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

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McMaster Students for Health Innovation
Health Seminar, Nov. 26th, 2013

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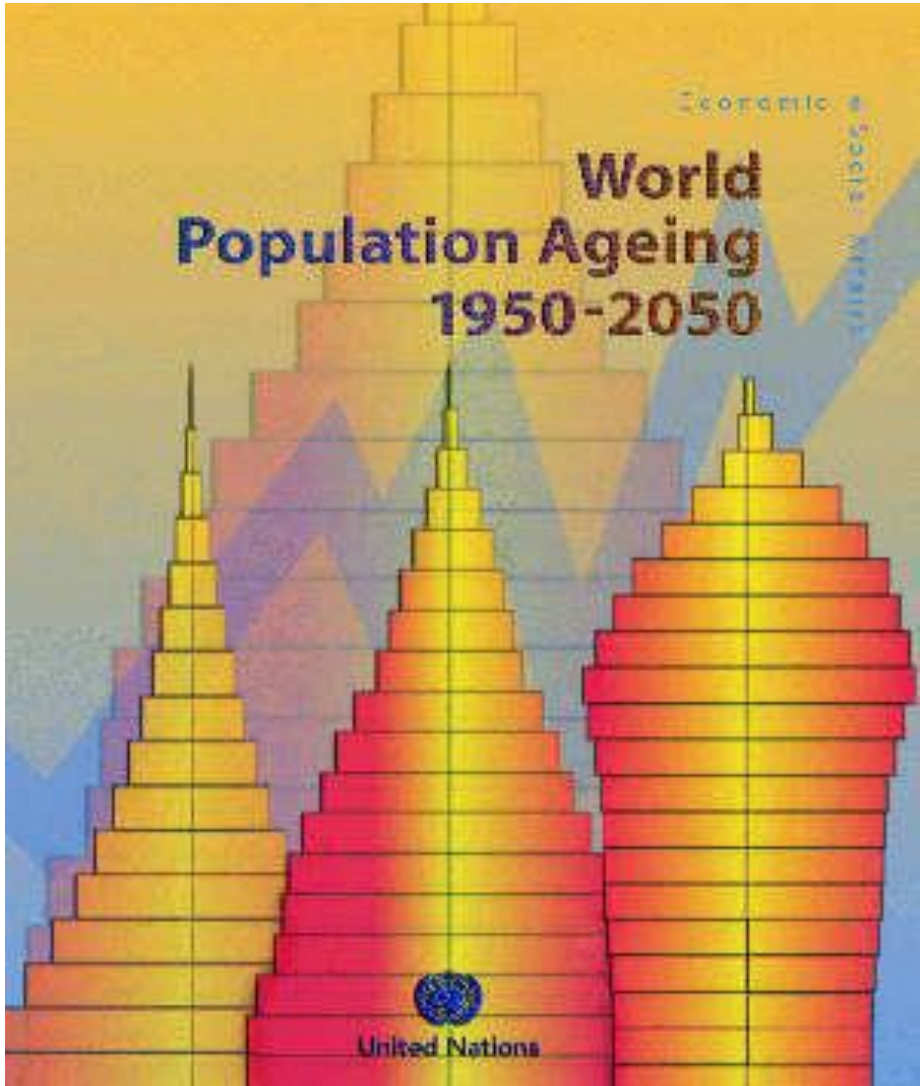
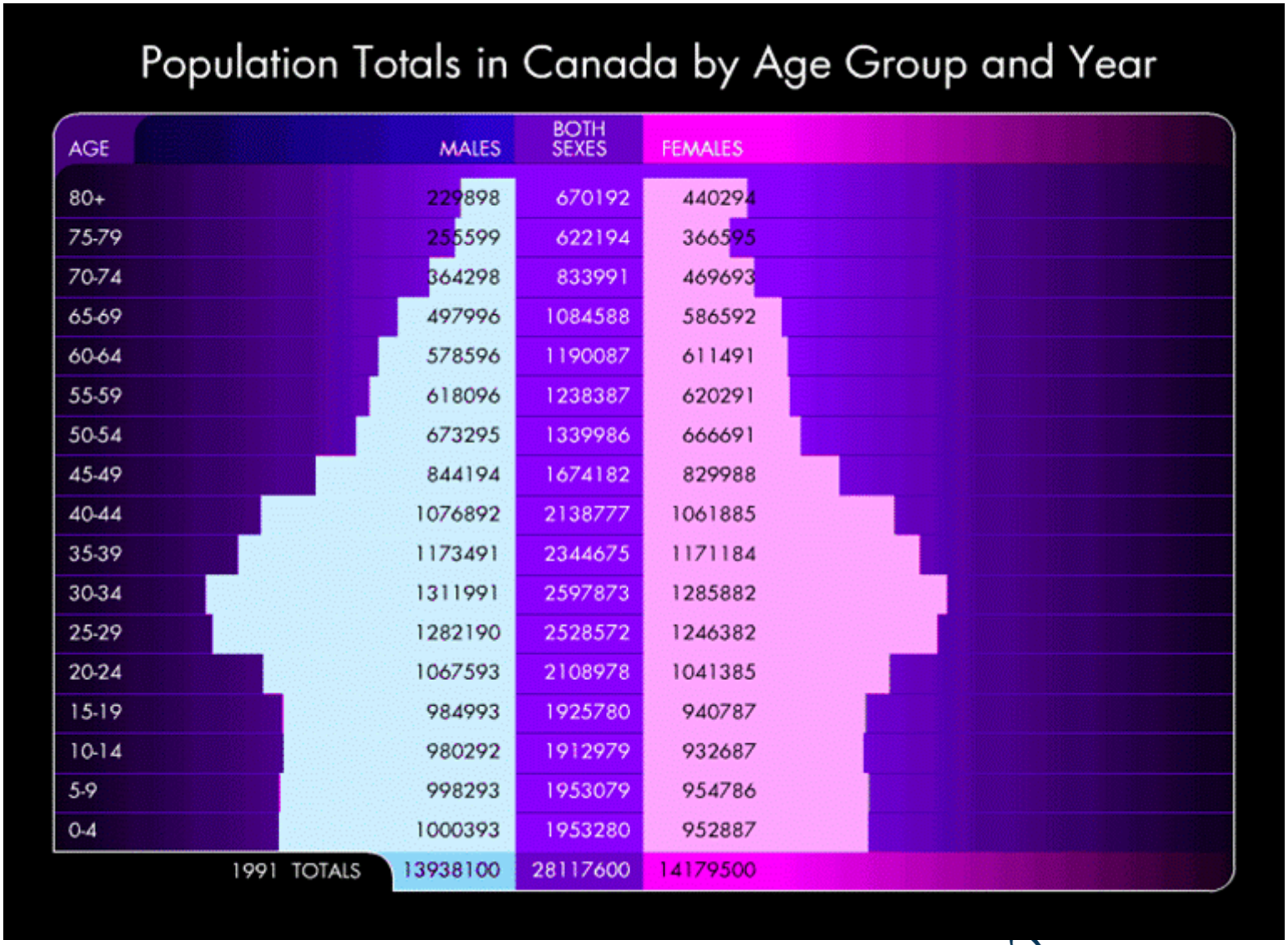
Population aging

