



***Transforming Everyday Life
into Extraordinary Ideas***



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

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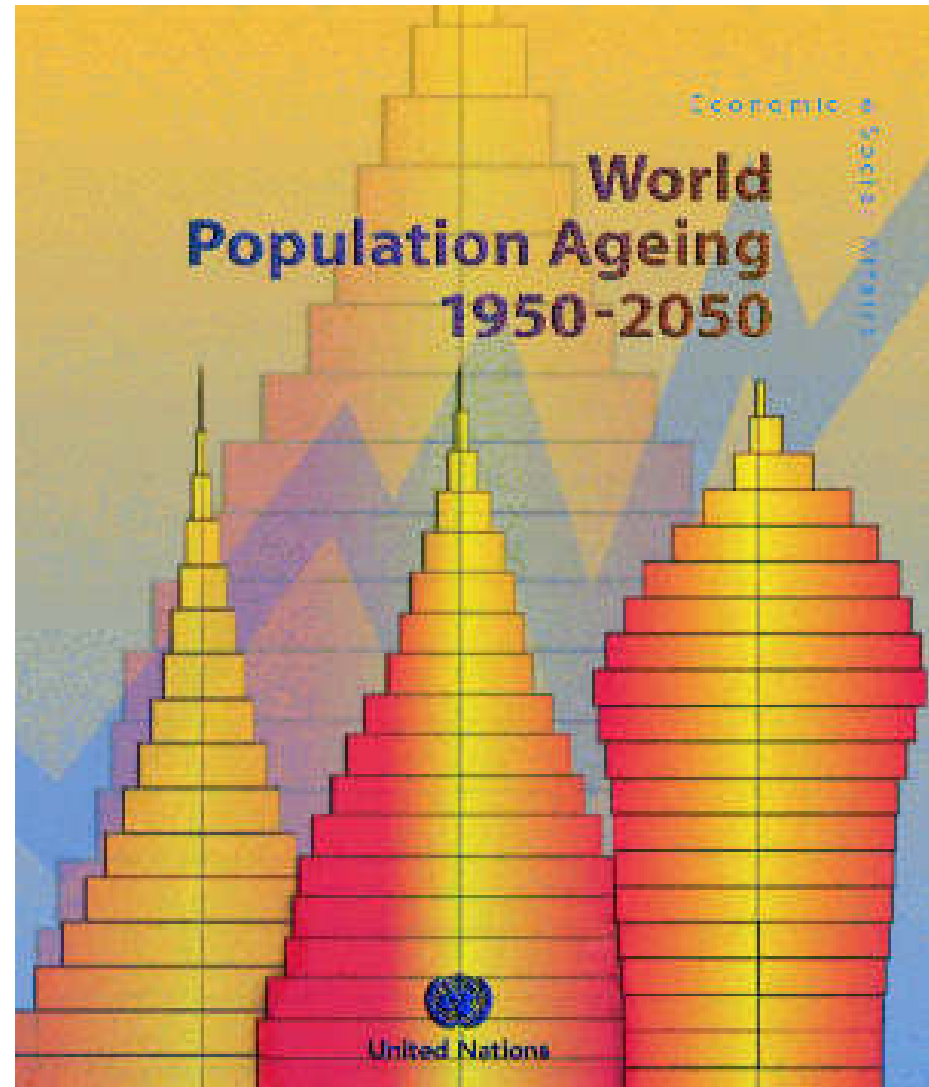
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Hamilton, November 30th, 2012

Population aging

- Due to declining fertility and increasing longevity (demographic transition)
- Unprecedented, accelerating, shifts will be permanent
- Profound implications for human life, including health



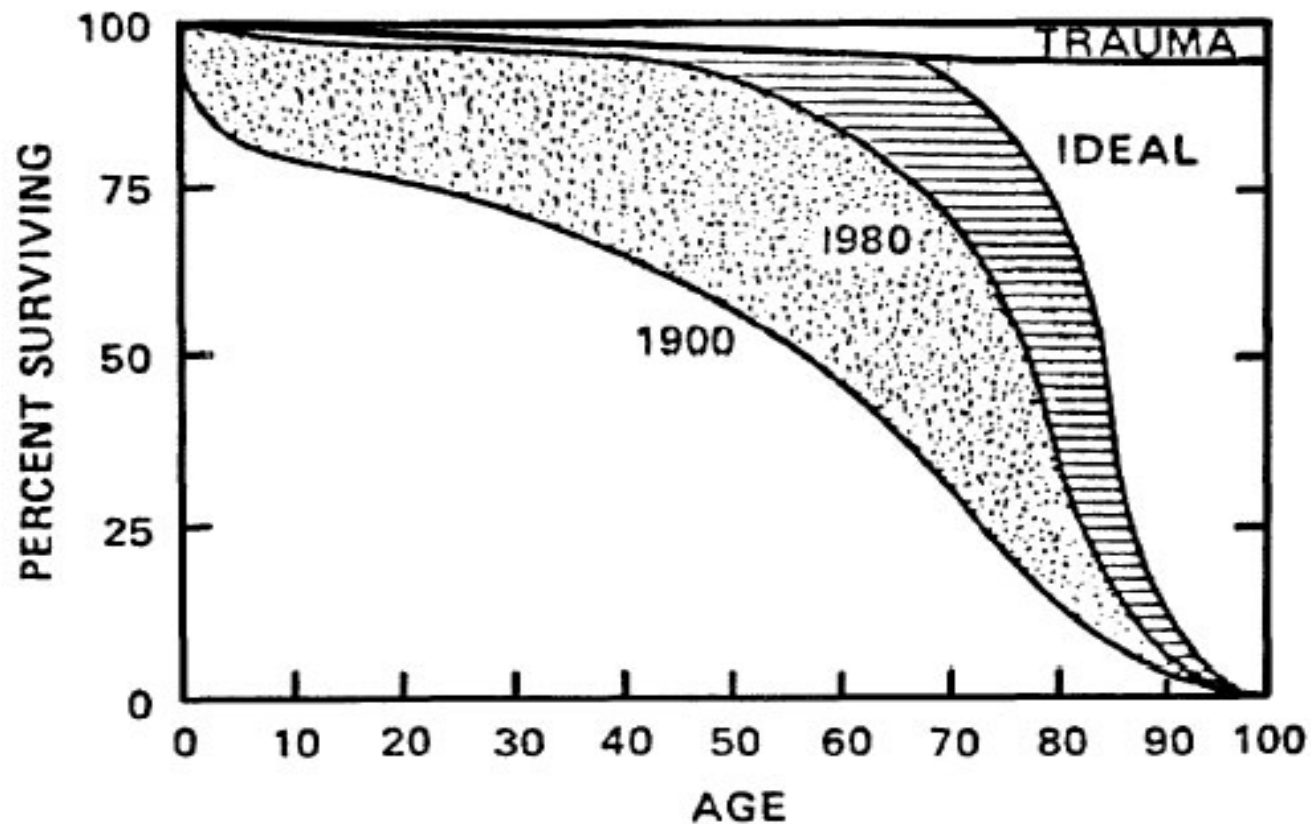
Population Totals in Canada by Age Group and Year

