Transforming Everyday Life into Extraordinary Ideas

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Canadian Longitudinal Study on Aging
Étude longitudinale canadienne sur le vieillissement

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

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Lyon, France November 6th, 2012

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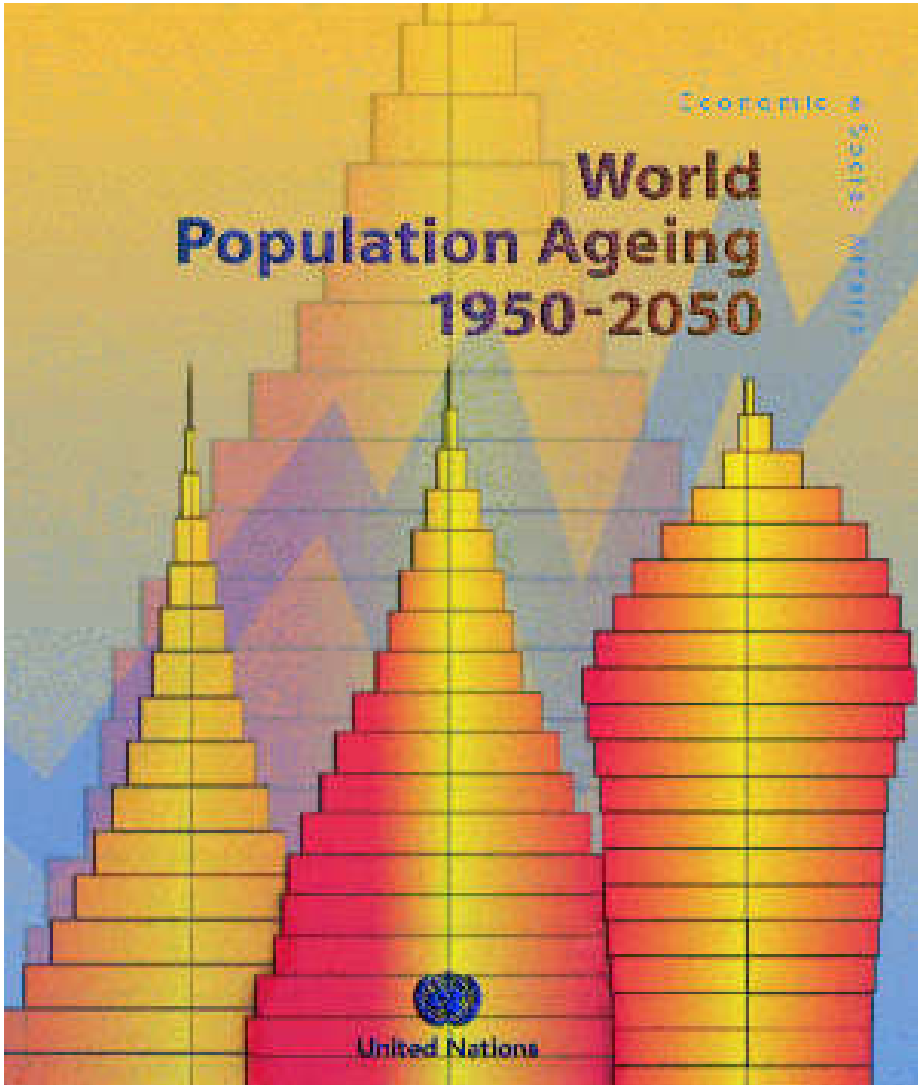
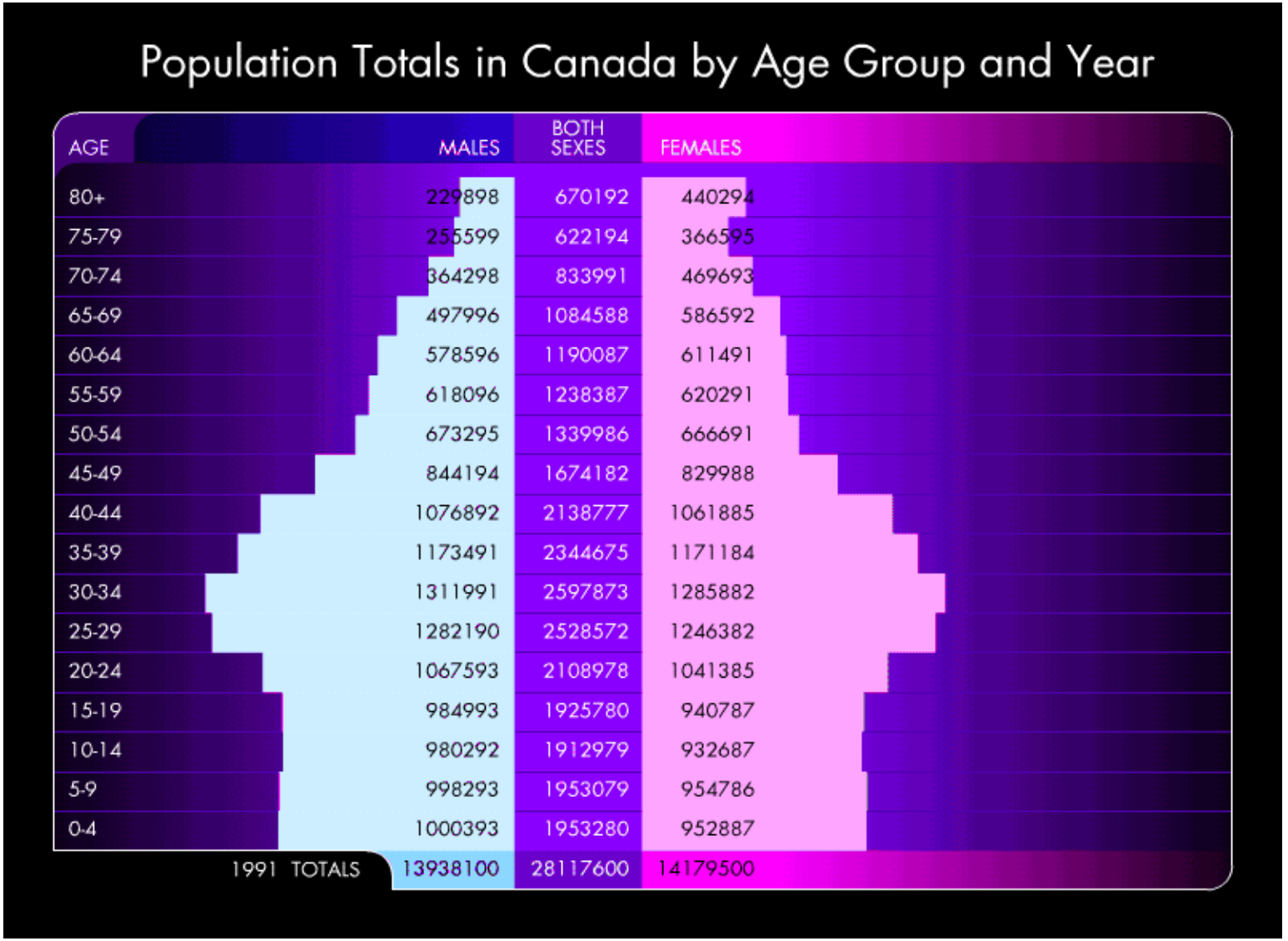
Population aging