- 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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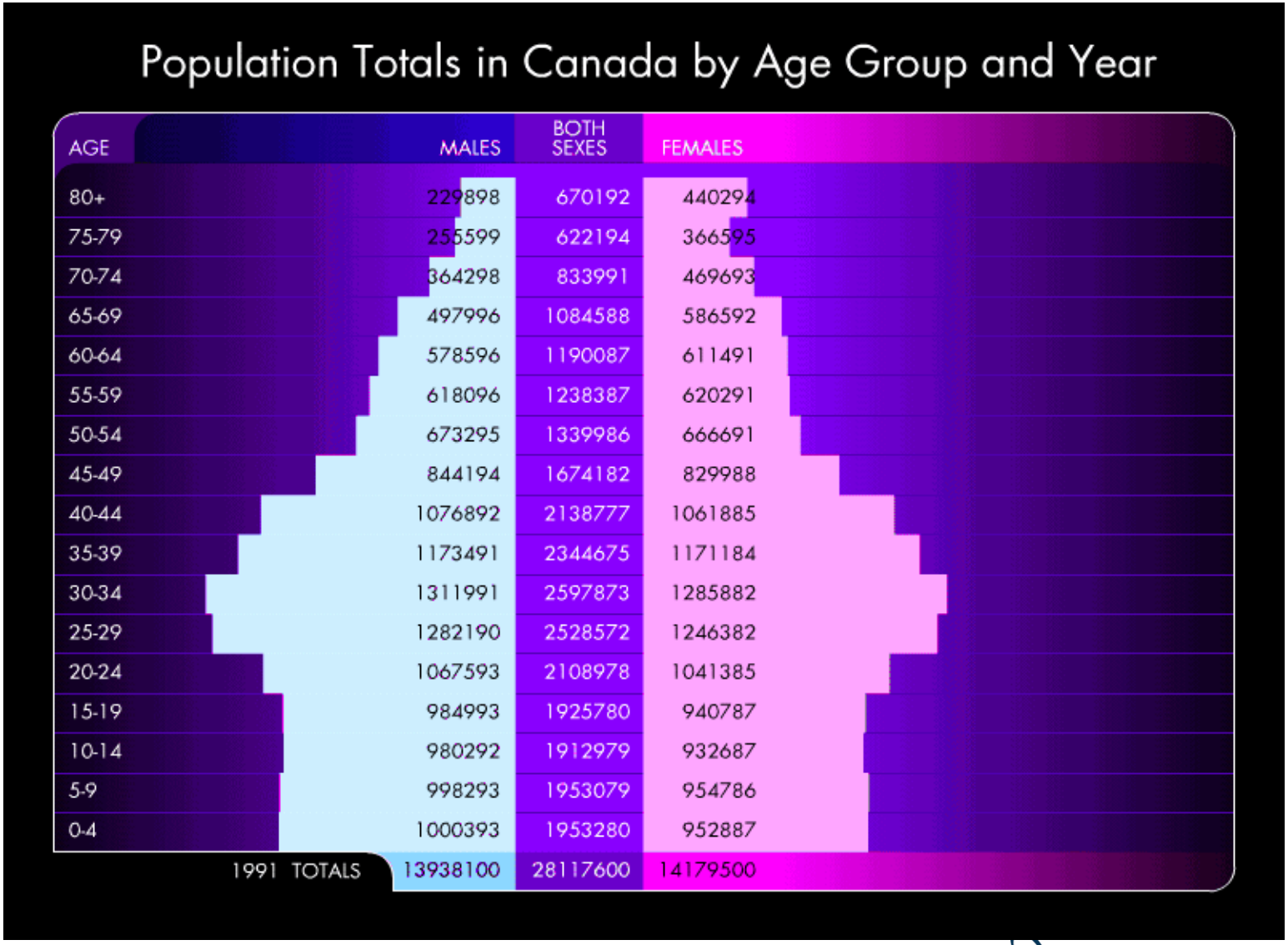

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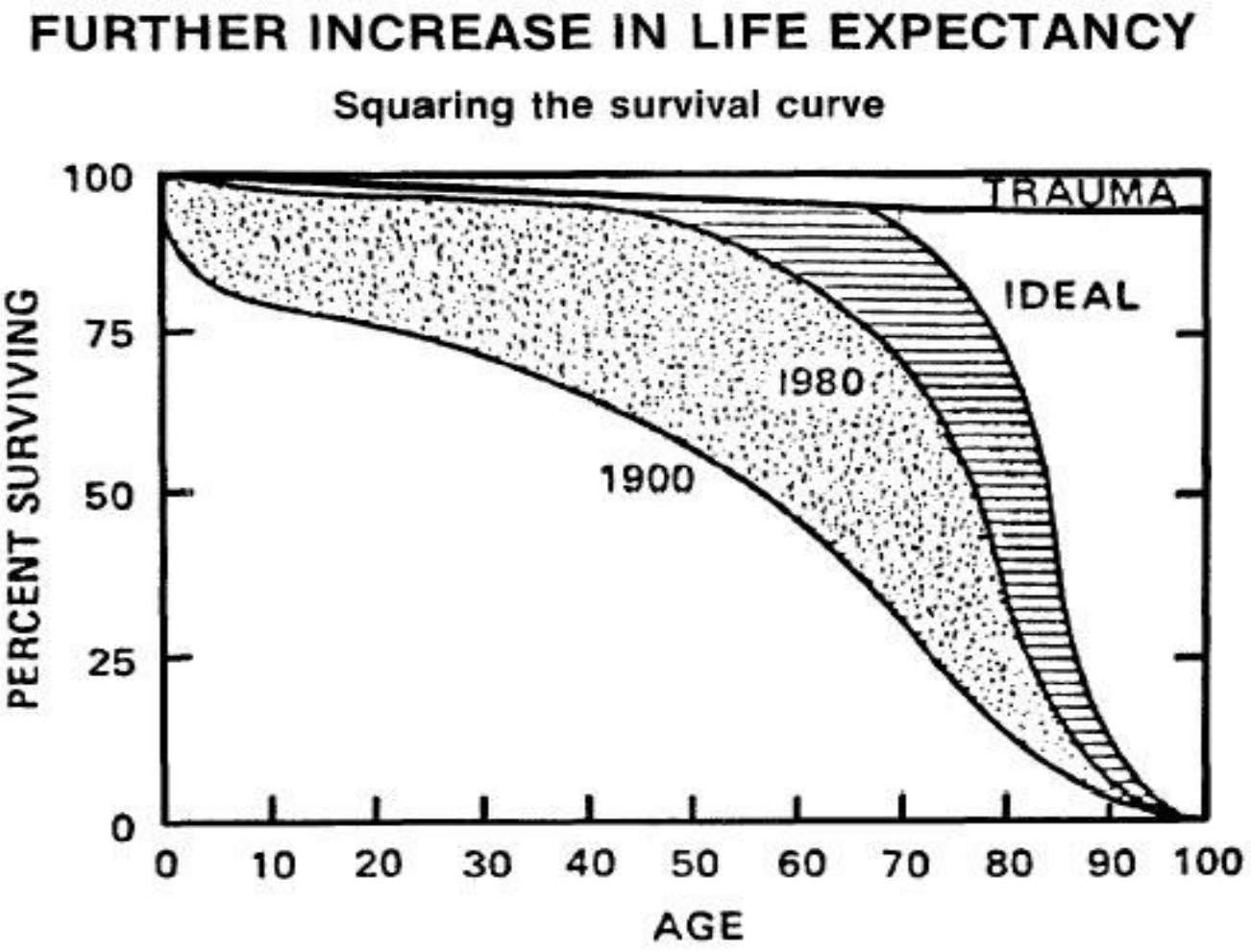
Rectangularization of the survival curve