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

Rectangularization of the survival curve

FURTHER INCREASE IN LIFE EXPECTANCY

Squaring the survival curve



Compression of morbidity

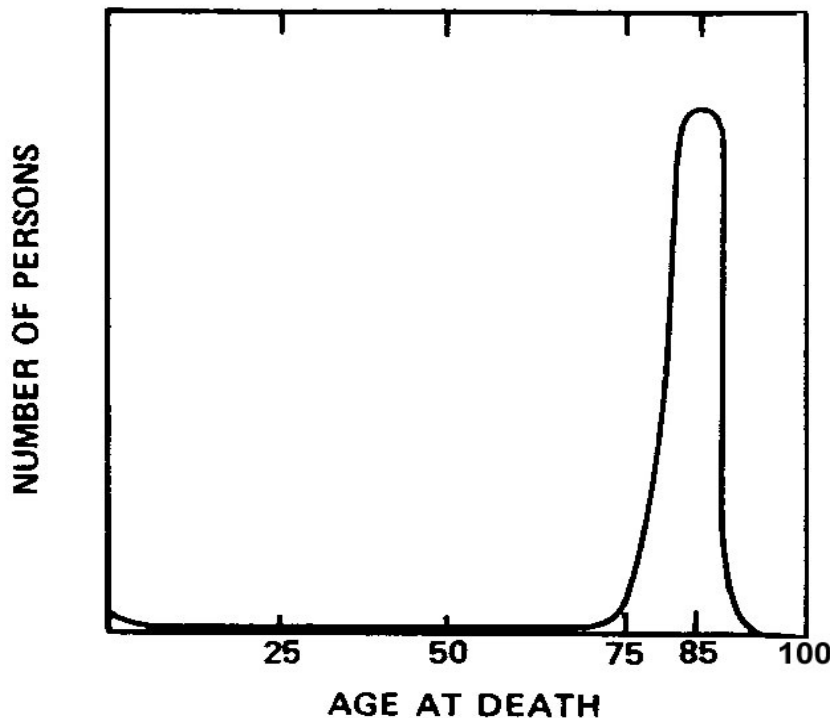


Figure: Mortality According to Age in the Absence of Premature Death

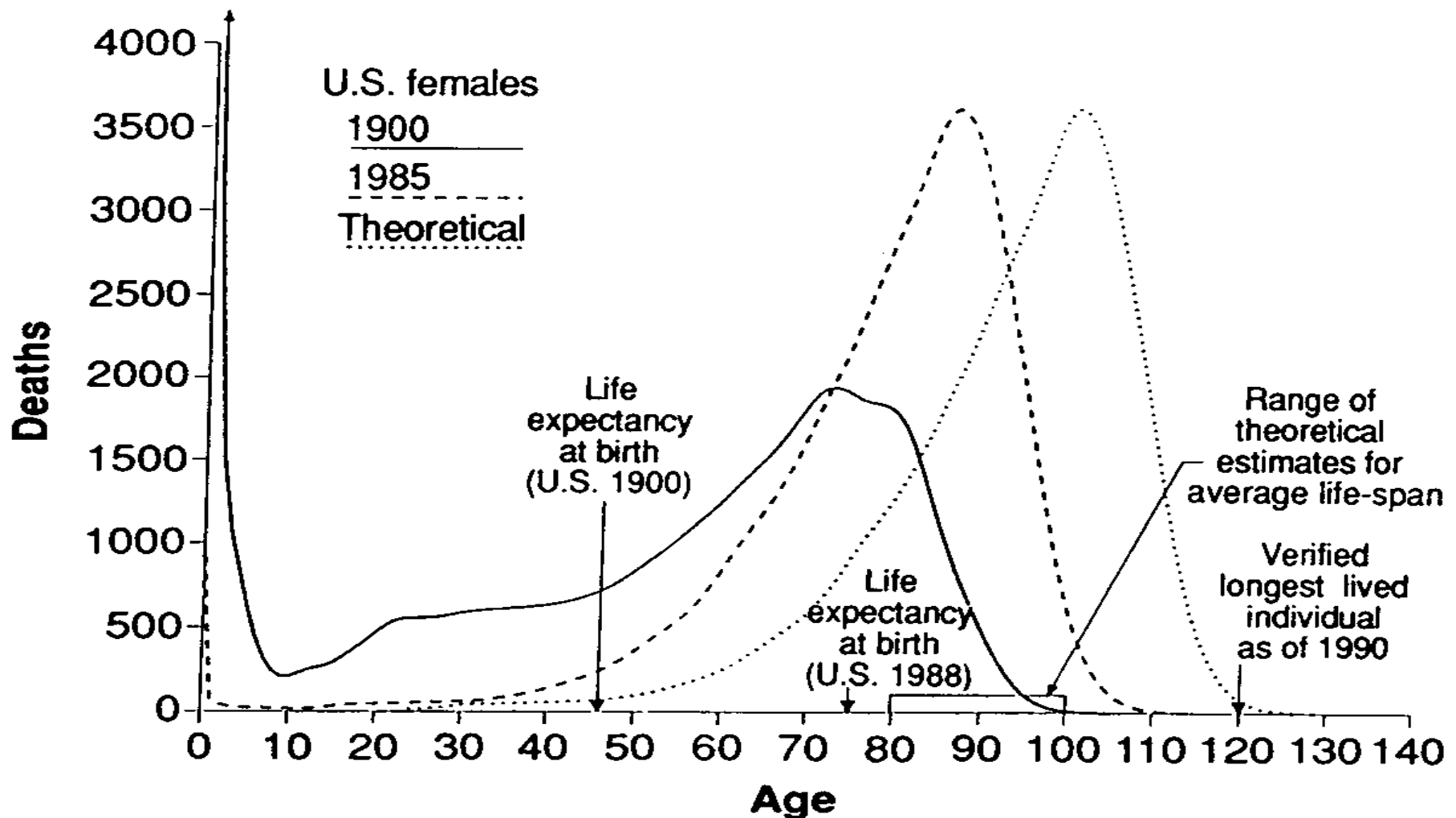
- Morbidity compressed into a short period prior to death
- Represented an important shift in thinking
- Departure from the medical model of aging, which assumed that death always occurred as a result of a disease process, and that older age was a period of inevitable decline

