The Canadian Longitudinal Study on Aging:

Understanding the complexity of aging through interdisciplinary research

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DALHOUSIE UNIVERSITY
Inspiring Minds

Hallman Visiting Professor
Waterloo, May 2007

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Outline

- Conceptual framework
- Study design
- Content
- Process
- Progress
- Challenges
- Opportunities

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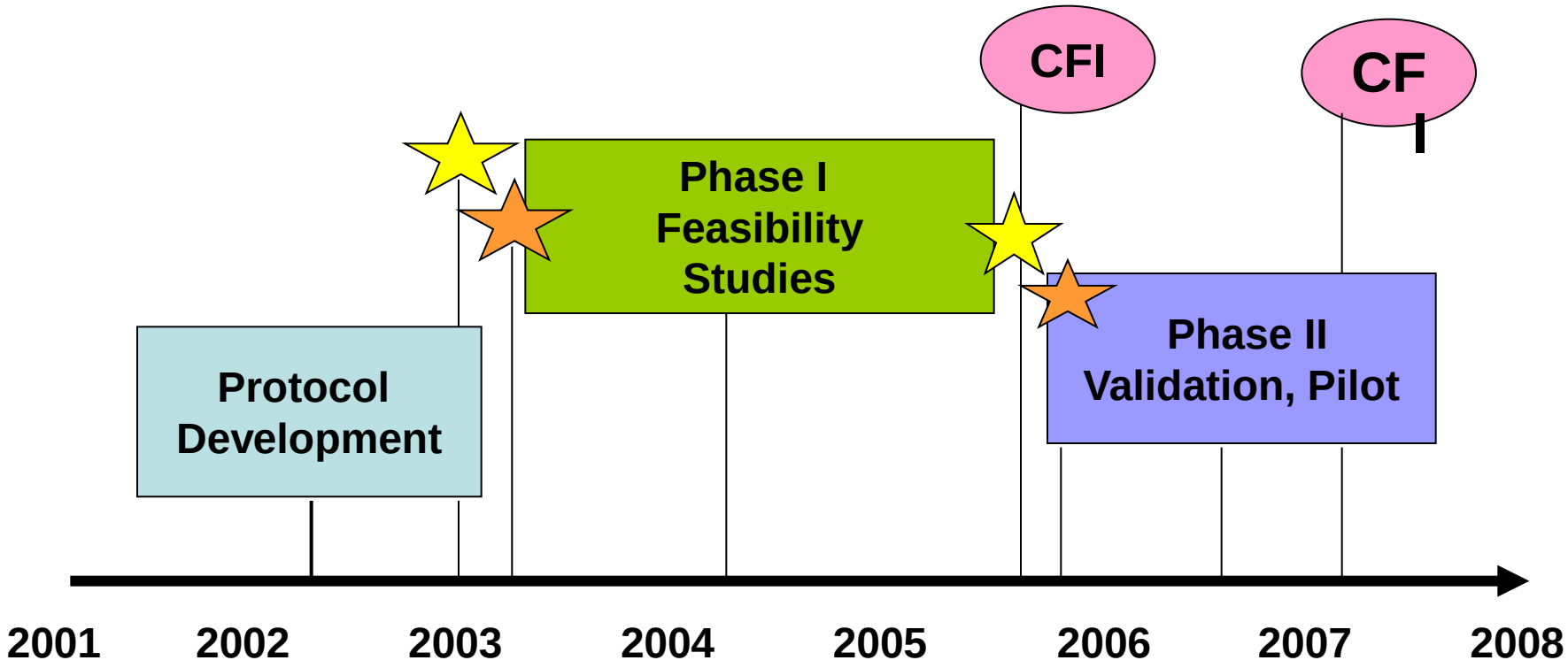
The aging of an academic: Development of the CLSA



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The Canadian Longitudinal Study on Aging (CLSA)

- A key component of the Canadian Lifelong Health Initiative, a strategic initiative of CIHR
  - The Canadian National Birth Cohort
  - The Canadian Longitudinal Study on Aging
- 3 principal investigators, more than 160 researchers from 26 institutions
- Multidisciplinary - biology, genetics, medicine, psychology, sociology, demography, economics, epidemiology, nursing, nutrition, health services, biostatistics, population health

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Rationale for CLSA

- Aging of Canadian population
- Longer life expectancies
- Baby boomers begin turning 65 in 2011
- Different needs, expectations
- Implications for health care system, social programs
- Need for evidence based decision making
- Generation of new knowledge

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CLSA Research Team

- 3 Principal Investigators
  - Susan Kirkland, Dalhousie University
  - Parminder Raina, McMaster University
  - Christina Wolfson, McGill University

- 4 Senior Advisors
- 3 Institutional Advisors
- 13 Theme Leaders/ Key Co-Investigators
- 200 Collaborators

Representing 26 institutions
in 10 provinces

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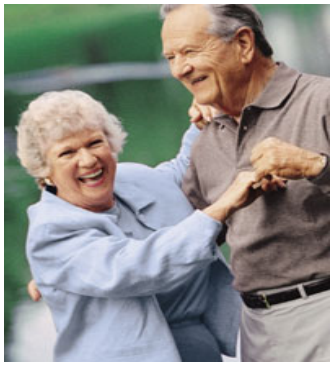
Overall Aims of the CLSA



- To examine aging as a dynamic process.
- To investigate the inter-relationship among intrinsic and extrinsic factors from mid life to older age.
- To capture the transitions, trajectories and profiles of aging.
- To provide infrastructure and build capacity for sustained high quality research on aging in Canada.

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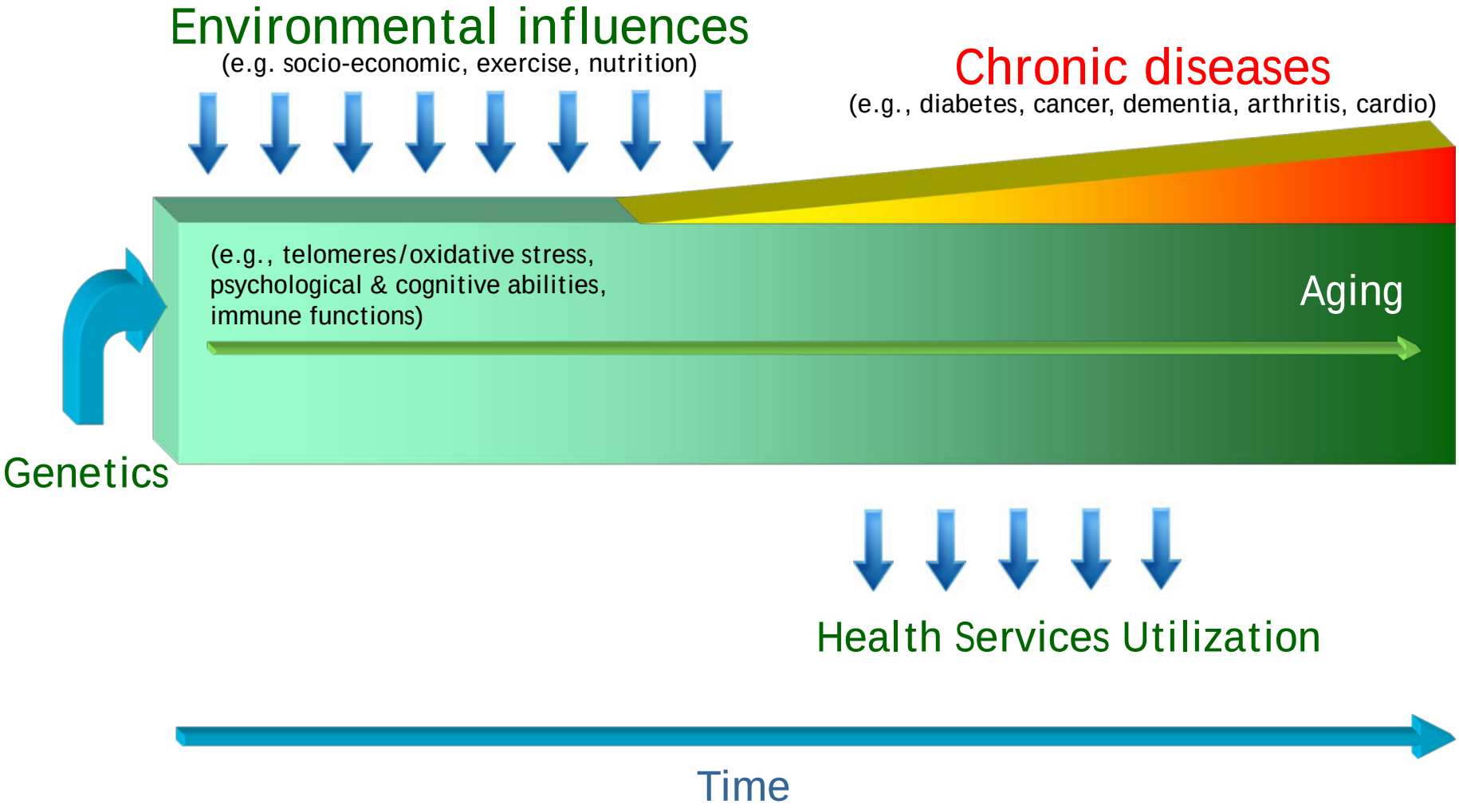
Aging as a process