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

Compression of morbidity

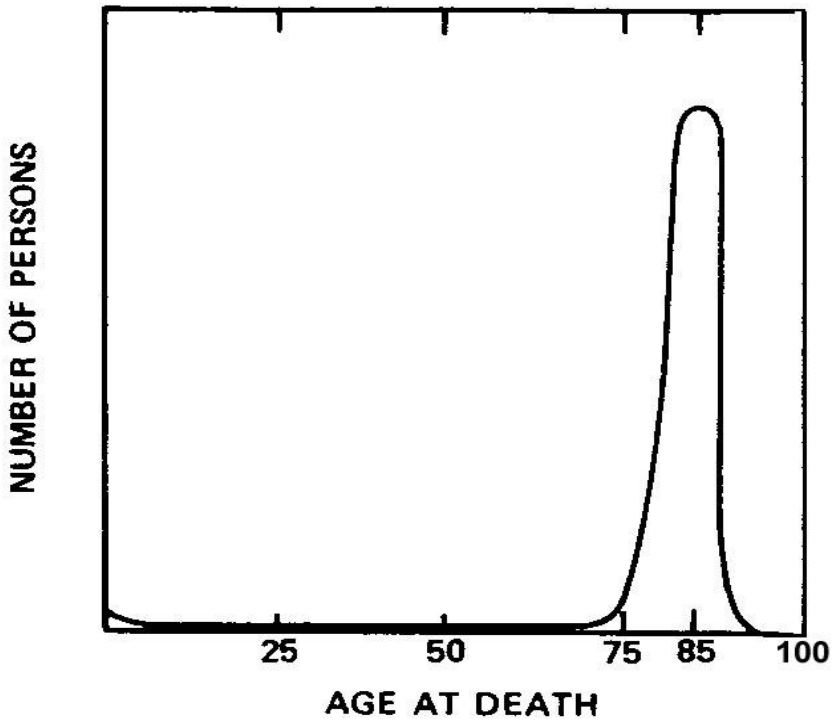


Figure: Mortality According to Age in the Absense of Premature Death

- 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

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

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

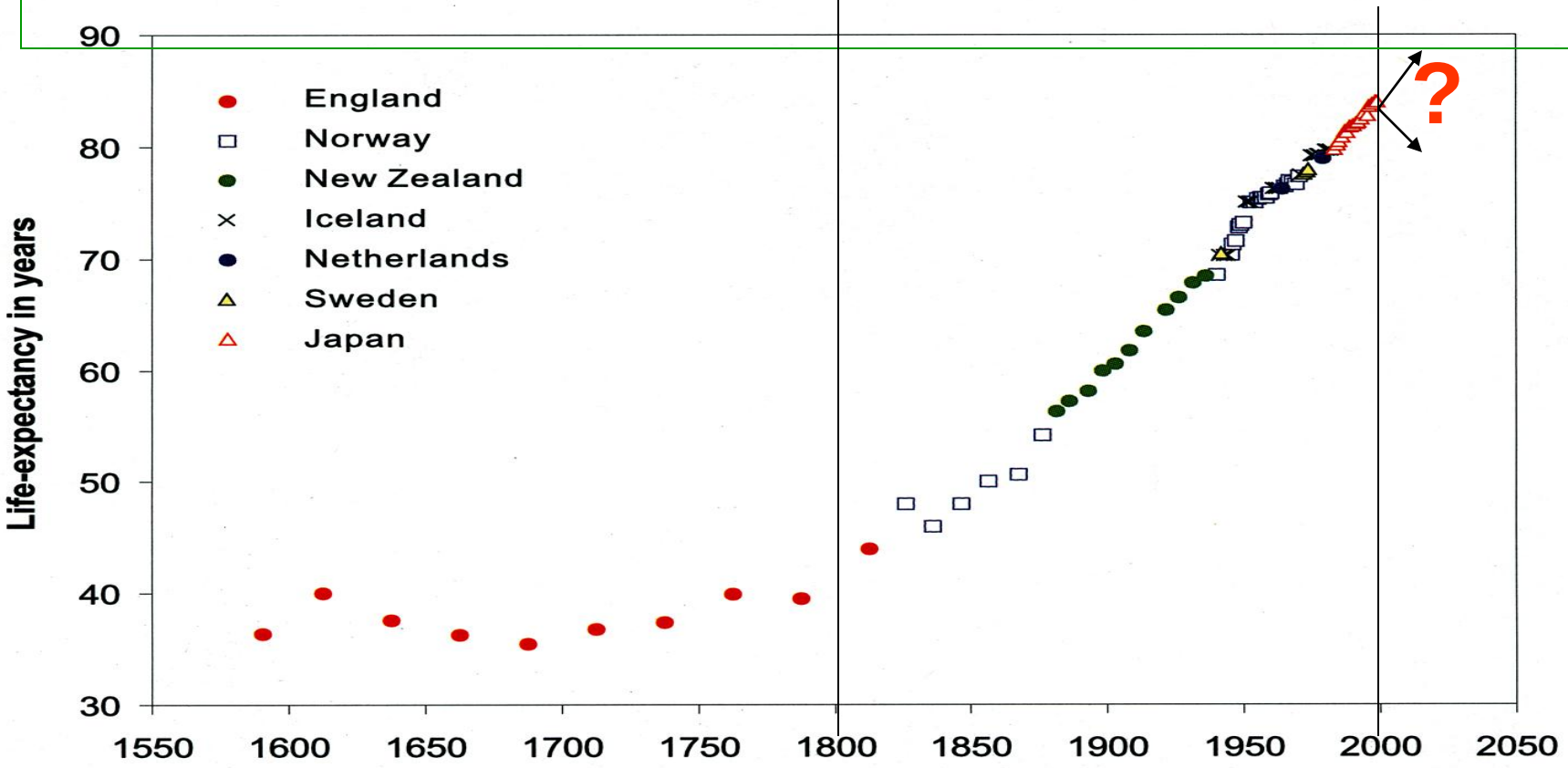
Historical increases of life expectancy

Oeppen and Vaupel, Science 2002; C Finch adaptation

Phase 1
early urban

Phase 2
sanitation-nutrition

Phase 3?
regeneration
modern medicine
Social Policy Innovation



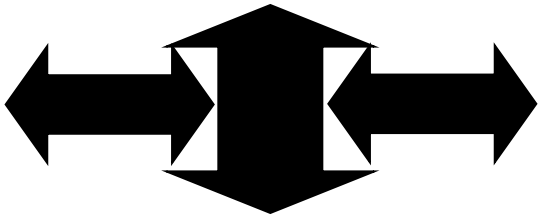
Demographic Futures

- 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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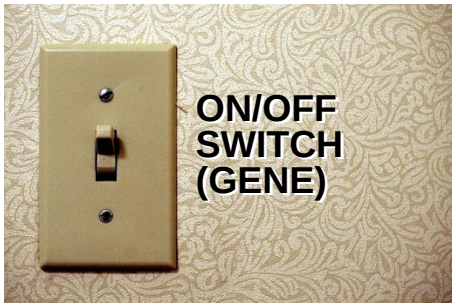
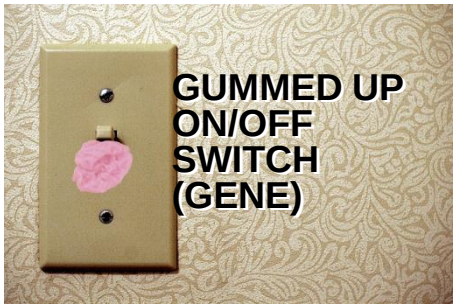
EPIGENETICS





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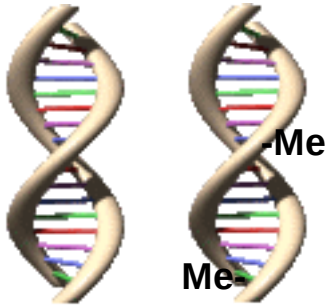


