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

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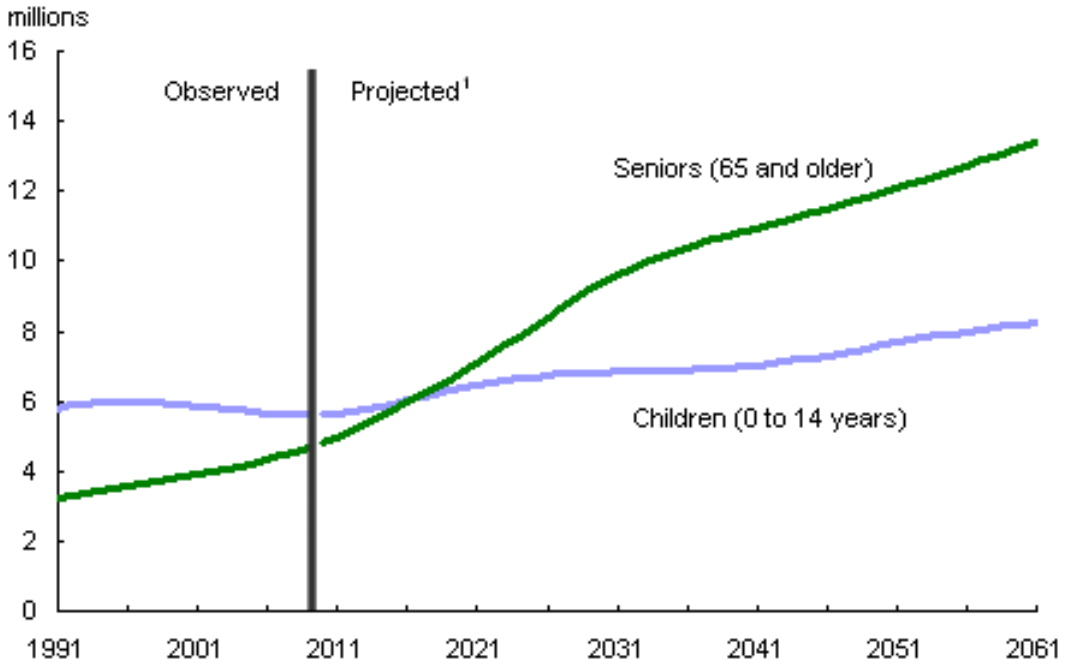
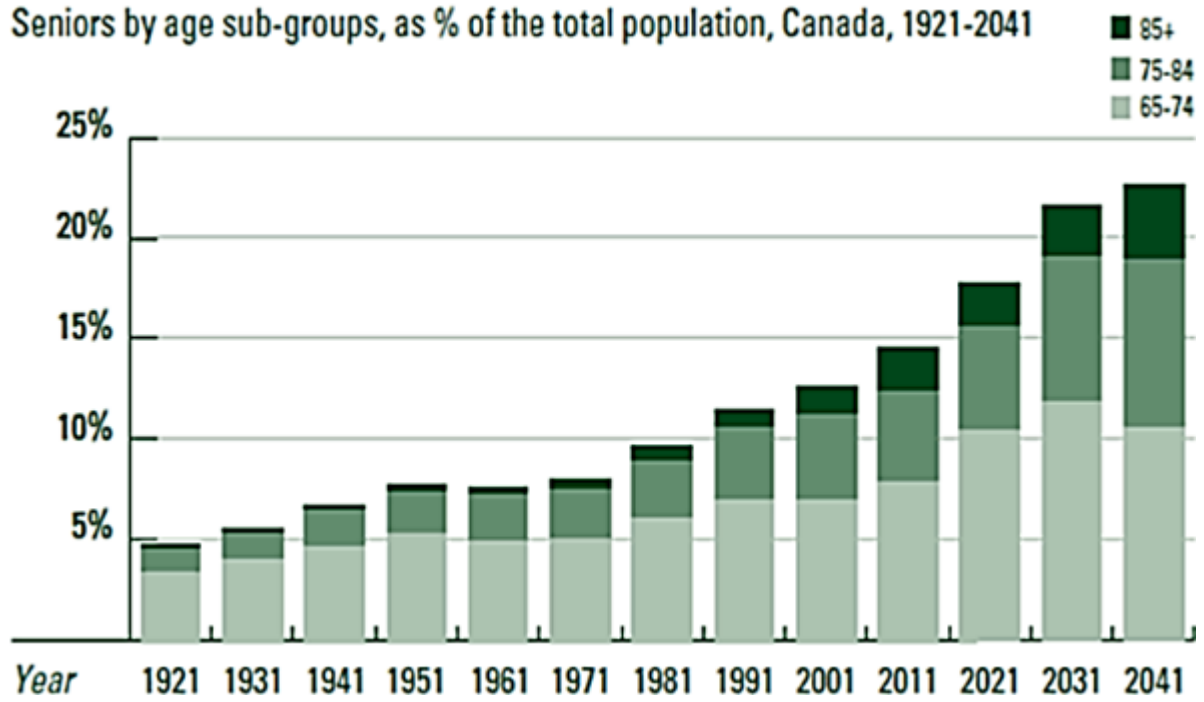
A need to study aging adults:

The population is getting older



1. Medium-growth scenario.

Source: Statistics Canada, CANSIM tables 051-0001 and 052-0005.



