Opportunities to include embedded or add-on studies of First Nations peoples and some of the larger ethnic groups as well as new immigrants to Canada will continue to be explored during the development phase.

4.3 Sampling strategy

The CLSA investigators have worked closely with statisticians at Statistics Canada to examine various strategies to use for sampling individuals to participate in the CLSA. As stated above, the use of the CCHS as a recruitment vehicle has been determined not to be optimal and other avenues (in particular the use of administrative databases) are currently under study.

One of the major objectives of the CLSA, and clearly one its innovative features is the long-term follow-up of a large cohort on which comprehensive information on biological, social, physical and psychological factors is regularly collected. The collection of in-depth data will require the availability of a sophisticated infrastructure across the country that will ensure the collection of all types of information in a standardized fashion. Given Canadian geography and the distribution of the population across the country, the only logistically and economically feasible approach is to undertake such a study in a small number of geographically contained sites.

4.4 Follow up assessments

Data will be collected every three years for the youngest age groups (40-79) and every year for the oldest group (80 or over). The follow-up schedule will be age-group specific such that when cohort members age into the oldest group, they will undergo follow-ups yearly. Each individual will be followed for 20 years or until death. Participants will be considered as censored if they are lost to follow-up, refuse continued participation or are still alive at the end of the study period. In addition to the primary follow-up, each cohort member will be contacted between major follow-up assessments for an interim follow-up. Between the major follow-ups those aged 40-79 years will be contacted once a year, and those aged 80 years and over will be contacted every 6 months.

4.5 Data linkage

For all 50,000 CLSA participants, primary data collected will also, with permission of study subjects, be linked to existing health care administrative databases, mortality files, cancer registries, the diabetes surveillance system and environmental databases that include information related to pollution, climate and other environmental variables. Developmental studies are underway to clarify the approach needed to be able to conduct these linkages and ensure confidentiality. Using data linkage, a number of disease outcomes (e.g., cancer, diabetes, etc) can be examined using the full CLSA cohort of 50,000.

5.0 Study coordination and management

5.1 CLSA Coordinating Centres

Three coordinating centres will be based at the three CLSA host institutions (i.e., Dalhousie University, McMaster University and McGill University). While all three centres will carry out many common tasks, they will also carry unique but complimentary functions. The goal in setting up the coordinating centres in this fashion is to simplify procedures for the data collection sites and to maintain data security at the highest possible level.

The McGill University coordinating centre will take primary responsibility for coordination of subject recruitment activities, working closely with the data collection sites. In addition the McGill University site will house the Statistical Analysis Centre. The McMaster University coordinating centre will coordinate all activities related to primary data collection of the clinical and biological data again working closely with the data collection sites. McMaster University will also house the Biological Processing Centre that will oversee the collection, processing and storage of biological specimens.

The coordinating centre based at Dalhousie University will take responsibility for data collection and retrieval conducted by CATI. This will include primary data collection for the 20,000 not undergoing in-depth assessment as well as the interim telephone contacts with all 50,000 study subjects.

An application to the Canada Foundation for Innovation is in preparation for the 15 February 2006 deadline. This application is a request for funding for the infrastructure for the 3 host institutions to put in place the capabilities to mount the CLSA. McMaster University is taking the lead on this application with McGill University and Dalhousie University as the two other CLSA coordinating centers. A further 6 centres across Canada are partners in this application.

5.2 Data collection sites

Data collection sites will be located in six urban centres within six regions of Canada. The sites will have a site director, who will be a CLSA co-investigator. Investigators in each of the six data collection sites will be responsible for implementing data collection and will oversee the performance of interviewers and clinical staff at their site. The McGill coordinating centre will take responsibility for the development of training procedures related to recruitment of the study subjects and completion of informed consent. The McMaster coordinating centre will coordinate the development of training procedures for the interviewers as well as the technical staff involved in primary data collection. However, the site investigators will be responsible for assessing the accuracy of data collected, monitoring interviewer performance, entering the site-specific data into standardized data software and transmitting data to the McMaster coordinating Centre. Ethical review will be required at each site. All study sites will adhere to procedures put in place and monitored by the coordinating centres.

5.3 Data collection

As described, questionnaire data will be collected using CATI as well as through in person interviews. Using CATI, the interviewers will read questionnaire items, and respondents' answers will be entered directly into a computer. The interviews will be conducted from a CATI laboratory based at Dalhousie University. The process for in person interviews to be conducted with the sub sample of 30,000 undergoing in-depth assessment, although still under

development, will generally proceed as follows: Interviewers will schedule an in-home face-to-face interview to explain the study in detail, obtain consent and schedule an appointment at the data collection site. The interviewer will leave a short self-administered questionnaire to be completed and returned to study staff at the time of the clinical assessment at the data collection site. At the time of the clinic visit to the data collection site, members of the will also undergo a face-to-face interview. The details of the content of these interviews (both CATI and in person) are the subject of the Phase II development activities (2006).