CLSA Conceptual Framework

- Healthy aging
- Lifecourse approach
- Determinants of health
- Continuum of micro to macro levels
- Gene-environment interactions
- Dynamic and changing face of Canadians

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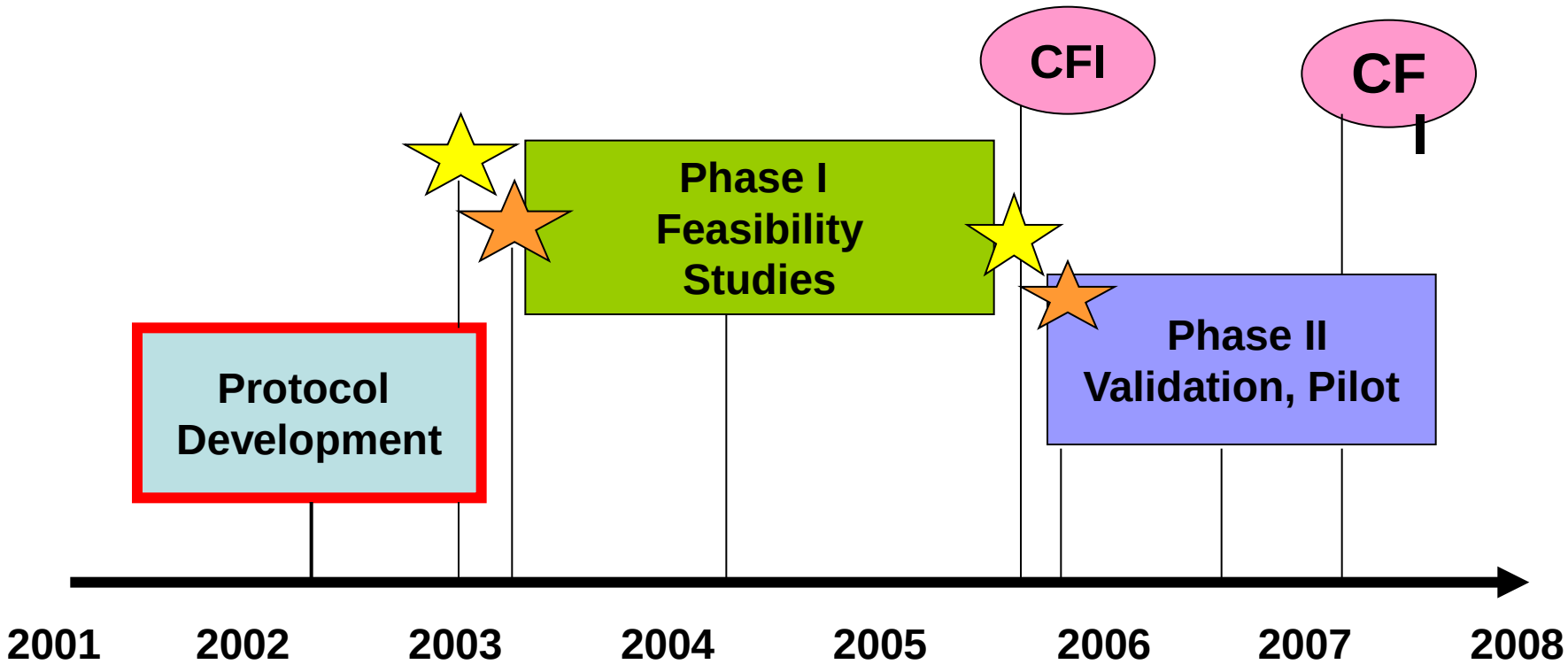
CLSA Timeline



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CLSA Protocol Development

- Development on multiple fronts
- Concurrent, iterative
  - Conceptual framework
  - Study design
  - Research questions
  - Study domains, content

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Review of 70 longitudinal studies on aging worldwide

- Majority study people over the age of 65; very few look at the aging process from mid-life to old age
- Many collect information on social factors or retirement but lack detailed information on physical health, or vice versa
- Very few capture the changing individual within a changing context and incorporate multiple levels of inquiry: the cell, the individual and society
- Very limited intersection between biology, clinical, and psychosocial dimensions of aging
- Very few focus on how individuals cope or adapt to changing circumstances and how it impacts their well-being

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Aging research in the genomics era

- Development of large scale biobank studies
- Gene-gene interactions, gene-environment interactions
- Study of quantitative traits (continuous endpoints)
- Antecedents of disease/systems markers of aging:
  - eg serum cholesterol, vital capacity, systolic blood pressure
- Longitudinal study of gene-environment interaction throughout the lifespan

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Conceptual framework: Models of healthy/successful aging

Literature dominated by two models:

Rowe and Kahn

- *Differentiates successful aging from usual aging*
- *Based on the assumption that successful agers engage in behaviours that modify risk factors to allow them to meet a high degree of physical, mental and social functioning*

Baltes and Baltes

- *Selection, optimization, compensation*
- *Based on the assumption that decline is an inevitable part of aging, and that successful agers are those who engage in processes that help them to adapt to change in order to meet their own goals*

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A conceptual model for the CLSA

- Central tenet that aging is multi-dimensional
- Chose to use the term “healthy aging”
- Recognize that there are many different ways that an individual can age
- Establish a framework to incorporate multiple elements to guide our thinking

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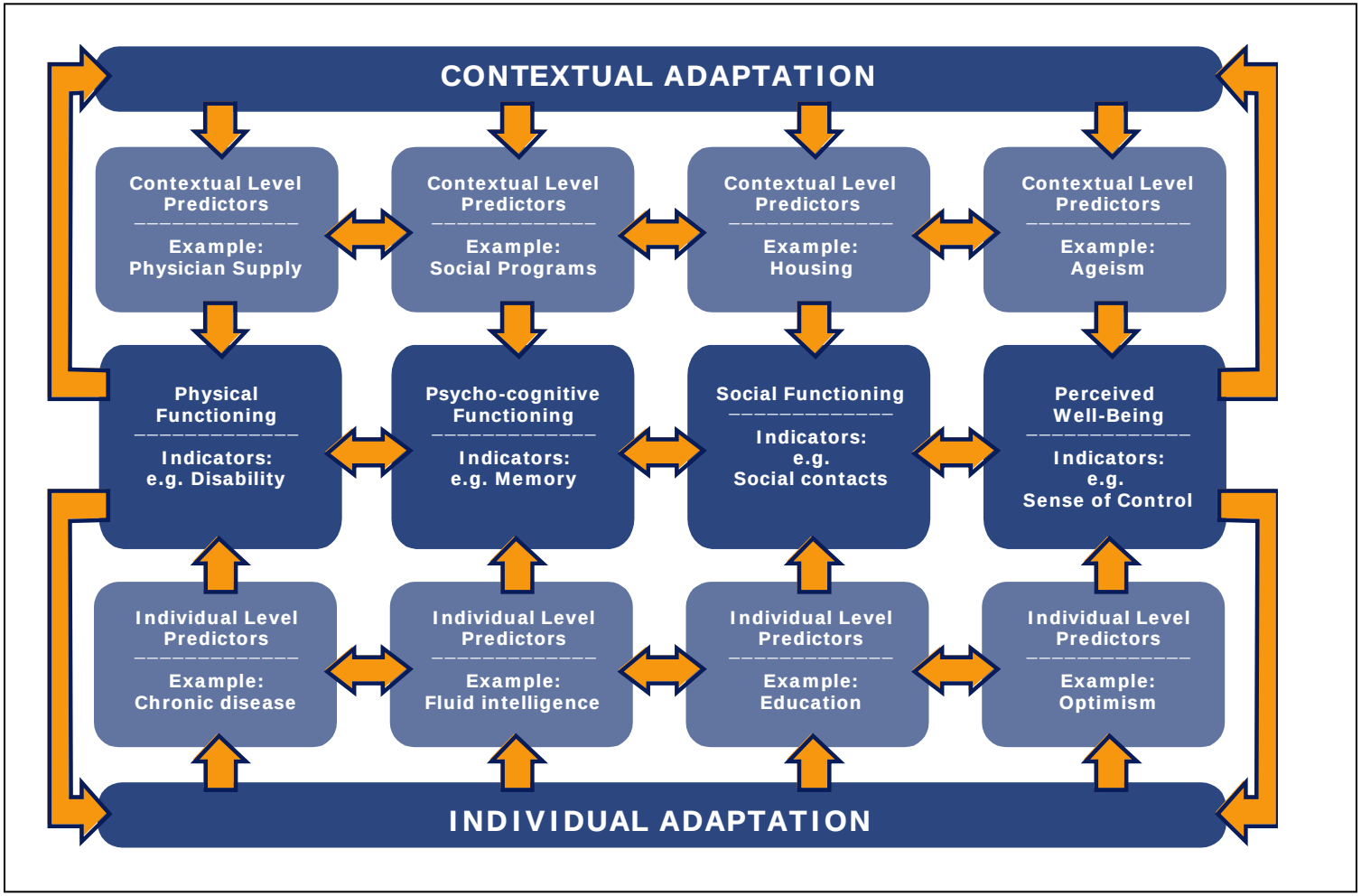
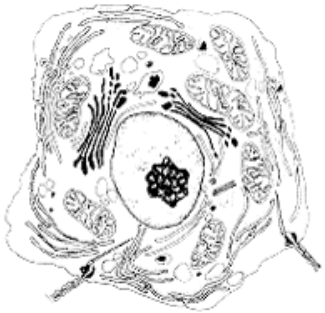
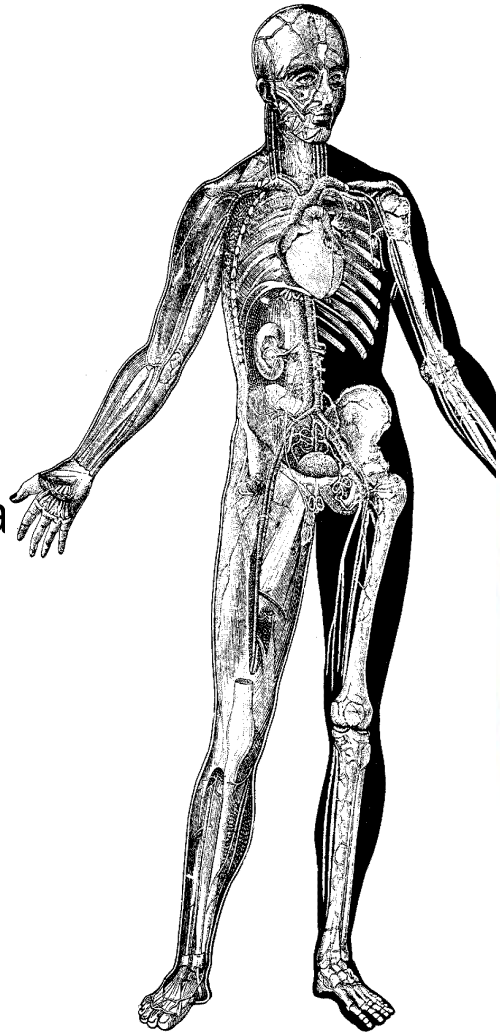
CLSA Model of Aging