Source: *Elections Canada*

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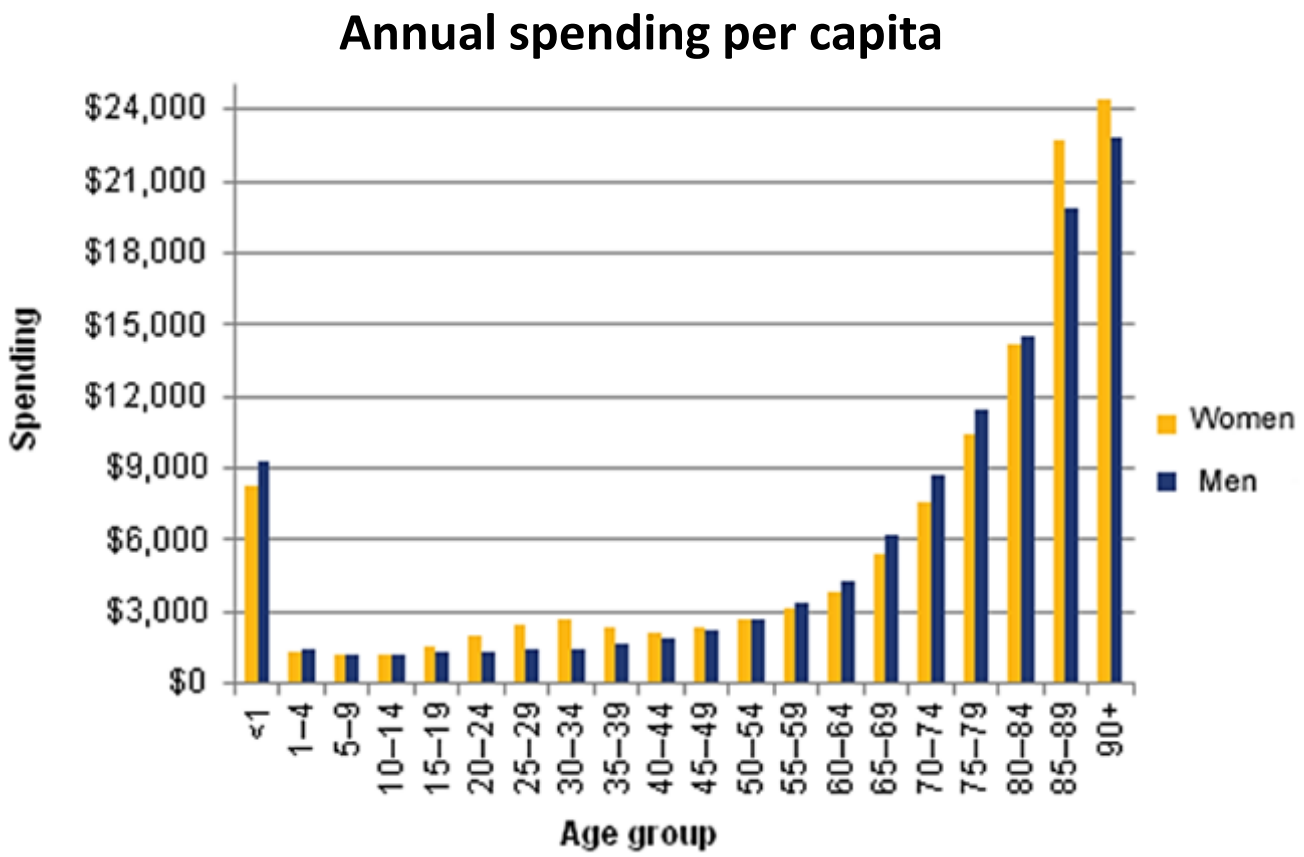
A need to study aging adults:

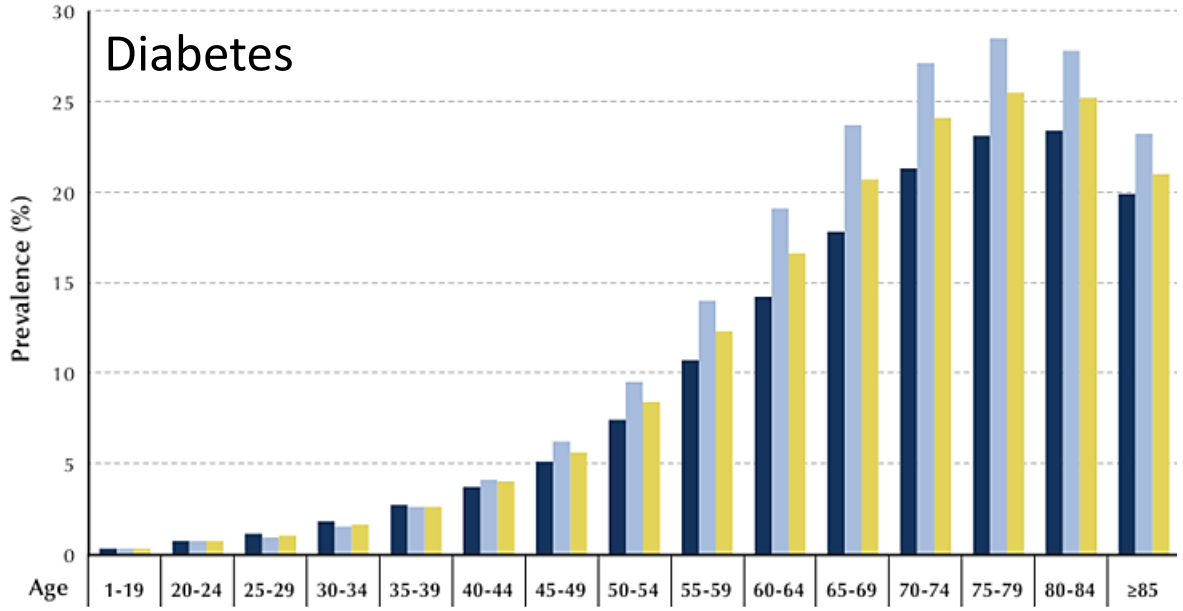
Health-care costs rise with age…

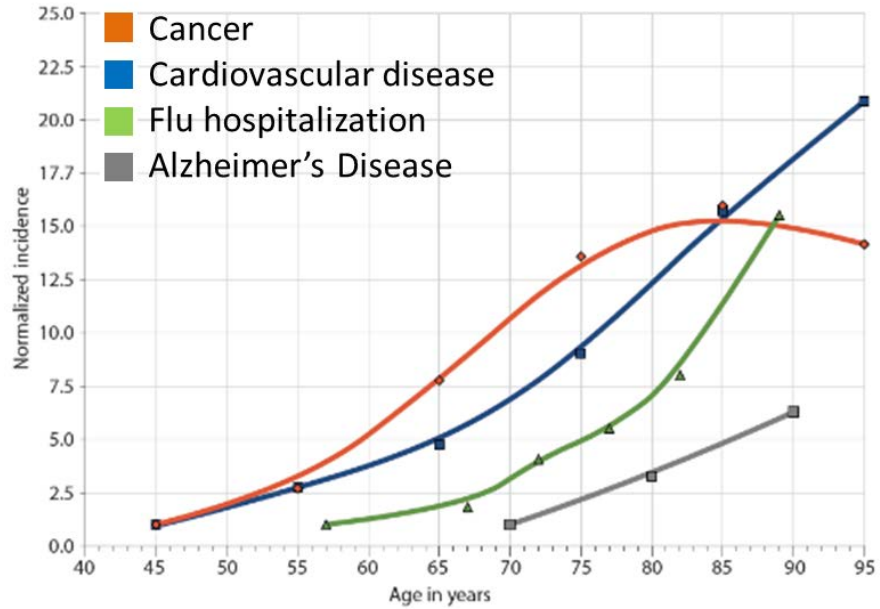


Source: *CIHR*

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: $$$$$

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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

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The Canadian Longitudinal Study on Aging (CLSA)

Lead Principal Investigator
Parminder Raina (McMaster)

Co-principal Investigator
Christina Wolfson (McGill)

Co-principal Investigator
Susan Kirkland (Dalhousie)

