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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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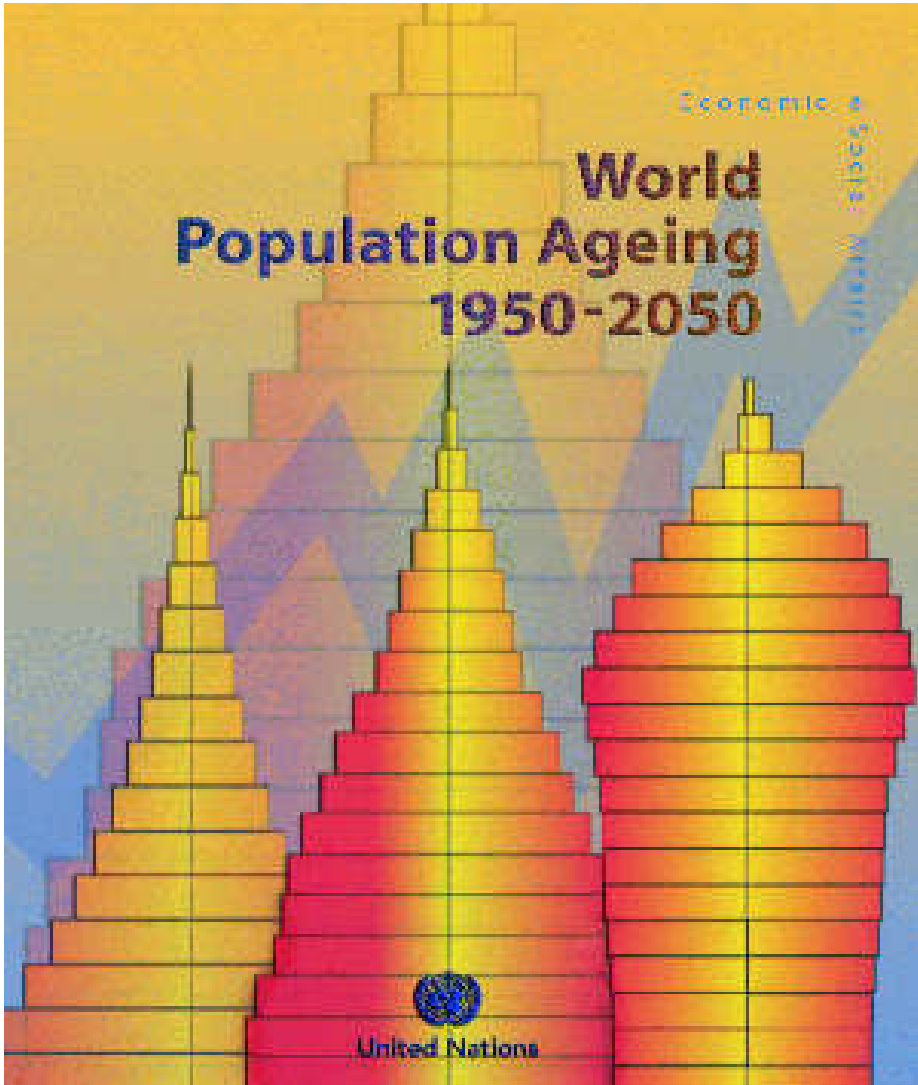
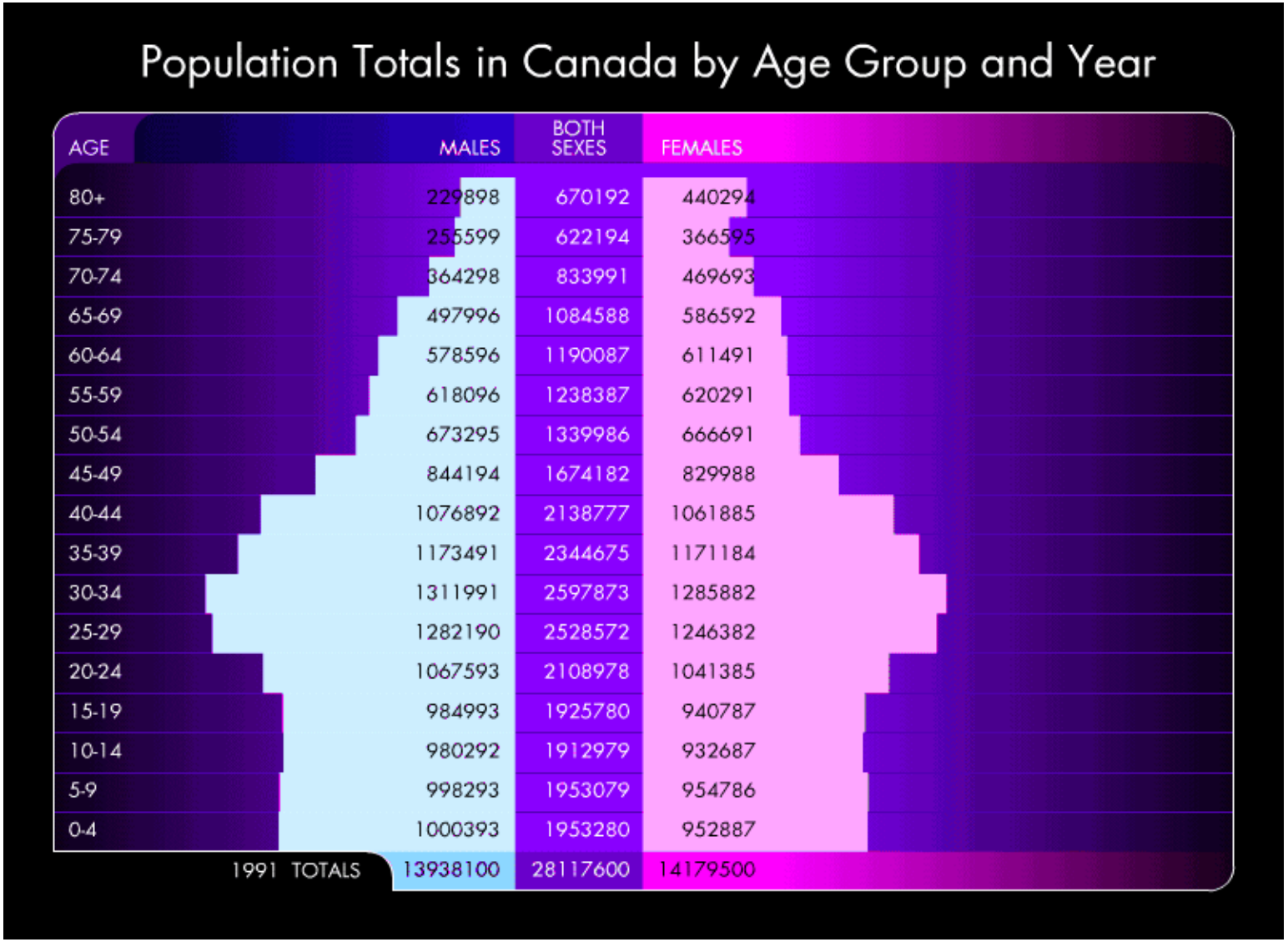
Population aging

