Canadian Longitudinal Study on Aging: A Multi-disciplinary Platform for Health Sciences Research

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University of Guelph, HHNS
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A need to study aging adults:

The population is getting older

Source: Elections Canada

1. Medium-growth scenario.

Source: Statistics Canada, CANSIM tables 051-0001 and 052-0005.
A need to study aging adults:

*Health-care costs rise with age...*

Source: CIHR
A need to study aging adults: ... because we don’t get any healthier

Can we prevent age-related disease? Can we live forever?

THE KEY: understand the demographic, biological, psychosocial and economic factors that influence “healthy aging”

THE PROBLEM: $$$$$
The Canadian Longitudinal Study on Aging (CLSA)

• Strategic initiative of CIHR; on Canadian research agenda since 2001
• A platform to provide the infrastructure and build capacity for state-of-the-art, interdisciplinary, population-based research and for evidence-based decision making needed to support the nation as it transitions into several decades of rapid population aging.

Raina et al., 2009: Can J Aging
The Canadian Longitudinal Study on Aging (CLSA)

• More than 160 researchers and collaborators – 26 institutions
• Multidisciplinary – biology, genetics, medicine, psychology, sociology, demography, economics, epidemiology, nutrition, health services
• Largest research platform of its kind in Canada for breadth and depth
• Following 50,000+ Canadians aged 45-85 at baseline for 20 years
Study Design and Timeline

Participants aged 45 to 85 at baseline (51,000+)

Enrolled

Tracking Cohort (n=20,000)
Age: 45-54 55-64 65-74 75-85
n: 6,000 6,000 4,000 4,000
(Telephone interviews)

Comprehensive Cohort (n=30,000)
Age: 45-54 55-64 65-74 75-85
n: 9,000 9,000 6,000 6,000
(In-person interviews and physical/biological assessments)

Data and Biological Sample Repositories

Active follow-up (FU) every 3 years

- Questionnaire
- Physical assessments
- Biological specimens
- Health-care utilization
- Disease registries
- Mortality databases

TIME: 20 Years

2010 - 2015

2015 2018
Data preview portal

https://datapreview.clsa-elcv.ca/datasets
# Interview data

## HEALTH INFORMATION
- Chronic disease symptoms (11 chronic conditions)
- Medication and supplement intake & compliance
- Women’s health (menopause and HRT)
- Self-reported health service use
- Oral health
- Administrative data linkage health services, drugs and other administrative databases (CIHI, ICES)

## PSYCHOSOCIAL
- Social participation
- Social networks and support
- Caregiving and care receiving
- Mood, psychological distress
- PTSD
- Injuries and consumer products
- Work-to-retirement transitions
- Personality traits
- Retirement planning
- Social inequalities
- Mobility-lifespace
- Built environments and contextual factors
- Income, wealth and assets

## LIFESTYLE & SOCIODEMOGRAPHIC
- Smoking and Alcohol consumption
- Physical activity (PASE)
- Nutrition (nutrition risk and food frequency)
- Ethnicity/race/gender
- Birth location
- Marital status
- Education
Interview data: Physical activity and nutrition

• PASE: Physical Activity Scale for the Elderly
  – Used to assess activities commonly engaged in by older persons
  – Correlates with age, sex, socioeconomic status, major conditions, functioning capacity, environment
  – Over 100 questions pertaining to types and duration of physical activity

• Nutritional risk (SCREEN II)
  – Used to identify risk for impaired nutritional states in community-living older adults
  – 11 questions pertaining to weight loss/gain, meals consumed, and eating

• Short food frequency Diet Questionnaire (SDQ)
  – a food frequency questionnaire designed to measure intake of total fat, fatty acids, cholesterol, trans fat, dietary fibre, calcium and vitamin D, and servings of fruits and vegetables.
  – Consists of 30 food and six beverage items, and consumption frequency (day, month, week, year)
Interview data: Chronic diseases, injuries and infections

• Falls (types, causes, injuries and other outcomes)
• Circulatory (Age of: CVA, angina, heart attack, hypertension, CVD, etc)
• Diabetes (Type, age begun insulin, other medications)
• Infections (In the past year: Flu/Pneumo, UTI, Eye/Ear, “other”)
• Cancers
• Arthritis (rheumatoid, osteoarthritis (Age, location and complications))
• Mental and neurological (anxiety, depression (age of), Parkinson’s (drugs and symptoms), dementia)
• Pulmonary (Asthma, COPD/emphysema, drugs taken)
• Allergies
Comprehensive Disease Ascertainment Algorithms

• Self-reported disease status can be inaccurate
    • Hypertension (κ=0.72), Diabetes (κ=0.82)
    • Asthma (κ=0.66), Depression (κ=0.40)
• Accurate clinical diagnosis is not realistic in a large epidemiological study
Comprehensive Disease Ascertainment Algorithms

- Algorithms have been developed that will utilize multiple data sources to diagnose disease.

- Performed for the following...