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

Distribution of life table deaths

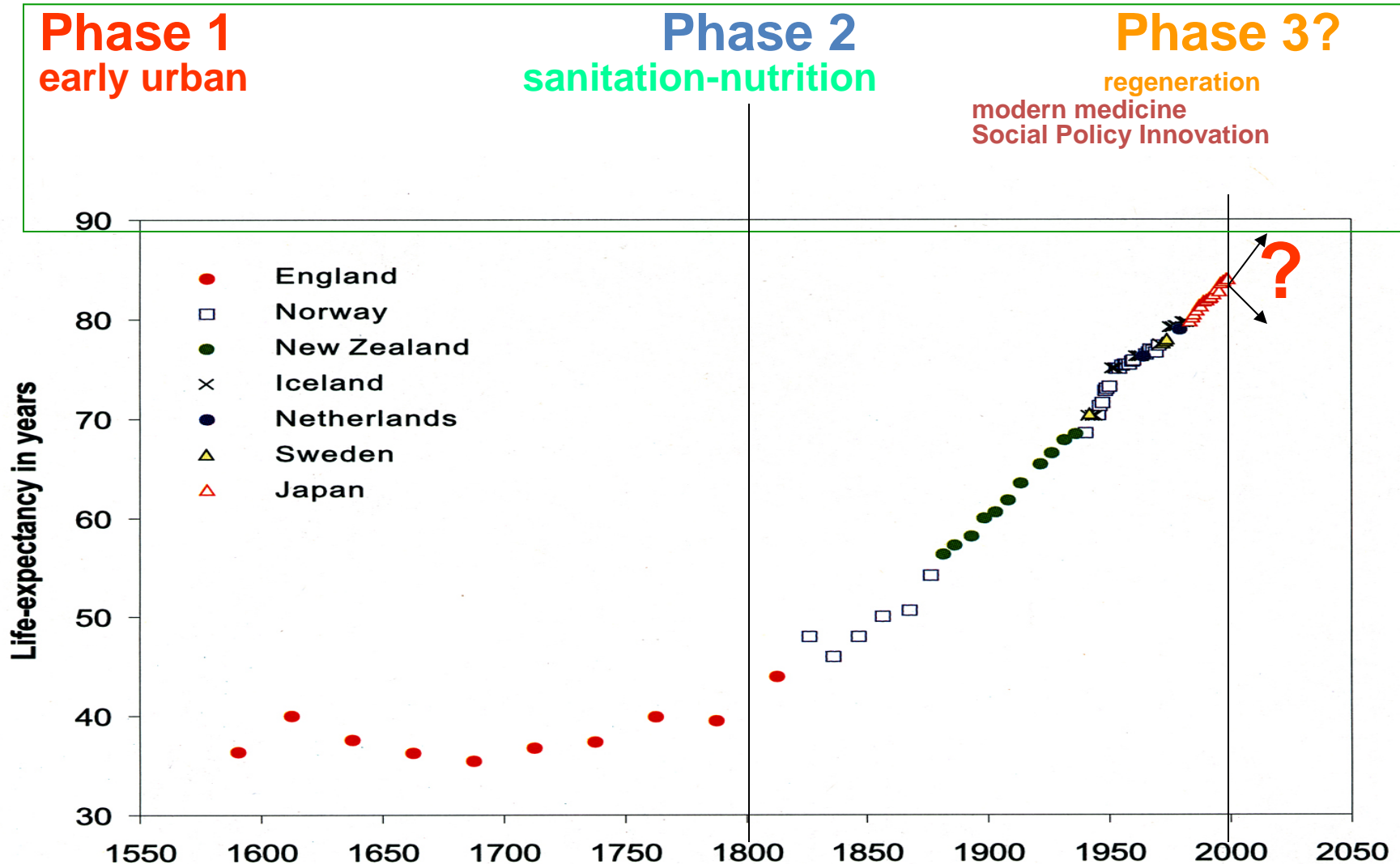


Evidence suggests otherwise

- 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

Oepen and Vaupel, Science 2002; C Finch adaptation



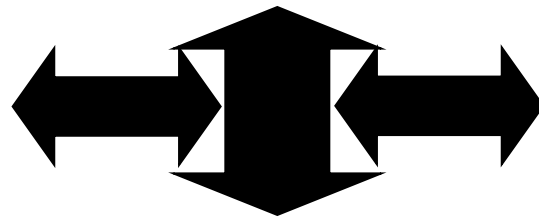
Demographic Futures

- 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 4

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

Genetic Heritability of Human Lifespan

Cournil & Kirkwood *Trends in Genetics* 2001

Twin Studies

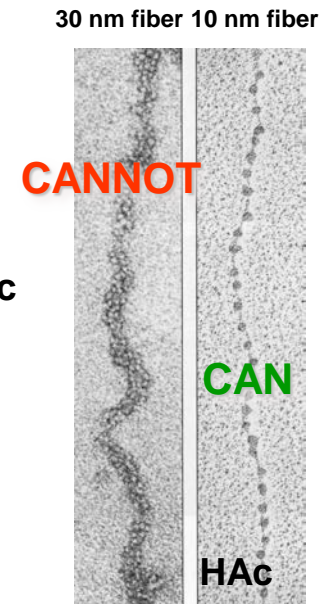
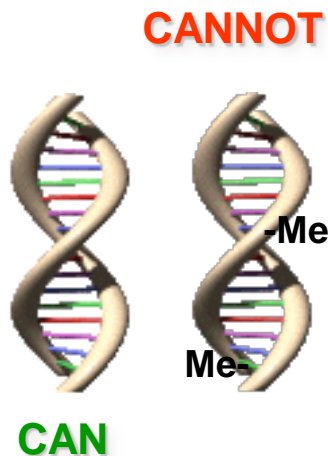
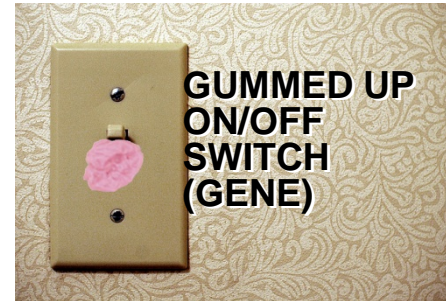
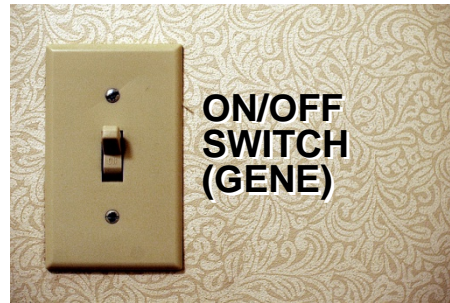
- McGue et al (1993) 0.22
- Herskind et al (1996) 0.25
- Ljungquist et al (1998) <0.33

Traditional Family Studies

- Philippe (1978) 0-0.24
- Bocquet-Appel & Jakobi (1990) 0.10-0.30
- Mayer (1990) 0.10-0.33
- Gavrilova et al (1998) 0.18-0.58
- Cournil et al (2000) 0.27

Genes account for 25% of what determines disease and longevity

EPIGENETICS



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)

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

Inflammation

Aging

Epigenetics



infections

Health & Social Services Utilization

Time (Longitudinal Study)



Canadian Longitudinal Study on Aging
Étude longitudinale canadienne sur le vieillissement

Genetics



The Canadian Longitudinal Study on Aging (CLSA)

- ▶ A key strategic initiative of CIHR
 - ▶ The Canadian Longitudinal Study on Aging
- ▶ More than 160 researchers - 26 institutions
- ▶ Multidisciplinary - biology, genetics, medicine, psychology, sociology, demography, economics, epidemiology, nursing, nutrition, health services, biostatistics, population health



Canadian Longitudinal Study on Aging (CLSA)

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.



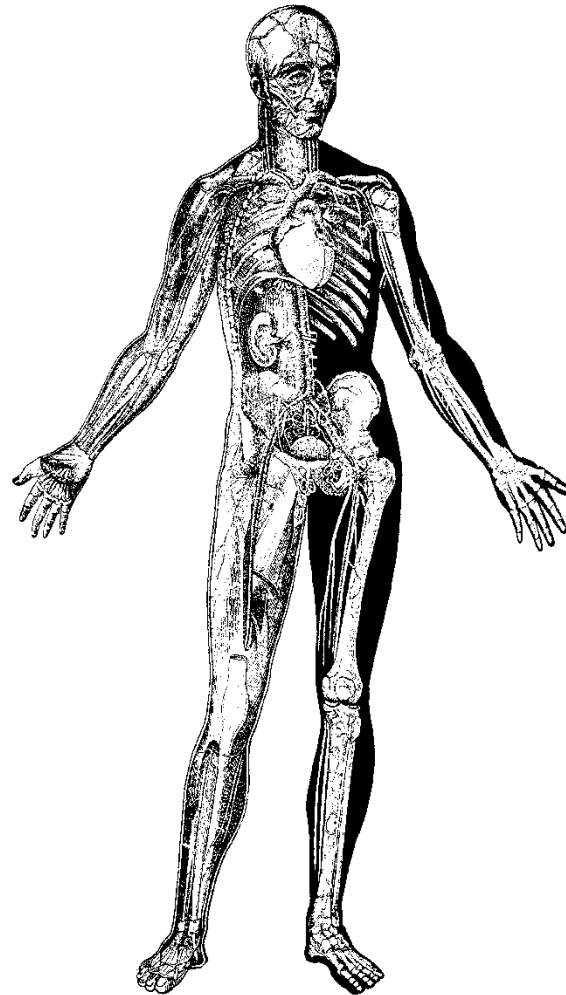
Our Aim

To study aging as a dynamic process and the inter-relationship among intrinsic and extrinsic factors from mid-life to older age.





