Advancing the Science of Population Health and Aging through Interdisciplinary Research: The Canadian Longitudinal Study on Aging

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Regroupement des organisations de santé publique de la Capitale-Nationale, April 27th, 2015
Population aging

- Due to declining fertility and increasing longevity (demographic transition)
- Unprecedented, accelerating, shifts will be permanent
- Profound implications for human life, including health
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1991 TOTALS: 13938100, 28117600, 14179500
Rectangularization of the survival curve

Compression of morbidity

- Morbidity compressed into a short period prior to death
- Represented an important shift in thinking
- Departure from the medical model of aging, which assumed that death always occurred as a result of a disease process, and that older age was a period of inevitable decline

Figure: Mortality According to Age in the Absence of Premature Death
Compression of morbidity

Fries’ paradigm based on the premise that:

- The length of human life is fixed
- AND
- Chronic disease can be postponed

- Predicted that the increase in life expectancy would plateau in the coming decades, particularly life expectancy from age 65 which excludes early life mortality
Evidence suggests otherwise

- Is average life expectancy approaching an upper limit to life expectancy?
  - the evidence that the average life span is 85 years is unconvincing
  - there is no evidence for further rectangularization of survival curves

- Will age at first infirmity increase?
  - there is no evidence for over-all declines in incidence of morbidity: on the contrary
  - evidence for actual “(de)compression” of morbidity is ambiguous
Historical increases of life expectancy
Oeppen and Vaupel, Science 2002; C Finch adaptation

Phase 1
early urban

Phase 2
sanitation-nutrition

Phase 3?
regeneration
modern medicine
Social Policy Innovation

Life expectancy in years

1550 1600 1650 1700 1750 1800 1850 1900 1950 2000 2050
Upward trend in life expectancy continue, cease, or reverse?

+ Effective interventions against age-related diseases
+ Improved environment for ageing
+ Life-cycle deceleration (delayed reproduction)

- Adverse effects of excess nutrition
- Adverse effects of alcohol and drug abuse
- Adverse effects of increasingly sedentary lifestyles
- Life-cycle acceleration (early maturation)
Why aging occurs

Intrinsic

Extrinsic

How aging is caused
# Genes Associated With Avoiding Late-Life Disease in Humans

<table>
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<tr>
<th>GENE</th>
<th>BIOCHEMICAL FUNCTION</th>
<th>COMMENTS</th>
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<td>APOE</td>
<td>Lipoprotein metabolism</td>
<td>E2 variant is frequent in centenarians while E4 variant as a risk factor for Alzheimer’s disease is rare in centenarians.</td>
<td>Schachter et al. 1994</td>
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<tr>
<td>ACE</td>
<td>Angiotensin-converting enzyme</td>
<td>Plays a role in regulating blood pressure.</td>
<td>Schachter et al. 1994</td>
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<tr>
<td>PAI1</td>
<td>Plasminogen activator inhibitor 1</td>
<td>Plays a role in blood clotting, thus affecting risk of stroke and heart attack.</td>
<td>Mannucci et al. 1997</td>
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<tr>
<td>HLA-DR</td>
<td>Histocompatibility locus antigen</td>
<td>DR variant is frequent in centenarians; resists infection and inflammation?</td>
<td>Ivanova et al. 1998</td>
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<td>WRN</td>
<td>Possesses both DNA helicase and exonuclease activity</td>
<td>Gene responsible for Werner’s Syndrome; mutation leads to a variety of aging-related pathologies, e.g., cataracts, cancer, osteoporosis, slow wound healing, etc.</td>
<td>Yu et al. 1996, Huang et al. 1998, Martin and Oshima 2000</td>
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<td>B3AR</td>
<td>B-3 adrenergic receptor</td>
<td>Allelic form present affects time of onset of Type 2 diabetes.</td>
<td>Walston et al. 1995</td>
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<tr>
<td>MTHFR</td>
<td>5-, 10-methylenetetrahydrofolate reductase</td>
<td>Deficiency leads to increased levels of homocysteine and DNA hypomethylation; increases risk of cardiovascular disease and cancer.</td>
<td>Heijmans et al. 2000</td>
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<tr>
<td>KLOTHO</td>
<td>Membrane protein with β-glucosidase activity?</td>
<td>Homozygous variant form is underrepresented in elderly individuals.</td>
<td>Arking et al. 2002</td>
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Genetic Heritability of Human Lifespan
Cournil & Kirkwood *Trends in Genetics* 2001

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</table>

Genes account for 25% of what determines disease and longevity
EPIGENETICS

ON/OFF SWITCH (GENE)

GUMMED UP ON/OFF SWITCH (GENE)

CANNOT CAN

30 nm fiber 10 nm fiber

CANNOT CAN

DNA AND CHROMOSOME LEVELS
Non-Biological/Medical Determinants of Aging?