<table>
<thead>
<tr>
<th>Diabetes</th>
<th>Hypertension</th>
</tr>
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<tbody>
<tr>
<td>Chronic Airflow Obstruction</td>
<td>Depression</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>Hyper/Hypothyroidism</td>
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<tr>
<td>Ischemic Heart Disease (Hand, Hip, Knee)</td>
<td>Osteoarthritis</td>
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<tr>
<td>Stroke</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>Dementia</td>
<td></td>
</tr>
</tbody>
</table>

- Release dependant on data used
Data Collection Sites
Physical and cognitive assessments and biospecimen collection
DCS: Physical and cognitive assessments

PHYSICAL ASSESSMENTS
- Height, Weight, BMI, Waist-to-hip ratio
- Bone Density (hip, spine, whole body), Body Composition, Aortic Calcification, Vertebral fractures (Hologic DXA)
- Lean muscle mass (Hologic DXA)
- Blood Pressure and heart rate (BpTRU)
- Electrocardiogram (MAC 1600)
- Carotid Intimal-Medial Thickness (GE Vivid Doppler ultrasound)
- Pulmonary Function (Easy on-PC spirometer)
- Vision (Chart, IOP, retinal imaging)
- Hearing (Tremetrics RA 300+)

PERFORMANCE TESTING
- Timed to get up and go
- Chair rise
- 4 metre walk
- Grip strength (Tracker Freedom Dynamometer)
- Standing balance test

COGNITIVE ASSESSMENTS
- Neuropsychological Battery
  - Memory
  - Executive function
  - Reaction time
DCS: Biospecimen collection

- 50 mL blood
- Urine sample
- Hematological tests completed on site
- Remainder frozen, within 2 hours
- Stored in 0.5ml matrix tubes in LN2.
DCS: Hematological analysis

White blood cells
Lymphocytes (absolute and relative number)
Monocyt (absolute and relative number)
Granulocytes (absolute and relative number)

Red blood cells
• Hemoglobin
• Hematocrit
• Mean corpuscular volume
• Mean corpuscular hemoglobin
• Mean corpuscular hemoglobin concentration
• Red blood cell distribution width

Platelets
• Mean platelet volume
First Follow-Up: New Content

- Child maltreatment
- Elder abuse
- Epilepsy
- Arterial stiffness
- Decedent information
- Transition to institutions
- Unmet health-care needs
- Workability
- Preventive health behaviours
- Enhanced hearing, oral health and transportation
- Sexual orientation and gender identity
- Subjective cognitive decline
- Loneliness
Coming soon: (More) Biomarker data
Expected release in 2017-2018

Comprehensive Cohort
(n=30,000)

Soluble Markers
Calgary Laboratory Services
(n=30,000)
- Albumin
- Alanine Aminotransferase
- C-Reactive Protein, High Sensitivity
- Creatinine, serum
- Total Cholesterol, HDL Cholesterol, Calculated LDL Cholesterol, Triglycerides
- Ferritin

Genome-wide Genotyping
McGill University and Génome Québec Innovation Centre
(n=10,000)
- Buffy coat DNA extracted on all 30,000
- Genotyping by the ~820K UK Biobank Axiom Array (Affymetrix)
- Imputation (~6 million SNPs) performed by Brent Richards (McGill University)

Metabolomics (n=3,000)
- Performed on participant serum in Japan using a mass spectrometry approach

DNA Methylation Profiling
UBC Genetics and Epigenetics Centre
(n=2,000)
- Performed in the laboratory of Dr. Michael Kobor, UBC
- PBMCs used for DNA extraction
- Profiling by 850K Infinium MethylationEPIC BeadChip (Illumina)

~2,000 participants with matching soluble, genetic, epigenetic and metabolomic marker data
Data and Biospecimen Access

- 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 resources that will be used optimally to support research to benefit all Canadians
  - No preferential or exclusive access
Data preview portal

https://datapreview.clsa-elcv.ca/datasets

DataPreview Portal

SMART TIPS
- Variables from all Baseline interviews are preselected by default. To limit your search, select/deselect each under the 'Dataset' tab on the left
- Search for Areas of Information or Scales using the search bar below
- For Variable Names and Labels, use the search fields under the 'Variable' tab
- When searching multiple terms, default search mode is (OR). To switch to (AND), use the Advanced option

Variable    Dataset

Variable properties
- Name
- Label

Areas of Information

Clear  CMQ | COM | TMCQ | TRM

Variables (210) Datasets (2)

<table>
<thead>
<tr>
<th>Name</th>
<th>Label</th>
<th>Dataset</th>
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<tr>
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<td>TMCQ</td>
</tr>
<tr>
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<td>PASE scale: Engaged in caring for another person - past 7 days</td>
<td>CMCO</td>
</tr>
</tbody>
</table>

Also… CLSA Protocol

https://clsa-elcv.ca/doc/511
Who can apply?