- 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

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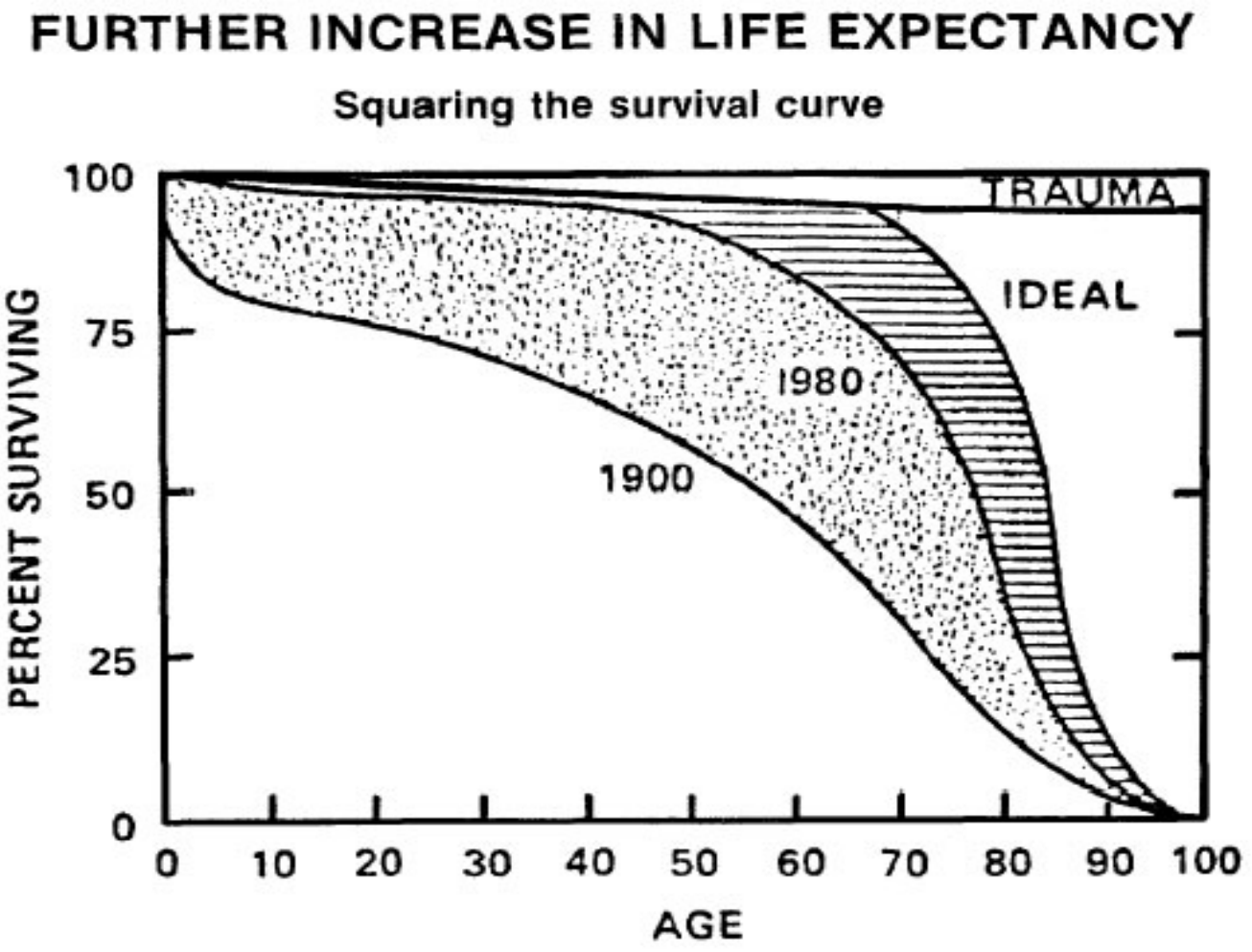
Rectangularization of the survival curve



JAMES F. FRIES, M.D., THE NEW ENGLAND JOURNAL OF MEDICINE, JULY 17, 1980.