Innovation - Cell to Society

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



CLSA Cohort Assembly

- Representative sample of Canadian population
  - Stratified by age, sex,province
- Options for sampling frame:
  - National: Census (2006), CCHS
  - Provincial: Health insurance files, enumeration records, telephone directories

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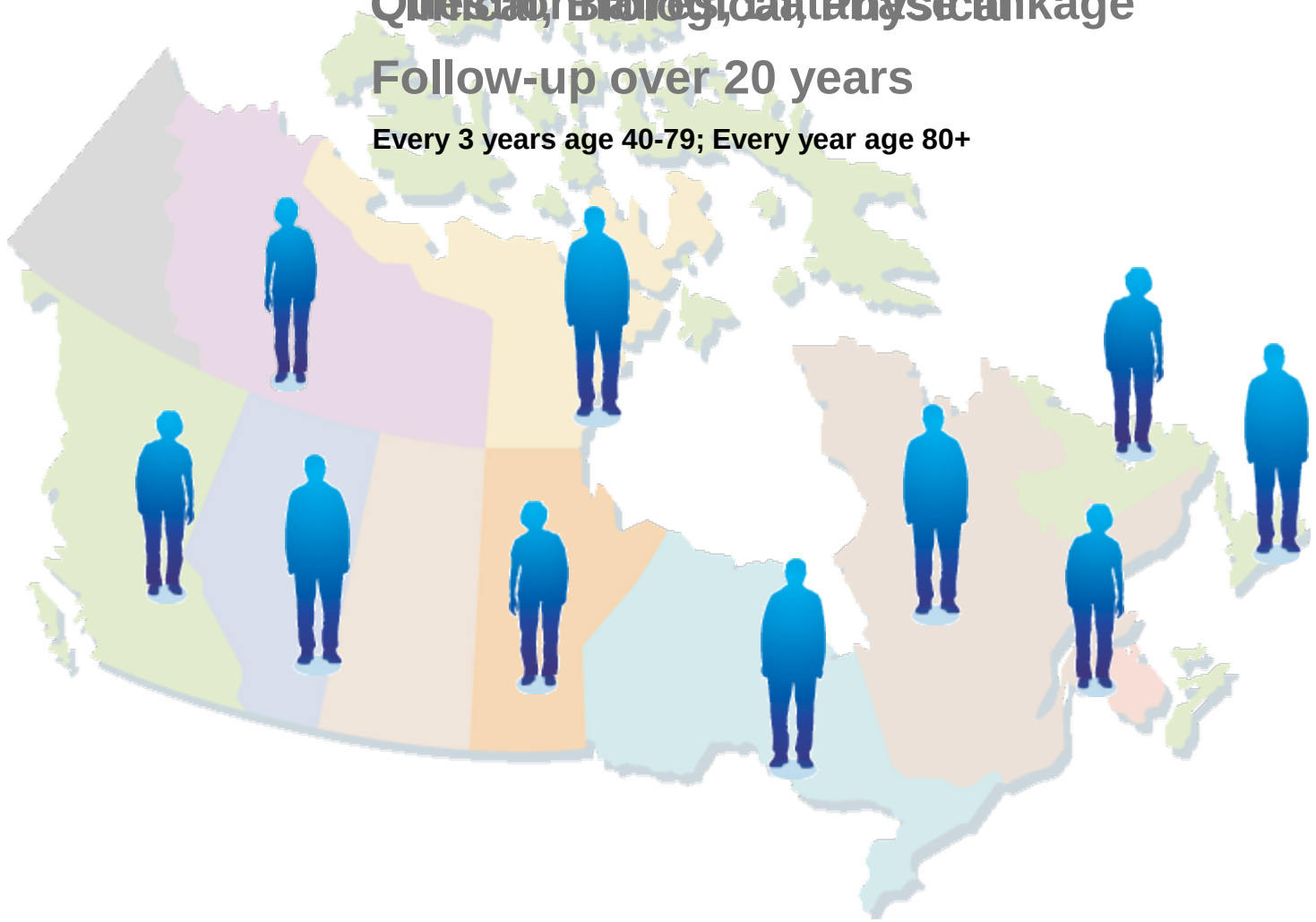
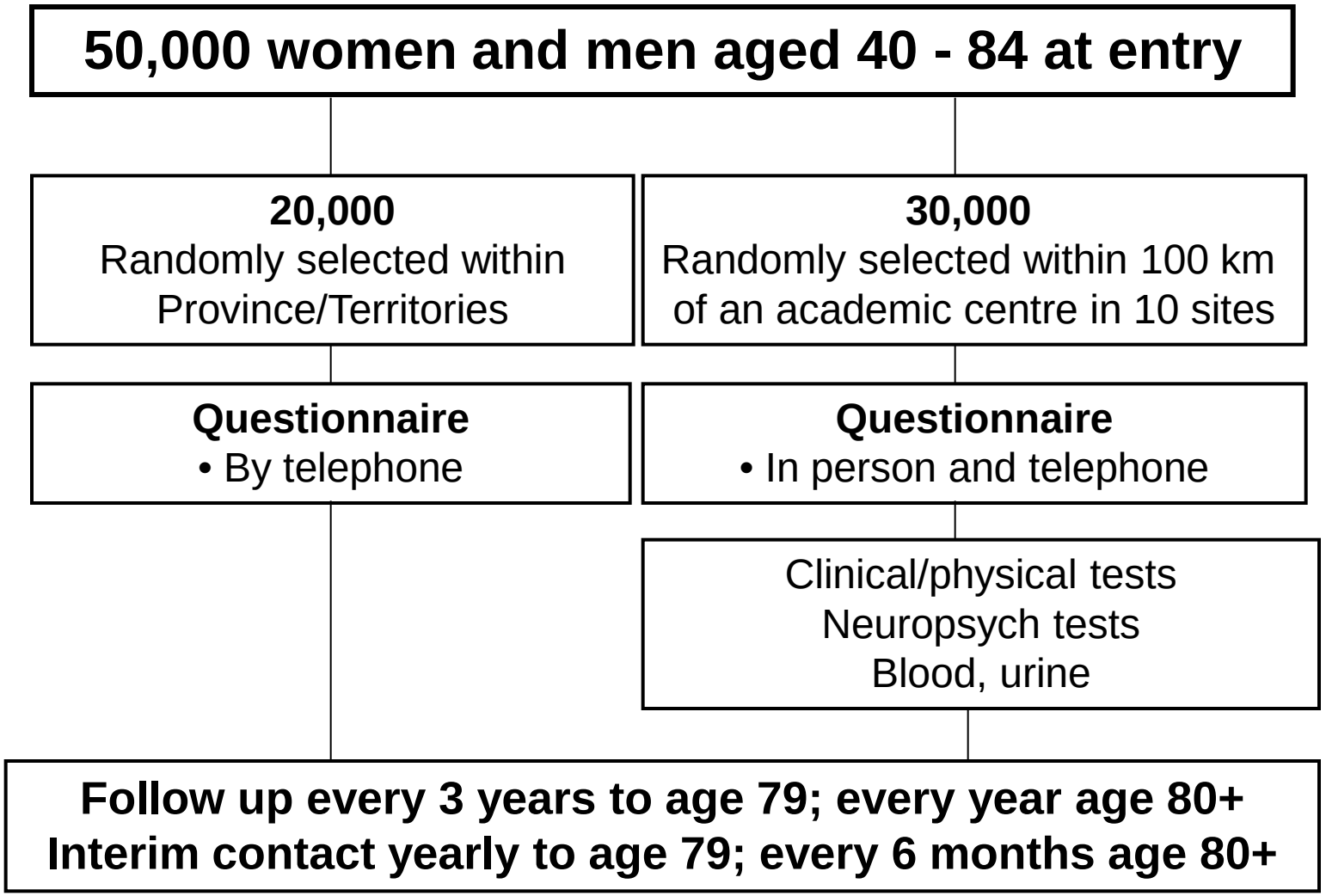
CLSA Architecture