- 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

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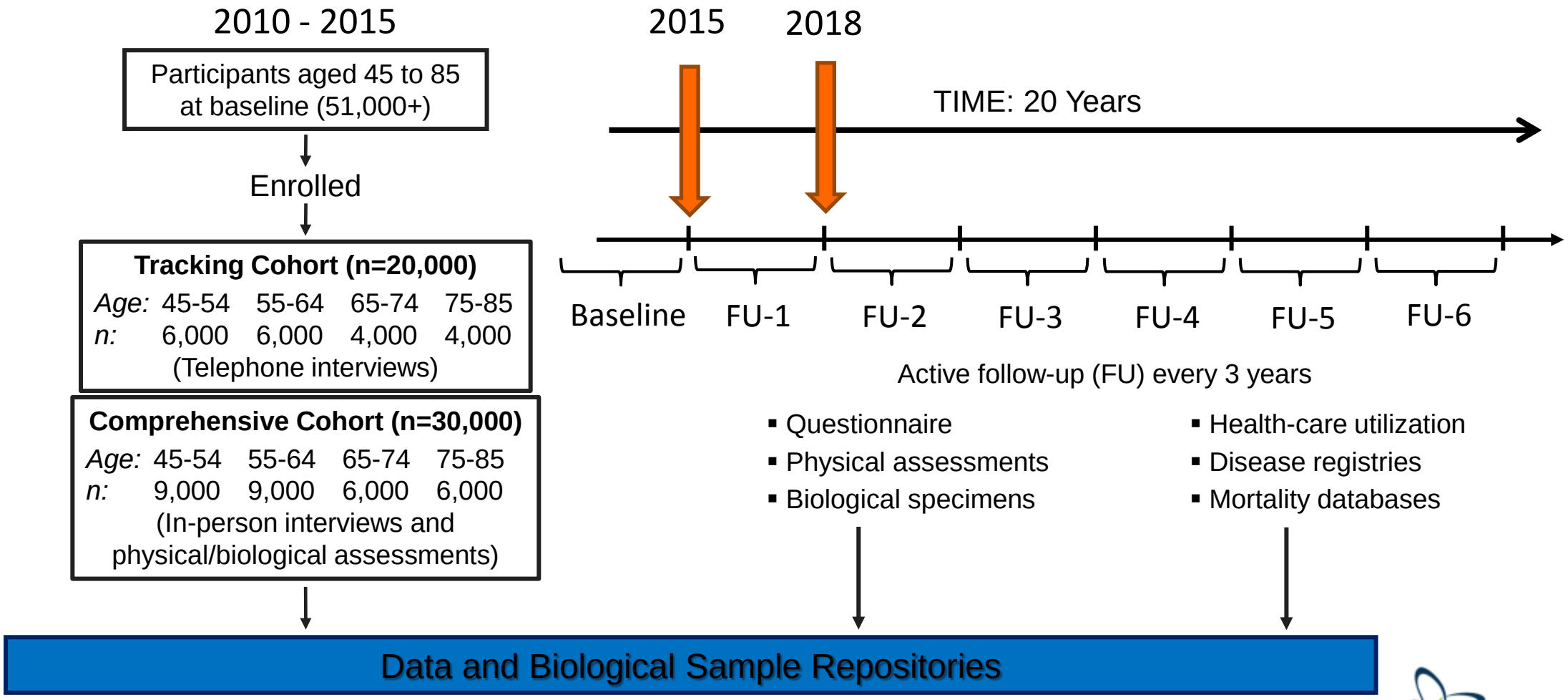
Study Design and Timeline



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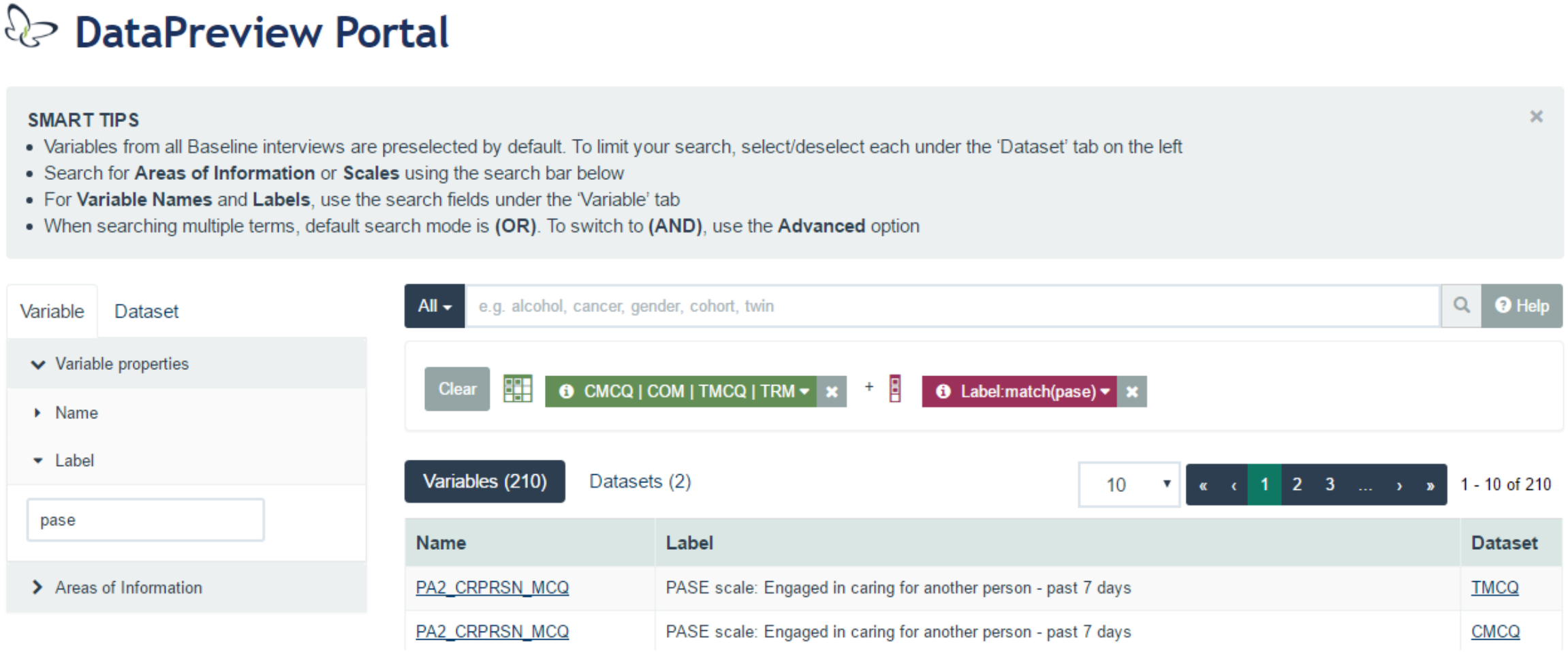
Data preview portal

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



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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)

LIFESTYLE & SOCIODEMOGRAPHIC

- Smoking and Alcohol consumption
- Physical activity (PASE)
- Nutrition (nutrition risk and food frequency)
- Ethnicity/race/gender
- Birth location
- Marital status
- Education

