



# COMPASS-ND, the COMPrehensive ASSEssment of Neurodegeneration and Dementia: Signature cohort study of the Canadian Consortium on Neurodegeneration in Aging (CCNA)

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# Disclosure statement



## ***Research Support***

CIHR  
NIH  
Alzheimer Society Canada  
Physician Services Incorporated  
Lawson Health Research Institute

## ***Consultant and CME Programs & Clinical Trials Funding***

Pfizer  
Janssen-Ortho  
Novartis  
Lundbeck  
Eli Lilly  
Merck  
Roche  
Biogen

## ***Clinical Trials Funding***

Purdue-Pharma  
Neotherapeutics  
HMR  
Pharmacia  
Boehringer-Ingelheim  
Sanofi-Synthelabo  
Myriad Pharmaceuticals  
ONO Pharma USA  
Neurochem  
Elan, Elan/Wyeth  
Eli Lilly  
Hoffman La Roche  
Bristol Myers Squibb  
Baxter  
Biogen  
Genentech  
Transtech  
Forum  
Merck  
Roche  
Cassava  
Alector

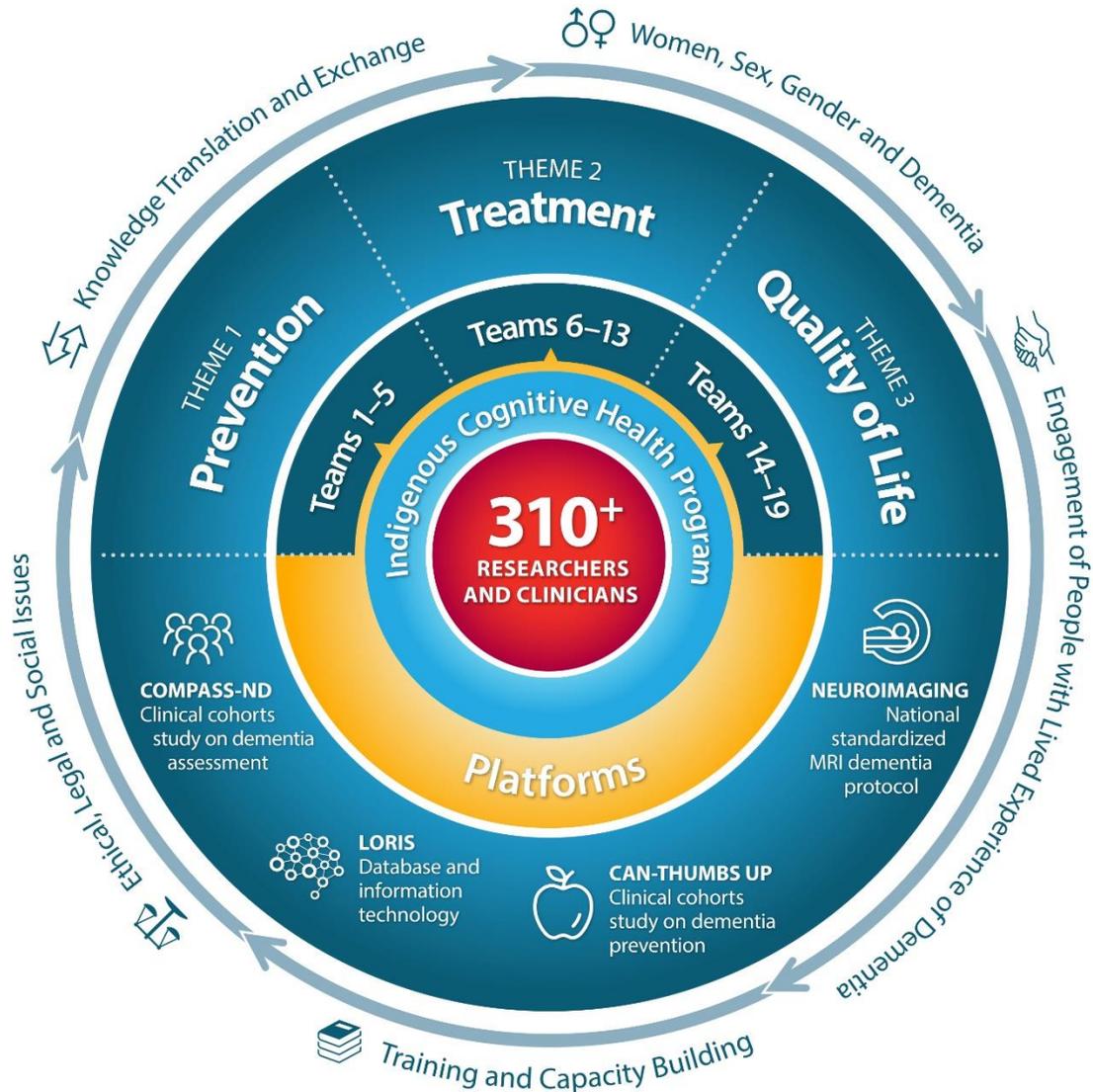
**No funding support has been received for this presentation**