- 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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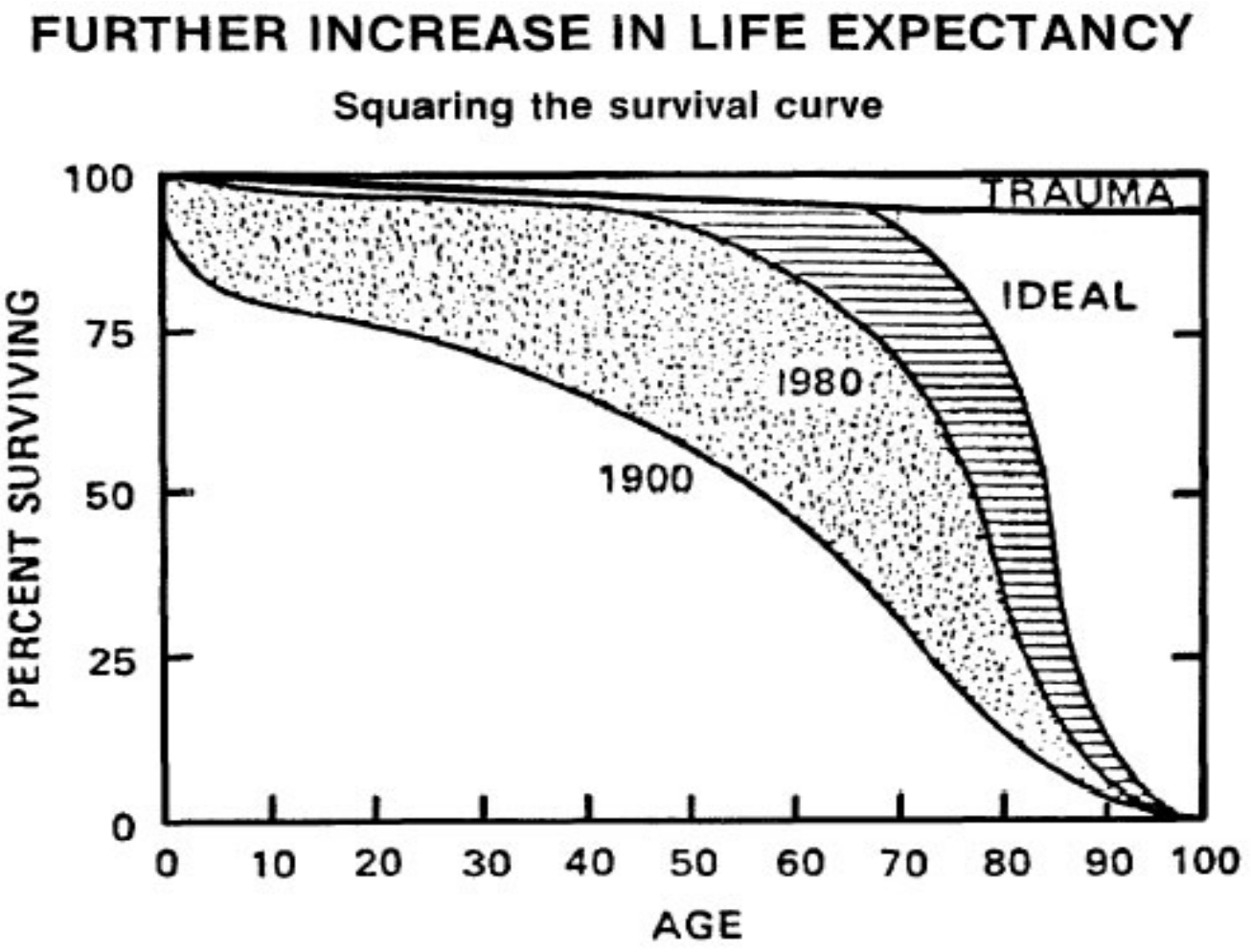
Rectangularization of the survival curve