Compression of morbidity

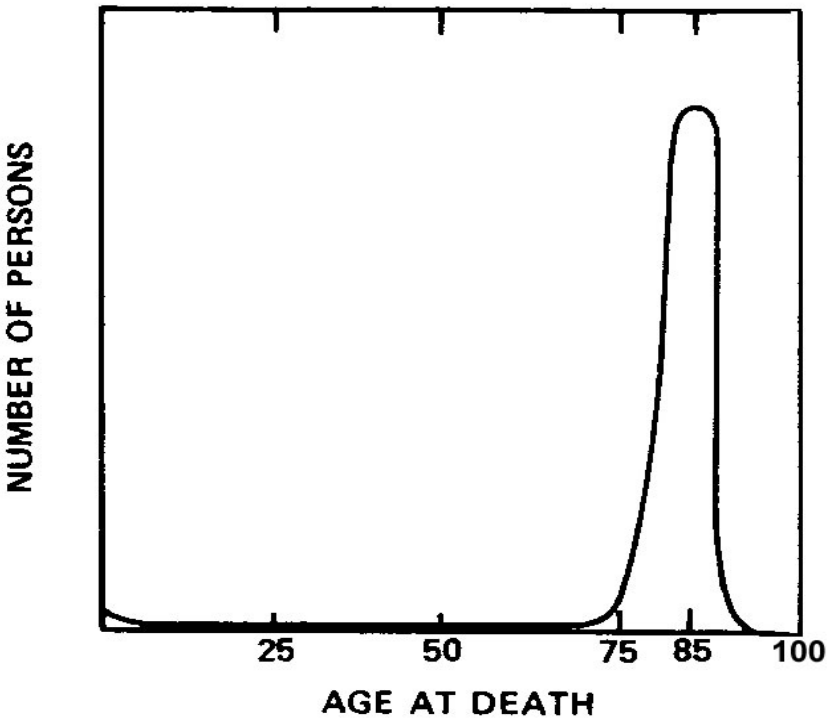


Figure: Mortality According to Age in the Absense of Premature Death

- 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

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Compression of morbidity

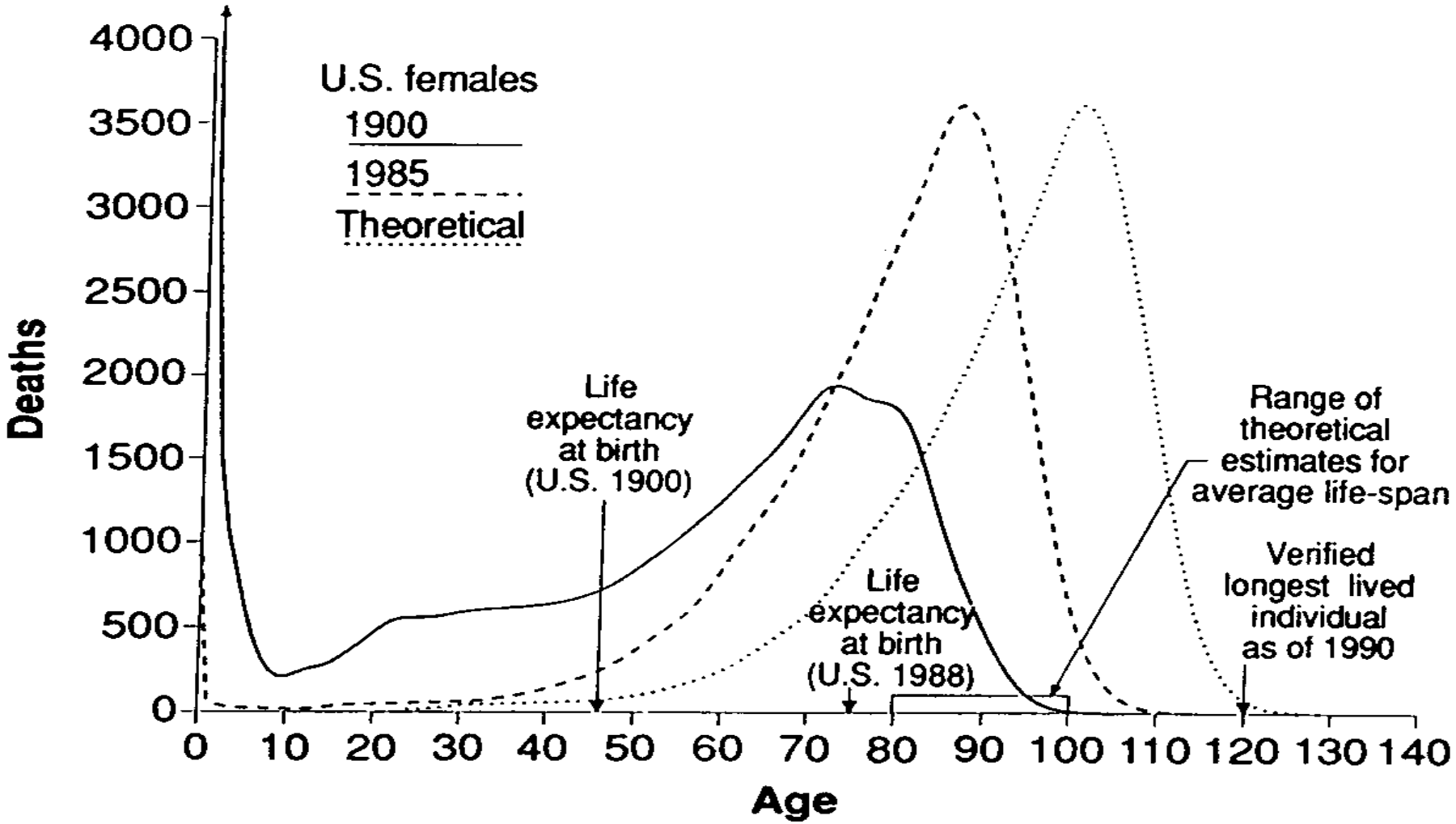
Fries' paradigm based on the premise that:

- 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

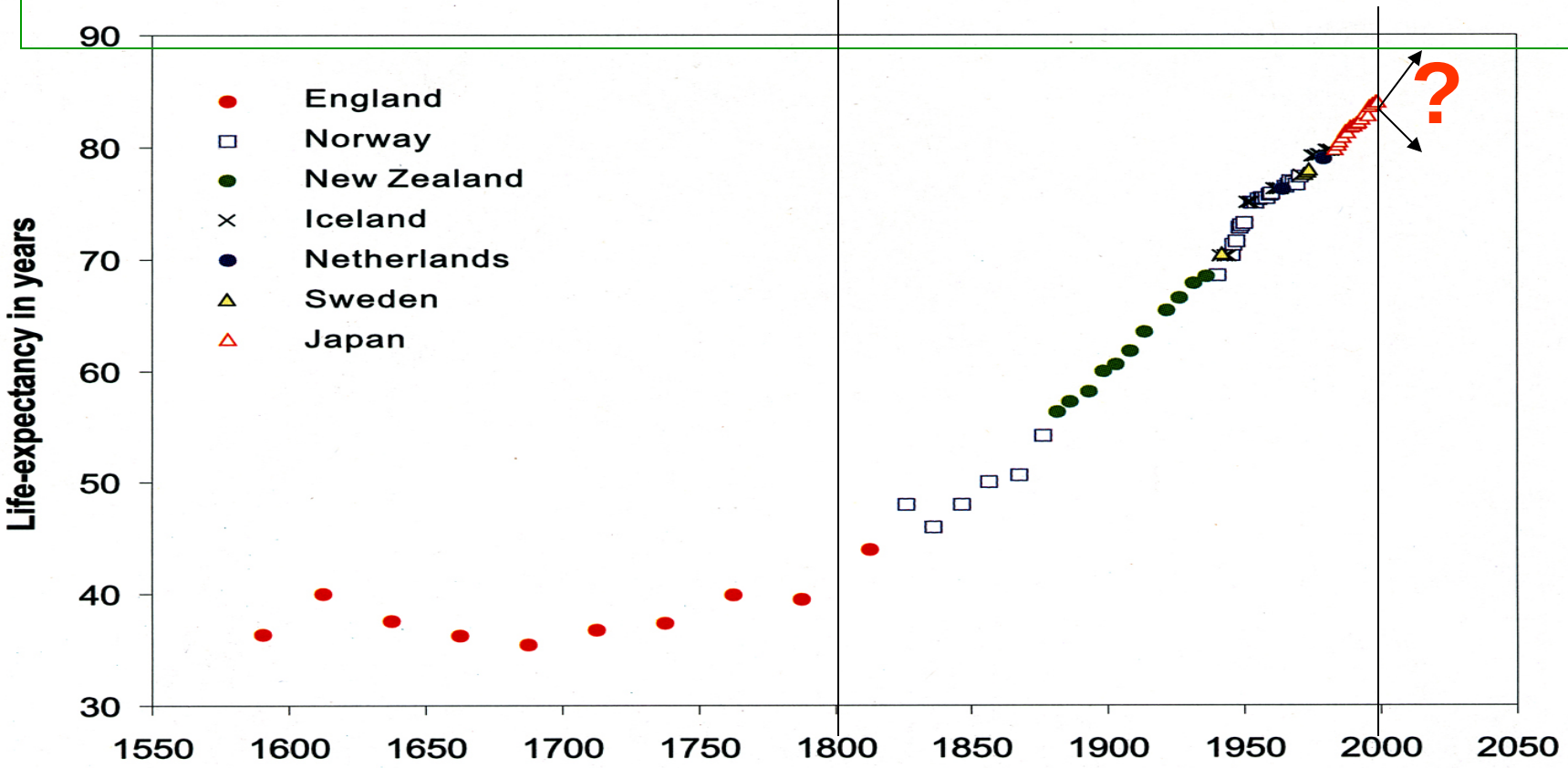
Historical increases of life expectancy

Oepen and Vaupel, Science 2002; C Finch adaptation

Phase 1
early urban

Phase 2
sanitation-nutrition

Phase 3?
regeneration
modern medicine
Social Policy Innovation



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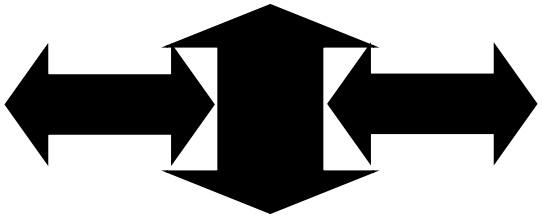
Demographic Futures

- 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

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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	Histocompatability 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-methylenetetra-hydrofolate 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

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Non-Biological/Medical Determinants of Aging?