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

Interview data: Physical activity and nutrition

- PASE: Physical Activity Scale for the Elderly
  - Washburn et al., 1993: J Clin Epidemiol.
  - 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)
  - Keller et al., 2005: Eur J Clin Nutr.
  - 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)
  - Shatenstein et al., 2005: Can J Diet Pract Res.
  - 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

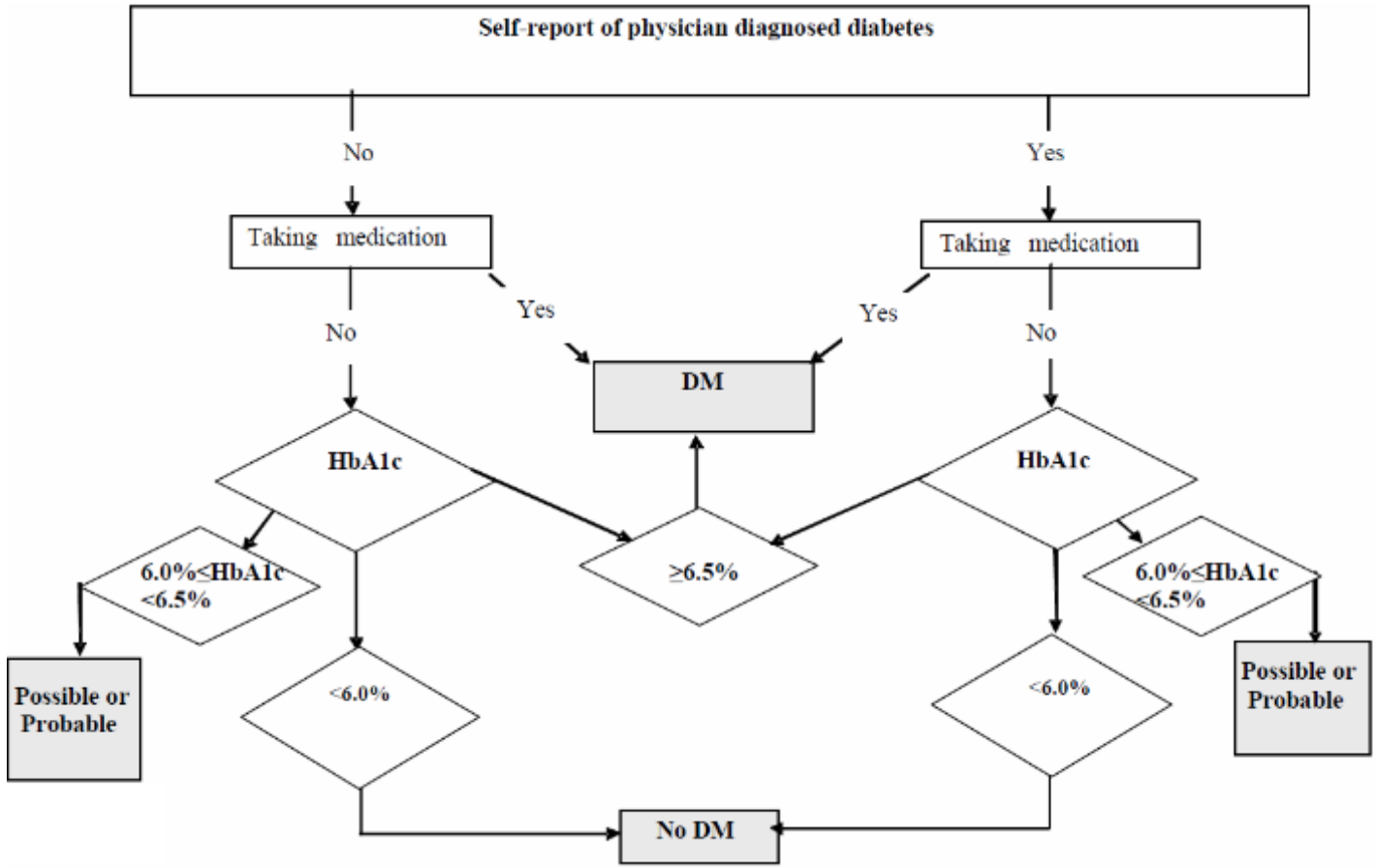
- Self-reported disease status can be inaccurate
  - Chun et al., 2016: Osong Public Health Res Perspect.
    - Hypertension (κ=0.72), Diabetes (κ=0.82)
  - Leikauf and Federman, 2009: J Am Geriatr Soc.
    - Asthma (κ=0.66), Depression (κ=0.40)
- Accurate clinical diagnosis is not realistic in a large epidemiological study

Comprehensive Disease Ascertainment Algorithms

- Algorithms have been developed that will utilize multiple data sources to diagnose disease.
- Performed for the following…

Diabetes	Hypertension
Chronic Airflow Obstruction	Depression
Parkinsonism	Hyper/Hypothyroidism
Ischemic Heart Disease	Osteoarthritis (Hand, Hip, Knee)
Stroke	Osteoporosis
Dementia	

- Release dependant on data used



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Data Collection Sites

Physical and cognitive assessments and biospecimen collection

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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