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

Compression of morbidity

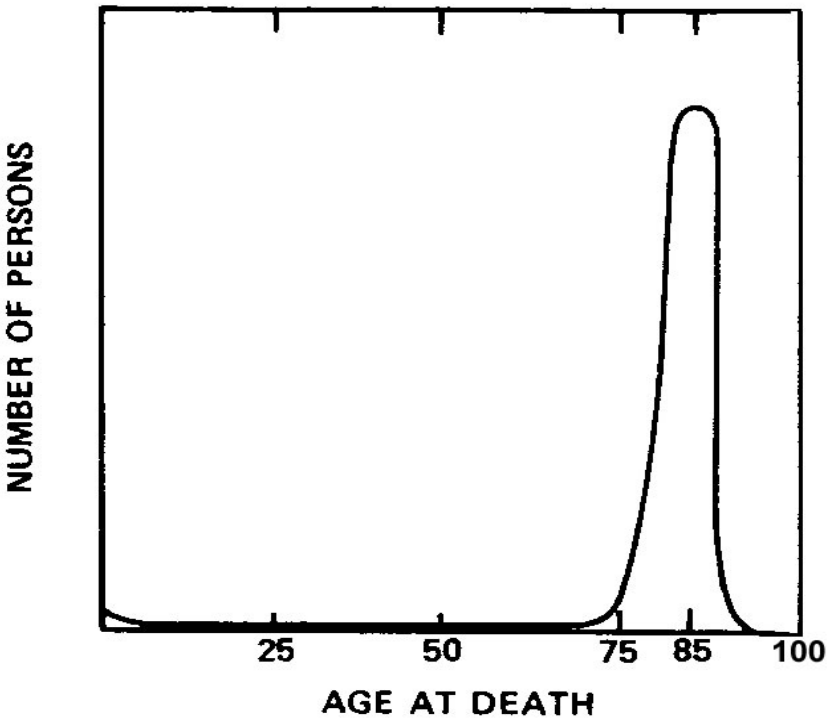


Figure: Mortality According to Age in the Absense of Premature Death

- 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

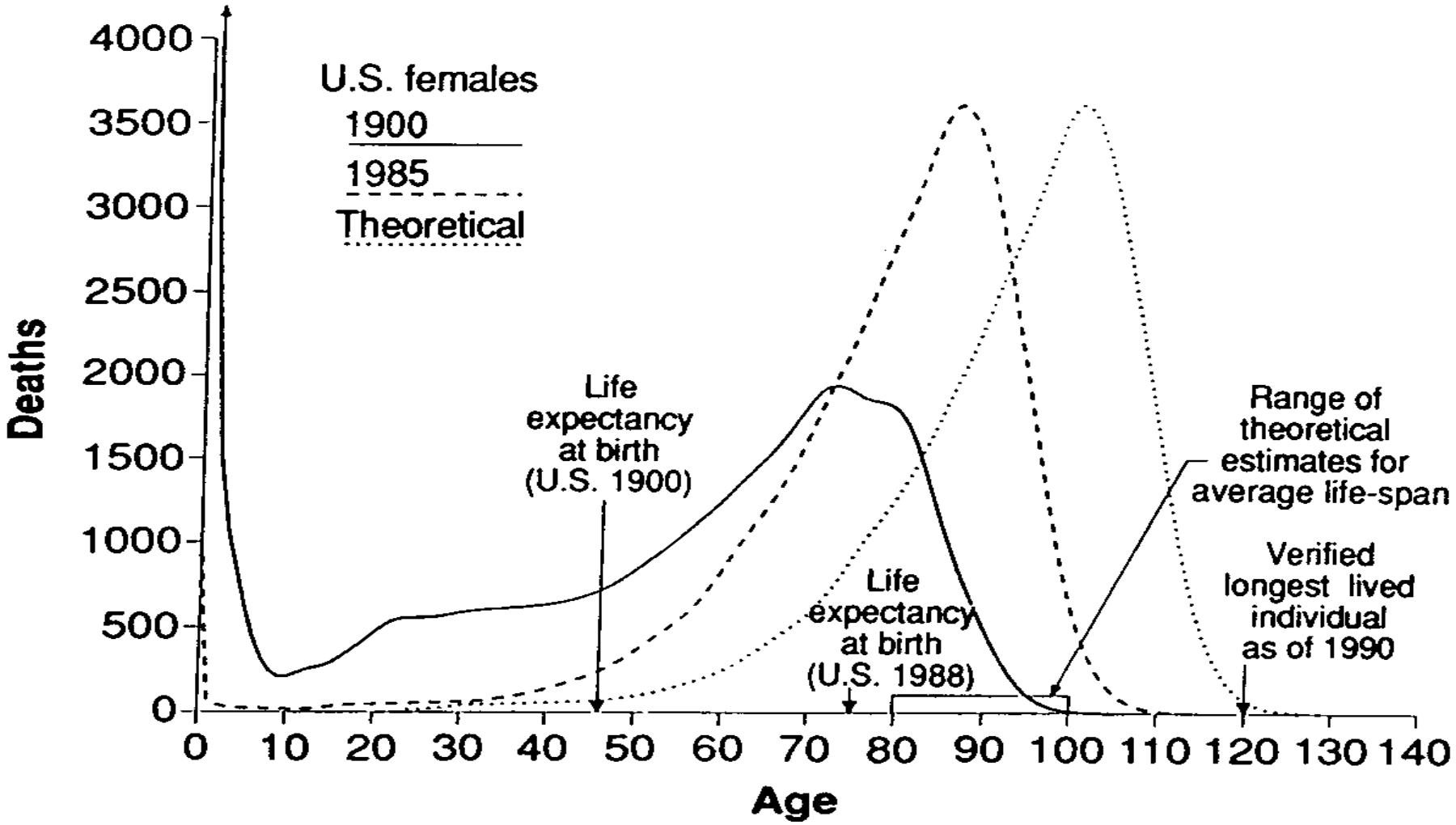
Fries' paradigm based on the premise that:

- 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

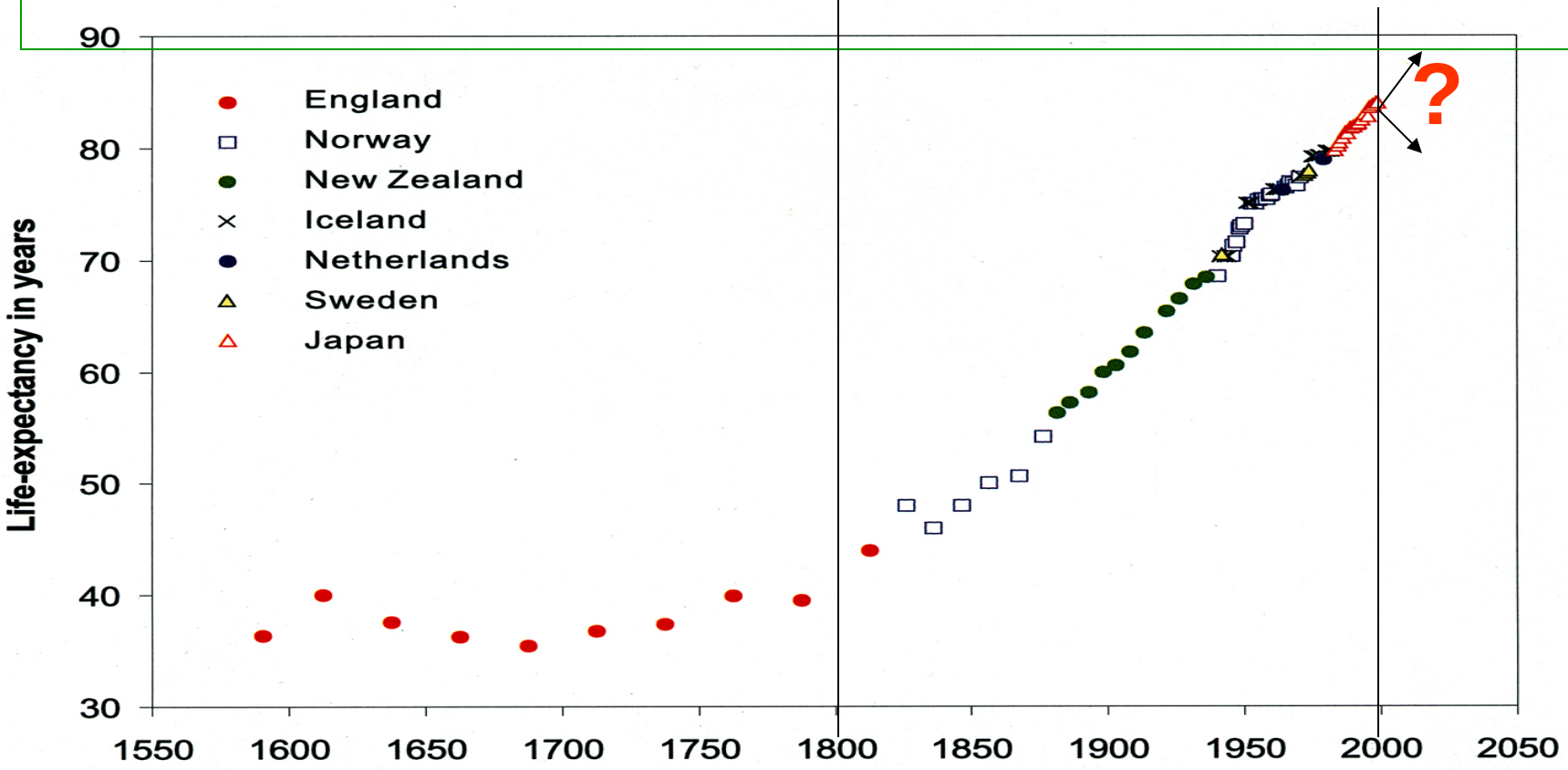
Historical increases of life expectancy

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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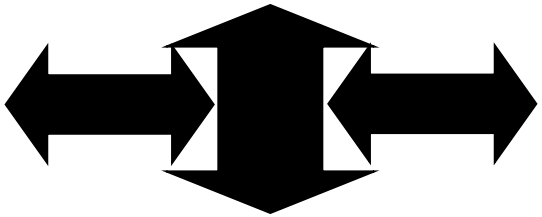
Demographic Futures