- Nutrition
- Lifestyle
- Environment
  - Physical
  - Social
  - Economic
  - Work Place
  - Psychological
- Chance

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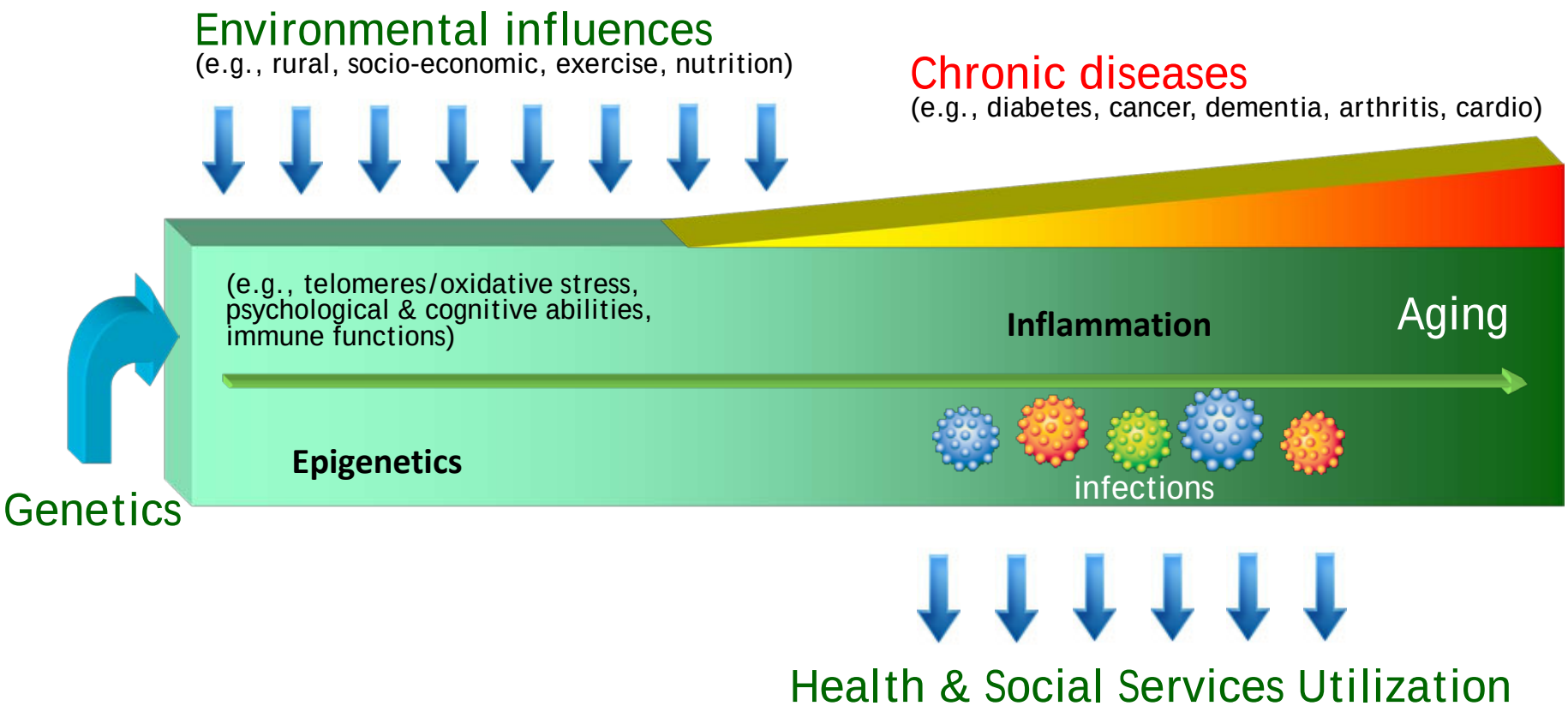
Intrinsic and Extrinsic Factors



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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

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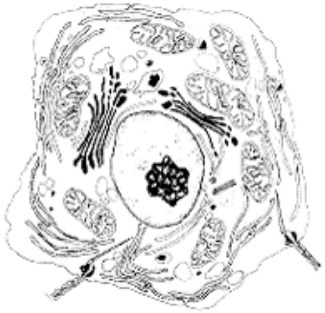
Canadian Longitudinal Study on Aging (CLSA)

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.

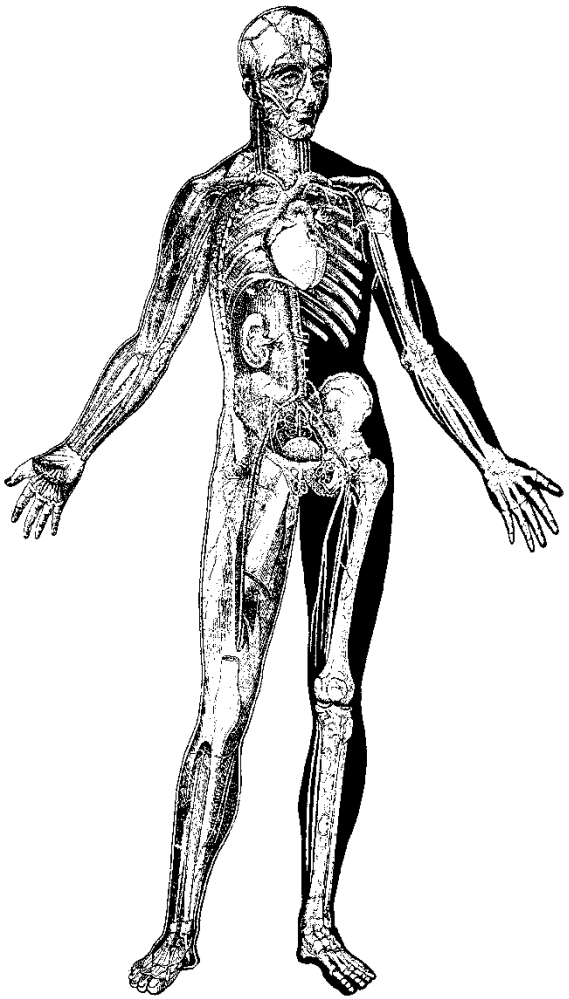
Our Aim

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



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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