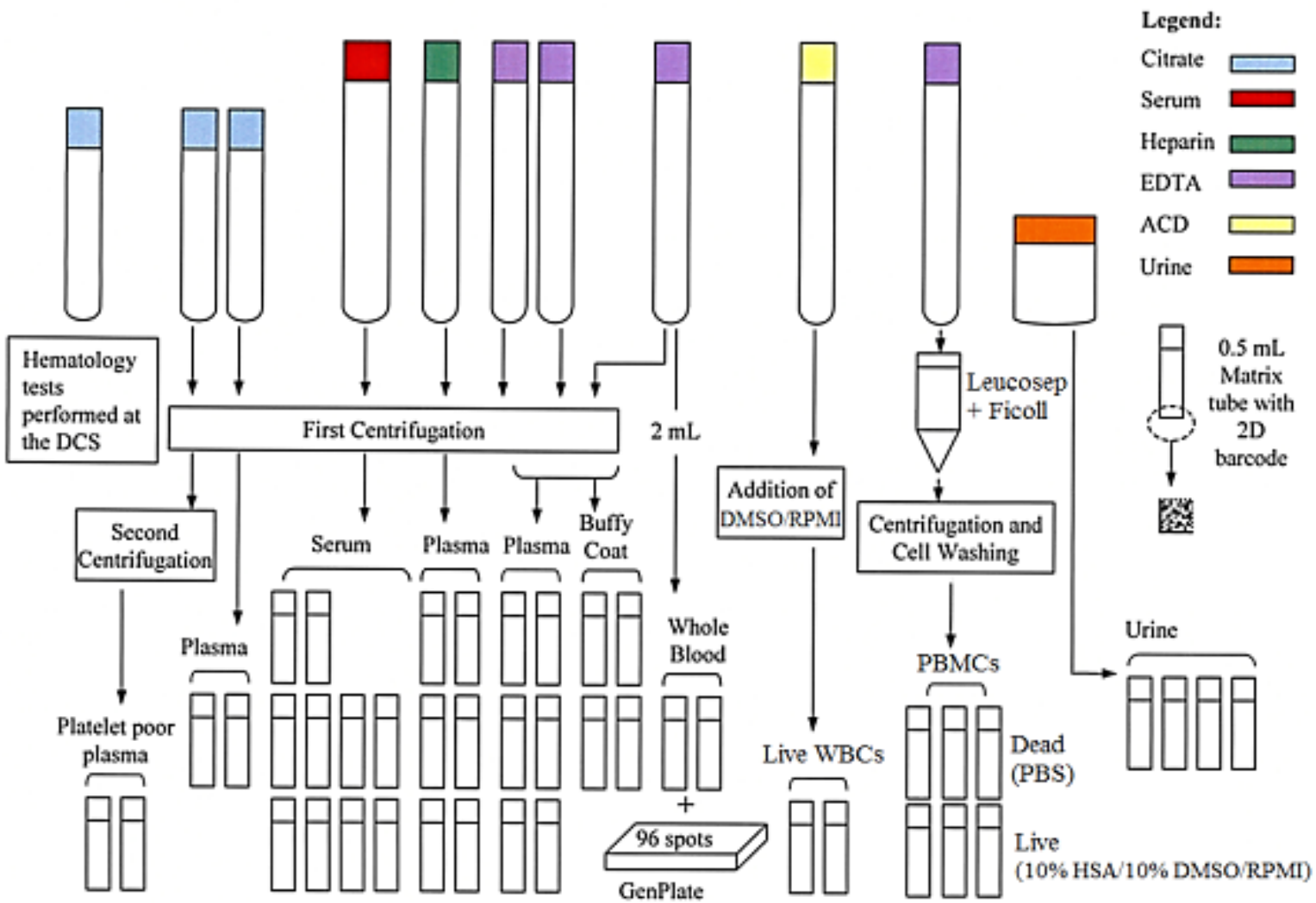
- Timed to get up and go
- Chair rise
- 4 metre walk
- Grip strength (Tracker Freedom Dynamometer)
- Standing balance test

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

Beckman Coulter AcT Diff

White blood cells

Lymphocytes (absolute and relative number)

Monocytes (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)

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

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
- Free T4
- Hemoglobin A1c
- Thyroid Stimulating Hormone
- Total 25-Hydroxyvitamin D

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)

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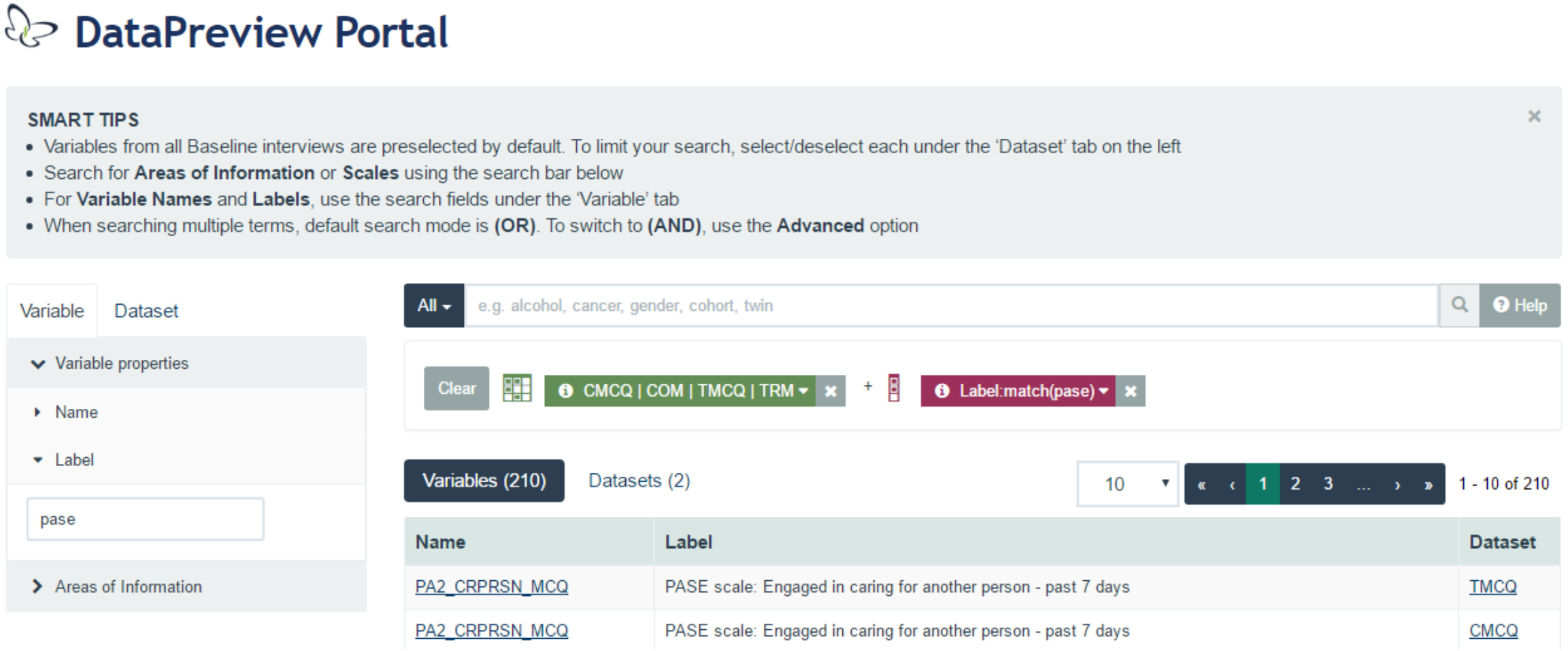
Data and Biospecimen Access

- **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



Also… CLSA Protocol
https://clsa-elcv.ca/doc/511

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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

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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

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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

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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)