- 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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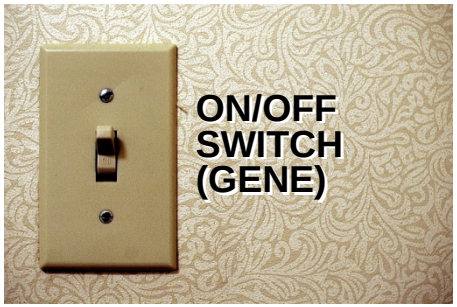
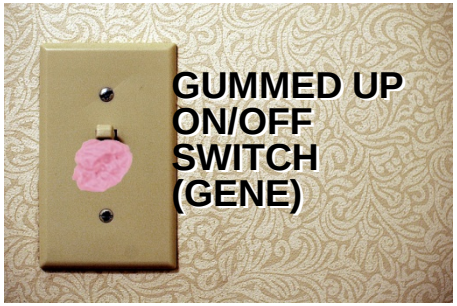
EPIGENETICS





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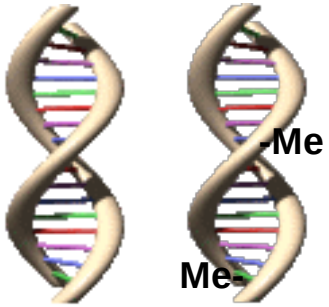

CAN

GUM

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30 nm fiber 10 nm fiber

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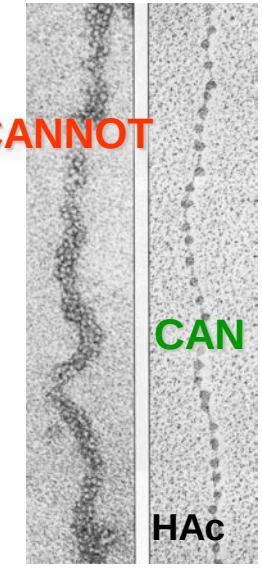

DNA AND CHROMOSOME LEVELS

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Non-Biological/Medical Determinants of Aging?

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

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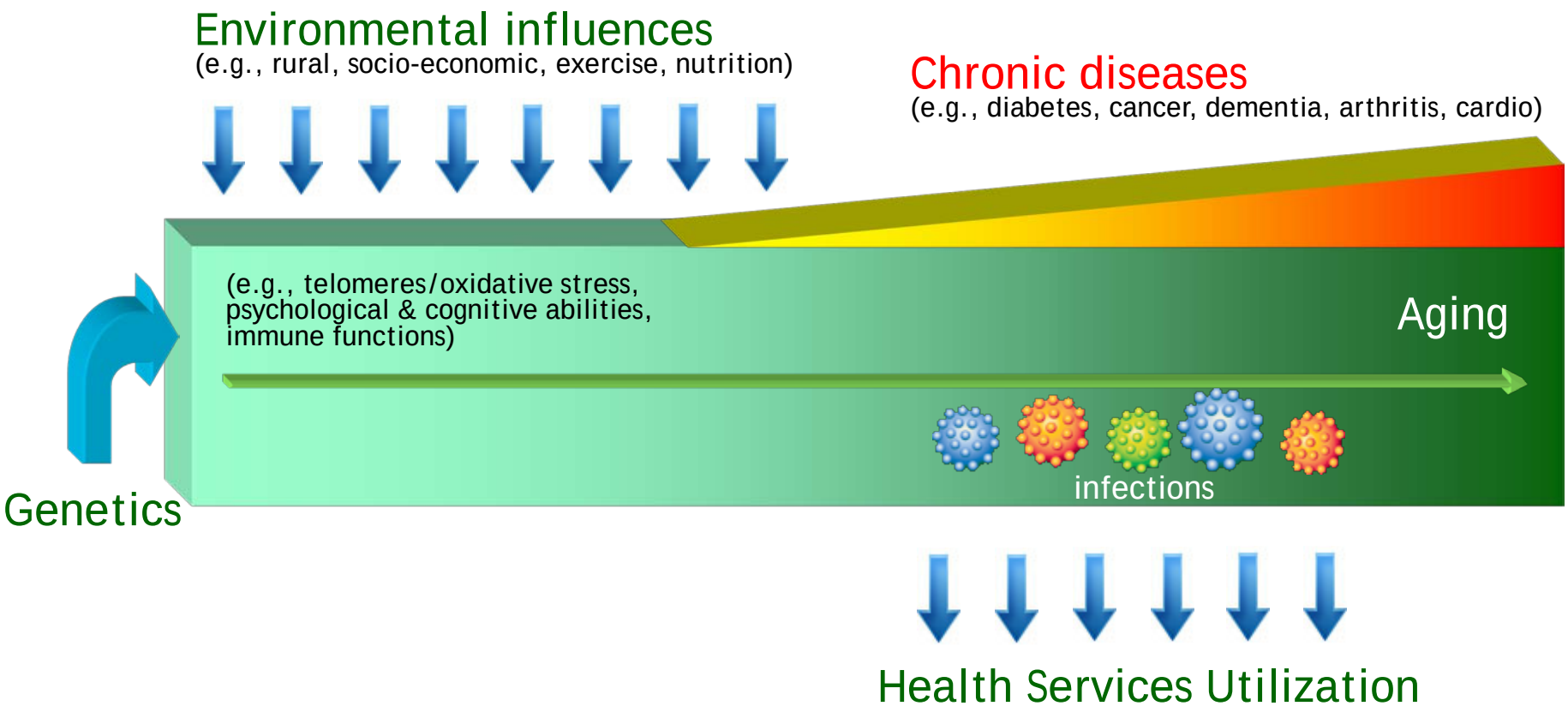
Intrinsic and Extrinsic Factors



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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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CLSA- The Concept

The Vision

A research platform - - infrastructure to enable state-of-the-art interdisciplinary population based *research* and *evidenced-based* decision making.