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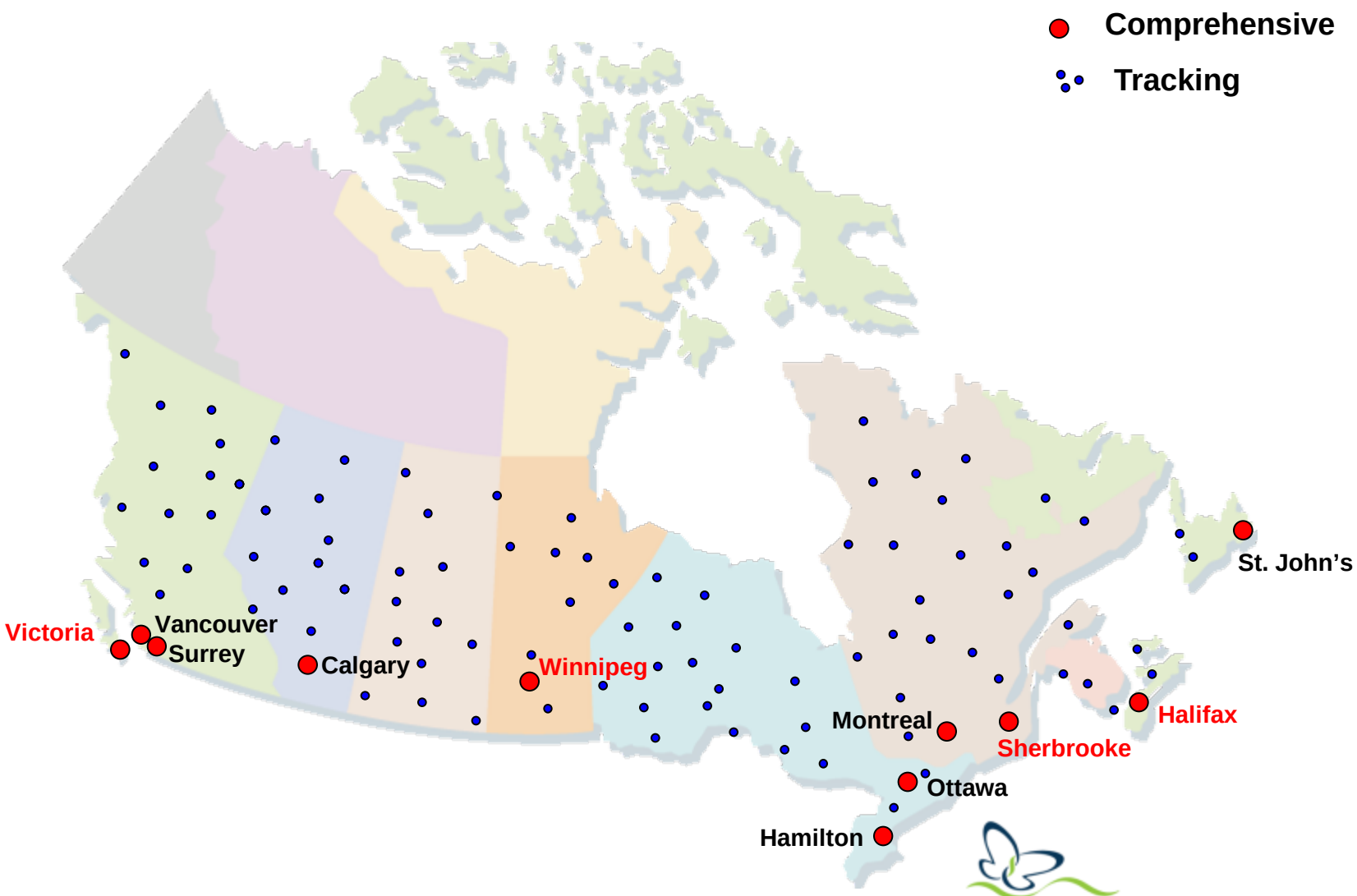
Participant Recruitment



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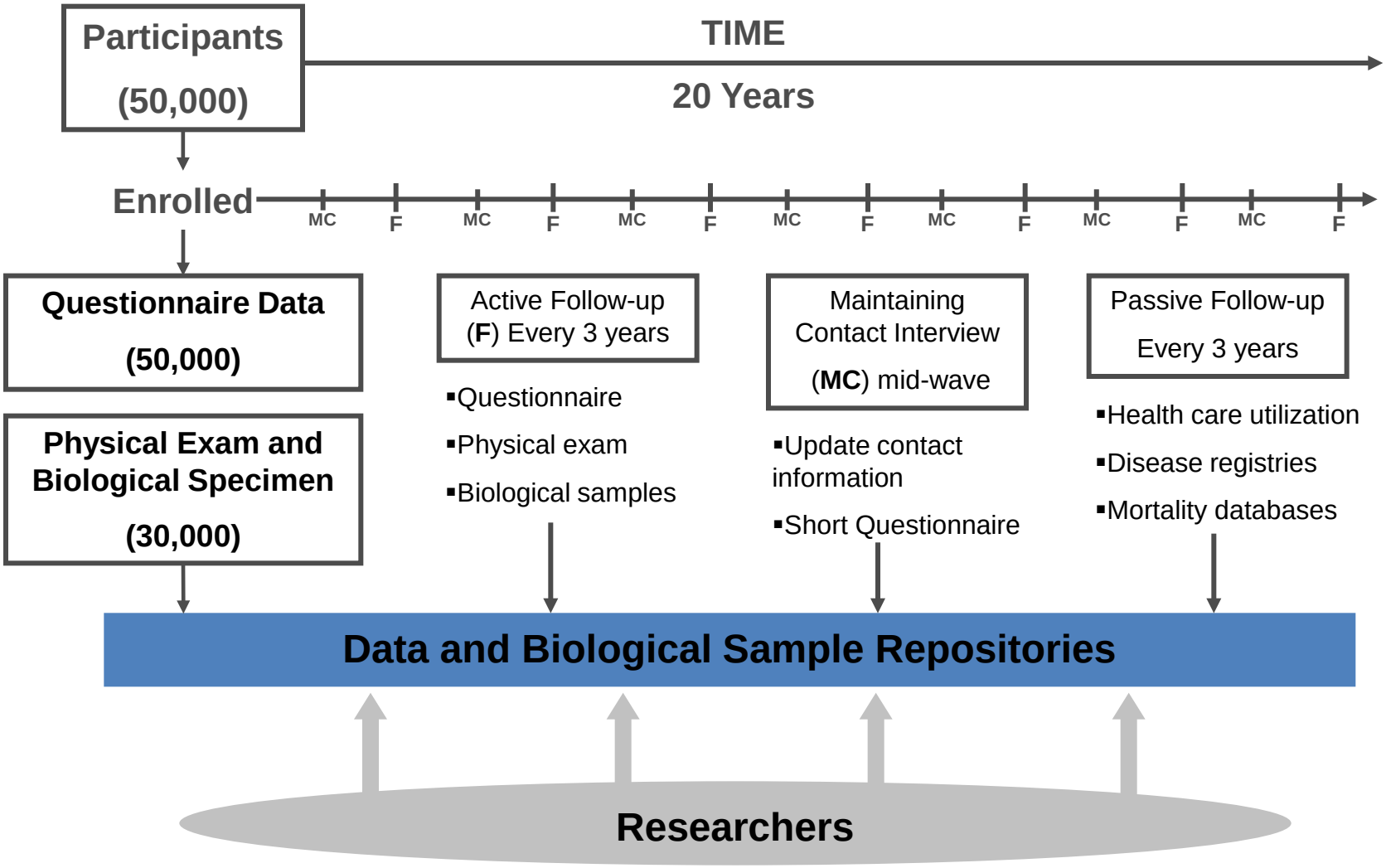