Innovation - Cell to Society

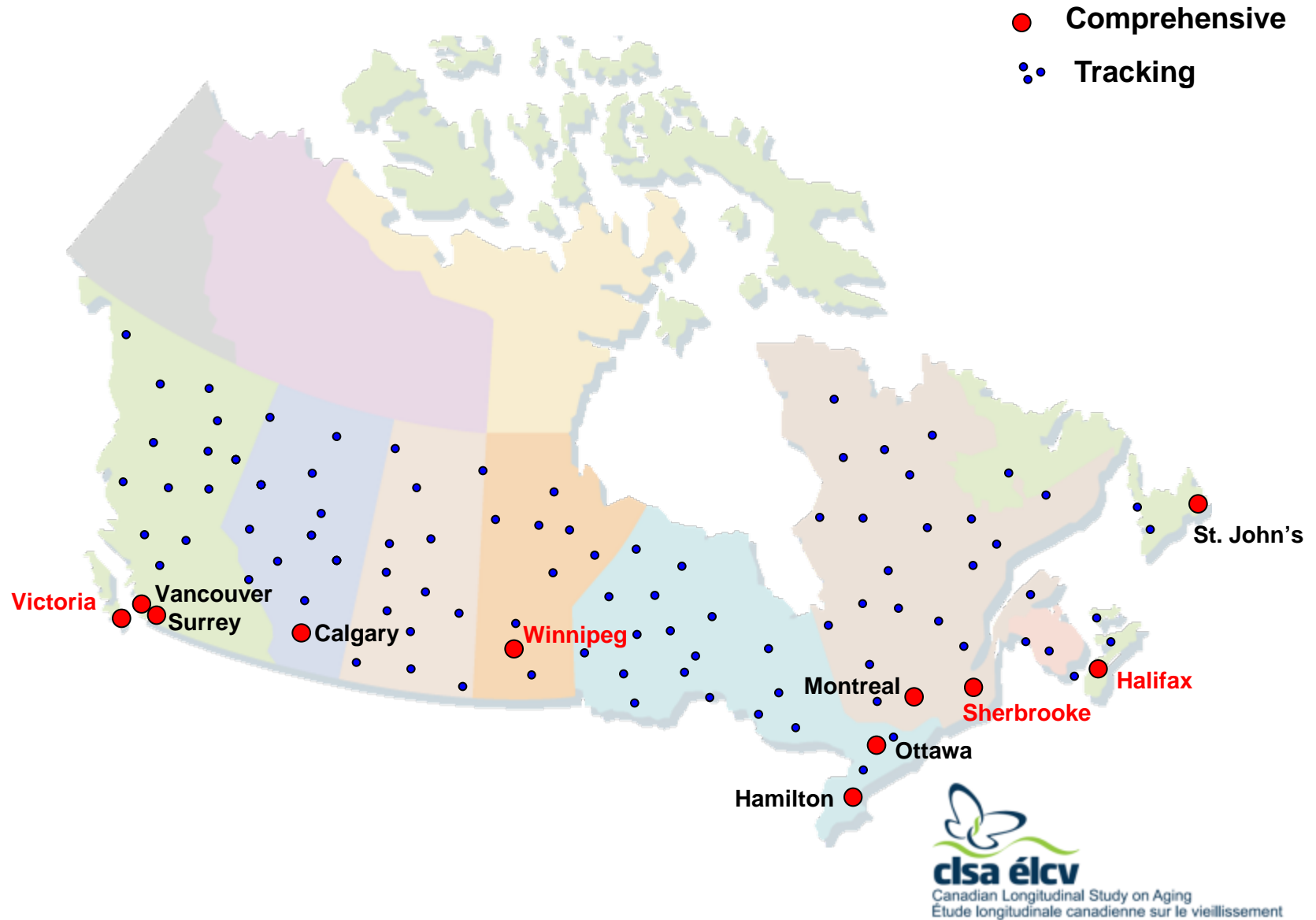


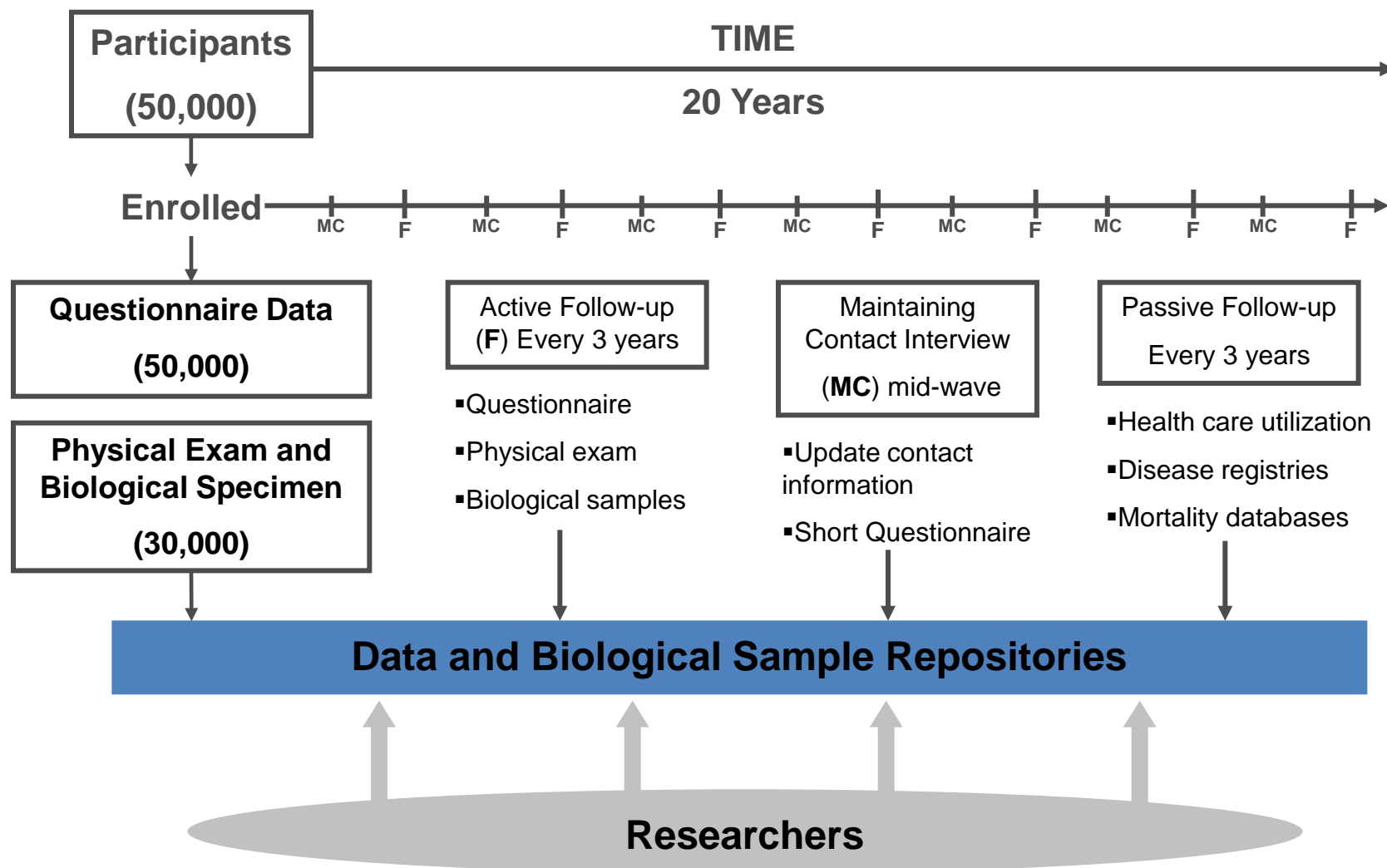
- ▶ Mid life to old age
- ▶ Quantitative traits
 - ▶ Physical
 - ▶ Social
 - ▶ Psychological
- ▶ Gene-environment interactions
- ▶ Disease, disability, psychosocial consequences
- ▶ Adaptation

Overall Aims of the CLSA

- The progression of **health** from middle-age to early old age to older old age
- The determinants of **well-being and quality of life**
- Risk Factors (including genetics) of **Chronic diseases**
- **Cognitive functioning** and **mental health**
- **Disability** and the compression of morbidity
- The examination of socioeconomic and health **inequalities** in an aging population
- **Social participation, social relationships and care giving** in an aging population
- **Retirement** and **post retirement** labor market activity

Participant Recruitment





Depth and Breadth of CLSA

PHYSICAL & COGNITIVE MEASUREMENTS

- Height & weight
- Waist and hip measurements
- Blood Pressure
- Grip strength, timed up-and-go, chair raise, 4-m walk
Standing balance
- Vision (retinal imaging, Tonometer & visual acuity)
- Hearing (audiometer)
- Spirometry
- Body composition (DEXA)
- Bone density (DEXA)
- Aortic calcification (DEXA)
- ECG
- Carotid Plaque sweep (ultrasound)
- Carotid intima-media thickness (ultrasound)
- Cognitive assessment (30 min. battery)

HEALTH INFORMATION

- Chronic disease symptoms (**disease algorithm**)
- Medication and supplements intake
- Women's health
- Self-reported health service use
- Oral health
- Preventative health
- **Administrative data linkage health services & drugs & other administrative databases**

PSYCHOSOCIAL

- Social participation
- Social networks and support
- Caregiving and care receiving
- Mood, psychological distress
- PTSD
- Coping, adaptation
- Injuries and consumer products
- Work-to-retirement transitions
- Retirement planning
- Social inequalities
- Mobility-lifespace
- Built environments & Contextual Factors
- Income, Wealth and Assets

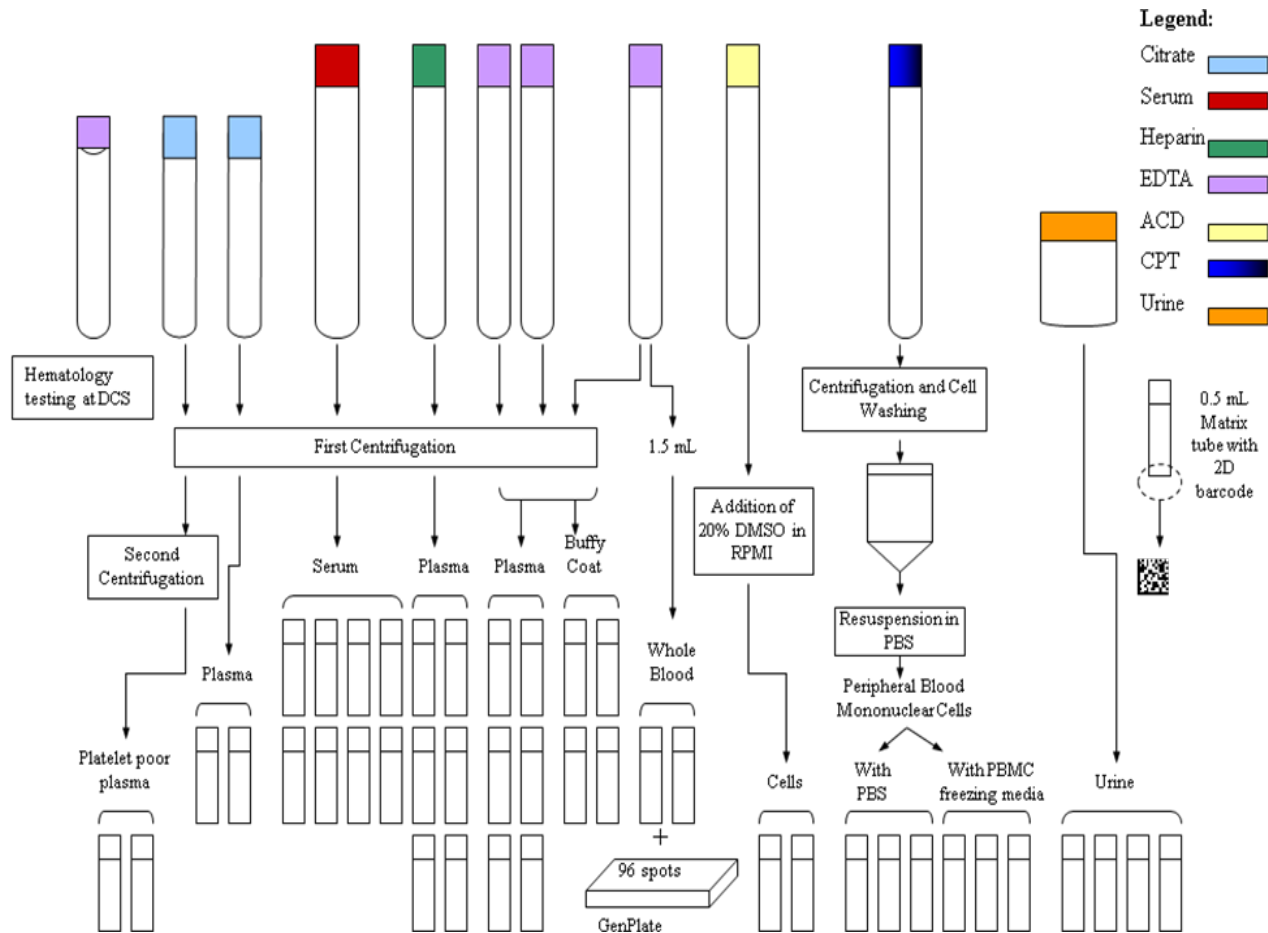
LIFESTYLE & SOCIODEMOGRAPHIC

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



Canadian Longitudinal Study on Aging
Étude longitudinale canadienne sur le vieillissement