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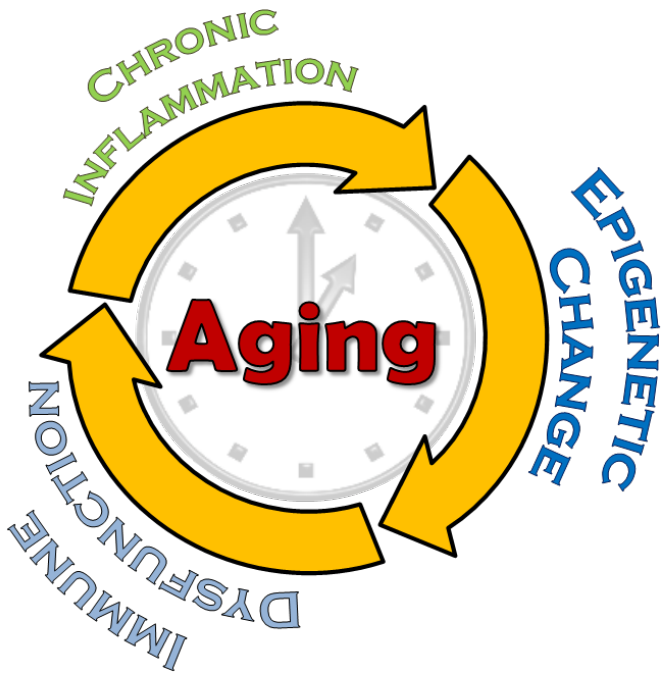
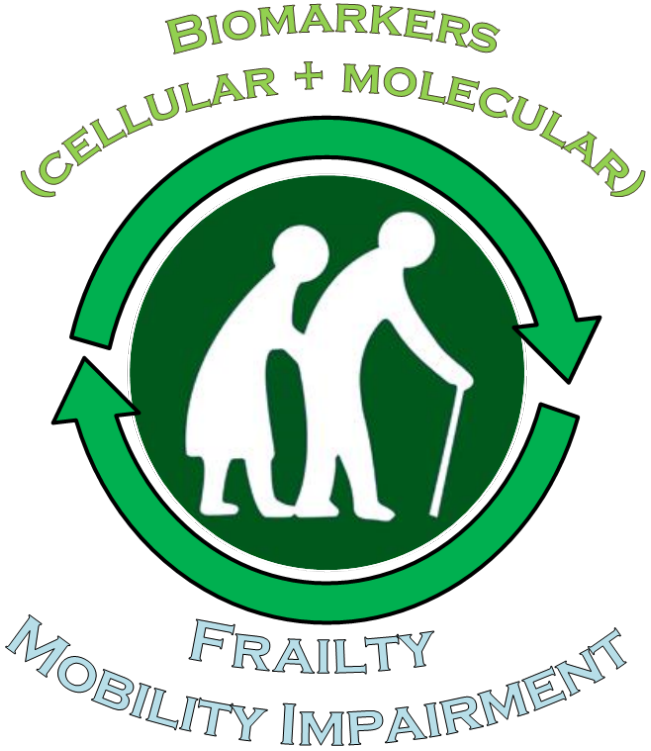
My Current Research Areas

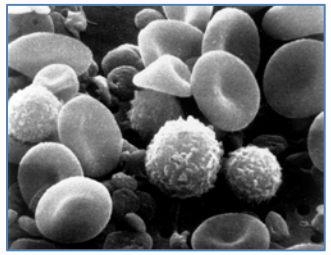
Past and Present



… and Beyond



Peripheral blood cells



Physical Frailty

Robust Pre-frail Frail

1) **Grip strength**
2) **Timed-to-up-and-go**
3) **Gait speed**
4) **Exhaustion**
5) **Weight loss**

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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

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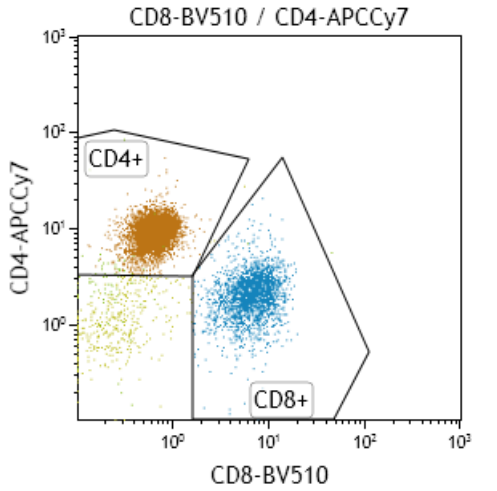
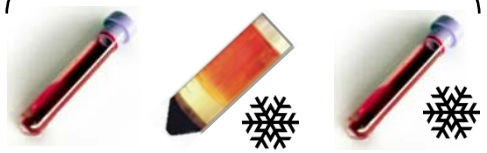
The CLSA Laboratory

Current Work





Fresh WB | Frozen PBMCs | Frozen WB

??

Flow Cytometry

Tissue culture facilities

Automated liquid handler (Gerobot)

Plate reader/ spectrophotometer

Plate washer

Luminex 200

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CLSA Research Team

UVic: Debra Sheets, Lynne Young, Holly Tuokko

UBC: Teresa Liu-Ambrose, Michael Kobor, Max Cynader

SFU: Andrew Wister, Scott Lear

UCalgary: David Hogan, Marc Poulin, Eric Smith, Alex Chin, Hossein Sadrzadeh

UManitoba: Verena Menec, Phil St. John

McMaster: Parminder Raina, Cynthia Balion, Lauren Griffith, Andrew Costa, Harry Shannon, Christopher Patterson, Michael Veall, Guillaume Paré, Brenda Vrkljan, Dawn Bowdish, Stu Phillips, Maureen MacDonald, Andrea Gonzalez, Harriet MacMillan, Byron Spencer, Chris Verschoor

UOttawa: Vanessa Taler, Larry Chambers

McGill: Christina Wolfson, Ron Postuma, Brent Richards, Mark Lathrop

USherbrooke: Hélène Payette, Benoît Cossette

Dalhousie: Susan Kirkland

Memorial: Gerry Mugford, Patrick Parfrey

UToronto: Andrew Paterson

UWaterloo: Mark Oremus, Mary Thompson, Changbao Wu

Eindhoven University of Technology: Edwin van den Heuvel

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CLSA Funders and Partners

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Thanks! Any Questions?

www.clsa-elcv.ca

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Contact Information

Chris Verschoor, cversch@mcmaster.ca

Data access? access@clsa-elcv.ca

Biospecimen access? bbc@clsa-elcv.ca

Connect with us

info@clsa-elcv.ca
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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!

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Population Totals in Canada by Age Group and Year

AGE	MALES	BOTH SEXES	FEMALES
80+	229898	670192	440294
75-79	255599	622194	366595
70-74	364298	833991	469693
65-69	497996	1084588	586592
60-64	578596	1190087	611491
55-59	618096	1238387	620291
50-54	673295	1339986	666691
45-49	844194	1674182	829988
40-44	1076892	2138777	1061885
35-39	1173491	2344675	1171184
30-34	1311991	2597873	1285882
25-29	1282190	2528572	1246382
20-24	1067593	2108978	1041385
15-19	984993	1925780	940787
10-14	980292	1912979	932687
5-9	998293	1953079	954786
0-4	1000393	1953280	952887
1991 TOTALS	13938100	28117600	14179500