- Established following Canada's commitment to tackle dementia following G8 Summit in 2012
- Funders : CIHR (Institute of Aging) and partners
  - Phase I (2014 – 2019) = \$33 million
  - Phase II (after peer review 2019 – 2024) = \$42 million
- Research strategy to accelerate discovery, innovation and adoption of new knowledge, directed at the **prevention**, **treatment**, and **management** of the neurodegenerative diseases of aging

**Goal: To improve the quality of life of individual Canadians living with these diseases**

# CCNA Phase II at a glance



## 310+ RESEARCHERS AND CLINICIANS

Over 310 Canadian scientists in 19 research teams are collaborating on preventing, treating, and curing age-related neurodegenerative diseases (NDD), and on improving the quality of life of people with lived experience of dementia.

## INDIGENOUS COGNITIVE HEALTH PROGRAM

Members of CCNA's Team 18 are working on Indigenous cognitive health, on supporting capacity building across CCNA, and are supporting CCNA researchers in exploring questions related to Indigenous health and healthcare.

## 3 RESEARCH THEMES AND 19 TEAMS

<i>Theme 1:</i>	<i>Theme 2:</i>	<i>Theme 3:</i>
Teams aim to identify and prevent the causes of NDD.	Teams aim to improve early detection and treatment of NDD.	Teams aim to improve the quality of healthcare and quality of life of those living with NDD.

## 4 NATIONAL PLATFORMS

The platforms enable teams to test their research hypotheses and foster collaborations by collecting, processing, and pooling big data.

## 5 CROSS-CUTTING PROGRAMS

Cross-cutting programs support the work of CCNA's 19 teams and accelerate idea uptake.

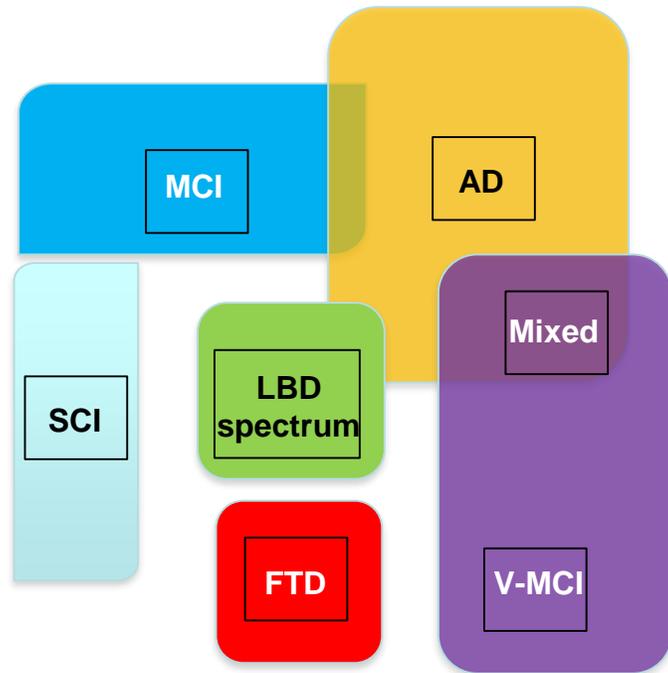
## PARTNER ORGANIZATIONS PROGRAMS

CCNA is a Government of Canada initiative, also supported by several national, provincial and non-profit organizations.