- Participant recruitment: 50,000 30,000 (at 10 sites)
- Questionnaire, Biologic, Data, Physician
- Follow-up over 20 years

Every 3 years age 40-79; Every year age 80+



Overview of the CLSA



Questionnaire

	Content	Time
Demographics	Age, sex, education, occupation, income, employment, wealth, pension, housing, ethnicity, household, family, transportation	15 mins
Psychology	Cognitive function, everyday competence, adaptive functioning, coping, personality, emotion, psychological distress, values, pain	20 mins
Social	Social networks, social support, work and retirement, participation, stability and change of place, structural inequalities	20 mins
Health Services	Services, medications, informal supports complementary therapies, assistive devices, health care access, costs, continuity of care	20 mins
Health Status	Quality of life, oral health, arthritis, diabetes, hypertension, communication, hearing, frailty, injuries, vision, chronic diseases	55 mins
Lifestyle	Alcohol, exercise, leisure activities, diet, nutrition, vitamin and mineral supplements, smoking, sleep, weight history	20 mins

2.5 hrs

In person follow up (30,000) Protocol at Data Collection Sites

Component	Time
Face to face Interview	75 min
Neuropsych Testing	20 min
Physical/clinical	80 min
TOTAL	**175 min** **~3 hrs**

+

Blood, urine collection	30 min
OGTT	2 hrs

Methodological Challenges

- **Population subgroups**
  - Geography: remote, urban/rural
  - Residence: community dwelling, institutional
  - Ethnicity: ethnic minorities, immigrants, aboriginal population
- **Sample size calculations**
  - Multiple endpoints
  - Multiple analytic approaches
- **Attrition**
  - Simulations using age specific mortality, loss to FU in NPHS
- **Missing Data**
  - Partial, wave
  - Imputation, re-weighting
- **Responder burden**
  - Vary modules according to age, sex
  - Embedded substudies
  - Participant engagement

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CLSA Content Development

- Expert working groups responsible for development of theme-specific content
- 30 minutes per working group as a guide
- Domains, research questions, predictors, outcomes, measures
- Guiding principles for content development: longitudinal, niche, aging

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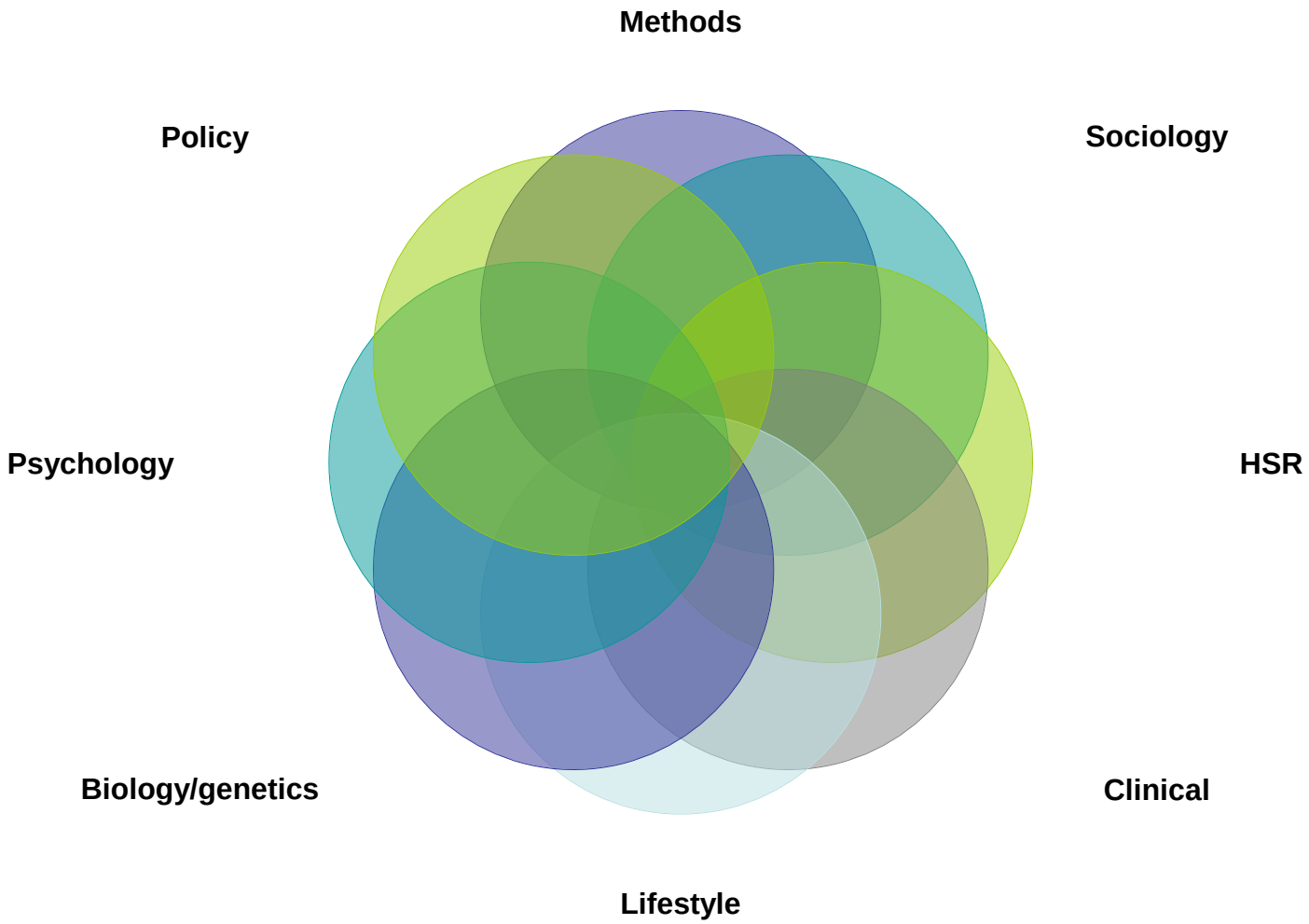
Interdisciplinary Research Agenda



Research Questions

- Overarching research questions
- Working group-specific research questions
- Individual level research questions

- Precursors, quantitative traits, consequences

Example Research Questions: Cognition as a Quantitative Trait

Cognition as a precursor:

- Is decline in cognitive functioning (memory, executive function and psychomotor speed) in mid and later life associated with subsequent adverse health related (or biological) outcomes?

- Is decline in cognition (memory, executive function and psychomotor speed) in mid and later life associated with changes in social participation?

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Example Research Questions: Cognition as a Quantitative Trait

- How do individuals with cognitive change adapt to maintain performance in everyday functioning?

- Are general lifestyle activities (e.g. physical activities, social activities, domestic activities, community service, etc) associated with cognitive functioning and/or change in cognition over time after adjustment for sensory impairment?

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Example Research Questions: Cognition as a Quantitative Trait

Cognition as a mediator

- How do cognitive functions mediate or moderate relations between biological/physical status and adaptive functioning and/or social participation?

Cognition as an outcome

- Are changes over time in cognition (memory, executive function and psychomotor speed) associated with specific biological states?