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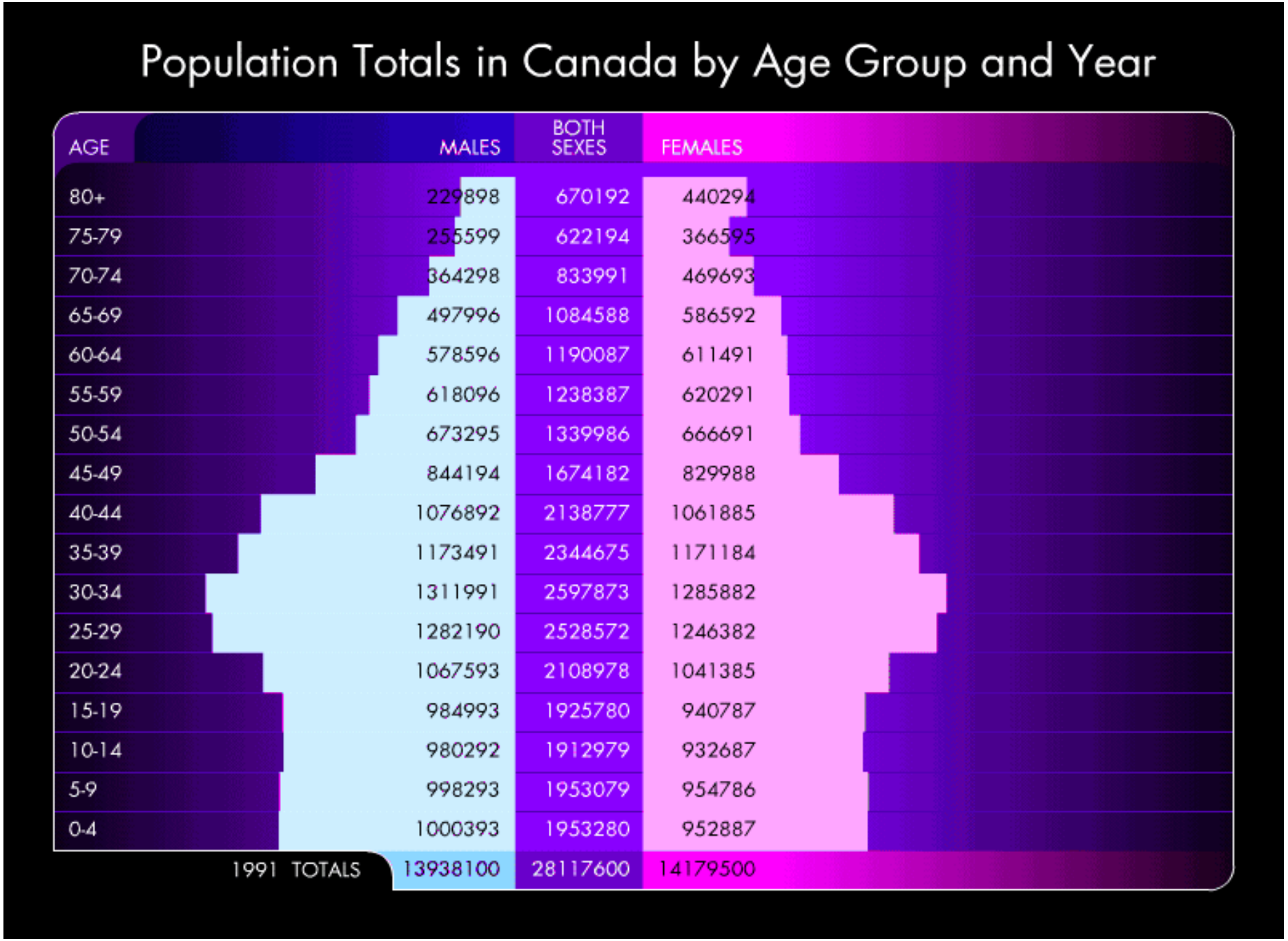
Population Totals in Canada by Age Group and Year



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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

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The CLSA Laboratory: Current Projects