# Overview of COMPASS-ND

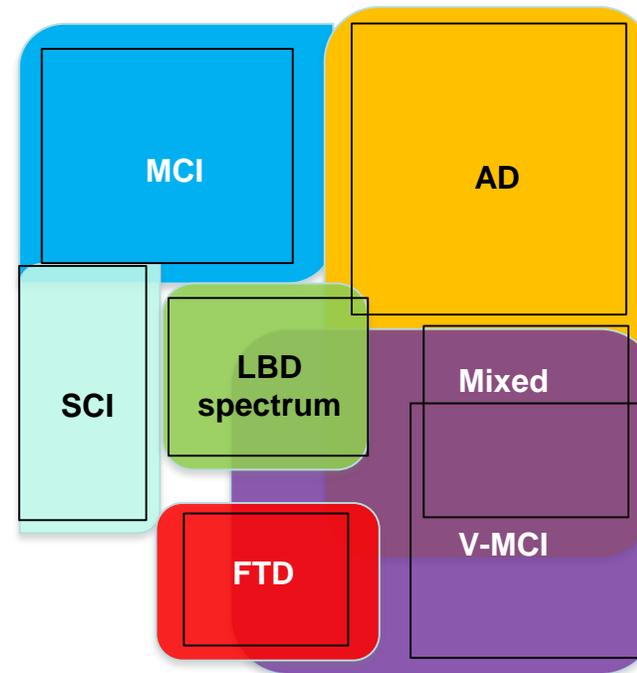


- Includes “ecologically-validated” groups, such as **mixed dementia**, and individuals with **multiple morbidities**, filling an essential knowledge gap in the research community by including individuals who represent the reality of clinical practice



**Narrowly-focused criteria** will produce homogeneous groups that represent a small fraction of the dementia population (e.g., ADNI)

May exclude co-morbidities and mixed dementias



**Broadly-inclusive criteria** will produce heterogeneous groups that cover the entire dementia population

Include almost all co-morbidities and mixed dementias

# Overview of COMPASS-ND



- COMPASS-ND is both:
  - **Cross-sectional**, with in-depth data collection across 11 cohorts
  - **Longitudinal**, repeating an abbreviated protocol 2–3 years later
- **Over 30 sites across Canada** have recruited participants
- Sites include:
  - memory clinics
  - stroke clinics
  - movement disorder clinics
  - behavioural neurology clinics
  - academic and private research groups



# Cohorts at a glance



- Major goals:
  - To learn about **dementia risk factors**
  - To understand **role of vascular factors** across the dementias
  - To evaluate **dementia subgroups**
  - To better understand **dementia biomarkers**
- Participants from **across the dementia spectrum**
- Includes **non-AD dementia** and **other risk groups** not found in other studies, including:

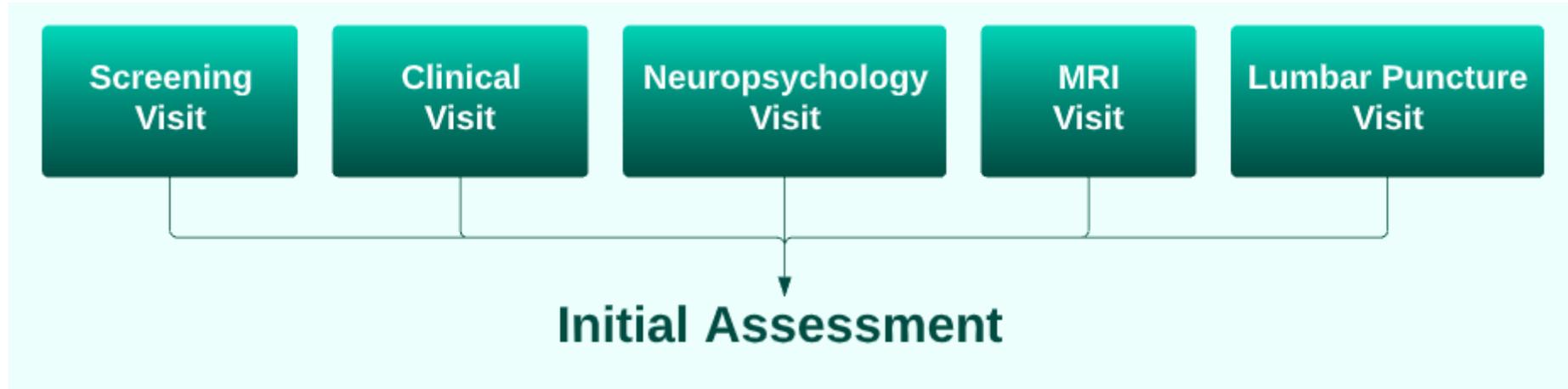
Cohort	Count	Women
Cognitively Unimpaired	177	62.1%
Subjective Cognitive Impairment	157	65.6%
Mild Cognitive Impairment	272	38.6%
Mild Cognitive Impairment with silent vascular lesions	151	45.7%
Alzheimer's disease	111	43.2%
Mixed dementia	84	48.8%
Frontotemporal dementia	41	46.3%
Parkinson's disease	82	45.1%
Parkinson's disease with Mild Cognitive Impairment	47	14.9%
Parkinson's disease dementia	15	6.7%
Lewy body disease	32	18.8%
Other dementia	4	--
<b>OVERALL</b>	<b>1,173</b>	<b>46.5%</b>

Age	Years	Education	Years	Testing language	Count	Ethnicity	Count	Community	Count
Minimum	42.1	Minimum	3	English	1,048	White	1,079	Urban	59.0%
Maximum	91.0	Maximum	23	French/bilingual	125	Visible Minority	92	Suburban	30.7%
<b>Mean</b>	<b>71.9</b>	<b>Mean</b>	<b>15.2</b>	<b>% French/bilingual</b>	<b>10.7%</b>	<b>% Visible Minority</b>	<b>7.9%</b>	Rural	10.3%

# Data collection timeline



- COMPASS-ND collects participant data over multiple, 2–3 hour visits:



- The data collected at each of these visits is entered into the **online database, LORIS**
- Study PDFs and audio files are also uploaded to LORIS, where the Monitoring and Data Validation Teams can evaluate and clean the data

# Neuropsychology assessment



## Premorbid IQ

- WAIS-III Vocabulary Test

## Attention, working memory, and processing speed

- WAIS-III Digit Span Test
- WAIS-III Digit Symbol – Coding

## Visual perception and construction

- Birmingham Object Recognition Battery Object Decision Task – Easy B
- Judgment of Line Orientation Test
- Brief Visuospatial Memory Test – Revised (Copy)

## Memory

- Rey Auditory Verbal Learning Test
- Brief Visuospatial Memory Test – Revised (Recall)
- CCNA–CIMA-Q Face-Name Association Task
- WAIS-III Digit Symbol – Incidental Learning
- Envelope Test

## Complex attention and executive functions

- D-KEFS Letter Fluency Test
- Trail Making Test
- D-KEFS Color-Word Interference Test
- CCNA–CIMA-Q Sentence Inhibition Task
- CCNA Reaction Time Task
- Social Norms Questionnaire
- Social Behavior Observer Checklist *[FTD only]*

## Speech and language

- D-KEFS Category Fluency Test
- Word Reading Test
- Semantic Word-Picture Matching Test
- Semantic Associates Test
- Northwestern Anagram Test (Short Form)
- Sentence Repetition Test
- Sentence Reading Test
- Noun and Verb Naming Test
- Boston Diagnostic Aphasia Exam Cookie Theft Picture Description

# Neuroimaging assessment



- We developed and used the **Canadian Dementia Imaging Protocol (CDIP)** to gather neuroimaging data for over **1,083 participants** (93% of the participant cohort)