The Aim

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

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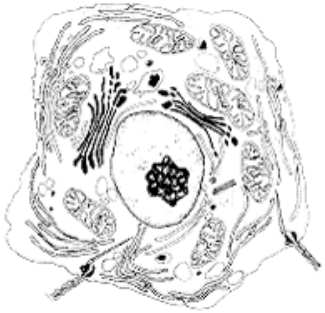
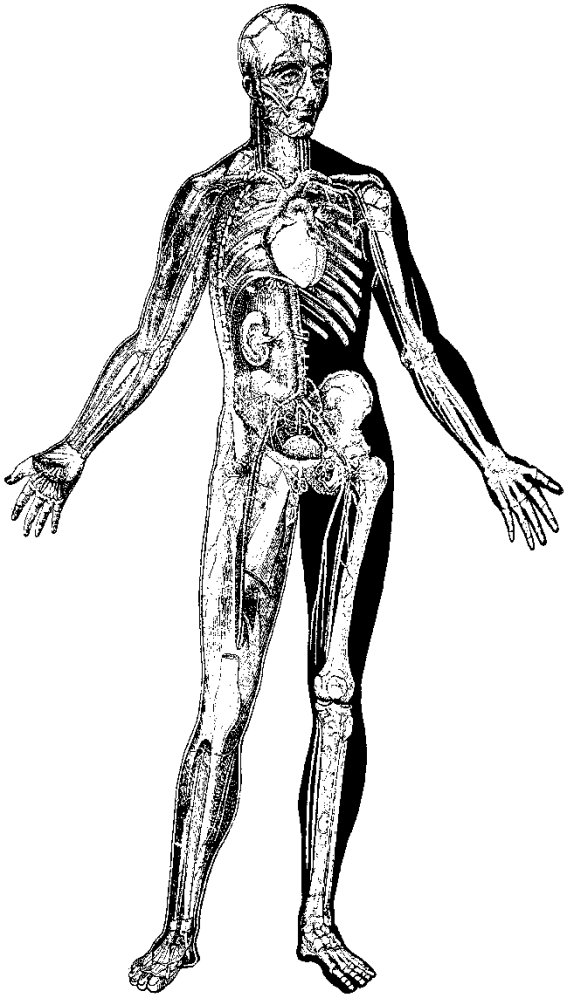


Innovation - Cell to Society

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



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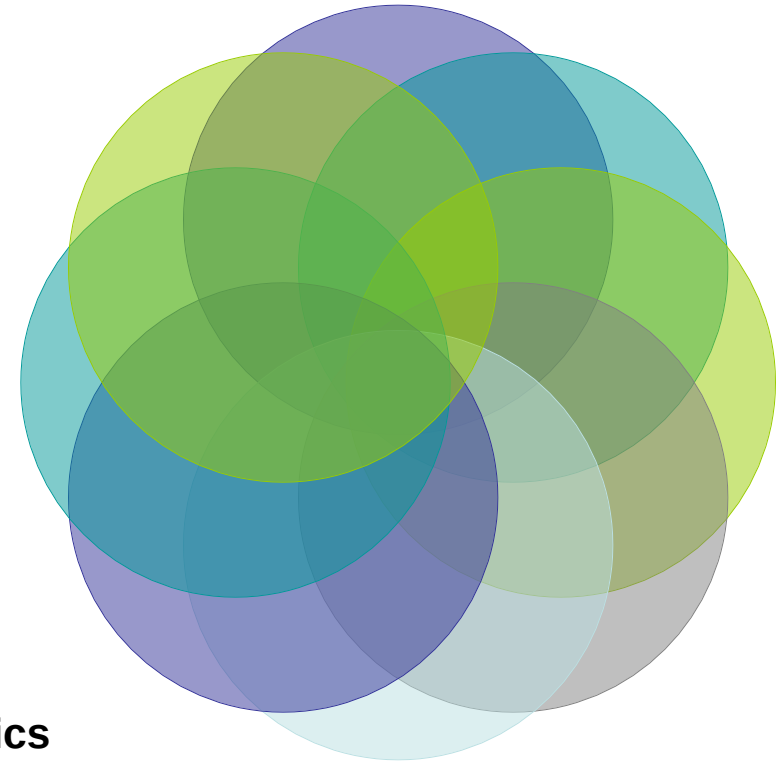
Interdisciplinary Research Agenda



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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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CLSA Architecture

Inception Cohort total 50,000

In-Depth collection on 30,000 (at 11 sites)

Questionnaires, Database linkage

Clinical, Biological, Physical

Follow-up over 20 years

Every 3 years age 45-85

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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

CLSA – CCHS Healthy Aging

Multi-stage sampling

- Sampling frame 2006 Census
- Selection
  - Clusters based on Census dissemination area blocks
  - Dwellings within cluster
  - Person within dwelling
- Response Rate
  - Household-level 80.8%
  - Person-level 92.1%
  - Overall 74.4%

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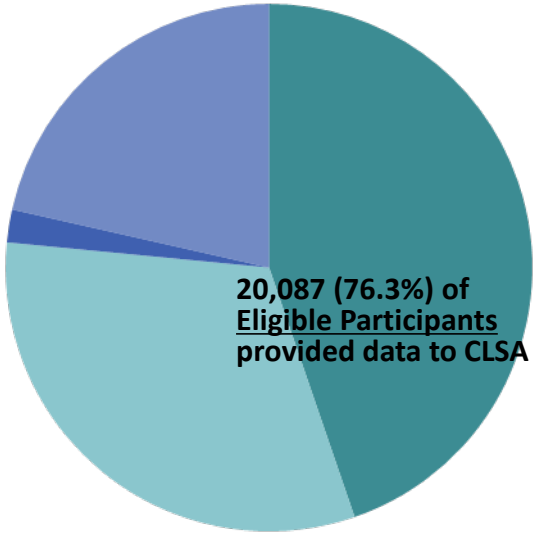
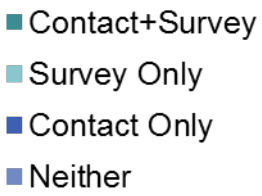
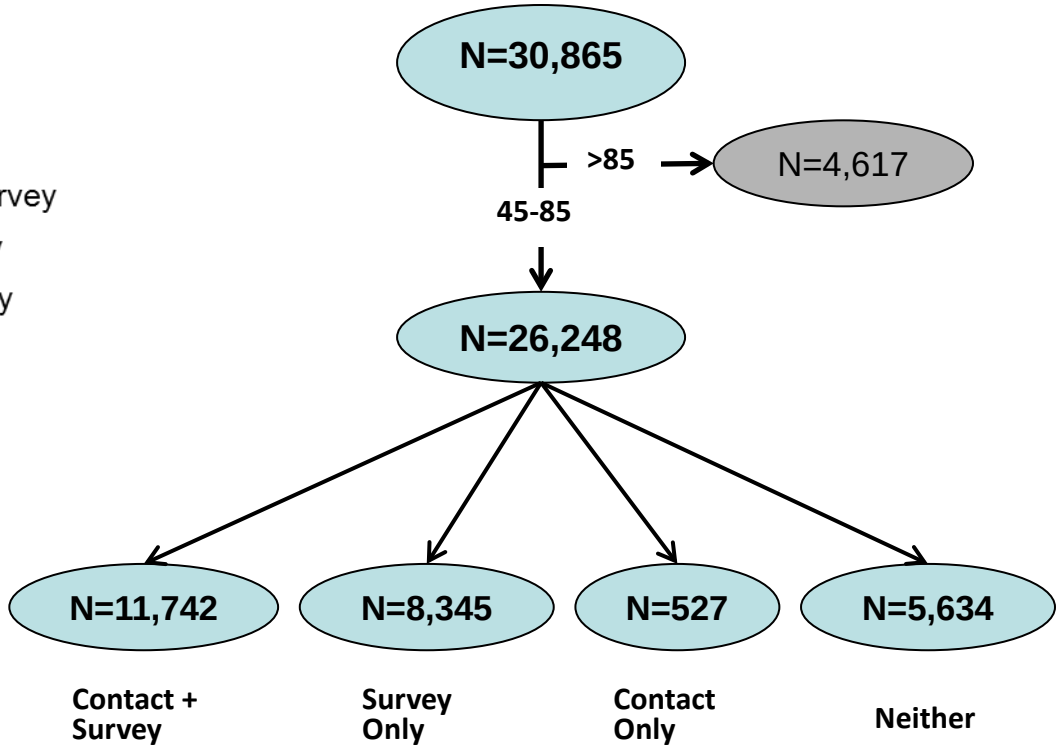
CLSA – CCHS Healthy Aging