The basic clinical examination will be designed to collect data on anthropometric parameters (e.g., height, weight, skin fold thickness, and mid upper-arm circumference) and clinical parameters (e.g., blood pressure, grip strength, balance, respiratory function, hearing and visual acuity). In addition, a series of physical performance tests and neuropsychological tests will be administered in accordance with standardized protocols. Blood will be drawn and urine collected for biochemical measurements following a 12-hour overnight fast at the beginning of the clinical assessment. The clinical examination will take approximately 2 hours; the entire clinic visit will take approximately 3 hours.

To ensure that sufficient quantities of material are collected for proposed testing and to provide versatility for unforeseen research needs, a range of specimen types will be collected (e.g., serum, plasma, blood cells, urine and skin cells). The amount of blood collected will be 60mL per participant per cycle. State-of-the-art storage systems will be used for safe, secure and stable retrieval of specimens. The establishment of blood and tissue cells will allow CLSA to conduct genotyping, small nucleotide polymorphism (SNP), proteomic, gene expression, and telomere studies for the measurement of cellular aging.

5.4 Developmental pre-testing and pilot studies

The three-year period in which CLSA developmental work and pilot studies will be undertaken began in early 2004. During Phase I of the developmental activities, the CLSA principal investigators planned and are currently conducting several studies to address various process issues proposed for the CLSA. In a parallel activity, the protocol is undergoing further refinements and specification of content. In Phase II, studies targeted to the content of the study will be conducted. For example, further development and refinement of study materials, including translation and back translation of measures and reliability and validity studies, as needed, will also be carried out. Harmonization of scales, instruments and measures with other longitudinal studies on aging will be accomplished where possible. Strategies will be put in place to identify and select the data collection sites. During the last phase (Phase III) of the developmental activities, a full-scale pilot study of the entire protocol will be conducted likely in 2007.

Each of the 3 host institutions has taken major responsibility for the coordination of several developmental studies. Ethics approval for all developmental studies has been obtained (or is being obtained) from all 3 host institutions following a procedure set up with the Chairs of the Ethics committees in the three institutions.

6.0 Dissemination

Strategies for the dissemination of research results will be designed to meet the needs various audiences (e.g., the general public, health service providers, managers, researchers and policy makers). An advisory board will be formed including stakeholders from health care

organizations, members from different level of governments, from non-governmental organizations and participants in national seniors groups. Dissemination will also occur through presentation of findings in peer-reviewed scientific journals and national and international conferences. Lay summaries of research findings will be circulated directly to clinicians; federal, provincial and municipal departments; health charities; CIHR Institutes and seniors' organizations. In addition, all research findings, working papers, reports, published journal articles and lay summaries will be made available on the CLSA web site. The CLSA will produce regular newsletters describing the progress and highlighting the new and important findings from the study. These newsletters will be mailed to the study participants annually.

The co-principal investigators have developed a general information website (www.clsa-elcv.ca) and have printed brochures (in French and in English) that are being distributed widely to inform the public as well as the scientific and medical community about the overall goals of the CLSA.

7.0 Building capacity

The CLSA will enhance research capacity by attracting Canadian graduate students and new investigators to the field of aging research and by garnering resources and creating opportunities to recruit and retain new and established researchers in Canada. A high-priority activity of the CLSA, in collaboration with the CIHR and other funding agencies, will be the development of scholarship programs for graduate students and postdoctoral and clinical fellows in a variety of areas such as genetics, biology, psychology, behavioural and social sciences, nutrition, bioinformatics, epidemiology, health services, clinical sciences and biostatistics. These graduate students and new investigators will be identified as CLSA scholars and will be located across the country. One of the major objectives of the CLSA is to serve as an infrastructure and platform for novel future research in many areas of science.

8.0 Governance and organizational structure

The CLSA will require a sustained plan for governance throughout the conduct of the study. The CIHR mandated Steering Committee began work on the development of a governance structure for the CLSA and this work continues. The scientific governance of the study is under development by the CLSA research team.

9.0 Ethical considerations

CIHR established a committee to address the Ethical Legal and Social Issues (ELSI) related to CLSA. This committee is composed of lawyers, ethicists, geneticists, biologists, epidemiologists, philosophers, sociologists and a privacy commissioner. The ELSI committee has a full time legal scholar to coordinate the ELSI agenda for this project. ELSI challenges associated with the CLSA will be evaluated on a continuing basis by the CLSA researchers together with the ELSI Advisory Committee. The conduct of CLSA will conform to the ethical and legal guidelines that will be developed by this committee. Ethical aspects of CLSA are the subject of ongoing collaboration and consultation with ELSI.