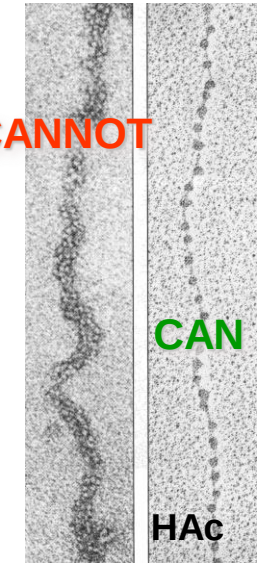
CAN

GUM

GUM

30 nm fiber 10 nm fiber

CANNOT



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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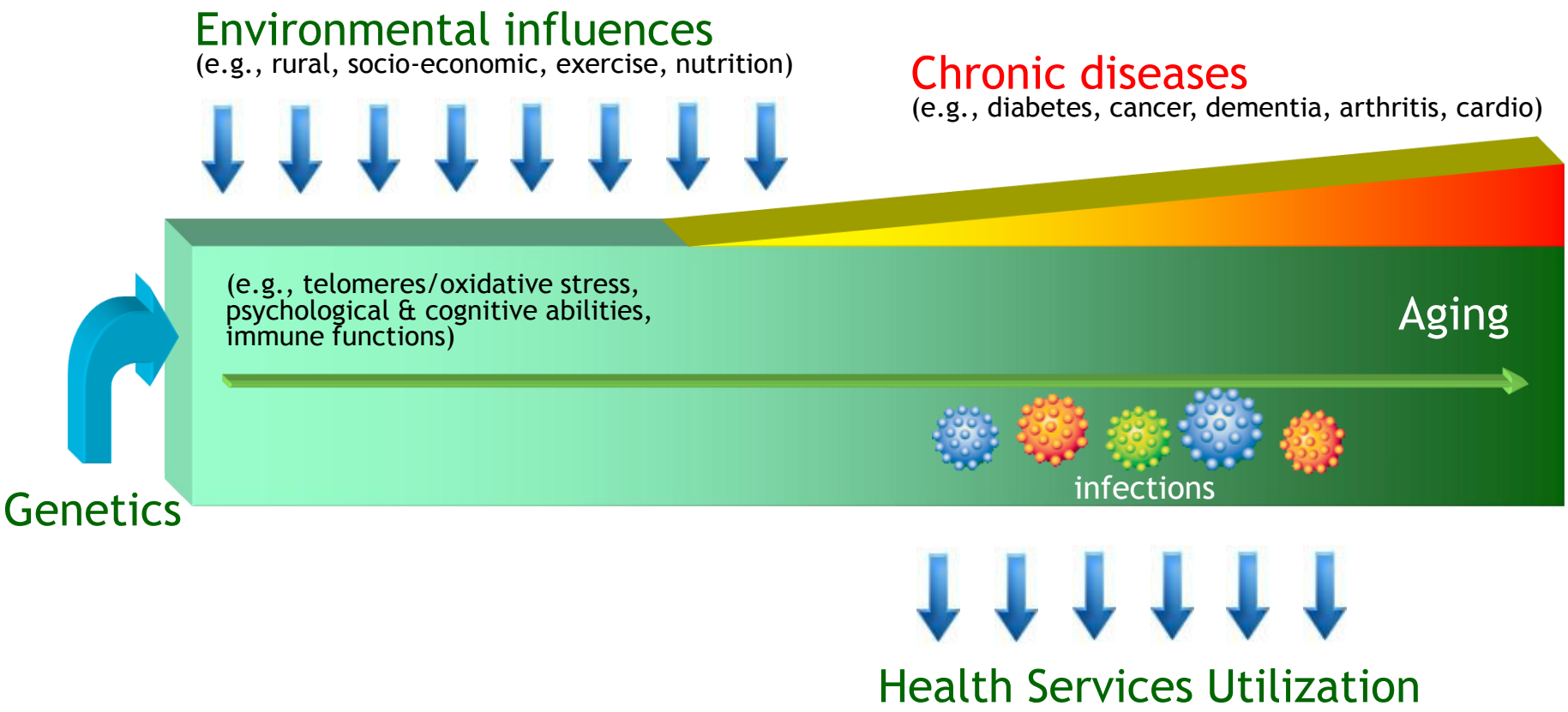
Intrinsic and Extrinsic Factors



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Canadian Longitudinal Study on Aging (CLSA)

- 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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Funders & Partners

- Strategic initiative of the Canadian Institutes of Health Research (CIHR)
- Funded by CIHR and the Canada Foundation for Innovation (CFI)
- Provinces and universities across Canada

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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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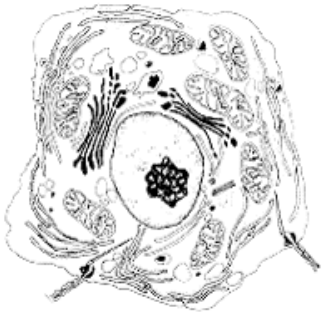
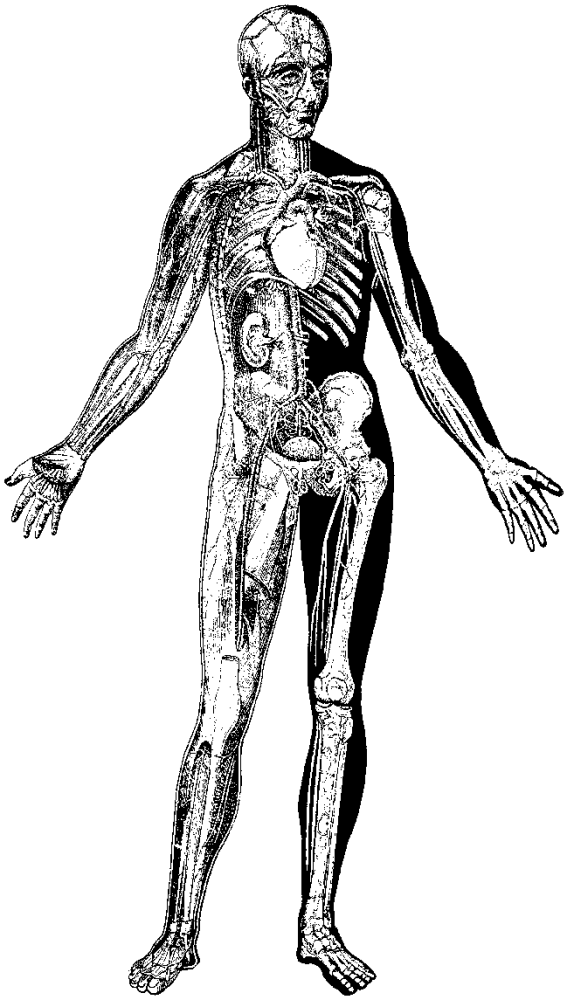


Innovation - Cell to Society

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



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Selected Research Goals

- The progression of **health** from middle age to early old age to older old age
- The determinants of **well-being and quality of life**
- **Social participation, social relationships and caregiving** in an aging population
- The examination of socioeconomic and health **inequalities** in an aging population
- **Retirement** and **post-retirement** labour market activity
- **Cognitive functioning** and **mental health**
- **Disability** and the compression of morbidity