Participants were asked to share:

- Their contact information with the CLSA (for recruitment)
- Their survey responses with the CLSA (for analysis)







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Aims of 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:
  - Using provincial health registries
  - Random digit dialing
- In Alberta and maybe BC, it appears we cannot use registries

Example of requirement by province
Tracking cohort

Alberta

	45-54		55-64		65-74		75-85		Total
	M	F	M	F	M	F	M	F	
# Required	306	306	306	306	204	204	204	204	2,040
# Providing Contact Info	121	128	153	193	108	138	74	107	1,022
# Anticipated through CCHS	28	35	56	82	53	64	33	25	376
# Additional Participants	278	271	250	224	151	140	171	179	1,664
# Need to Sample*	X	X	X	X	X	X	X	X	X

*** This will depend on the recruitment rate per number sampled**

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RDD approach

- Randomly sample numbers as far as possible in specified area codes and with next 3 digits in relevant area
- Identify eligible people at that number
- Randomly choose one person
- Recruit willing participants

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Issues in using RDD

- Identifying numbers in specified area
- Having up-to-date list of numbers
- Ability to compute sample weights
- Presence of landlines and/or cellphones
- Eligibility within household – changes over time
- Method of initial contact
- Households without phones
- Numbers may be businesses, out of order, etc.
- People away from home (snowbirds, etc.)

Obtaining lists of numbers

- Commercial organization, ASDE, in Quebec
- Can supply randomly chosen numbers
- Will state recency of population list of numbers
- If number is ‘listed’, can provide name and address attached to number (harder for cellphones)
- We are recruiting over 3 years, we will need ‘refreshed’ lists every so often
- Might over-sample in areas with many older people

Cell phones and landlines

- Statistics Canada survey December 2010
- Supplement to Labour Force Survey
- Households using cellphones exclusively:
  - Overall: 13%
  - Age 18-34 50%
  - Over 35 8%
  - Over 55 4%
- Increasing over time
- Landlines reach nearly all our eligibles

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Combining samples from cellphones and landlines

- Methods have been described
- Need to determine all phones in each household
- Keep logs of unfilled quotas (age-sex numbers)
- Interviewers construct rosters of eligibles within households and randomly choose one

Some issues with cell phones

- Ethical: incoming calls may cost user; privacy; activity when answering (driving, etc); children
- Cost: AAPOR states at least 2x, maybe 3-4x cost of landline survey
- Getting addresses
- Quality of data (may be similar to landlines)

Source: AAPOR

‘Cold calling’ vs prior contact/letters

- Time and expense of mailing letters (only possible when we have name and address)
- May increase willingness to talk to interviewers (call display)
- Perhaps try both initially and then move to using one

Contacting subjects

- On average, anticipate making many calls to recruit a single person
  - Up to 7-10 calls to obtain response
  - Leave message?
  - Willingness to participate
- Working on assumption of 20% ‘recruitment rate’ for health registry data (15% in 75-85 age group)
- Exclude households without a phone

Some questions

- How often should we refresh samples of numbers?
- Should we try both cold calling and prior contact?
- Is it OK to exclude households without a phone?
- Should we leave a message after n calls fail to contact anyone at the number?
- Should we exclude cell phones?

Depth and Breadth of CLSA

PHYSICAL & COGNITIVE MEASUREMENTS

- Height, Weight
- Waist and hip measurements
- Bioimpedence
- Arterial pressure
- Mean heart rate
- Grip strength, timed up-and-go, chair raise, 4-m walk
- Standing balance
- Vision
- Hearing
- Spirometry
- Bone density
- Aortic calcification
- ECG
- Carotid intima-media thickness
- Cognitive Assessment

HEALTH INFORMATION

- Chronic disease symptoms (11 chronic conditions)
- Medication intake & Compliance
- Women's health
- Self reported Health service use
- Oral health
- Preventative Health
- Administrative data Linkage Health Services & Drugs
- Other Administrative Data bases

PSYCHOSOCIAL

- Social participation
- Social networks and support
- Care giving and Care receiving
- Mood, Psychological distress
- Coping, Adaptation
- Work to retirement transitions
- Job-Demand/Effort Reward
- Retirement Planning
- Social Inequalities
- Mobility-Lifespace
- Built Environments
- Wealth

LIFESTYLE & SOCIODEMOGRAPHIC

- Smoking
- Alcohol consumption
- Physical activity
- Nutrition
- Birth location
- Ethnicity/Race/Gender
- Marital status
- Education
- Income

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Biological Samples

BIOCHEMICAL & HEMATOLOGICAL ANALYSIS (50 ml Blood; Urine)