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Depth and Breadth of CLSA

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

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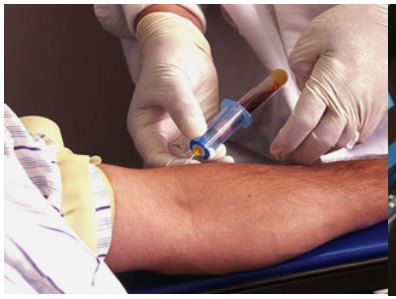
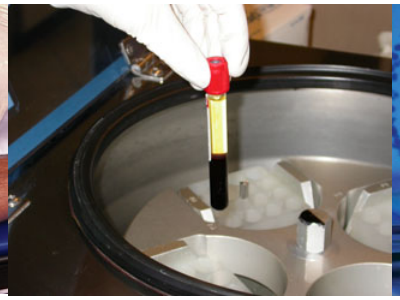
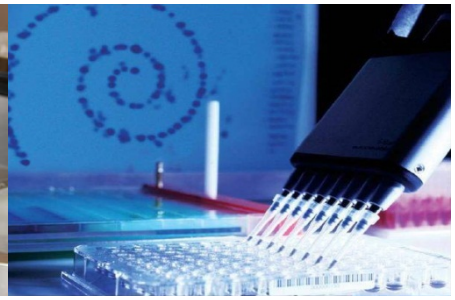
Data Collection Sites (DCS)

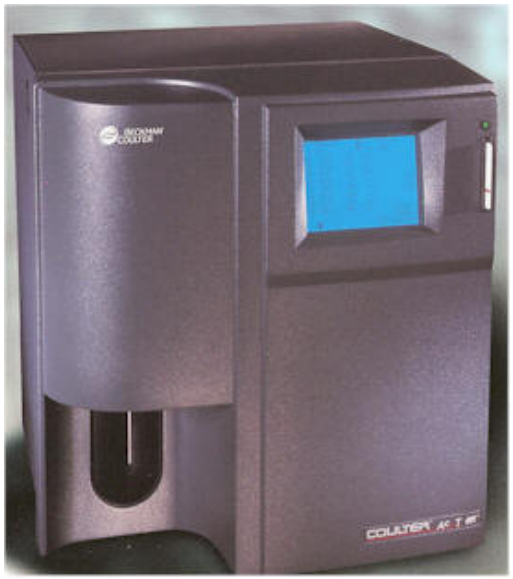
11 ACROSS CANADA

- **5 participants per day (40 weeks)**
- **50 mL blood**
- **Urine sample**
- **Hematology tests (AcT DIFF, Beckman Coulter)**









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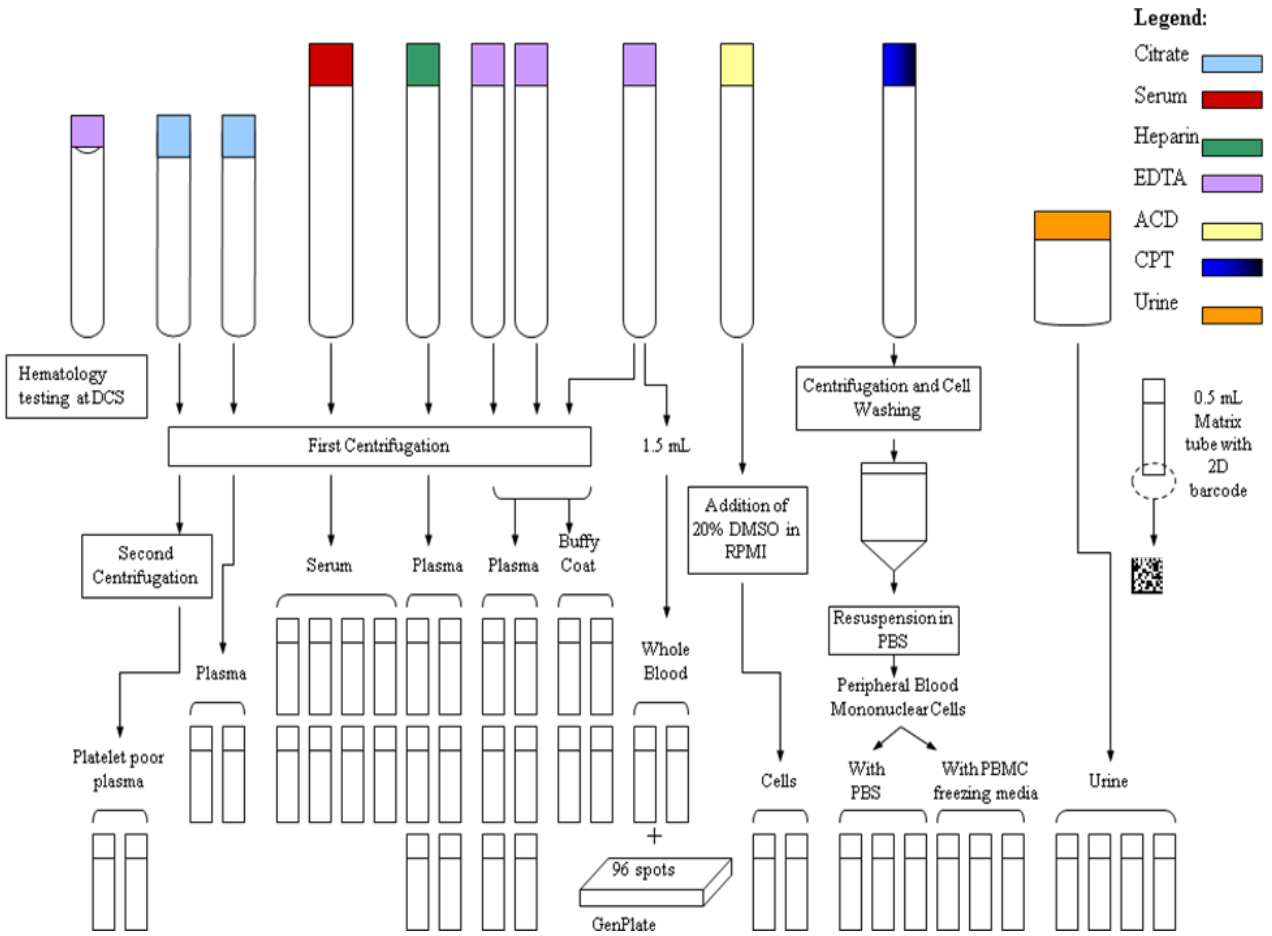
Bio specimens
42 aliquots per participant



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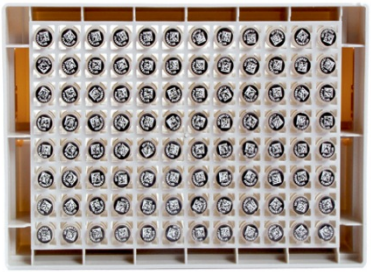
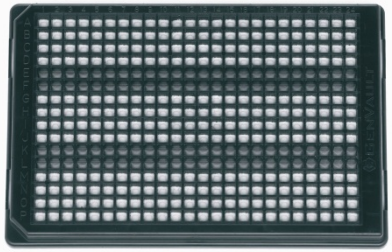
Storage System



Tubes

- 500-µL V bottom, screw- top tubes (Matrix Tubes, Thermo Fisher Scientific)
- Open-bottomed boxes for fast scanning
- Standard 96 well format
- Potential for 'pick and place' robotic retrieval and storage box compression ('defragging')