- Nutrition
- Lifestyle
- Environment
  - Physical
  - Social
  - Economic
  - Work Place
  - Psychological
- Chance
Intrinsic and Extrinsic Factors

Environmental influences
(e.g., rural, socio-economic, exercise, nutrition)

Chronic diseases
(e.g., diabetes, cancer, dementia, arthritis, cardio)

Genetics
(e.g., telomeres/oxidative stress, psychological & cognitive abilities, immune functions)

Aging

Time (Longitudinal Study)

Health Services Utilization

Infections
50,000 Participants from across Canada

Aged 45-85 at baseline

20 year study with major data collection every 3 years

More than 160 researchers in 26 institutions

biology, genetics, medicine, psychology, sociology, demography, economics, epidemiology, nursing, nutrition, health services, biostatistics, population health
The CLSA Vision

A research platform – infrastructure to enable state-of-the-art, interdisciplinary population-based research and evidenced-based decision-making that will lead to better health and quality of life for Canadians.
Innovation - Cell to Society

- Mid life to old age
- Quantitative traits
  - Physical
  - Social
  - Psychological
- Gene-environment interactions
- Disease, disability, psychosocial consequences
- Adaptation
Design Overview

50,000 women and men aged 45 - 85 at baseline

- n=20,000* Randomly selected within provinces
- n=30,000 Randomly selected within 25-50 km of 11 sites

Questionnaire
- By telephone (CATI)
- In person, in home (CAPI)

Clinical/physical tests
- Blood, urine
  - At Data Collection Site

Full follow up every 3 years
Maintaining Contact in between waves

Data Linkage
1. Partnered with Statistics Canada
   – CCHS 4.2 Healthy Aging Survey
     • 2006 Census as an area frame to select households
   – Agreed to share contact information

2. Partnered with provincial Ministries of Health (MOH)
   – Health Card Registration databases
   – Mailouts, return Consent-to-Contact form

3. Random Digit Dialing
   – Pre-recruitment
Exclusion Criteria At Baseline

CCHS exclusion criteria

- Residents of the 3 territories
  - i.e. Northwest Territories, Nunavut, Yukon
- Living in an institution
- Living on First Nations Reserves
- Full time members of the armed forces
- Temporary visa holders
- Cognitive impairment
- Unable to communicate in French or English
Standardized Paperless Process

Pre-recruitment

Participants Consent to Participate in CLSA

Participants Provide Questionnaire Data (n=50,000)

Biological Data Processing
- Blood
- Urine

DATA COLLECTION SITE VISIT
Physical/Neuropsychological Data

n=20,000 Telephone Interview

n=30,000 Home Interview

Stored at Biorepository and Bioanalysis Centre

Data Stored at Statistical Analysis Centre and disseminated to researchers

Questionnaire data processing

Canadian Longitudinal Study on Aging
Étude longitudinale canadienne sur le vieillissement
Content: Tracking Modules

60 minute Computer Assisted Telephone Interviews

- Sociodemographics
- Veteran identifier
  - PTSD screen
- Lifestyle
- Health
  - General, women’s, vision, hearing, chronic conditions
- Functional Status
- Cognition
  - Rey Auditory Verbal LT
  - Mental Alternation Test
  - Animal Naming
- Depression
- Satisfaction with life
- Social networks/support/participation
- Care-giving/receiving
- Injuries
- Labour Force
- Income
Content: Comprehensive
InHome Computer Assisted Personal Interviews

- The Tracking CATI
- Short diet questionnaire
- Sleep
- Medications
- More extensive disease symptoms questionnaire
CLSA Data Collection
At the Data Collection Site

Physical Data Collected
- Bone Density, Body Composition
- Aortic Calcification
- ECG
- Carotid Intimal-Medial Thickness
- Pulmonary Function
- Vision and Hearing