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Precursors	**Quantitative Trait**	**Consequences**
Physical activity	COGNITION	Dementias
Medication use	Memory	Depression
Education	Intelligence	Social engagement
Sleep	Exec function	Quality of life
Self esteem	Psychomotor	Institutionalization
Head trauma		Cargiving
Hypertension		Injuries
Societal role exp		Work/occupation
Genes (APOE)		Abuse

Research Domains

Social

Social networks

Social support

Social participation

Work

Retirement

Income and wealth

Education

Housing

Demographics

Health services

Psychological

Cognition

Personality

Emotion/mood

Depression

Adaptive functioning

Lifestyle

Physical activity

Food consumption

Alcohol

Smoking

Weight/obesity

Physical

General health

Functional health

Disability

Chronic diseases

Oral health

Arthritis

Medication use

Biological

Biochemical markers

Genetics

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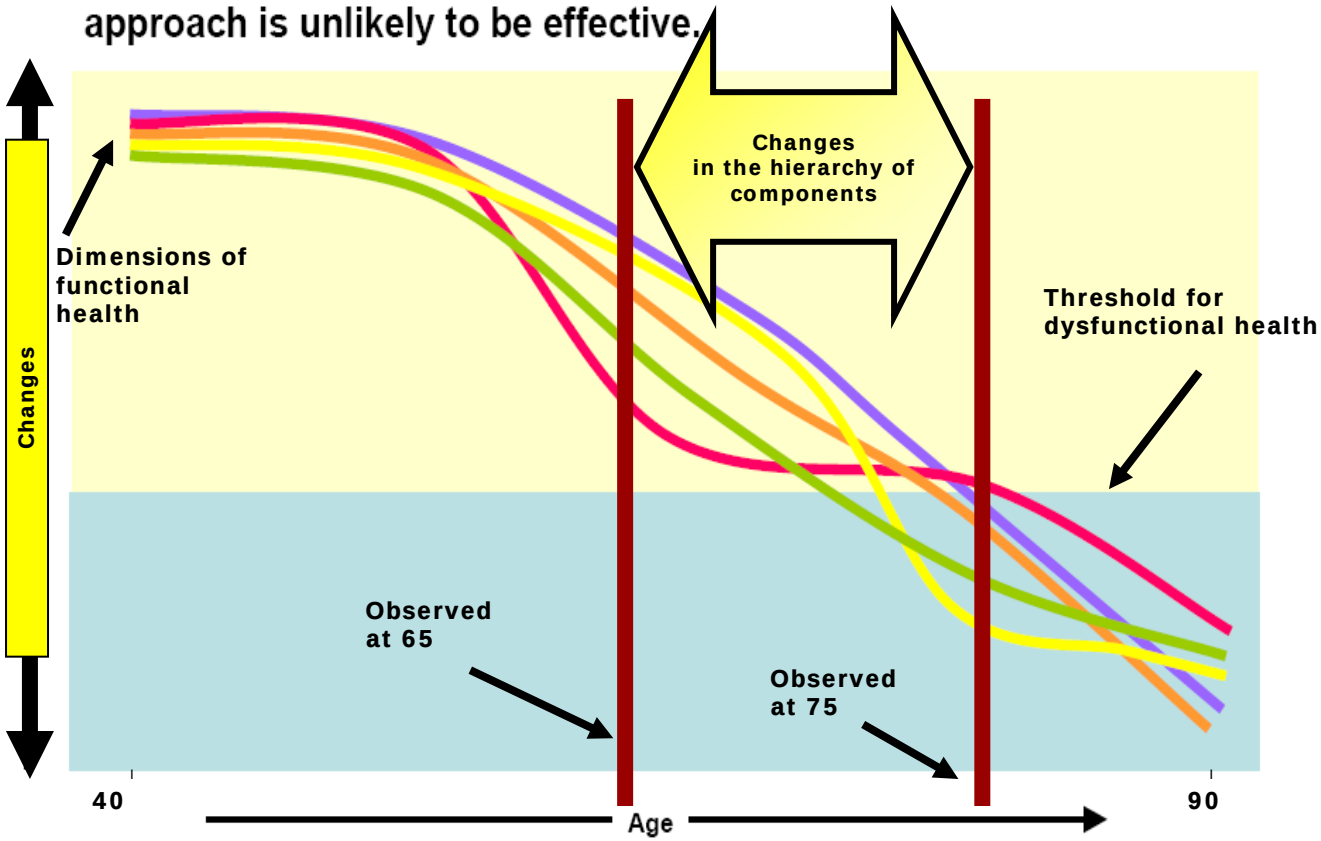
Trajectories of Aging



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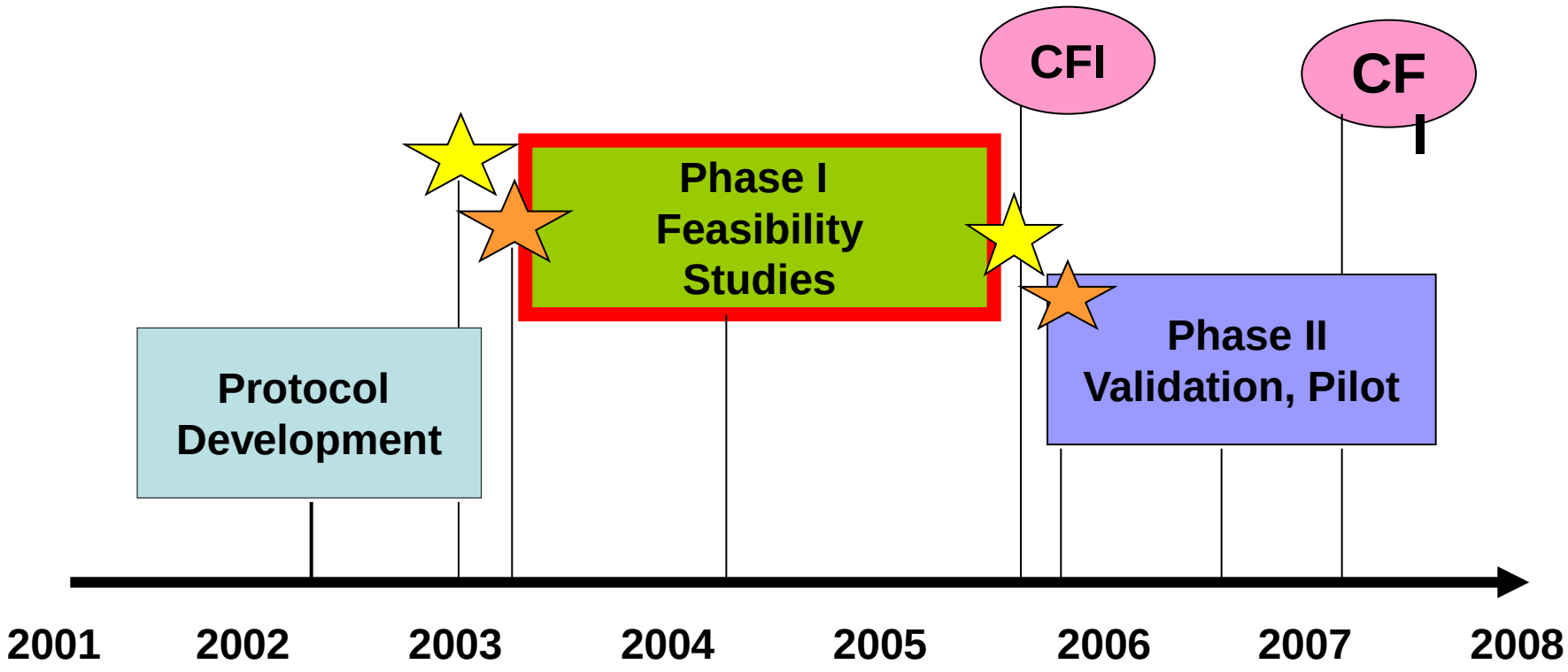

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Purpose of Feasibility Studies

- Assess logistics of proposed study design and its implementation
- Designed to be informative to the development of any large-scale, longitudinal study involving in-depth data collection
- Directly applicable to the CLSA
- Used to inform further refinement of the protocol

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Participant Recruitment and Retention Studies

Study 1:	Views of Canadians towards participation in a longitudinal, population-based study
Study 2:	Test consent to release coordinates of participants in the CCHS
Study 3:	Identification of the optimal consent process
Study 4:	Identification of possible alternative sample frames
Study 5:	Screening tools to assess capacity to consent to observational research
Study 6:	Development of optimal process for the baseline interview

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Data Collection and Data Flow Studies

Study 7:	Feasibility of proposed blood and urine sample collection/shipping/storage and analysis strategies
Study 8:	Strategies to enhance data linkage with health care utilization data bases and disease registries
Study 9:	Development and evaluation of disease identification algorithms
Study 10:	Issues related to the return of clinical information to study participants and/or general practitioners
Study 11:	Assessment of logistics of data collection methods, data transfer and security

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Views of Canadians

Methods

- Focus groups conducted in six Canadian cities: Vancouver, Calgary, Winnipeg, Hamilton, Montreal, Halifax

Key Findings

- Healthy aging considered important, timely
- Universities trusted to carry out the study; government to fund
- Private companies should not profit from the stud
- Providing blood and urine samples adds credibility
- Trust that confidentiality will be protected
- Concerns around the use of DNA
    - Information not be shared with third parties
    - Why needed, how would it be used, who would have access
- Altruism is a key motivator for most participants

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Key Messages

- **Willing to help others, but want to know that findings are put to use**

  "So any kind of study that will boost…health and people's situation in life, you can't help but do something good as long as it's not stuck in the shelf somewhere when it's done."

- **Want to feel appreciated contributing to something worthwhile**

  "…basically your primary reason for doing it would be to help others. So if they come back and say, hey, what you've done has helped in this way, that would be kind of nice, yeah."

  "…it'd be nice once in a while to get a phone call or a letter in the mail that said this was done, this was great, you know, updates; wouldn't have to be a monthly newsletter, but a once a year newsletter type of thing…"

- **Expect some kind of feedback on own health status**

  "…that could very well be one of the benefits, to have more information, more broader information, more precise information about your own and your family's health."