Bio specimens
42 aliquots per participant







CLSA Infrastructure

- National Coordinating Centre (McMaster)
- Biorepository and Bioanalysis Centre (McMaster)
- IT Infrastructure (McMaster)
- Statistical Analysis Centre (McGill)
- Genetics and Epigenetics Centre (UBC)
- 4 Computer-Assisted Telephone Interview Sites
 - Victoria, Winnipeg, Sherbrooke and Halifax
- 11 Data Collection Sites
 - Victoria, Vancouver, Surrey, Calgary, Winnipeg, Hamilton/Toronto, Ottawa, Montreal, Sherbrooke, Halifax and St.John's

Biorepository and Bioanalysis Centre (BBC)

HAMILTON

Biorepository

- § 31 nitrogen tanks (5 million aliquots)
- § Autofilled from a bulk nitrogen tank
- § Cryocarts
- § Personal Archive, dry storage at room temperature (humidity controlled)
- § LIMS (LabWare)
- § CryoMORE, (Air Liquide) safety monitoring system



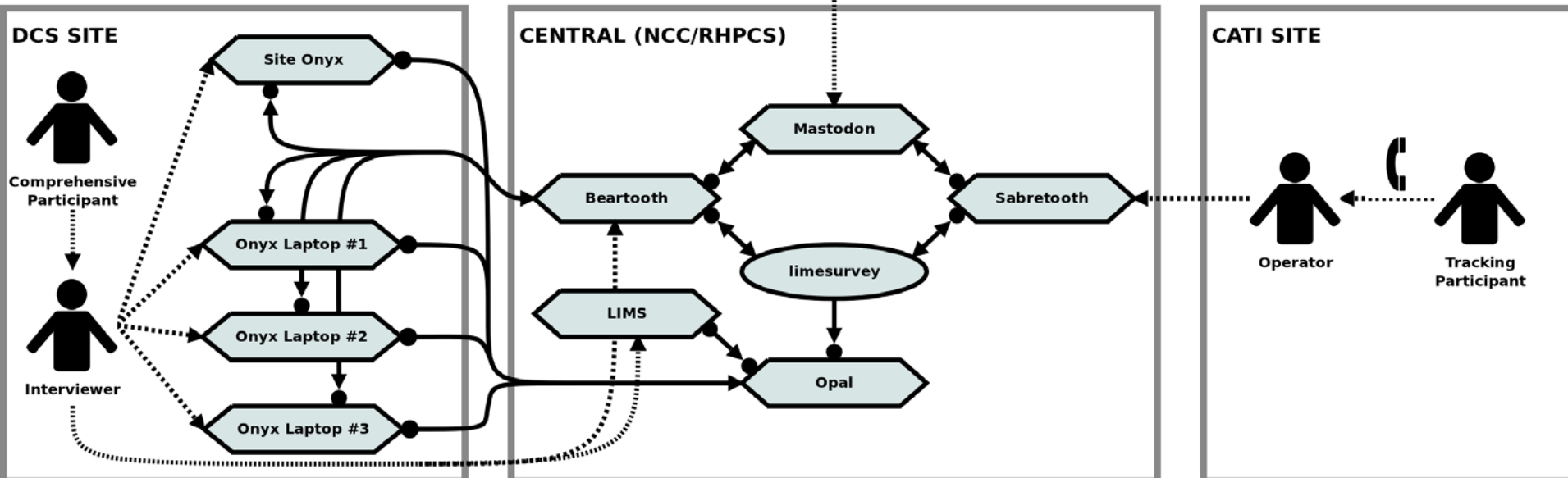
FUTURE

ASKION C-line®
work bench



A →● B Data flows by B pulling from A
 A ●→ B Data flows by A pushing to B
 A→ B Data flows by A providing information to B

 Web service (server)
 Application (non-server)



Sampling and Subject Selection

CLSA collaborated with Statistics Canada to develop Sampling Strategy

- Target population: People aged 45-85 living in private occupied dwellings in the ten provinces
- Excluded:
 - Residents of the three territories
 - Persons living on Indian reserves or Crown lands
 - Persons living in institutions
 - Full-time members of the Canadian Forces
 - Residents of some remote regions

Sampling

- Choose representative sample of eligible Canadians
 - 20K Tracking cohort; 30K Comprehensive cohort
 - Specified numbers in age-sex groups by province
- Options for methods of selection:
 - Statistics Canada
 - Using provincial health registries
 - Random digit dialing
- In Alberta and maybe BC, it appears we cannot use registries

Tracking Cohort of the CLSA (n=20,000)

Baseline Recruitment and Data Collection

- First selection of 20,000 started in late 2011
 - Pre-recruits via Stats. Can, RPDB and RDD~33,000
 - Completed 60 minute questionnaire by telephone on over 13,000 individuals
 - Plan to complete tracking by the end of January 2013
- Mid 2013 we will begin our maintaining contact interviews (30 minute telephone interview)
 - Minimize loss to follow-up
 - Collect additional data

Comprehensive Cohort of the CLSA (n=30,000)

Implementation Plan for the Comprehensive Cohort (n=30,000)

- ❖ Cohort of 30,000 persons to be recruited within 25 to 50 km radius of 11 data collection sites (DCS)
 - Victoria (3000), Vancouver (1500), Burnaby (1500), Calgary (3000), Winnipeg (3000), Hamilton (3000), Ottawa (3000), Montreal (3000), Sherbrooke (3000), Halifax (3000), St. John's (3000)

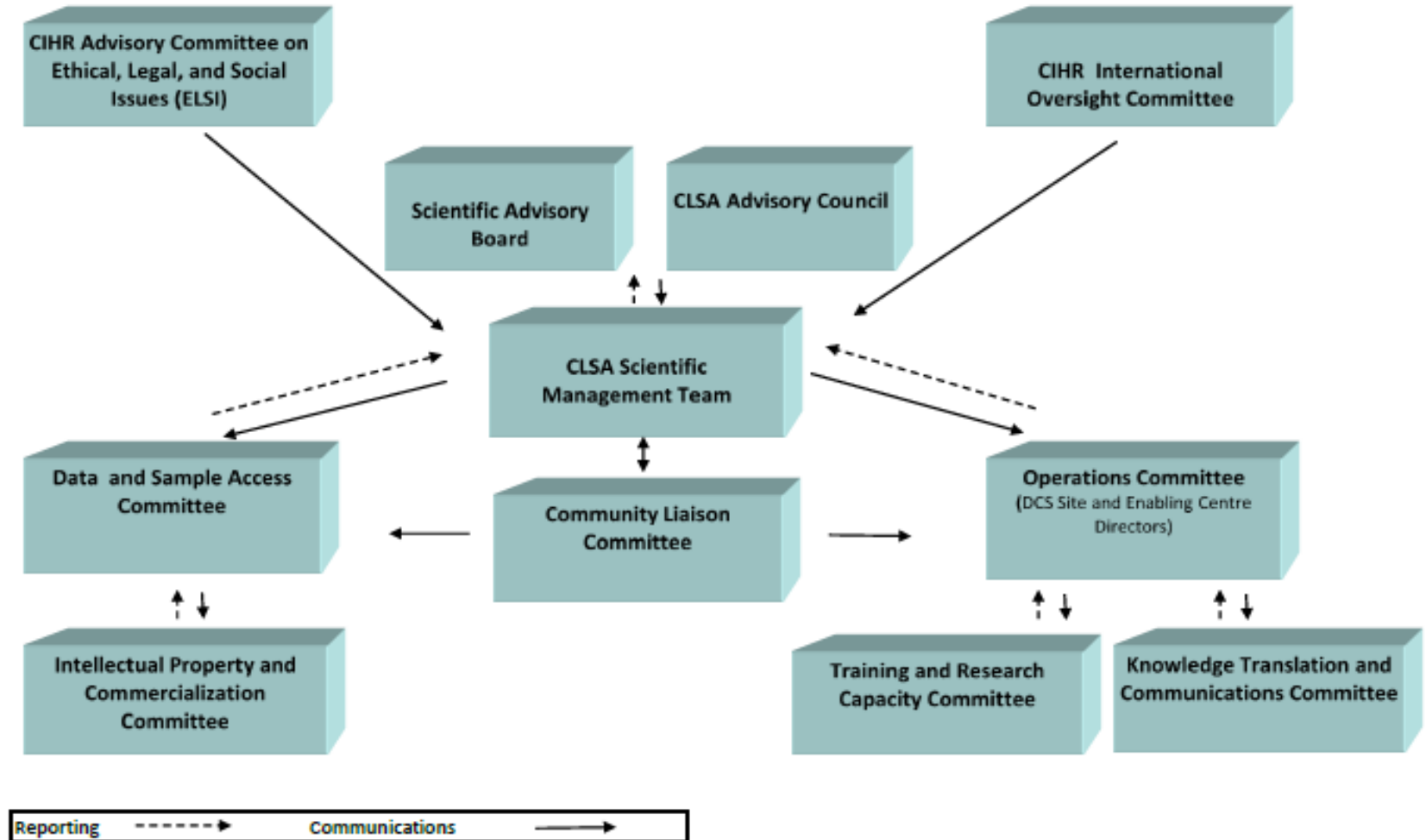
Comprehensive Cohort Rolling Recruitment