Biological Data Collected
- Blood
- Urine

Psychological Data Collected
- Neuropsychological Battery
- Performance Testing
- Anthropometric Measures

For more Information visit www.clsa-elcv.ca
Biological Samples

BIOCHEMICAL & HEMATOLOGICAL ANALYSIS (50 ml Blood; Urine)

General Hematology
- Basophils
- Eosinophils
- Neutrophils
- Lymphocytes
- Monocytes
- White blood count
- Red blood cells
- Hemoglobin
- Platelets

Lipid Profile
- HDL-cholesterol
- LDL-cholesterol
- Tryglycerides
- Glucose
- Fasting blood sugar

Genetic and Epigenetic Markers
Content: Maintaining Contact

30 minutes CATI

- Falls
- Pain
- Oral Health
- Health Care Utilization
- Dietary Supplement Use
- Nutritional Risk
- Physical Activity
- Social Inequality
- Online social networking
- Transportation, migration, mobility
- Built Environment
- Wealth

- Parkinsonism (T)
- Medication (T)
- Psychological Distress (C)
- Personality Traits (C)
Status

As of April 24th, 2015
Recruitment & Data Collection Update

Telephone Interviews

- Recruitment of 20,000* participants, 60 minute telephone interviews every 3 years:
  - From….Provincial Health Care Registries
  - From….Statistics Canada CCHS on Healthy Aging
  - From….Random Digit Dialing

- Recruitment and baseline data collection are complete!

- Data available for release to researchers‡
  - Maintaining contact interviews initiated 2013 (14,674 completed, ~4% lost)

- First full follow-up begins summer 2015

*21,241 result of over sampling low SES
‡ cognition data and some open text in second release
Recruitment & Data Collection Update
Home Interviews and Data Collection Site Visits

- Recruitment of 30,000 for Home Interviews and Data Collection Site Visits:
  - From…Provincial Health Care Registries
  - From…Random Digit Dialing

- Baseline data collection 2012 to 2015:
  - In Home Interviews: 29,063
  - DCS visits: 27,969
  - Data release target: Spring 2016
  - Maintaining Contact 10,792 to date (~4% lost)

- First full follow-up begins summer 2015
“Results”
Tracking Only

N=21,241

Acknowledgements to SAC team, Christina Wolfson, Jennifer Uniat, Susan Kirkland, Andrew Wister, Verena Menec; CAG presentations, 2014
## CLSA Tracking Telephone Interviews

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<td>432</td>
<td>2.0</td>
<td>1.9</td>
</tr>
<tr>
<td>Just about right</td>
<td>9492</td>
<td>45.0</td>
<td>46.0</td>
</tr>
<tr>
<td><strong>Satisfaction with Life</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dissatisfied</td>
<td>2068</td>
<td>9.8</td>
<td>9.8</td>
</tr>
<tr>
<td>Neutral</td>
<td>850</td>
<td>4.0</td>
<td>4.5</td>
</tr>
<tr>
<td>Satisfied</td>
<td>18264</td>
<td>86.2</td>
<td>85.6</td>
</tr>
</tbody>
</table>
CLSA Tracking Data

Work, Aging, Retirement and Health in the Canadian Longitudinal Study on Aging
Canadian Workforce

Percent of workers 55 years and older is on the rise

“Most older workers who leave career jobs return to work within a decade: Statistics Canada”
## CLSA Retirement Data

### Tracking - Weighted

<table>
<thead>
<tr>
<th>Retirement Status</th>
<th>45-64</th>
<th>65-85</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Completely Retired</td>
<td>17.0%</td>
<td>22.9%</td>
</tr>
<tr>
<td>Partly Retired</td>
<td>8.8%</td>
<td>8.2%</td>
</tr>
<tr>
<td>Not Retired</td>
<td>74.2%</td>
<td>68.8%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>45-64</th>
<th>65-85</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Retired and Returned to Work</td>
<td>7.8%</td>
<td>7.2%</td>
</tr>
</tbody>
</table>
Of those Retired:

• Retirement voluntary  \( n = 9,683 \ (78\%) \)

• Health/Disability/Stress  \( n = 2,935 \ (24\%) \) contributed to decision to retire
# CLSA Retirement Data