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CCHS as CLSA sample frame

Statistics Canada's Canadian Community Health Survey (CCHS) identified as a survey vehicle that could provide a sample frame for the recruitment of a representative sample of the Canadian population

Objectives

- Determine the willingness of CCHS participants to share **personal coordinates** (contact information) with CLSA
- Determine the willingness of CCHS participants to share **survey responses** with CLSA

Methods

- Additional CLSA content added to the activities of the CCHS 3.1 Pilot Test

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Results by Sex, Age, Location

	M	F	Total
Share contact info	64.7%	62.8%	63.8%
Share survey data	75.3%	76.4%	75.8%

	40-54	55-64	65-74	75+	Total
Share contact info	63.9%	76.8%	46.7%	55.3%	63.8%
Share CCHS data	73.7%	86.6%	64.4%	73.7%	75.8%

	Vancouver	Montreal	Halifax	Total
Share contact info	44.2%	78.1%	69.7%	63.8%
Share CCHS info	62.5%	90.5%	74.2%	75.8%

Note: 77% signed consent

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Consent to Release Coordinates

Consider…

n=429	100% of eligible sample
n=319	74.1% of those eligible agreed to participate in CCHS
n= 298	94.9% of those who agreed to participate in CCHS agreed to share their data with the MOH
n=229	77% of those who agreed to share with MOH signed consent to share contact info, share data with CLSA

Therefore… 53% of those originally eligible agreed to share contact info

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Data Linkage with Health Care Utilization Data Bases

Objectives

- Examine barriers and facilitators to accessing and linking with health care utilization databases
- Develop best practice guidelines for use of and access to health care utilization data

Methods

- Telephone interviews conducted with P/T Data Stewards (n=20) and P/T Information Privacy Commissioners / Ombudsmen (n=13)

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Key Findings

- Standard approach in all jurisdictions does not exist
- Informed consent: study questions, data accessed, for how long, where stored, how used, who has access, periodic re-consent
- Data access agreement: Provincial/territorial MOH
- Privacy Impact Assessment
- Provincial privacy legislation AND health information legislation is constantly evolving
- Lack of standardization of variables, coding, completeness, updating
- Requires extensive “up front” work with data stewards, managers
- Complex process, but possible

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Blood and Urine Sample Collection, Shipping, and Storage Strategies

Objectives

- Document the infrastructure of existing laboratory services
- Compare the feasibility, logistics and cost of collecting specimens in private community-based and hospital-based clinical laboratories
- Assess the ability to accommodate study participants, execute standardized protocols

Methods

- At each site and lab type, participants randomized to:
  - Collection of 93mL of (fasting) blood and a urine specimen OR
  - Collection of 93mL of (fasting) blood and a urine specimen AND Oral Glucose Tolerance Test (OGTT)

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Methods

- Participants recruited by family physicians in Vancouver, Hamilton, Montreal
- Processing time approximately 1 hour, to be conducted within a 2 hour window
- Frozen, stored, shipped to central location in batches
- Evaluated for volume, number of aliquots per tube, evidence of hemolysis, labelling errors

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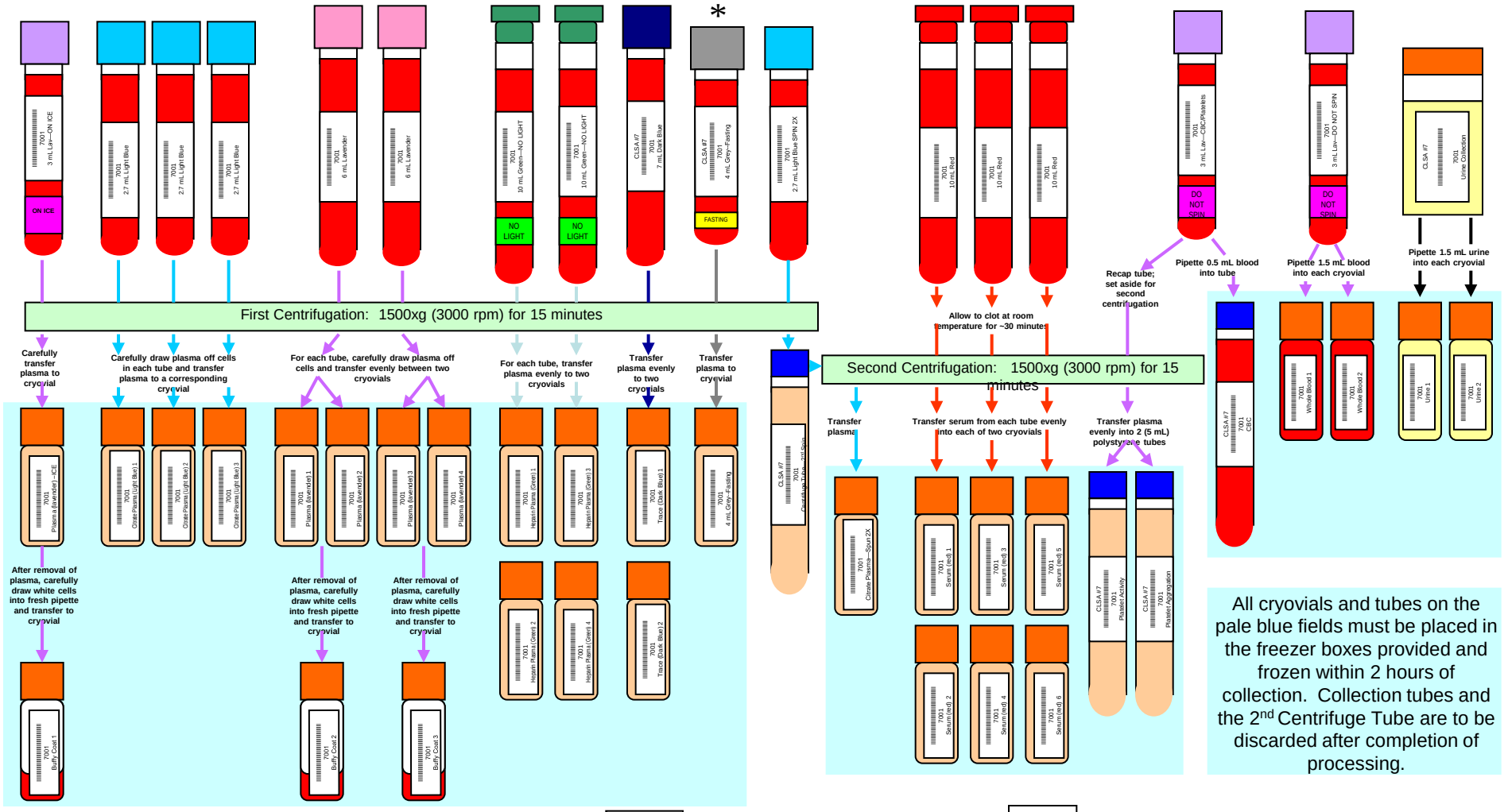
Specimen Processing for the **C**anadian **L**ongitudinal **S**tudy on **A**ging: Biological Specimen Collection Feasibility Study



All cryovials and tubes on the pale blue fields must be placed in the freezer boxes provided and frozen within 2 hours of collection. Collection tubes and the 2nd Centrifuge Tube are to be discarded after completion of processing.

* For Grey tube labeled CLSA #7 7001 4 mL Grey Post 2 hr OGTT, processing is identical; plasma is transferred to cryovial labeled CLSA #7 7001 4 mL Grey—2 hr OGTT

Key Findings

- Not all provinces have private labs
- Instability in private sector
- Considerable variation in capacity among private labs and hospital labs
- Reasons for declining participation: current demands, space and time constraints, complex, demanding protocol
- Average lab charges per participant: $144 (range $66 to $270) in hospital labs and $254 (range $96 to $535) in private lab settings
- Withdrawal rate 22%
- Participant satisfaction high

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Return of Clinical Information

Objective

To explore the issues involved in returning individual clinical rest results to research participants and/or their family physicians

Methods

- Internet survey of 68 relevant longitudinal studies.
- Focus groups to explore potential participants' views of the importance, the type of information they would like to receive, and how they would like to receive it.
- Telephone interviews with PIs of 13 longitudinal studies

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Return of Clinical Information

Type of measure	Collected	Returned if collected
Anthropomorphic measures	85%	35%
Functional ability	50%	20%
Neuropsych exam	45%	33%
Blood pressure	75%	63%
EKG	65%	75%
Advanced clinical tests	22%	83%
Vision	32%	63%
Hearing	42%	67%
Oral health	10%	50%
Blood biomarkers	70%	79%
Urine biomarkers	45%	44%
Biosample for genetics	60%	0%

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Key Findings: Survey

- Majority of studies returned some individualized information to study participants
- Ethical considerations identified as most important factor in deciding whether or not to return results
- 75% of respondents recommended return of individualized test results; 25% recommended no return
- Reasons in favour of returning individualized results: ethical considerations, participant retention, benefits to participants
- Reasons against returning individualized results: ethical considerations, tests not done in clinical settings, reliability too low, results not readily interpretable

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Key Findings: Focus Groups

- Participants well-informed health care consumers
- Strong perceived onus on health studies to return individual results, especially adverse findings
- Participants overwhelmingly want their own individual results or want their physician to have them
- No expectation of interpretation or counseling
- Return of results seen as a benefit of participation and an incentive to continue
- Focus group perceptions and expectations around the return of individual test results mirrors an emerging trend among researchers and funding bodies