- ❖ First batch of 1000 people to be recruited/site (mid-2012 to mid-2013)
 - ❖ Pre-recruits via RPDB and RDD~11,000
 - ❖ We have completed home interviews on 3500 individuals and DCS visit on over 2500 individuals
 - ❖ Maintaining contact by phone (end of 2013- end 2014)
- ❖ Second batch of 1000 people to be recruited/site (mid-2013 to mid-2014)
 - ❖ Maintaining contact: (end of 2014-end of 2015)
- ❖ Third batch of 1000 people to be recruited/site (mid-2014 to mid 2015)
 - ❖ Maintaining contact: (end of 2015-end of 2016)

Data and Sample Access

- Data and Sample Access is Open
 - All researchers have access to data
 - No special access to the “creators” of the platform
 - Individual level data versus aggregate data
 - Genetic versus Health (Depression) versus Social data
- Ethical and Legal Considerations
 - How the data are used and what purpose?
 - Public sector versus Private sector access to data

CLSA Governance Structure



Use of the CLSA Platform: Examples





CLSA Program of Research on Bone Health

Objectives

- Theme 1:
 - What are the rare genetic variants associated with osteoporotic fracture?
 - How do such variants influence of risk of fracture?
 - Do such variants improve our ability to identify individuals at risk of fracture?
 - Require large sample sizes
 - Harmonization with other studies across the world

Objectives Contd..

- Theme 2:
 - How can osteoporosis and sarcopenia be defined for Canadian men and women using imaging, functional and clinical risk data?
 - Can measures combining volumetric bone density, muscle area, and muscle adiposity improve our ability to identify individuals at risk of fracture?
 - What are the longitudinal associations between loss of muscle mass, loss of muscle strength and loss of physical function by fracture types and gender?
 - Using techniques such as Peripheral Quantitative CT and MRI

Canadian Longitudinal Study on Aging (CLSA) Mobility Initiative-An Emerging Team in Mobility in Aging

CIHR Funded (investigator Initiated)

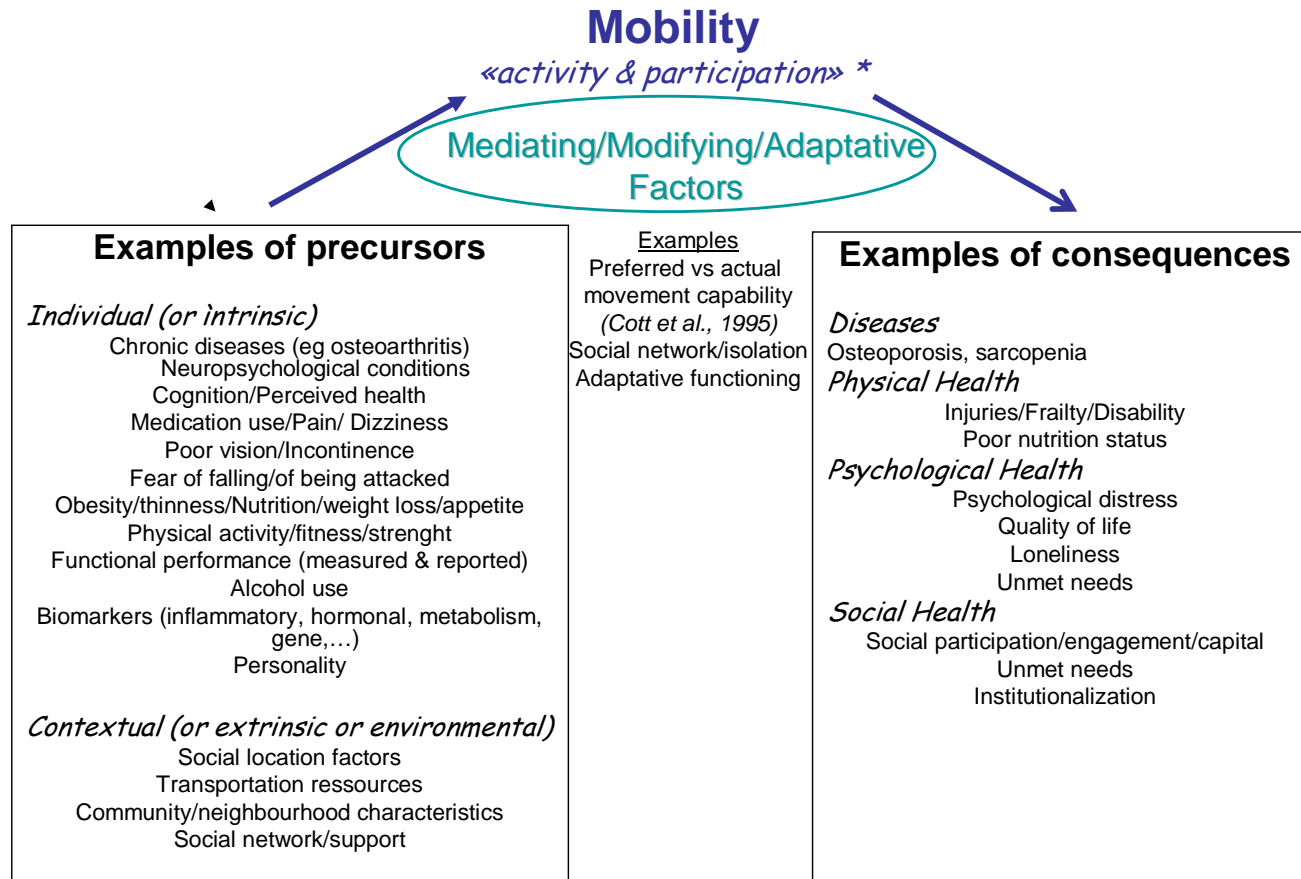


Canadian Longitudinal Study on Aging
Étude longitudinale canadienne sur le vieillissement

CLSA-MI Objectives

- Design a comprehensive assessment of mobility to be implemented as part of the CLSA cohort;
- Engage an inter-disciplinary team of researchers and decision-makers to focus and implement research on mobility in aging;
- Serve as a platform for researchers to advance knowledge in the field of mobility and aging
- Provide training opportunities in an interdisciplinary research focussed on mobility and aging;
- Implement knowledge translation and dissemination strategies

CLSA-MI Theoretical Framework



* Mobility is to be measured by the Life-Space Assessment questionnaire (Baker et al, 2003; Allman et al., 2004)