## Tracking – Weighted

<table>
<thead>
<tr>
<th>Of Those Not Retired</th>
<th>45-64</th>
<th>65-85</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Currently Working</td>
<td>92.2%</td>
<td>89.4%</td>
</tr>
<tr>
<td>More than 1 job</td>
<td>15.0%</td>
<td>15.5%</td>
</tr>
</tbody>
</table>
Extensive Work and Retirement Modules

- Age at retirement
- Spouse’s retirement status
- Reasons for retirement
- Preparation for retirement
- Return to work after retirement
- Reasons for return
- Full-time/Part-time, type of work
Retirement Planning Module

• Age plan to retire
• Preparation for retirement
• Contribution to pension
• Adequacy of income/investments to maintain standard of living
• Reasons for planned retirement
Richness of CLSA Telephone-Interview Data

- Socio-Demographic Characteristics
- Psychological Characteristics and Cognition
- Work and Retirement
- Injuries (including workplace injuries)
- Social Environment
- Physical Health and Physical Functioning
Access

Alphanumeric data from 21,241 CLSA participants who completed 60 minute CATIs
Data and Biospecimen Access

• Data and biospecimens will be available to the research community

• Fundamental tenets:
  • The *rights*, *privacy* and *consent* of participants must be protected and respected at all times
  • The *confidentiality* and *security* of data and biospecimens must be safeguarded at all times
  • CLSA data and biospecimens are unique resources that must be used optimally to support research to benefit all Canadians.
Data Access Steps

Tracking Data Only

Application process via CLSA DataPreview portal
1. Administrative Review
2. Data and Sample Access Committee Review
3. Recommendation to Scientific Management Team
4. Notification of applicant
   • Steps 1 to 4 take 3-4 weeks
5. CLSA Access Agreement preparation and signatures
   • Institutional review/signature timing is unpredictable
6. Raw data provided to approved investigator
   • Step 6 takes 5 working days following completion of step 5

acces@clsa-elcv.ca
Data Access Continued

• Costing

• Cost Recovery
  a. $1,000 for a straightforward dataset
  b. No cost for data for graduate student theses

• DSAC Meetings 2015
  • February, April, June, September, December

• Application deadlines
  • March 23rd, May 15th, August 14th, November 16th
DataPreview Portal
https://datapreview.clsa-elcv.ca/

Welcome to the DataPreview Portal for the Canadian Longitudinal Study on Aging (CLSA)! The CLSA data and biological samples are available to approved Canadian and international public sector researchers, with no preferential or exclusive access for any individual. As you navigate the site you will find information about the application process and requirements for data and sample access. If you are new to using the portal we recommend you begin by reading the Frequently Asked Questions.
Datasets

A Canadian Longitudinal Study on Aging (CLSA) dataset holds and describes variables collected from participants at each wave of data collection. The variable search tool enables researchers to locate items of interest within all available data collected from CLSA participants.

Currently, data emanating from the over 20,000 Tracking participants who completed the baseline 60-minute telephone interviews are available. Cognitive scoring is ongoing and these data will be available as part of the second CLSA data release in December 2014.

Datasets from future data collection events will be added when they are available.

Variables (June 2014)

Variables currently available in the first wave of the data release, with filtering and search options.

Variables (December 2014)

Variables that will be available in the second CLSA data release in December 2014.

Sampling weights

Description of sampling weights used in the CLSA.

Questionnaire

Baseline 60-minute Telephone Interview questionnaire (Tracking).

Study design

Study design of the Canadian Longitudinal Study on Aging (Tracking participants).
DataPreview Portal

Variables

Help: To obtain all the variables contained in a CLSA questionnaire module, type the two- or three-letter module prefix (e.g. SDC for socio-demographic variables) into the full-text search box.