• Researchers based in academic settings and research institutes in Canada

• International researchers may choose to collaborate with Canadian researchers to access data or biospecimens as long as the data and/or biospecimens are analyzed in Canada

• Graduate students and postdoctoral fellows based at Canadian institutions
Preparing an Application
https://www.clsa-elcv.ca/data-access

Complete the Data and/or Biospecimen Request Application
• Includes a 3 page proposal outlining the study background/relevance, objectives and hypotheses, design and methodology, and the data analyses proposed.
• Identifiable information will not be shared (e.g. six-digit postal codes, names, contact information).

For more information
• Consult the Data and Sample Access Policy and Guiding Principles
• Review the pertinent sections of the CLSA protocol and the CLSA questionnaires
• Visit the DataPreview Portal to search datasets
Review & Data Access Process

- **Submit**: March, June and October for review May, July and November
- **Review**: Administrative → Data and Sample Access Committee → Scientific Management Team
- **Approval**: Preparation of CLSA Access Agreement, verification of ethics approval
- **Release**: Raw data provided to approved investigator, cost recovery
- **Enhance**: Return of derived variables to CLSA dataset as appropriate

Queries should be sent to access@clsa-elcv.ca
Data and Biospecimen Access Fees

• Partial cost-recovery model
• $3,000 for a straightforward alphanumeric dataset for any number of participants
• Additional fees applied for requests that require more complex customization
• No cost for graduate students who use these data for their Master’s or PhD theses
• One free dataset for postdoctoral fellows
• Baseline biospecimen and biomarkers data release is expected soon, fees are still being determined (Questions? bbc@clsa-elcv.ca)
My Current Research Areas

Past and Present

- Grip strength
- Timed-to-up-and-go
- Gait speed
- Exhaustion
- Weight loss

Biomarkers (cellular + molecular)

Robust  Pre-frail  Frail

Peripheral blood cells

1) Grip strength
2) Timed-to-up-and-go
3) Gait speed
4) Exhaustion
5) Weight loss
Biorepository and Bioanalysis Centre (BBC)

- Central location for storage and analysis of the biological samples
  - 31 nitrogen freezers (-190°C)
  - Storage for 5 million aliquots
  - Dry storage, humidity controlled, room temperature

- Director: Dr. Cynthia Balion, McMaster University
The CLSA Laboratory

Current Work

Flow Cytometry

Automated liquid handler (Gerobot)

Tissue culture facilities

Plate reader/
spectrophotometer

Plate washer

Luminex 200

Flow Cytometry

Current Work

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CLSA Research Team

UVic: Debra Sheets, Lynne Young, Holly Tuokko
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SFU: Andrew Wister, Scott Lear
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UManitoba: Verena Menec, Phil St. John
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Dalhousie: Susan Kirkland
Memorial: Gerry Mugford, Patrick Parfrey
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UWaterloo: Mark Oremus, Mary Thompson, Changbao Wu
Eindhoven University of Technology: Edwin van den Heuvel
Thanks! Any Questions?

Transforming Everyday Life into Extraordinary Ideas

www.clsa-elcv.ca
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Data access? access@clsa-elcv.ca
Biospecimen access? bbc@clsa-elcv.ca

Connect with us

info@clsa-elcv.ca
www.clса-elcv.ca
The difficulty in studying trends of health and disease in community-dwelling adults

An ideal study should be:
- Representative – capture population heterogeneity
- Sufficiently powered (n)
- Cost-effective

Important considerations:
- Target(s)
- Effect size
- Prevalence or variability of target(s)
- Follow-up period

An inconvenient truth…

“Go Big or Go Home”

Wouldn’t it be great if there was a national platform to support this type of work!
Population Totals in Canada by Age Group and Year

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<tr>
<th>AGE</th>
<th>MALES</th>
<th>BOTH SEXES</th>
<th>FEMALES</th>
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First Follow-Up: Additional Considerations

- Changing circumstances
  - Moving
  - Cognitive impairment
  - Physical impairment
  - Sensory impairment
  - Institutionalization

- Accommodation strategies to maintain long-term participation
- Allows for flexible participation
- Baseline exclusion criteria no longer apply
The CLSA Laboratory: Current Projects

• Validating the use of cryopreserved whole blood for cellular immunophenotyping by multicolour flow cytometry.

Not feasible for large studies

Costly, Requires trained personnel

Cost-effective, Simple to prepare
Validating the use of cryopreserved whole blood for cellular immunophenotyping by multicolour flow cytometry

Testing: Total WBCs, Monocytes, Neutrophils, CD4/CD8 Lymphocytes, B-cells, NK cells, NKT cells, pDCs, Basophils

CD4 T-lymphocyte Frequency

- Fresh vs. Frozen Whole Blood
- Frozen Whole Blood vs. Frozen PBMCs
- Frozen/Frozen Whole Blood vs. CBC
Examining the relationship between blood biomarkers and frailty in older adults

- Approved by the CLSA Scientific Management Team and Data and Sample Access Committee, June 2016.

- **Hypothesis:** The frequency and phenotype of peripheral blood cells can discriminate individuals classified as healthy (robust), pre-frail and frail, although this relationship will depend on important demographics such as age, sex and socioeconomic status.