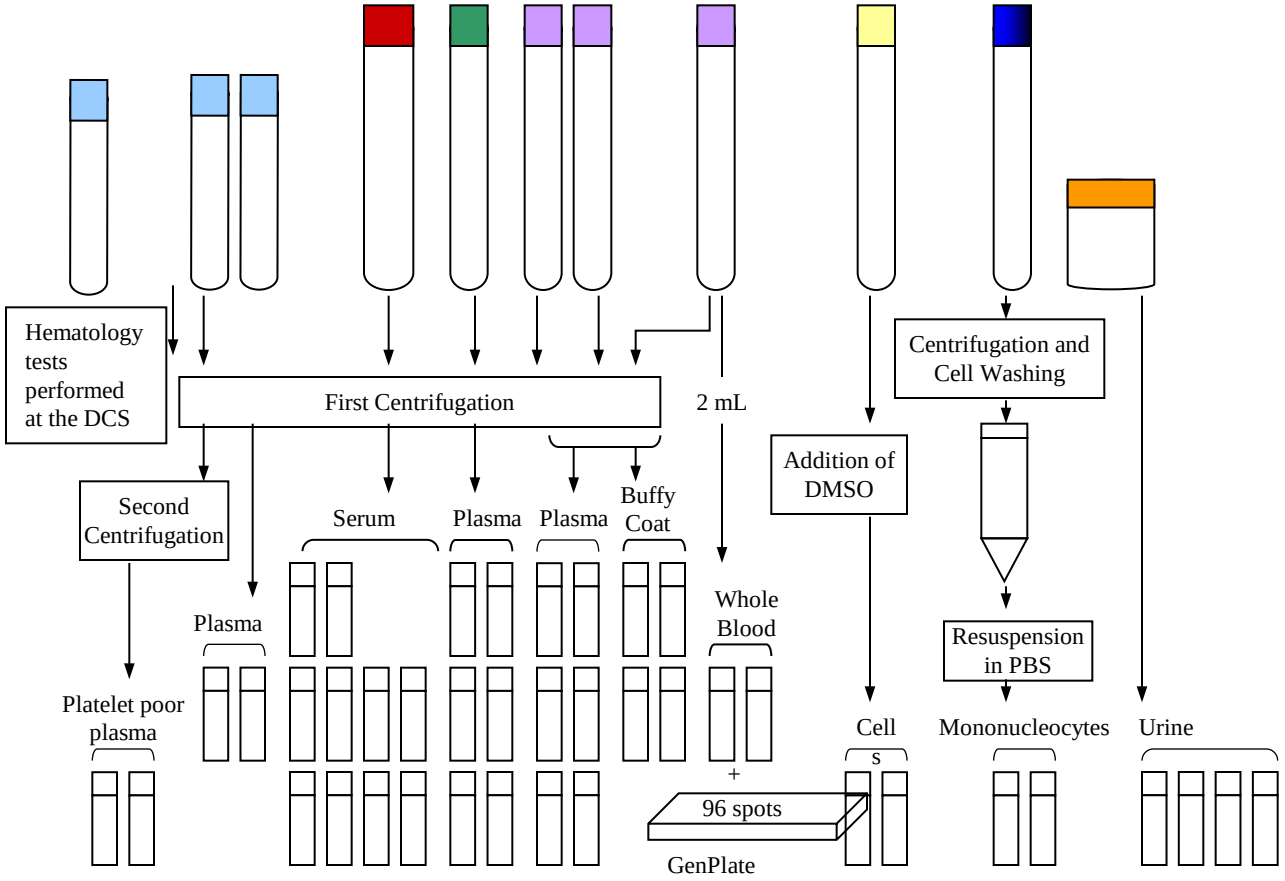
General Hematology

- 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



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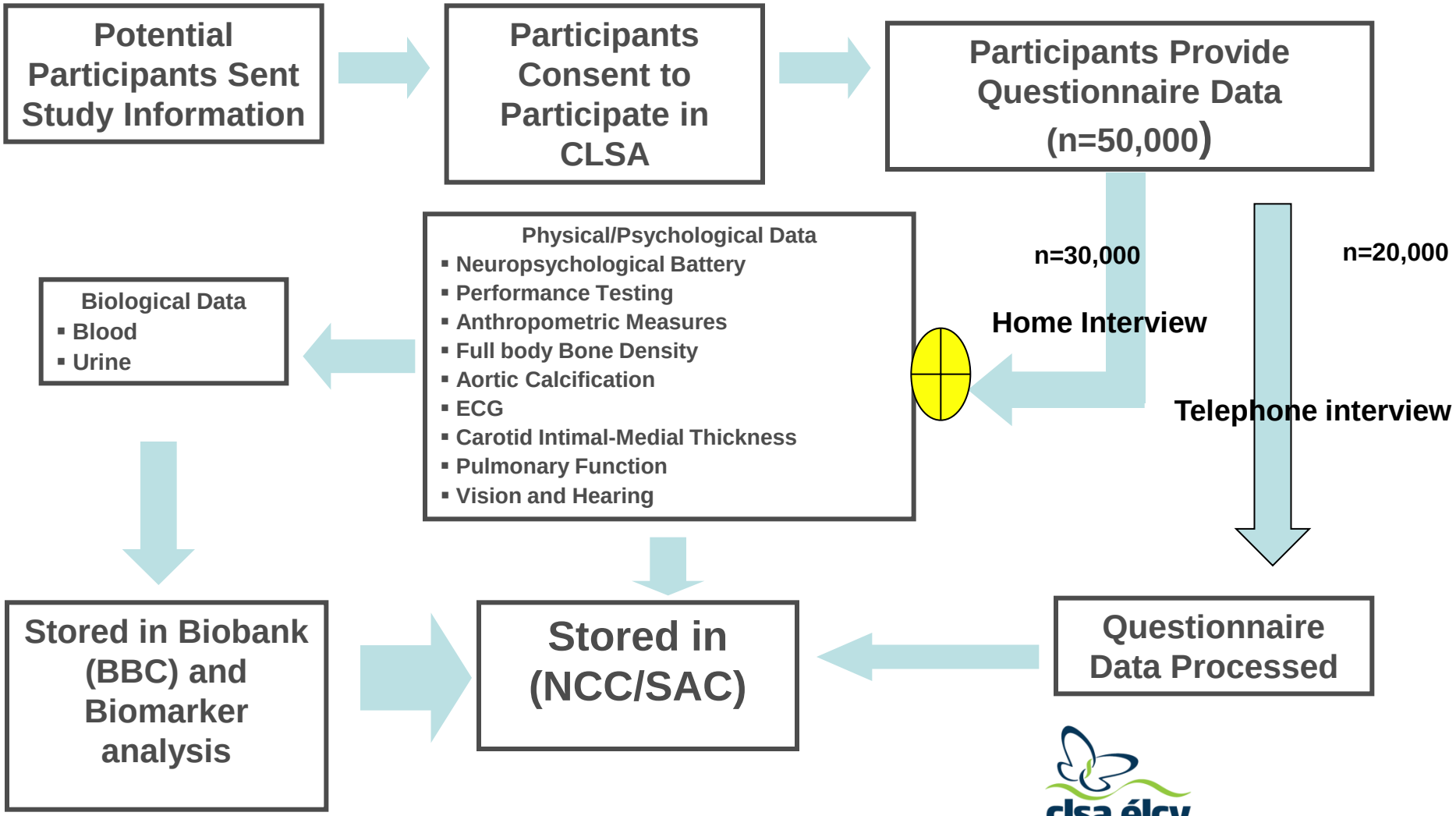
Data Collection Overview