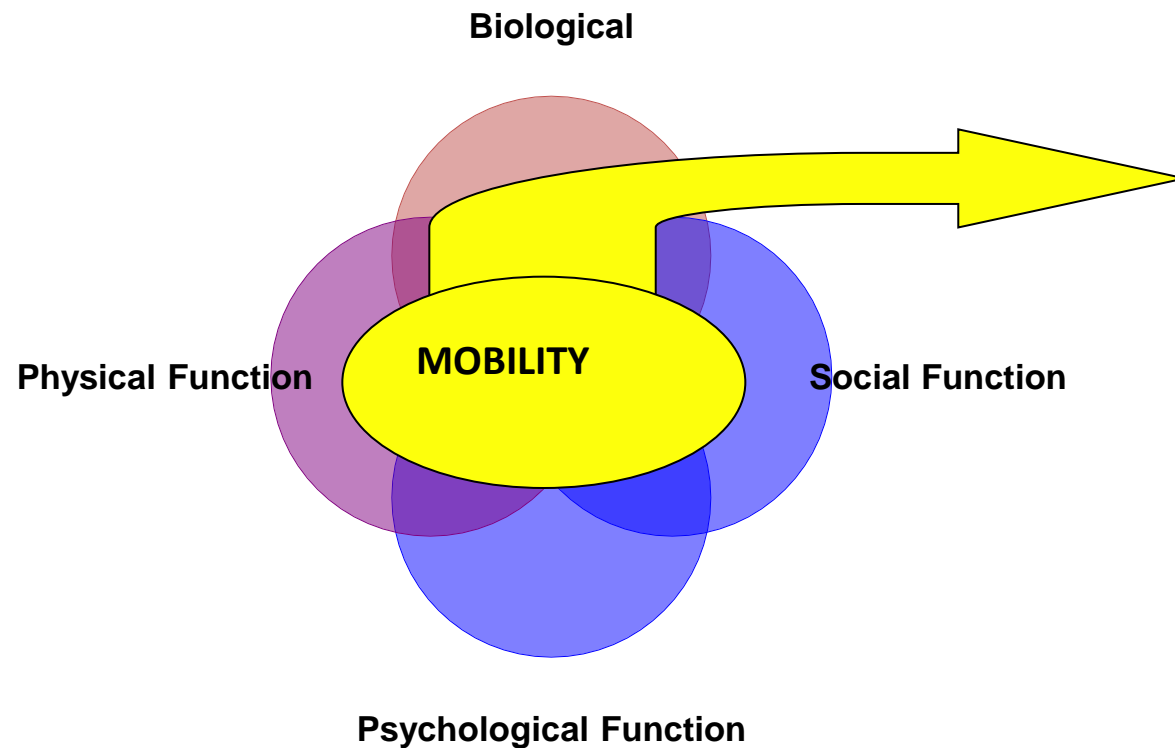
CLSA-MI – An Embedded Study

Measures in CLSA Core

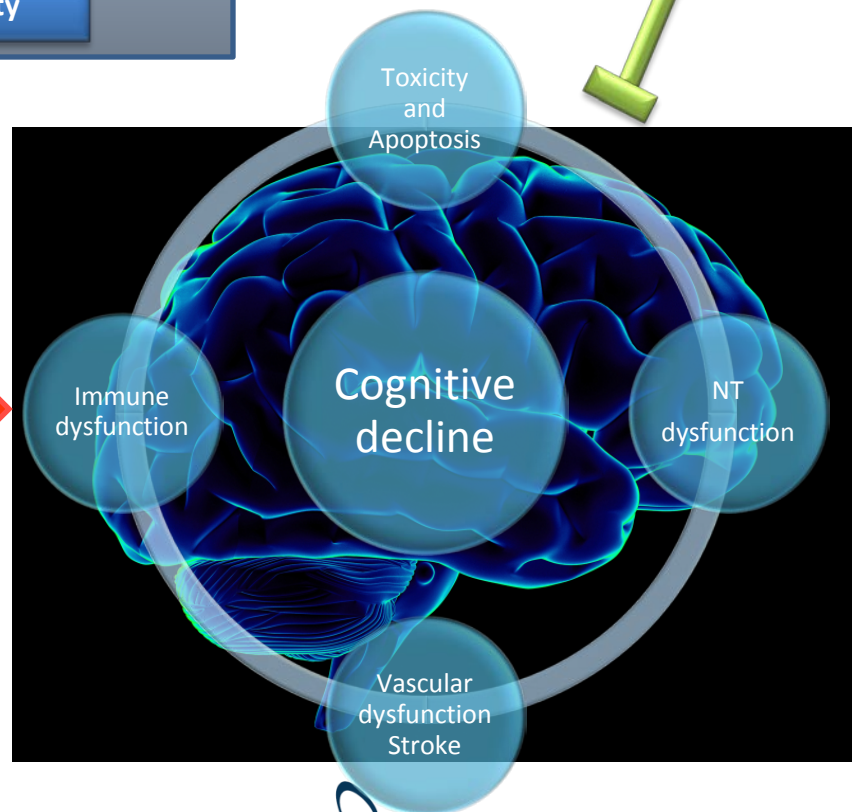
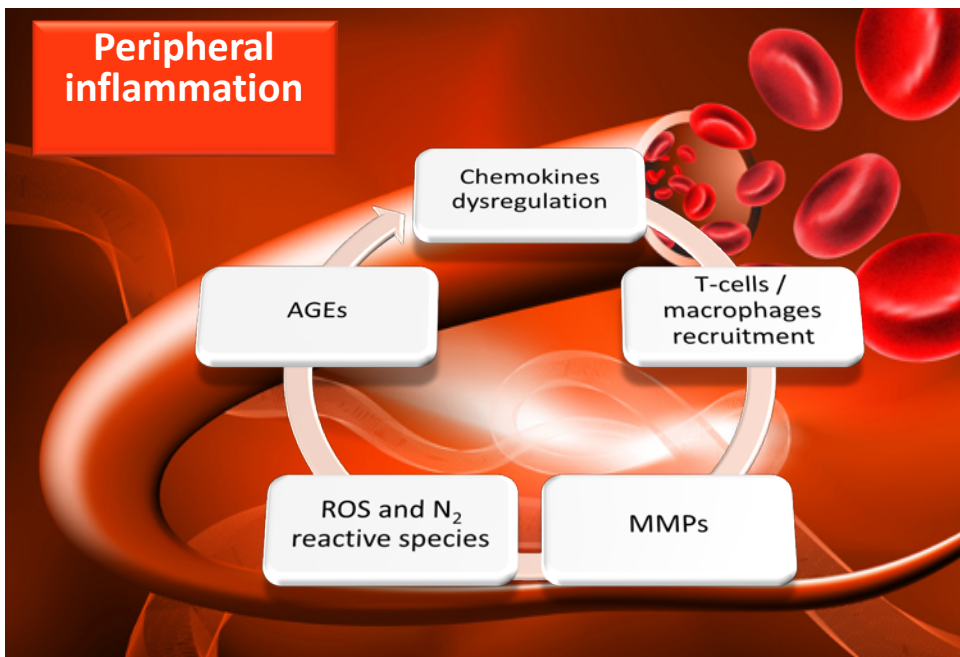
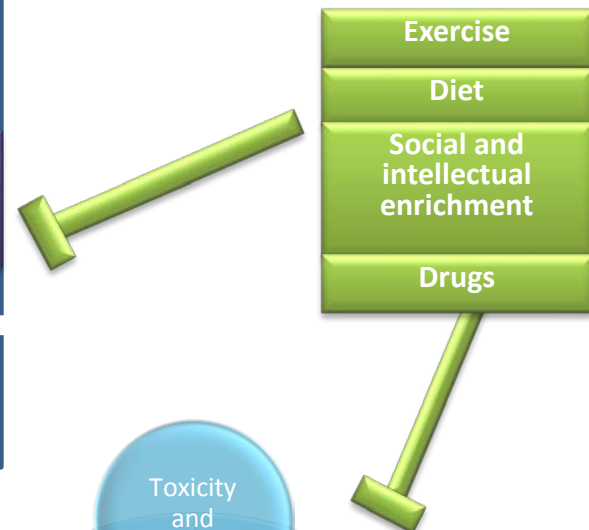
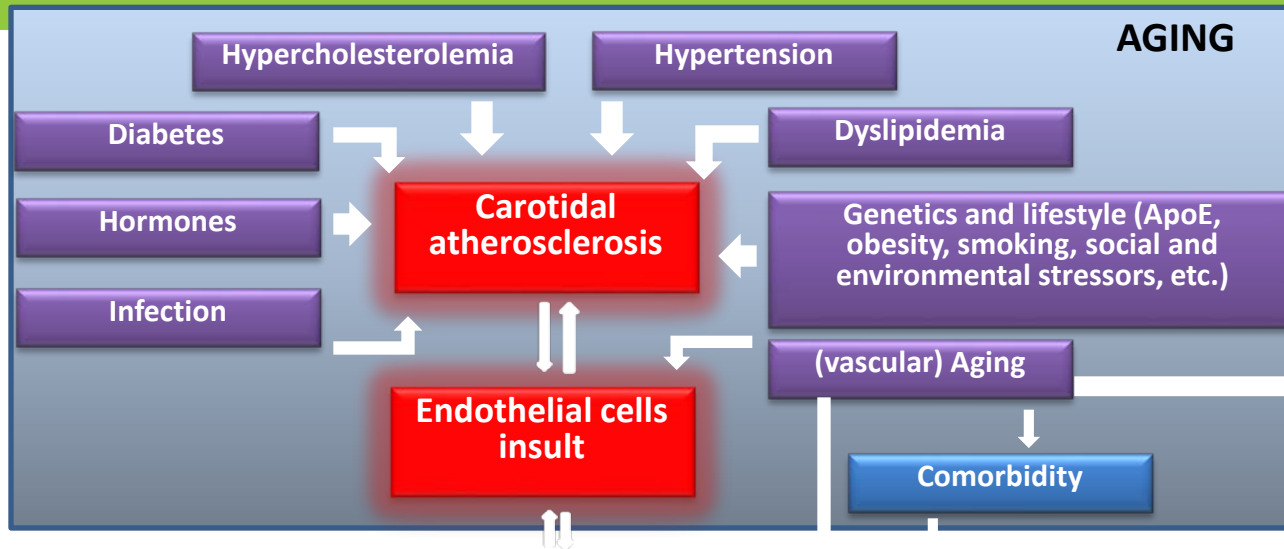
- Grip Strength
- 4 Meter Walk
- Functional Status
- ADL and IADL