Microwell Plates



- 3-section GenPlates (Genvault) with FTA paper
- Standard 96 well format
- Dried overnight in GenVault FastDryer and sealed with an adhesive foil cover

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Shipping

Matrix boxes

- Pre-charged vapor shippers (-160ºC)
- Weekly shipments to BBC (overnight courier)
- Equipped with data loggers

GenPlates

- Envelopes with dessicant

Quality

Standard protocols to minimize process variation

Supplies

- Received by the BBC and packaged for monthly shipments to the DCS
- Barcode labels for supplies generated at BBC
- Lot numbers and expiry dates tracked centrally

Biospecimens

- Scanned at each stage of processing and handling to provide a detailed history of the biospecimen
- Characteristics of samples documented
- Sample integrity maximized
  - Maximum time from collection to storage is 2 h
  - Storage at –160^{0}C

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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

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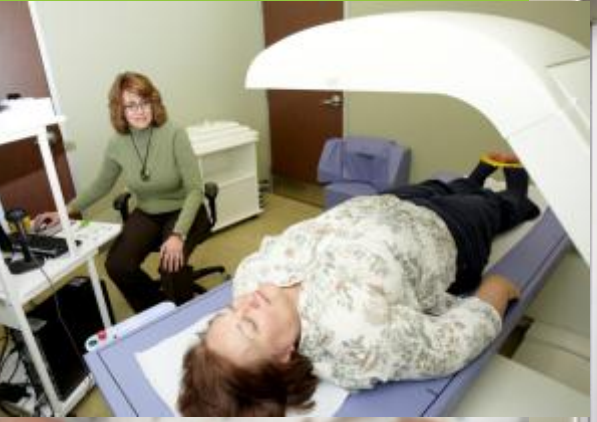


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N C V K D
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Biorepository and Bioanalysis Centre (BBC)

Biorepository

- **Installation May 2012**
- **LIMS implementation April**
- **Hiring BBC coordinator**

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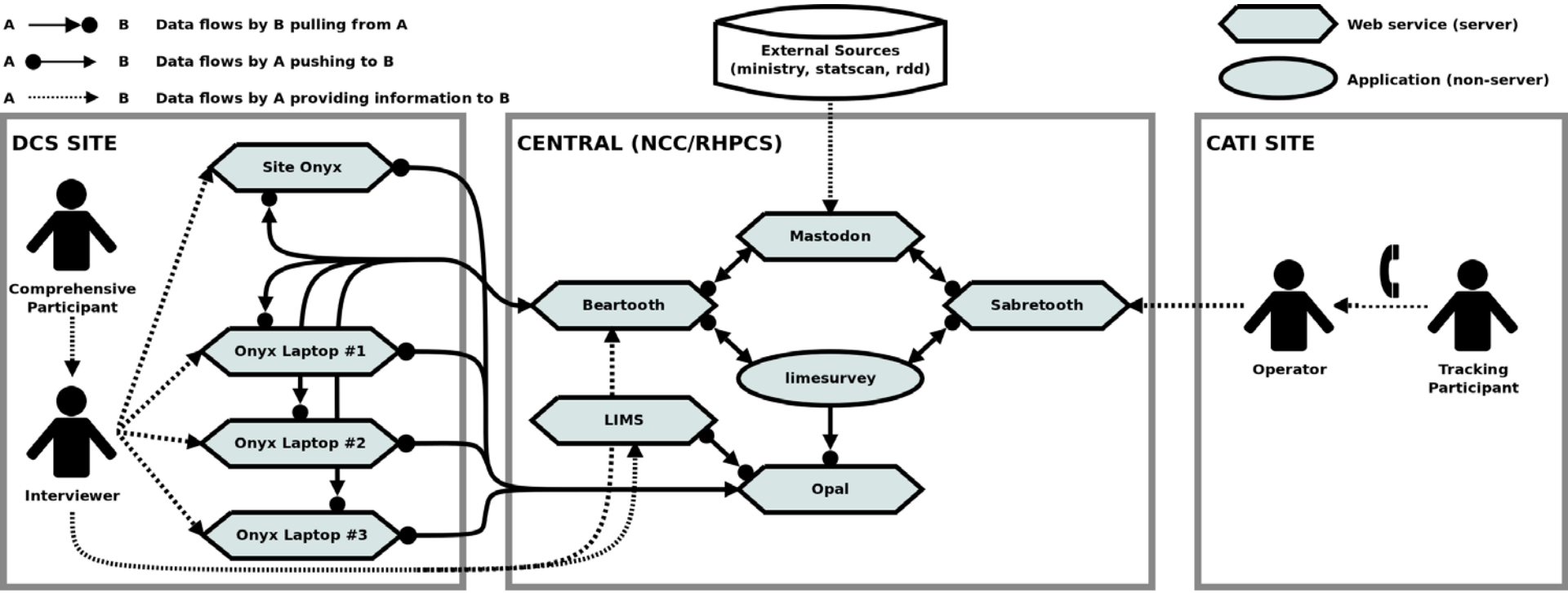
Biorepository and Bioanalysis Centre (BBC)

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



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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

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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)

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Baseline Recruitment and Data Collection

- First selection of 20,000 started in late 2011
  - Completed 60 minute questionnaire by telephone on about 12,000 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

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

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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)
  - 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)

What is required to create a Centralized Platform like CLSA?

- Good Governance
- Coordinated ongoing ethics approval process
- Transparent Data and Sample Access Policies
- Transparent Data Ownership and IP Policies
- Integrated IT infrastructure