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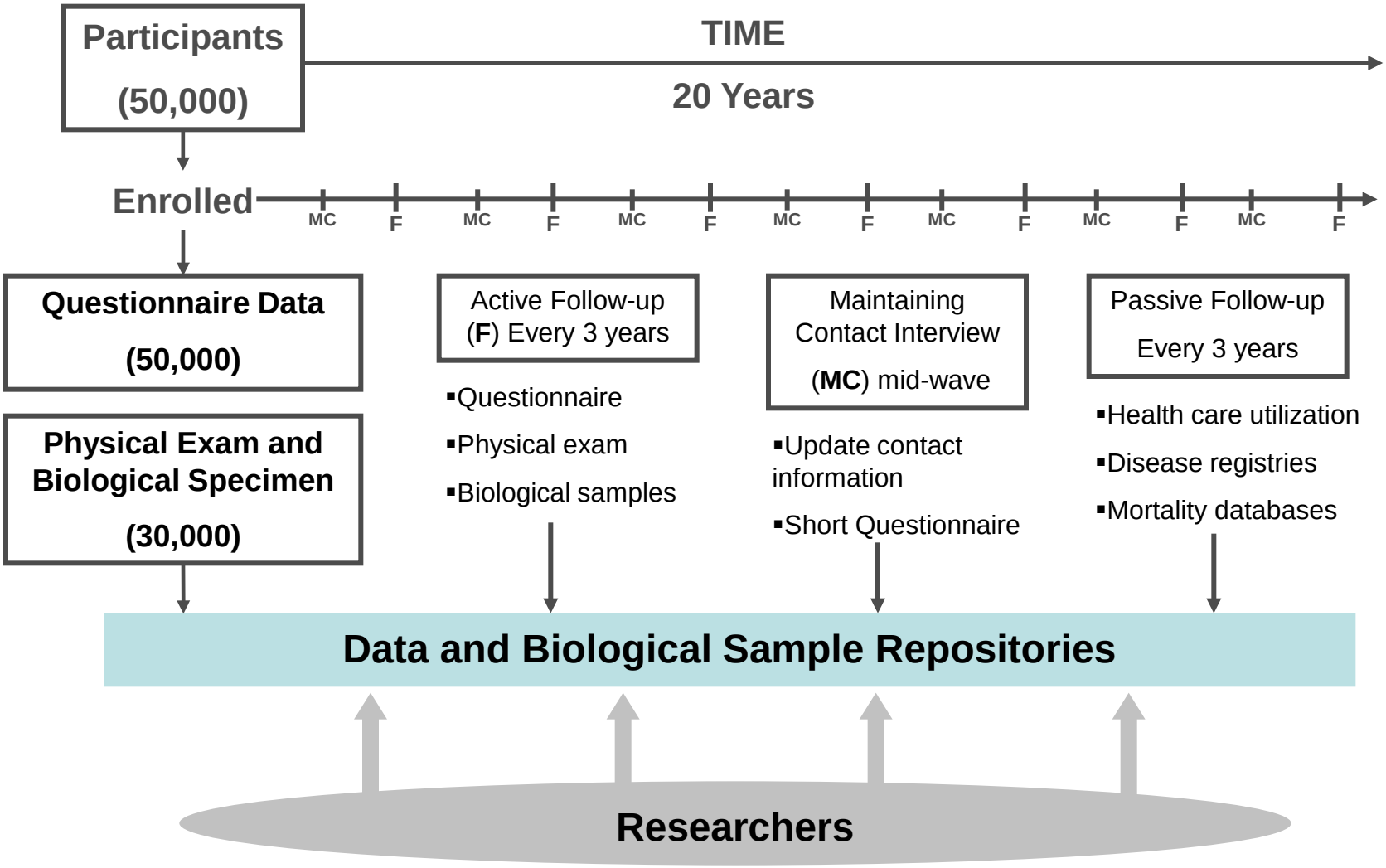

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Example

Physical Function

Mobility

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Mobility

«activity & participation» *

Examples of precursors

Individual (or intrinsic)

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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Mobility

Mobility as a precursor:

Is mobility in mid- and later life associated with physical, psychological and social functioning? Specifically:

- How do changes in mobility impact upon indicators of psychological health including, depression, psychological distress, satisfaction with life, adjusting for other factors?

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Mobility

Mobility as a mediator:

How does mobility in mid- and later life mediate relationships between determinants of health and health outcomes? Specifically:

– How does compromised mobility mediate the relationship between income and health?

Mobility

Mobility as an outcome:

How do physical, psychological, and social functioning in mid- and later life relate to changes in mobility? Specifically:

- What is the relationship between inflammatory biomarkers (e.g., IL-6, C reactive protein, albumin), hormonal biomarkers (e.g., IGF-1, T3, T4), metabolic (e.g., fasting glucose, cholesterol) or immunological markers (TNFα), oxidative stress (e.g. vitamin E and C), vitamin D, and (Epi) genetic markers (e.g., IGF-I and Apo-E) and changes in mobility and how is this relationship is modified by SES?

- What is the relationship between neighbourhood deprivation and incident mobility disability in aging population?

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

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Launch of the CLSA

- First selection of 20,000 started in late 2008 in collaboration with Statistics Canada CCHS Healthy Aging module (Tracking Cohort)
    - Approximately 12 500 have agreed to release their names to CLSA (5000 have been recruited)
- Remaining 15,000 for Tracking Cohort will be recruited in mid-2011
- Remaining 30,000 will be recruited in late 2011 (Comprehensive Cohort)
    - Provincial Client Registries or Random digit Dialing

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Implementation Plans for 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-2011 to mid-2012)
  - Maintaining contact by phone (end of 2012- end 2013)
- Second batch of 1000 people to be recruited/site (mid-2012 to mid-2013)
  - Maintaining contact: (end of 2013-end of 2014)
- Third batch of 1000 people to be recruited/site (mid-2013 to mid 2014)
  - Maintaining contact: (end of 2014-end of 2015)

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Future and Current Legacy of the CLSA Research Platform

Effective Design

- Multidisiciplinary Team
- Key initiative of CIHR
- Governance Structure
- Longitudinal Design
- Random selection
- Extensive data
- Extensive feasibility work
- Transparent data access policies
- Simple IP policy
- Harmonization with international cohorts
- State of the art facilities
  - Bio-repository
  - High Throughput biomarker labs
  - Statistical Analysis centre
  - Bioinformatics
  - Fully equipped data collection facilities

Strong Scientific Program

- Healthy Aging
- Association studies based on candidate genes & diseases-related QTs
- Unique Approach:
  - Chronic conditions as Precursor, mediator Outcome
  - Binary outcomes and quantitative traits
- Quality of life
- Chronic disease management
- Risk factor identification
- Psychosocial aspects of Health
- Environment & Health
- Methodological development
  - Statistical modelling
  - Biological sample collection and storage

Resource for the future

- CFI-funded research facilities
- Supporting biomarker discovery research
- Supporting and developing complex diseases screening methodologies
- Personalized medicine
- Informing health & Social care policy
- Commercialization
- Building research capacity
- Platform for sub-studies
- Advancing Science of Aging
- Improving the health of Canadians

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