Measures added by CLSA-MI

- Chair Stand
- Unipodal Standing
- TUG
- Life Space Assessment
- Transportation
- Built Environment



Environment and Biological Processes of Chronic Inflammation: Link between Vascular Aging and Brain Health



Data harmonization Platform

Building a Global Network of Harmonized
Cohorts



Canadian Longitudinal Study on Aging
Étude longitudinale canadienne sur le vieillissement

Prospective Harmonization

Harmonization achieved **before**
the initiation of data collection

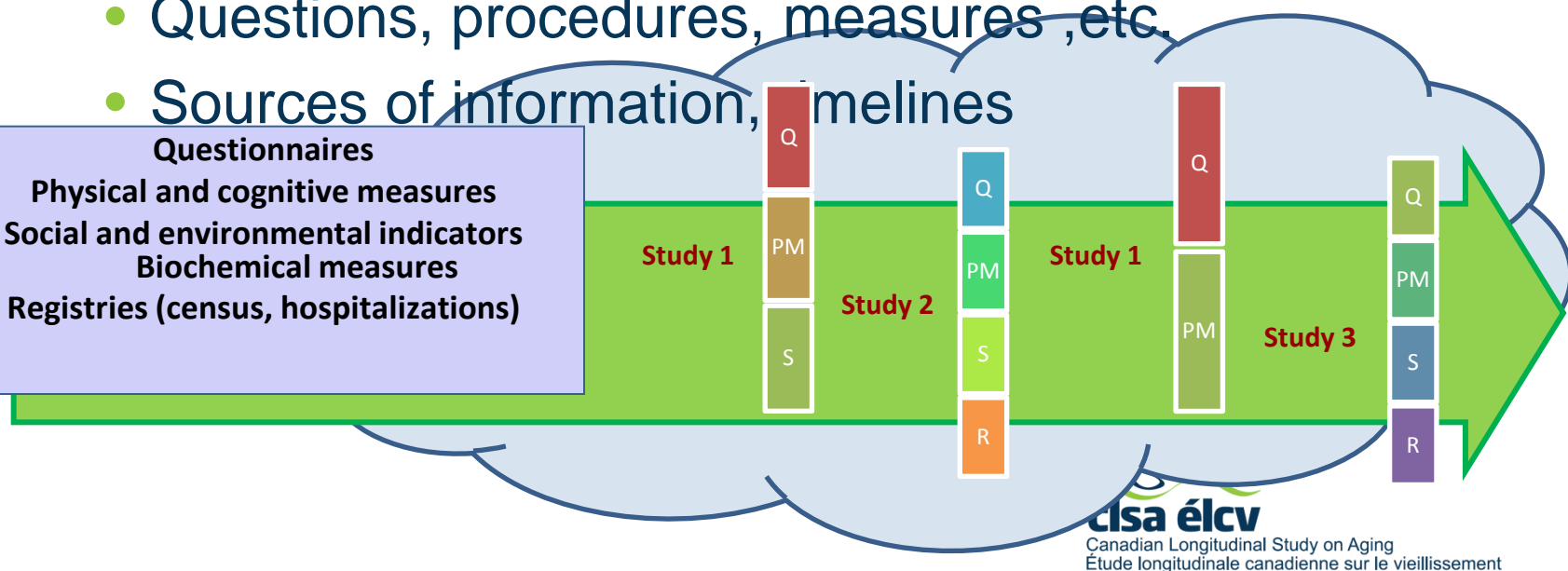
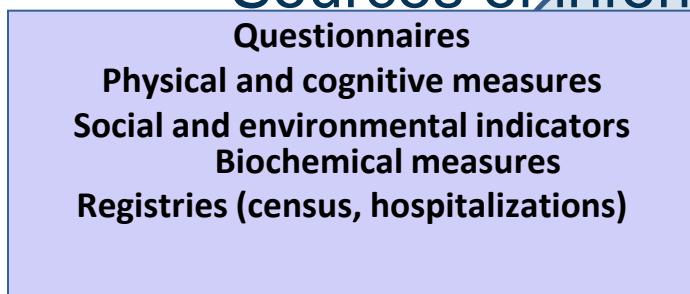
- Stringent or input harmonization
 - Same questions, same protocols, same measures: One common set of procedures
- Flexible or ex-ante output harmonization
 - Common set of target variables, but with a certain level of flexibility in the specific questions, protocols, measures, etc. **However, inferential equivalency must be ensured!**



Retrospective Harmonization

Harmonization making use of **existing** data

- Flexible or ex-post harmonization
 - Various...
 - Designs of studies
 - Questions, procedures, measures, etc.
 - Sources of information, timelines



To generate knowledge we need:



Quality



Range of information
Number of participants

YERİ
TARİHİ
OLCU
ALETLERİ
KESME
SIVILARI
ÇİC
KATKİLERİ
SERT
MADEN
UÇLARI
SERT
MADEN

Quantity



Usage

Global Landscape

Infrastructure

Tools

Research

Studies
(data and
bio-samples)

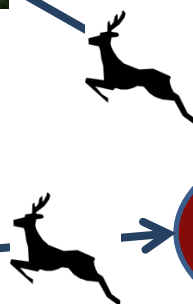
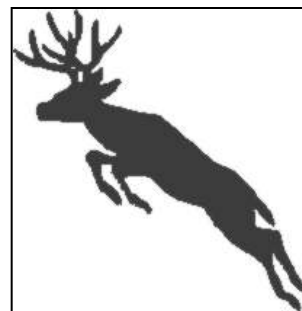
**Methods, software and
expertise supporting
harmonization and synthesis
of information in different
research areas**

**New
scientific
knowledge**



LifeLines



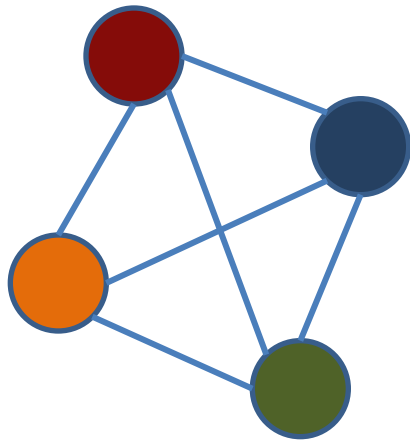


Need to generate compatible data!

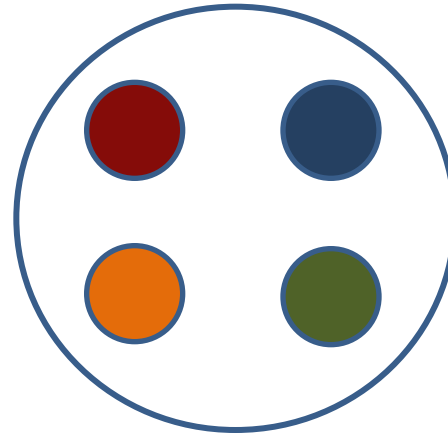


Thanks to Patricia Martens
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Identify variables and evaluate harmonization potential

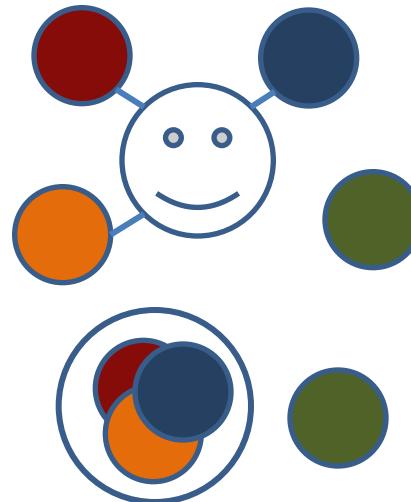


Multiple variables



**Generic variable
allowing to combine
the largest number
of studies**

**Variable selected based on its:
(1) Scientific relevance and
(2) Harmonization potential**



Pairing algorithms

Statistical models

clsa élcw

Canadian Longitudinal Study on Aging
Étude longitudinale canadienne sur le vieillissement

CLSA CORE TEAM

Lead PI	Parminder Raina (McMaster)
CO-PI	Christina Wolfson (McGill) and Susan Kirkland (Dalhousie)
Key Senior Co-Investigators	Gerry Mugford, Patrick Parfrey (Memorial), Helene Payette (Sherbrooke), Ron Postuma (McGill), Vanessa Taller, Larry Chambers (Ottawa), Harry Shannon, Cynthia Balion, Christopher Patterson, Lauren Griffith and Mark Oremus (McMaster), Mary Thompson and Chang Bo (Waterloo), Deb Sheets, Lynne young, Holly Tuokko, (Victoria), Verena Menec (Manitoba), David Hogan and Marc Poulin (Calgary), Max Cynader, Michael Hayden and Michael Kobor (UBC) and Andrew Wister, Scott Lear (SFU)
Scientific Working Group	See our website – www.clsa-elcv.ca



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CLSA funded by the Government of Canada through CIHR and CFI, and provincial governments and universities

www.clsa-elcv.ca