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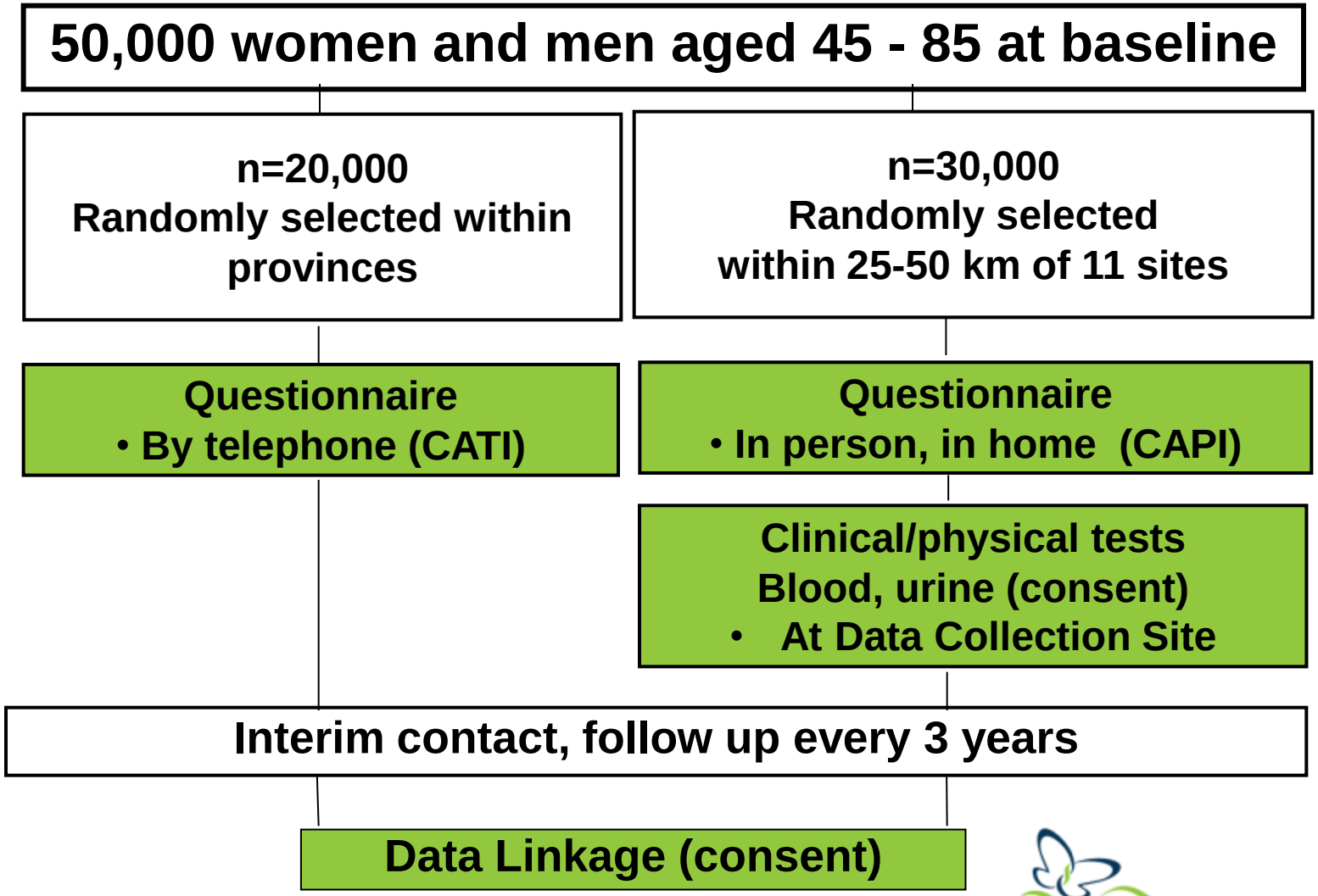
Study Overview



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CLSA Architecture

- Inception Cohort: 50,000 (at 11 sites)
- Questionnaires, Data 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

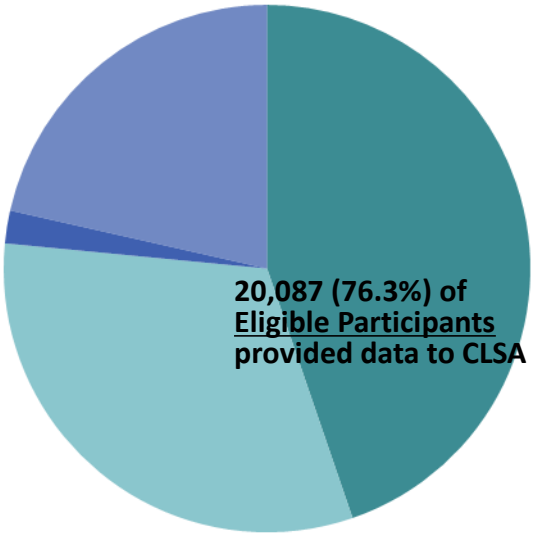
- Target population: People aged 45-85 living in private occupied dwellings in the ten provinces

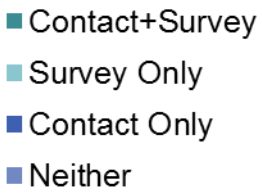
- Excluded:
  - Residents of the three territories
  - Persons living on Indian reserves or Crown lands
  - Persons living in institutions
  - Full-time members of the Canadian Forces
  - Residents of some remote regions

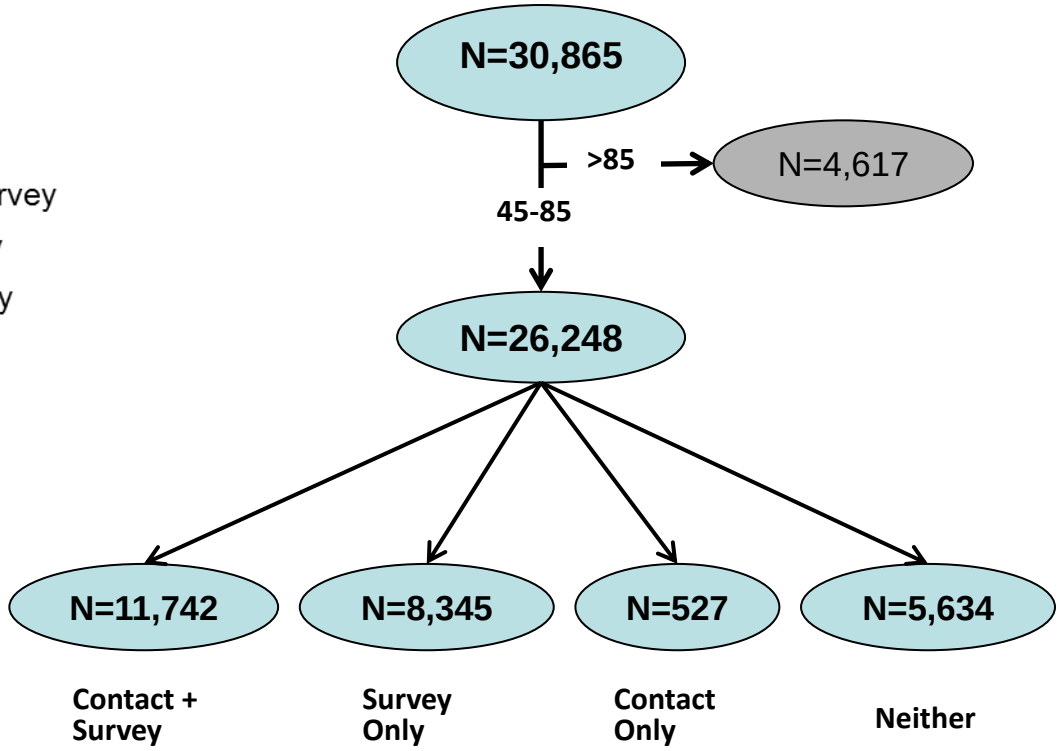
CLSA – CCHS Healthy Aging

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 Quebec, we could not use registries

Standardized, Centralized Process

Potential Participants Sent Study Information

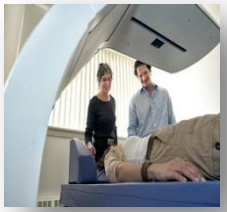
Participants Consent to Participate in CLSA

Participants Provide Questionnaire Data (n=50,000)

n=30,000 Home Interview

n=20,000 Telephone Interview

DATA COLLECTION SITE VISIT
Physical/Psychological Data



Biological Data

- Blood
- Urine

Stored at Biorepository and Bioanalysis Centre (BBC)

Stored at (NCC/SAC)