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Ethical and Legal Issues

- Informed consent
  - For 20 year duration
  - For storage of biological samples, clinical, questionnaire based information
  - Genetic and biochemical testing
  - Products from biological samples: cell lines
  - For unspecified research projects in the future
- Harmonization across provinces
  - Ethical approval from multiple REBs
- Privacy laws regarding use and disclosure of personal information across provinces

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Ethical, Legal, Societal Issues (ELSI)

- Lawyers
- Ethicists
- Philosophers
- Geneticists
- Epidemiologists
- Social scientists
- Privacy commissioner

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Informed Consent

I have read the Information Package for the Canadian Longitudinal Study on Aging.	yes ☐	no ☐
I understand the information I have read about the Canadian Longitudinal Study on Aging.	yes ☐	no ☐
I agree to participate in the Canadian Longitudinal Study on Aging. I understand this involves completing questionnaires, and having physical measures conducted at study centres.	yes ☐	no ☐
I agree to collection of biological samples.	yes ☐	no ☐
I understand biological samples and information about me will be stored for 20 years and even longer for studies related to human health in the aging process.	yes ☐	no ☐
I agree to linkage of information collected from me with databases held by public institutions.	yes ☐	no ☐
I agree that results of routine clinical tests will be mailed to me.	yes ☐	no ☐
I understand that attending a study centre for physical measures testing does not replace a visit to my doctor or other health care provider.	yes ☐	no ☐

I have had time to decide whether to participate in the Canadian Longitudinal Study on Aging. I have had a chance to ask questions about the Study. I understand that even though I have consented to some or all of the items on this form, I can still withdraw from participating in the Study at any time.

Name:
Signature:
Date:

Name of witness:
Signature:

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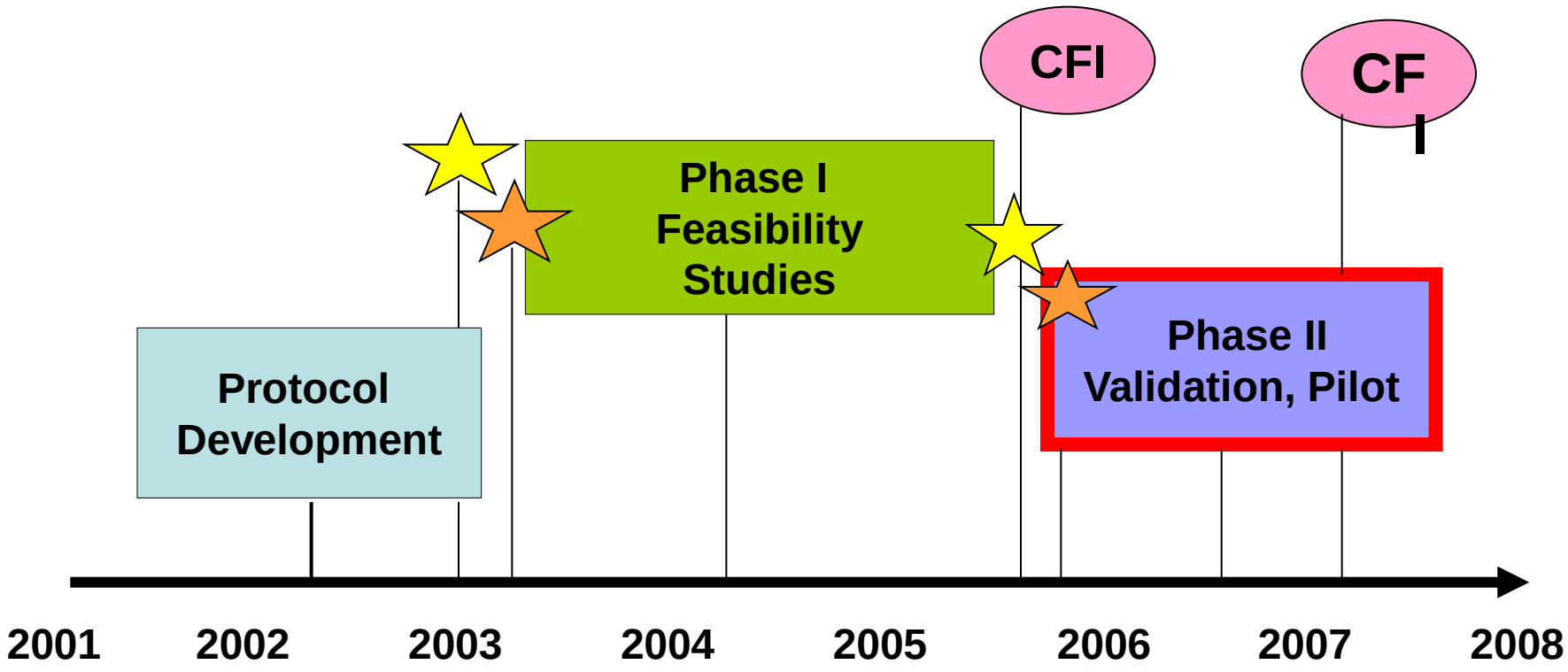

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Phase II Development Activities

- Refine, validate content and measures
- Priority setting, identification of gaps, overlaps
- Protocols, standard operating procedures for data collection & storage, data analysis plan
- Collaboration, harmonization with national, international studies
- Development of SC CCHS 4.2 survey on aging
- Comprehensive dress rehearsal
- Partnerships with community organizations, seniors, practitioners, policy makers, & private sector

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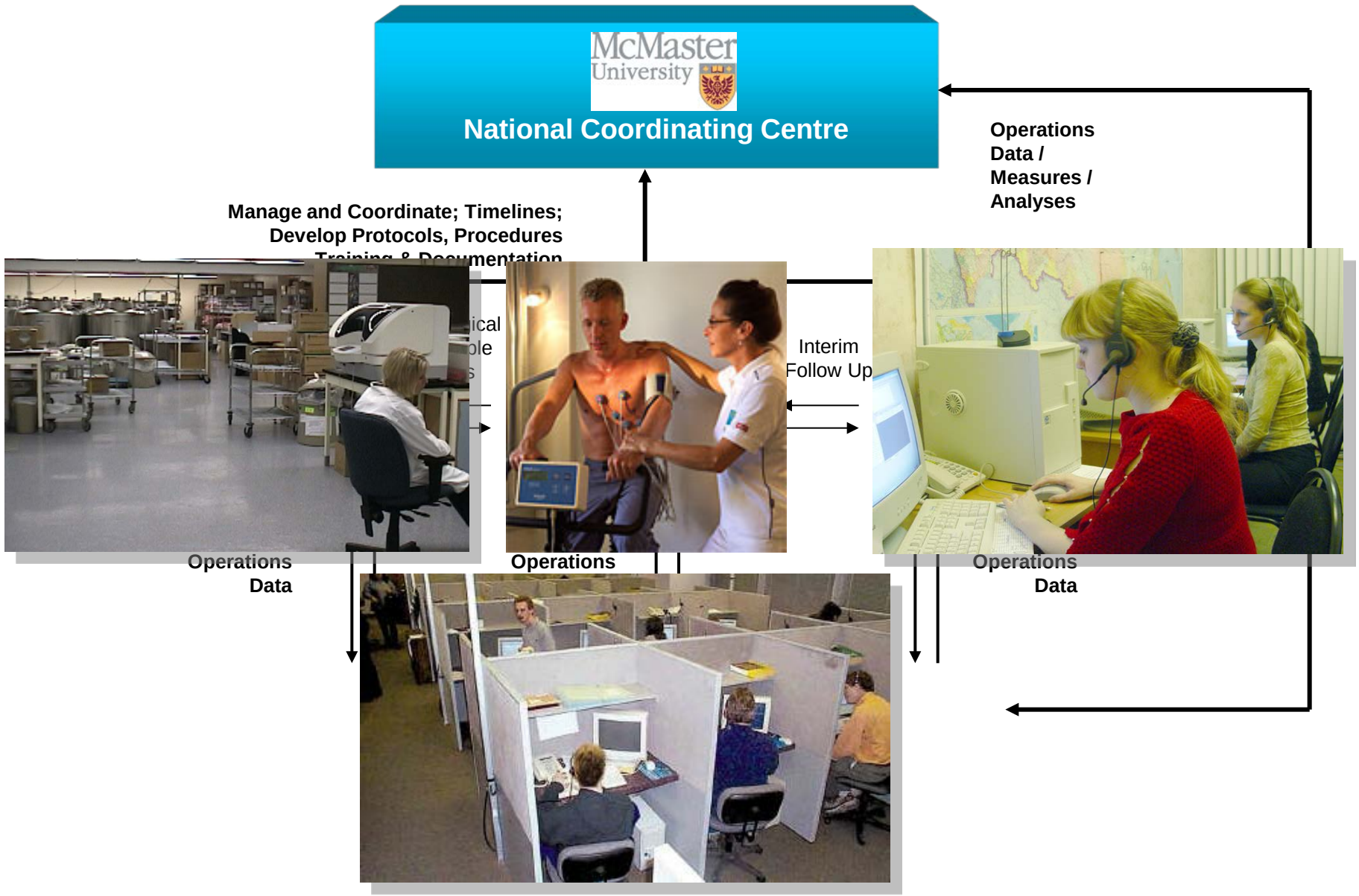
Infrastructure: Core Network of Facilities