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

Not feasible for large studies

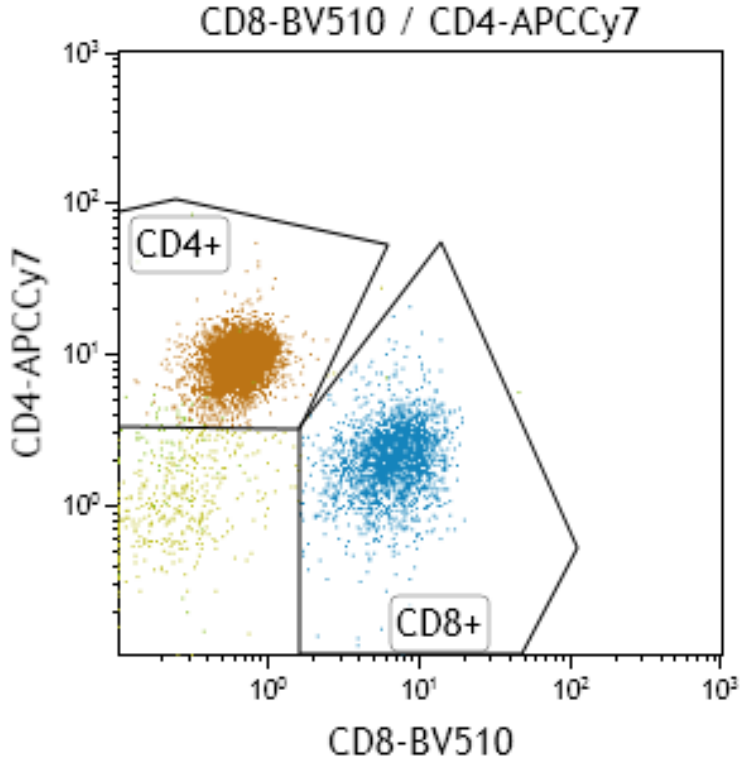
Fresh whole blood

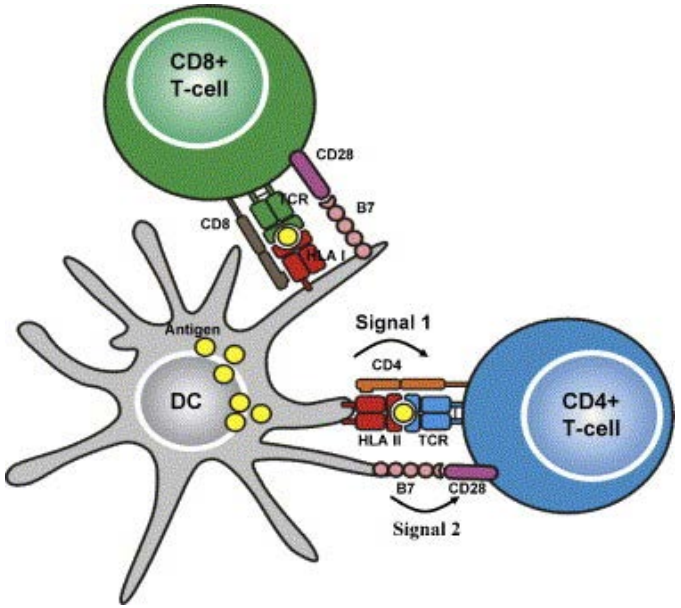
Costly, Requires trained personnel

Frozen PBMCs

Cost-effective, Simple to prepare

Frozen whole blood





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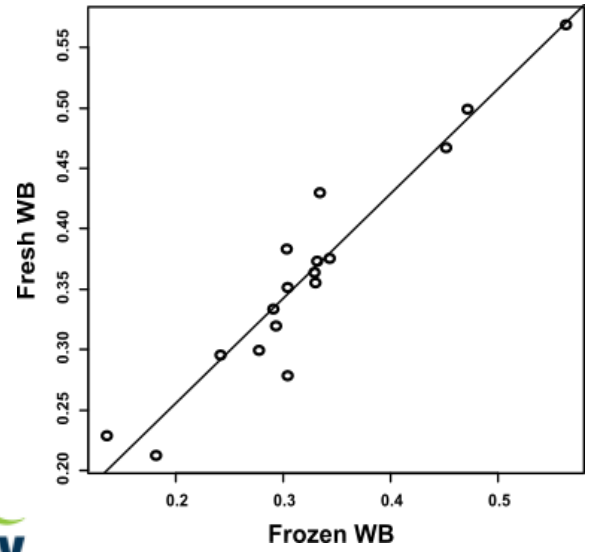
Validating the use of cryopreserved whole blood for cellular immunophenotyping by multicolour flow cytometry

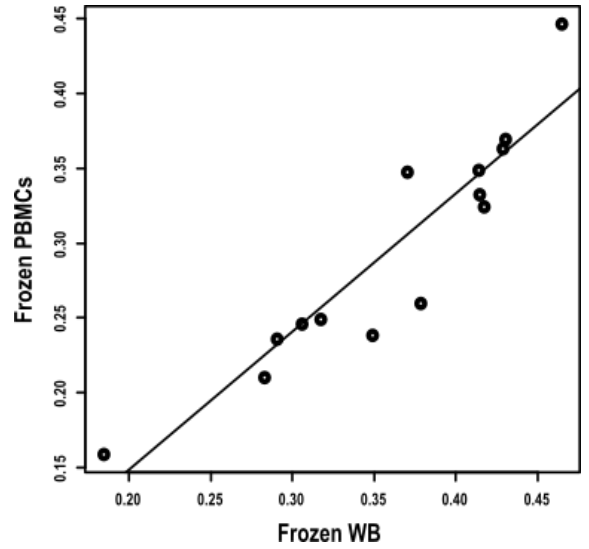
<u>Testing:</u> Total WBCs, Monocytes, Neutrophils, CD4/CD8 Lymphocytes, B-cells, NK cells, NKT cells, pDCs, Basophils

CD4 T-lymphocyte Frequency

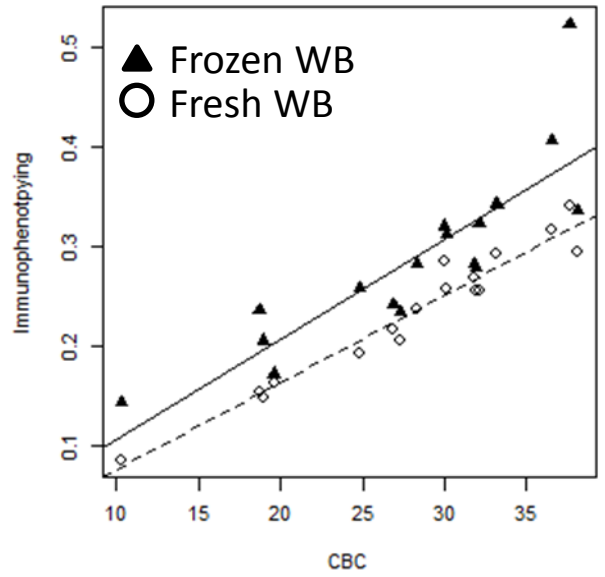
Fresh vs. Frozen Whole Blood



Frozen Whole Blood vs. Frozen PBMCs



Frozen/Frozen Whole Blood vs. CBC



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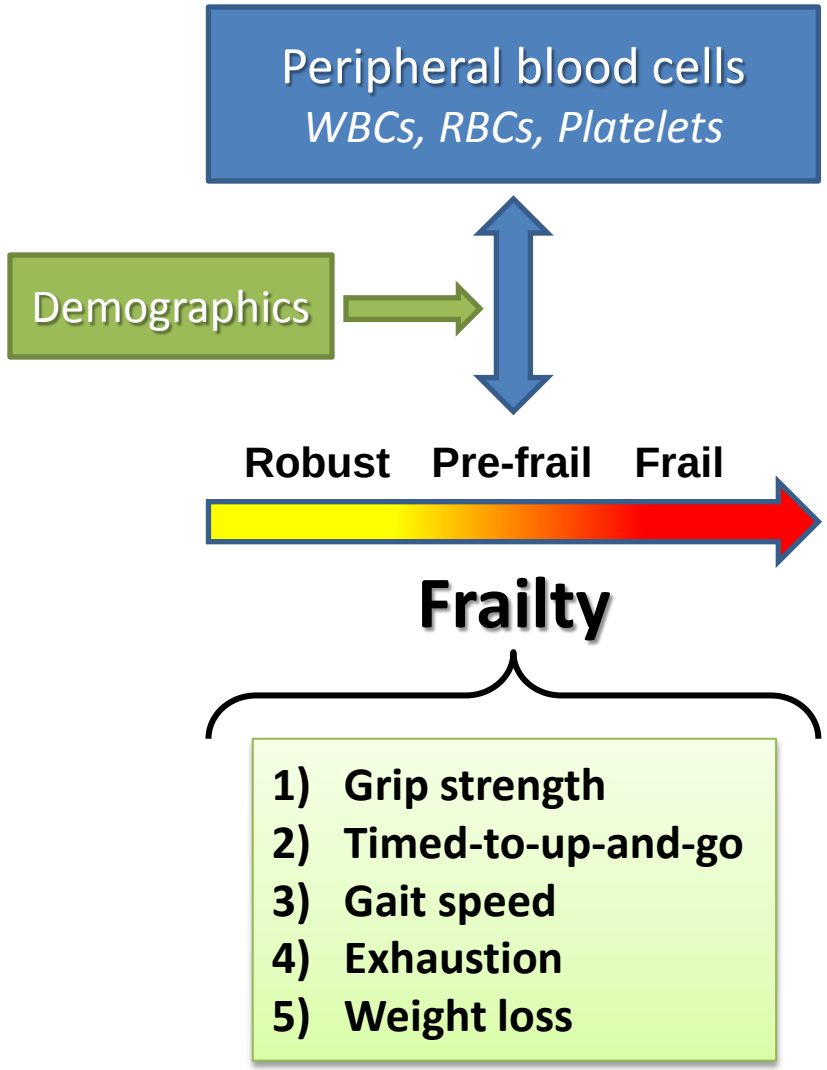
Examining the relationship between blood biomarkers and frailty in older adults



- 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.*

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Canadian Longitudinal Study on Aging
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