Questionnaire Data Processed

Linkage to Admin Data

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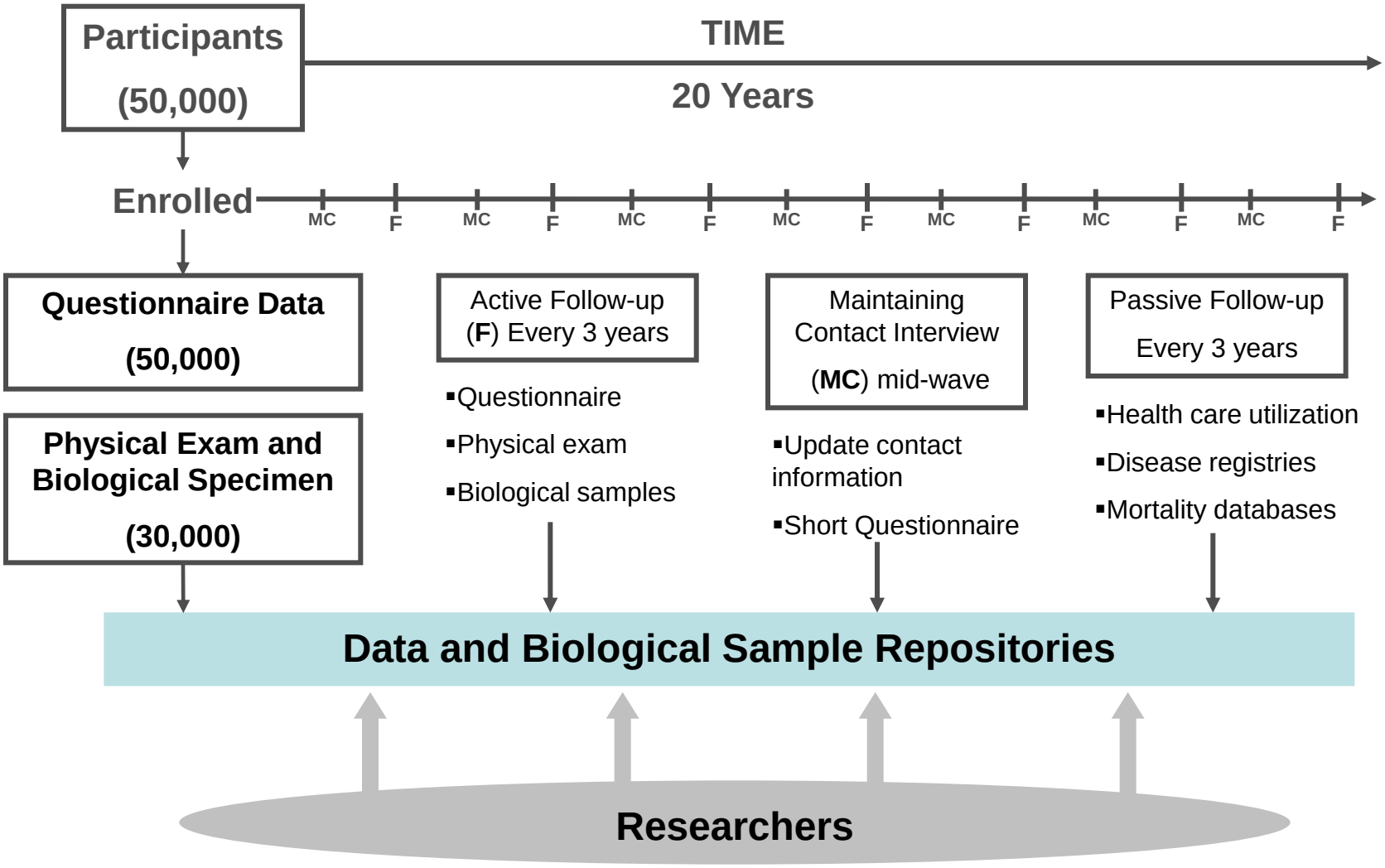

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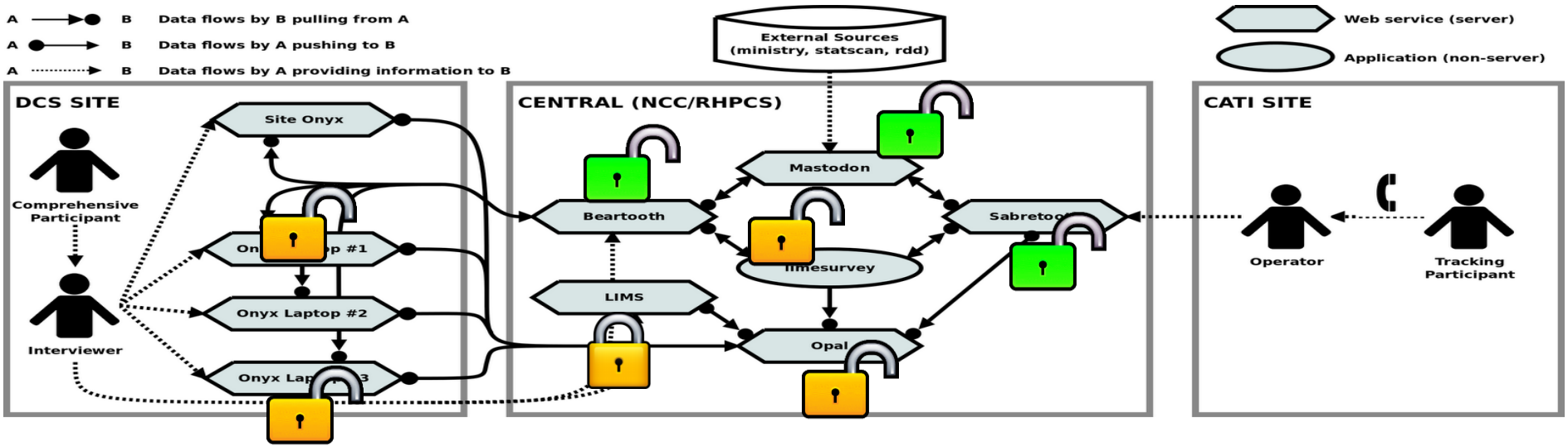
CLSA Software Architecture, IT Integration Systems for Paperless Data Collection



Mastodon - manages interactions with participants and securely stores identifying information

Sabretooth & Limesurvey – CATI software manages participant data collection, Interview scheduling and tracks the status of the interviews through to completion

Beartooth & Onyx – CAPI software used by the Data Collection Sites to coordinate the collection of questionnaire responses, physical measurements and biospecimens from participants

Opal – Central Data Repository – or databank – stores and manages all non-identifying data collected using Sabretooth, Beartooth and Onyx

Depth and Breadth of the CLSA

PSYCHOSOCIAL

- Social participation
- Social networks and support
- Caregiving and care receiving
- Mood, psychological distress
- Satisfaction with life
- Wealth
- Personality traits
- Work-to-retirement transitions
- Veteran identifier/ PTSD
- Retirement planning
- Social inequalities
- Mobility-lifespace
- Built environments

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Depth and Breadth of the CLSA

HEALTH INFORMATION

- Chronic disease and symptoms
- Medication and supplement use
- Women's health
- Self-reported health service use
- Oral health
- Administrative data linkage health services and drugs
- Other administrative databases
- General health
- Injuries
- Pain/discomfort
- Functional status
- ADL/IADL

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Depth and Breadth of the CLSA

LIFESTYLE & SOCIODEMOGRAPHIC

- Smoking
- Alcohol consumption
- Physical activity
- Nutrition
- Birth location
- Ethnicity/race/gender
- Marital status
- Education
- Income
- Transportation
- Home ownership

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At the Data Collection Site

Reception
Sign in
Bar code scan
Contraindications Q

↓

Measurement Room I
Hip Waist ratio
Height/Weight (BMI)
Heart rate & BP
ECG
c-IMT/Plaque sweep
Spirometry