Canadian Cohort Network

Large cohorts in development stages - CIHR

- Canadian National Birth Cohort
- Asthma/Allergy Birth Cohort
- Cancer/chronic disease cohort
- Multi-generational cohort

Large population based research studies

- Canadian Multicentre Osteoporosis Study (CaM*os*)
- Prospective Urban and Rural Epidemiology Study (PURE)
- Epidream
- Panel Study of Lifecourse Dynamics (PSLD)

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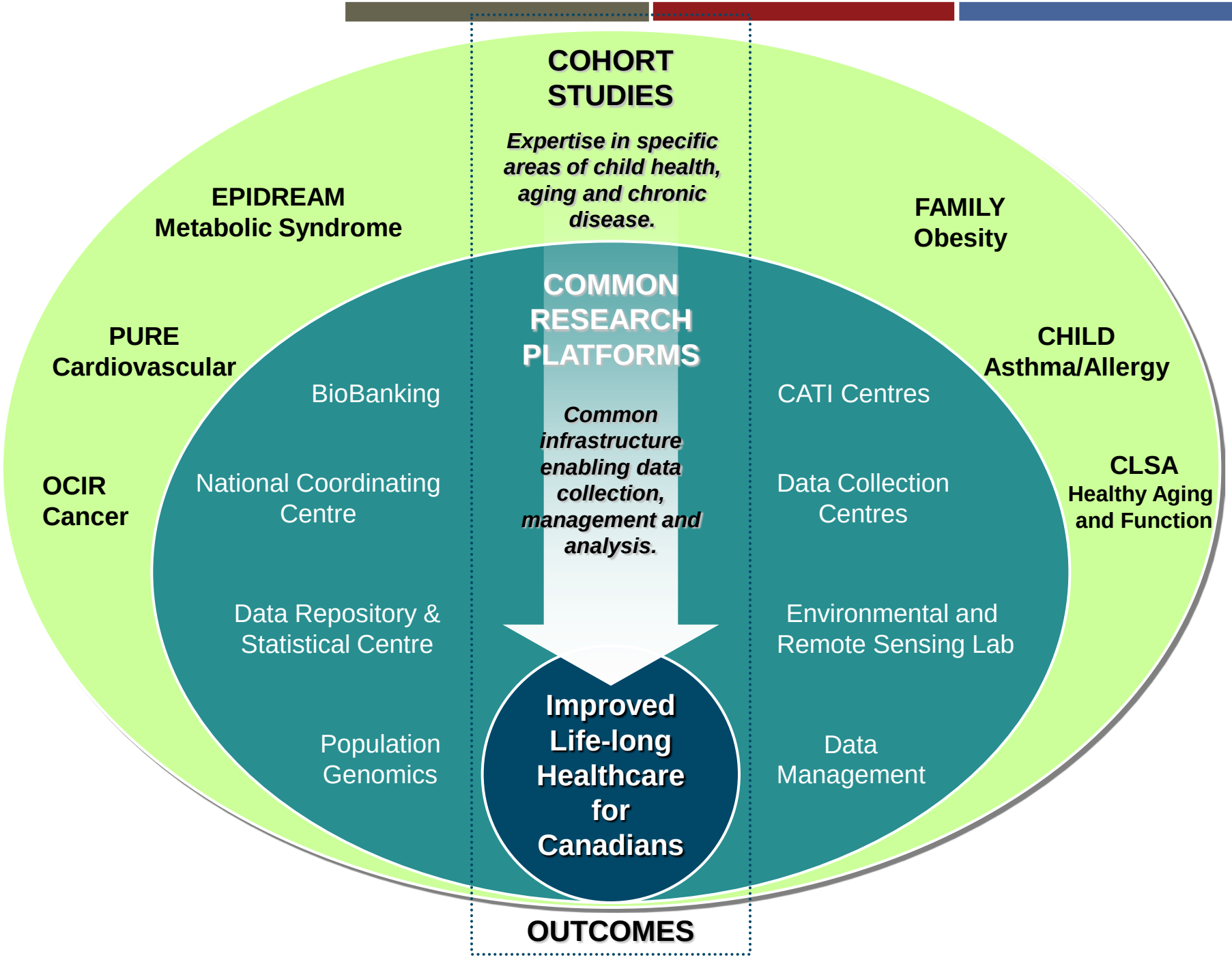
COHORT STUDIES
Expertise in specific areas of child health, aging and chronic disease.
EPIDREAM
Metabolic Syndrome
FAMILY
Obesity
PURE
Cardiovascular
CHILD
Asthma/Allergy
OCIR
Cancer
CLSA
Healthy Aging and Function
COMMON RESEARCH PLATFORMS
Common infrastructure enabling data collection, management and analysis.
BioBanking
CATI Centres
National Coordinating Centre
Data Collection Centres
Data Repository & Statistical Centre
Environmental and Remote Sensing Lab
Population Genomics
Data Management
Improved Life-long Healthcare for Canadians
OUTCOMES

Challenges

- Caught between strategic initiative and investigator driven project
- Political environment
- Scientific environment
- Large team dynamics, communication
- Funding

- Personal (academic) costs

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Opportunities

- Key population health issue
- Platform for research on aging for the broad research community
- Opportunity for capacity building, attracting new researchers
- “Big Science” initiative for Canada

- Personal (academic) growth

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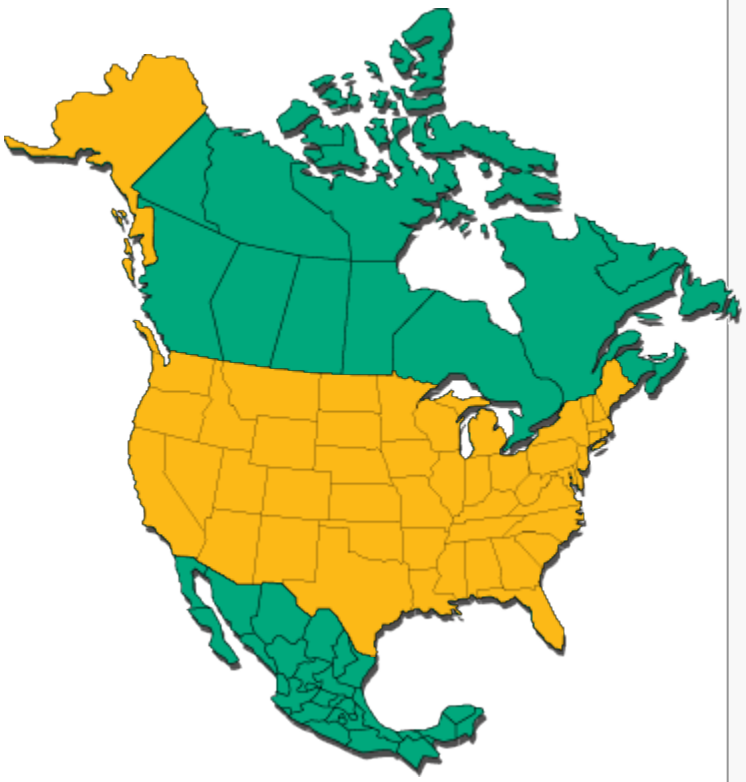
Partnerships

International Links



Womens Health and Aging Study - USA

Aging & Sexuality - USA

HRS - USA

British Birth Cohort - UK

UK Biobank - UK

ELSA - UK

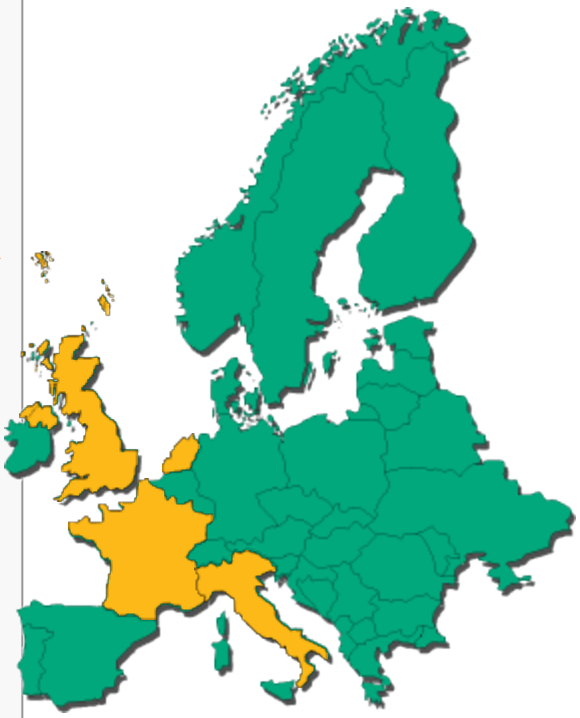
ALSPAC - UK

Cohorte Constances - FRANCE

LASA - Amsterdam

ILSA - Italy

InChianti - Italy



CLSA ELCV

CLSA launch date: 2008

CLSA ELCV

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