<table>
<thead>
<tr>
<th>Name</th>
<th>Label</th>
<th>Dataset</th>
</tr>
</thead>
<tbody>
<tr>
<td>startdate</td>
<td>Date and time at start of interview</td>
<td>Tracking - Baseline Interview</td>
</tr>
<tr>
<td>startlanguage</td>
<td>Language at start of interview</td>
<td>Tracking - Baseline Interview</td>
</tr>
<tr>
<td>AGE_NMBR_TRM</td>
<td>Age (years)</td>
<td>Tracking - Baseline Interview</td>
</tr>
<tr>
<td>SEX_ASK_TRM</td>
<td>Sex</td>
<td>Tracking - Baseline Interview</td>
</tr>
<tr>
<td>SDC_COB_TRM</td>
<td>Country of birth</td>
<td>Tracking - Baseline Interview</td>
</tr>
<tr>
<td>SDC_COB_OTSP_TRM</td>
<td>Country of birth other, Specify</td>
<td>Tracking - Baseline Interview</td>
</tr>
<tr>
<td>SDC_YACA_YR_TRM</td>
<td>Year arrival in Canada</td>
<td>Tracking - Baseline Interview</td>
</tr>
<tr>
<td>SDC_ETHN_CA_TRM</td>
<td>Parental ethnic background Canadian</td>
<td>Tracking - Baseline Interview</td>
</tr>
<tr>
<td>SDC_ETHN_FR_TRM</td>
<td>Parental ethnic background French</td>
<td>Tracking - Baseline Interview</td>
</tr>
</tbody>
</table>
## Approved Applications

<table>
<thead>
<tr>
<th>Applicant Title</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consumer Product related senior falls and injury risk assessment</td>
<td>Ontario</td>
</tr>
<tr>
<td>CLSA Neurological conditions initiative (CLSA-NCI)</td>
<td>Quebec</td>
</tr>
<tr>
<td>The association between hearing loss and social function in older Canadians</td>
<td>British Columbia</td>
</tr>
<tr>
<td>The Veterans’ Health Initiative within the CLSA (CLSA-VHI)</td>
<td>Quebec</td>
</tr>
<tr>
<td>Labour force participation: Retirement Transitions, Expectations and Planning</td>
<td>Ontario</td>
</tr>
<tr>
<td></td>
<td>Student application</td>
</tr>
<tr>
<td>Who is at risk of social isolation and loneliness?</td>
<td>Manitoba</td>
</tr>
<tr>
<td>Companion animals and the aging population: Exploring relationships, contexts, and opportunities to contribute to health equity</td>
<td>Alberta</td>
</tr>
<tr>
<td></td>
<td>Student application</td>
</tr>
<tr>
<td>Factorial invariance of the CES-D</td>
<td>Saskatchewan</td>
</tr>
<tr>
<td>The development of normative data and comparison standards for the cognition measures employed in the CLSA</td>
<td>British Columbia</td>
</tr>
</tbody>
</table>
Linking CLSA Data

• Linkage is key to CLSA research strategy
  • Enormous potential for collection of information that is difficult to get from participants due to time, accuracy limitations; unknown to participants

• Types of databases
  • Individual level administrative provincial health databases (priority)
  • Disease registries
  • Population level databases of community characteristics, climate, pollution
  • Individual level economic characteristics
First Follow Up (2015-2018)

- 1st follow up Tracking (September 2015)
  - Re-contacting 21,242 participants for their follow up telephone interviews

- 1st follow up Comprehensive (July 2015)
  - Re-contacting 30,000 participants for their follow up in-home interviews and DCS visits
First Follow Up
New Content

- Child maltreatment
- Elder Abuse
- Epilepsy
- Hearing handicap
- Arterial stiffness
- Workability
- Subjective cognitive decline
- Transportation
- Health care use
- Preventive health behaviours
Analysis of baseline biomarkers

Biomarker and epigenetic analyses repeated over time

- Panel of biomarkers: albumin, ALT, creatinine, CRP, ferritin, hemoglobin A1C, lipids (cholesterol, HDL, Triglycerides, LDL), thyroid stimulating hormone, free T4, 25-hydroxyvitamin D
  - n=28,000 (Calgary Laboratory Services)
- Proposed genotyping: Affymetrix UKBiorepository array assay 820,967 SNPs
  - n=10,000 (McGill Genome Centre)
- Proposed epigenetic analysis: targeted age-associated CpG methylation using pyrosequencing and Sequenom EpiTyper
  - n=5,000 (UBC Genetics and Epigenetics Centre)
- Proposals submitted to do miRNA and metabolomics
- Requires isolation of DNA from PBMCs
CLSA
Transforming Everyday Life into Extraordinary Ideas

griffith@mcmaster.ca
www.clsa-elcv.ca

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Questions? Comments?