↓

Measurement Room 2
DEXA (BMD, body composition, aortic calcification)

→

Measurement Room 3
Event PMT
Audiometer
Stroop & COWAT
(F,A,S) Choice Reaction
Social Network Q

↑

Hallway
4m walk
Timed Up and Go

↑

Measurement Room 4
Standing balance
Chair rise
Visual acuity
Fundus photograph
Occular pressure
Grip strength

→

Measurement Room 5
Timed PMT
Disease Symptoms Q

↓

Washroom
Urine Sample

↓

Biospecimen Room
50 ml blood draw
Sample processing

↓

Check out
Review of results
Snack
Honorarium

TOTAL TIME
2.5 – 3 HRS

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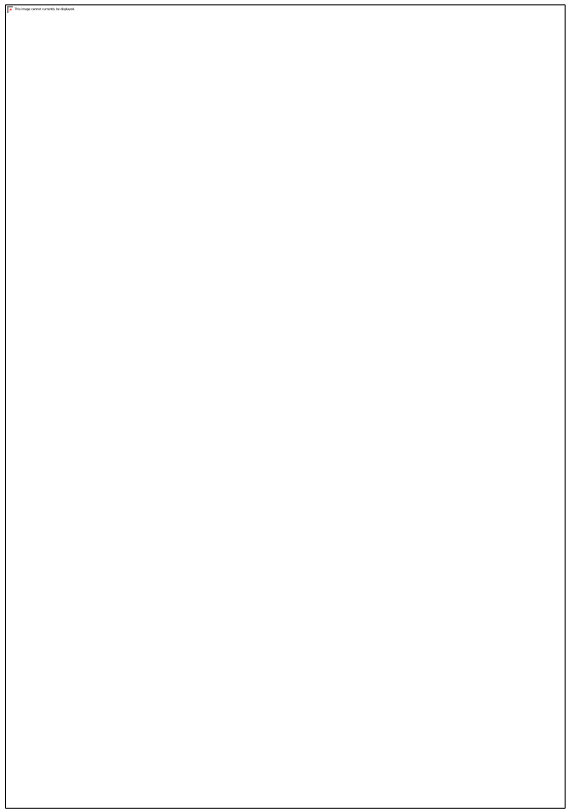
Biospecimen Room

Collection, processing, analysis

- 5 – 6 participants per day
- 50 mL blood
- Urine sample
- Hematology tests
- Collection to storage time
  2 hour



AcT DIFF, Beckman Coulter

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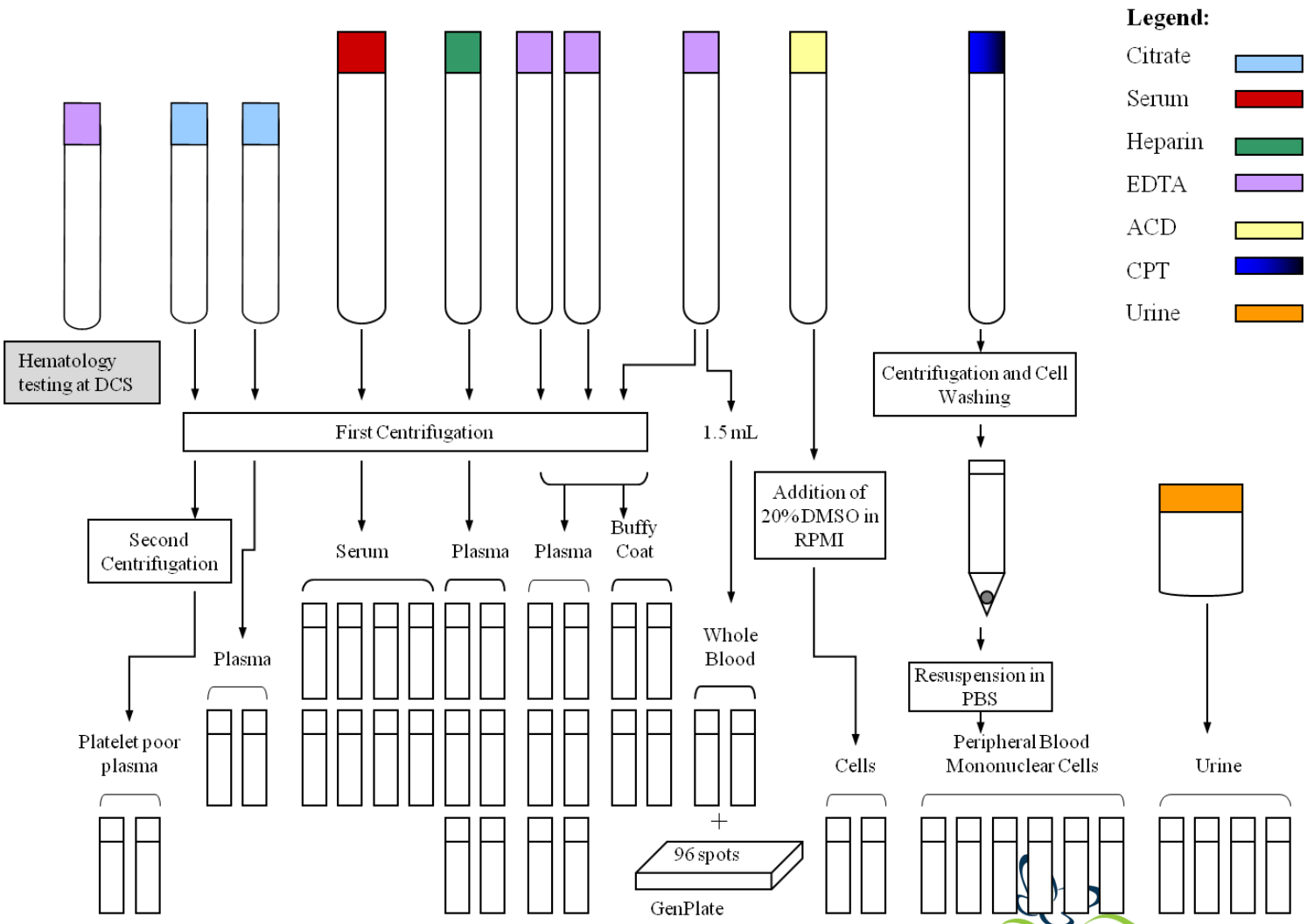
Biospecimen processing:
42 aliquots per participant



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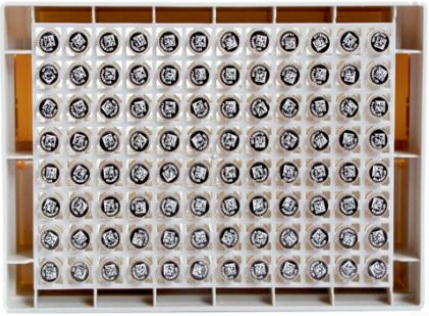
Storage & Shipping

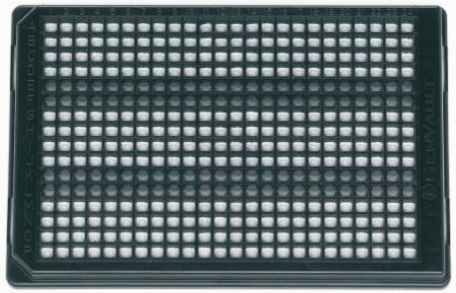
Matrix Tubes

- 500-µL V bottom screw top tubes
- Laser etched 2D unique barcode
- 96 well open-bottomed boxes for fast scanning
- Stored at DCS -80C for a maximum of 5 days



Microwell Plates

- 3 section GenPlates (IntegenX)
- 96 wells per participant (10 µL whole blood per well)
- Dried overnight, sealed with adhesive transparent cover



Shipping

- Precharged vapour shippers (-160C) with data logger
- Weekly to BBC via overnight courier