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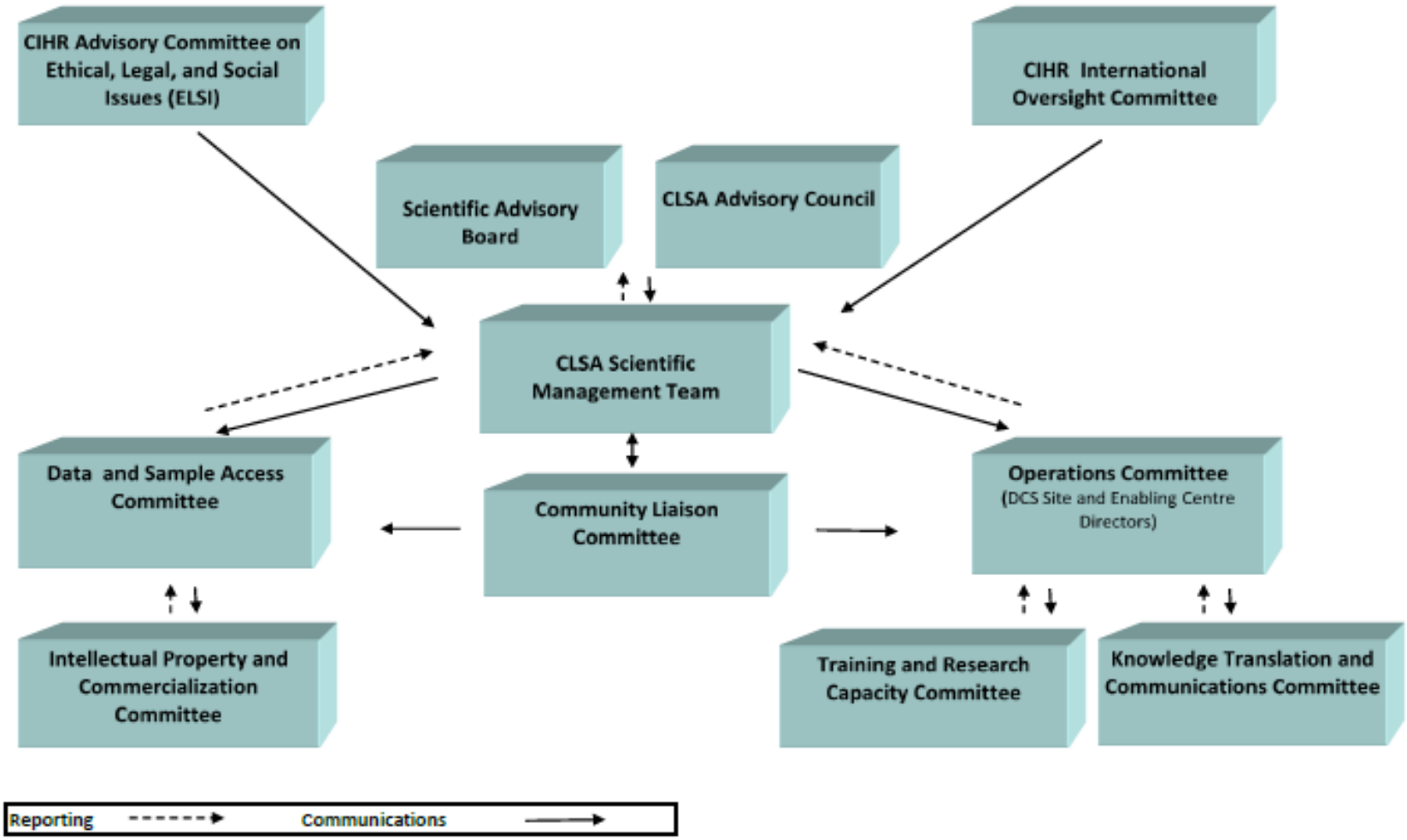
Data and Sample Access

- 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



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CLSA Partners

- Public Health Agency of Canada
- Veterans Affairs Canada
- Statistics Canada
- Ontario Ministry of Health and Long-Term Care
- Provinces
- Universities
- Large number of in-kind contributions from vendors and suppliers

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Use of the CLSA Platform: Examples

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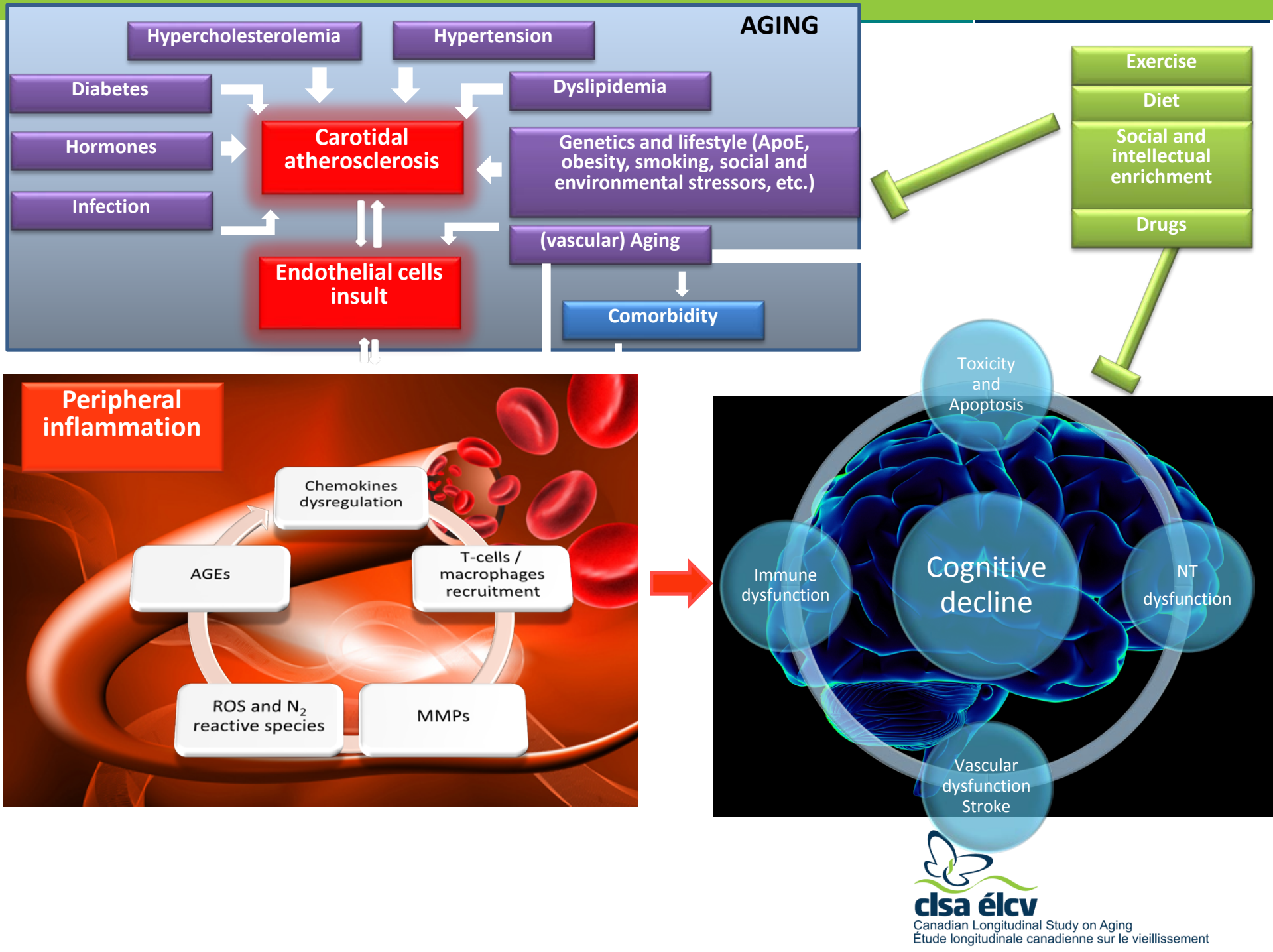

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Mobility

*«activity & participation» **

Examples of precursors

Individual (or ìntrinsic)

Chronic diseases (eg osteoarthritis)
Neuropsychological conditions
Cognition/Perceived health
Medication use/Pain/ Dizziness
Poor vision
Fear of falling/
Obesity/Nutrition/weight loss/appetite
Physical activity/fitness/strength
Functional performance (measured & reported)
Alcohol use
Biomarkers (inflammation, hormonal, metabolism, genetics, epigenetics)
Personality

Contextual (or extrinsic or environmental)

Social partcipation
Transportation resources
Community/neighbourhood characteristics
Social network/support

Examples of consequences

Diseases

Osteoporosis, sarcopenia

Physical Health

Injuries/Frailty/Disability
Poor nutrition status

Psychological Health

Psychological distress
Quality of life
Loneliness
Unmet needs

Social Health

Social participation/engagement/capital
Work Transitions
Unmet needs
Institutionalization

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Étude longitudinale canadienne sur le vieillissement

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

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