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Biorepository and Bioanalysis Centre (BBC)

- 31 nitrogen freezers (-180°C)
  - space for 5 million aliquots
- Personal Archive
  - dry storage, humidity controlled, at room temperature
- Laboratory Information System (LabWare)
  - Sample tracking system
  - Quality control
- Consumable warehouse

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Biomarker analysis

Disease Ascertainment Algorithms

- Diseases will not diagnosed by clinicians
- DAAs developed by CLSA Clinical Working Group
- Validated by pilot studies[1,2]

  - Osteoarthritis-knee, hip, hand
  - Parkinsonism
  - CAO
  - Diabetes
  - Hypo- and Hyperthyroidism
  - Ischemic heart disease
  - HBP
  - Stroke/Cerebrovascular event
  - Osteoporosis
  - Depression
  - Dementia

[1]*Raina PS, et al. Can J Aging 2009;28(3):275-85*

[2]*Oremus M, et al. Can J Aging 2013;32(3):232-9*

Proposed Data Linkages

- Regular linkage with mortality databases between waves of data collection
  - Decedent Questionnaire implemented for first follow-up
- Air pollution data (in collaboration with Health Canada)
- Administrative data linkage health services & drugs & other administrative databases for participant who provide consent

CLSA Recruitment: Where are we now?

Telephone-Administered Questionnaires

- Goal: Completion of all 20,000 baseline interviews Spring 2014
- As of last week:
  - 20,376 completed 60-minute baseline interview
  - 1,082 completed maintaining contact interview

In-home Interviews and DCS Visits

- Goal: complete first 8,000-10,000 baseline DCS visits by mid 2013
- As of last week:
  - 15,298 In home interviews completed
  - 12,777 DCS visits completed

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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 and secure IT infrastructure

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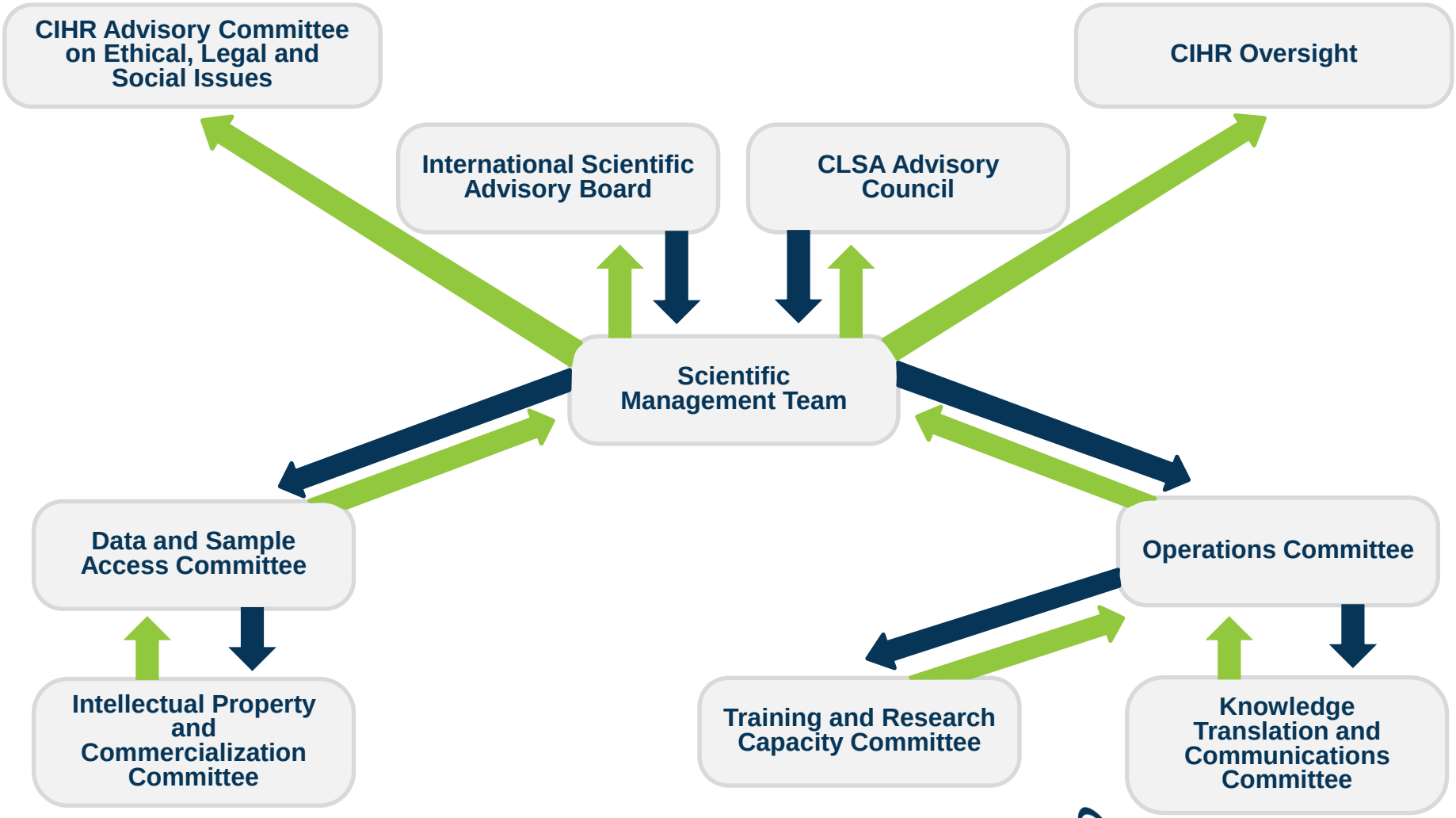
CLSA Governance Structure



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Coordinated REB Process

- First known coordinated approach for a national observational study in Canada
- 11 sites, 11 REBs, one standardized set of study documentation for informed consent
- Online documentation process developed by the Public Health Agency of Canada (PHAC)
- Submit to McMaster (lead) REB
  - Provisional approval, comments posted on PHAC portal for other sites to review
  - Sites post local reviews; one set of comments sent to CLSA team for response
- Annual amendments, coordinated ethics renewals

Data and Sample Access

- Data and samples available to the research community
- Fundamental tenets:
  - The rights, privacy and consent of *participants* must be protected and respected at all times
  - The confidentiality and security of *data and biological samples* must be safeguarded at all times
  - CLSA data and biological samples are resources that will be used optimally to support research to benefit all Canadians.

What is the process to access data?

- 20,000 CATI Interviews: anticipate data to be available mid-2014
- Application process via CLSA website portal
- Review: Administrative, Data and Sample Access Committee recommendation
- Approval, data/sample sharing agreements
- Raw data and/or samples to investigator
- Return of derived variables to CLSA dataset

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CLSA funded by the Government of Canada through the CIHR and CFI and by Provincial Governments

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CLSA Recruitment

Tracking Cohort

- Recruitment via CCHS complete
- Recruitment ongoing in all provinces through Ministry of Health (MoH) and/or Random Digit Dialing (RDD)
- Completion of all 20,000 baseline interviews by Spring 2013
- As of today:
  - 15,728 completed 60 minute baseline interview

Comprehensive Cohort

- Recruiting ongoing in all provinces through MoH and/or RDD
- Goal: complete first 8,000-10,000 baseline DCS visits by July 2013.
- As of today:
  - 5,029 in home interviews and 3,806 DCS visits completed (recruited)

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Milestones for 2013

- Complete recruitment for Telephone Interviews – 20,000
- Recruit first 10,000 participants for Comprehensive Assessment (DCS)
- Initiate Maintaining Contact Interview
- Data curation, derived variables and data cleaning
- Data access process, portal developed and tested
- Baseline tracking data released (Spring 2014)
- Planning and development for Wave 2

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