## Sequences

- 3D-T1w
- FLAIR
- Dual PD/T2
- T2\*
- DTI
- BOLD resting state
- Optional add-on sequences

## Synoptic Report & Visual Measurements

- Infarcts
- Hemorrhages
- Cortical superficial siderosis
- White matter hyperintensities
- Overall burden of cerebrovascular brain injury

## Volumetrics

- Hippocampus
- Entorhinal cortex
- Globus pallidus
- Putamen
- Caudate
- Cerebellum
- Thalamus
- Ventricles
- Total lobar GM & WM
- Total GM, WM, CSF, & intracranial volumes

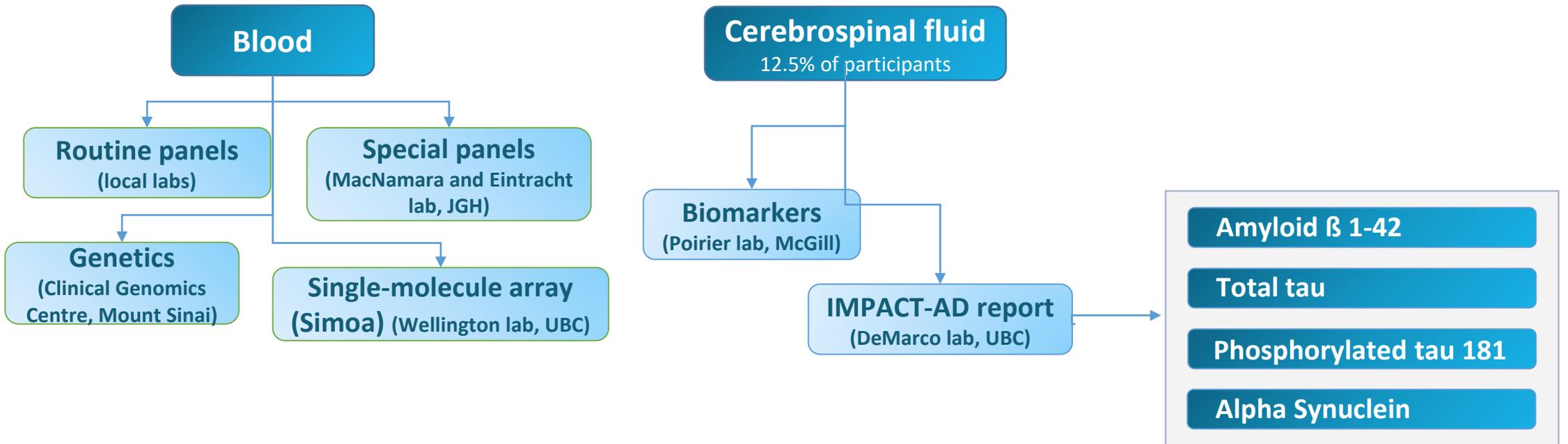
## Research Diagnosis Reappraisal

Screening and clinical data, along with MRI findings, yield the ***Final Research Diagnosis (Baseline)***

# Biosample collection



- In addition to the rich alphanumeric and neuroimaging data set, biosamples (blood, urine, saliva, buccal, fecal, and cerebrospinal fluid) have been collected from **1,100 participants** so far
- Collected biosamples include blood, urine, saliva, and cerebrospinal fluid; in addition, buccal and fecal swabs were collected for eventual **microbiome analysis**
- Routine **blood** and **CSF analyses** for all participant samples are undertaken at a few core labs:





- Ultimately, COMPASS-ND participants are asked if they would like to donate their brains after death
- The Brain Donation Program is centrally coordinated at UBC by Dr. Ian MacKenzie
- After autopsy and neuropathology assessment, brain tissue is banked at the **Douglas – Bell Canada Brain Bank** (Montréal, QC)
- Thus far:

**32**

autopsies have been done according to COMPASS-ND protocol

**251**

participants have consented to brain donation across all COMPASS-ND cohorts thus far

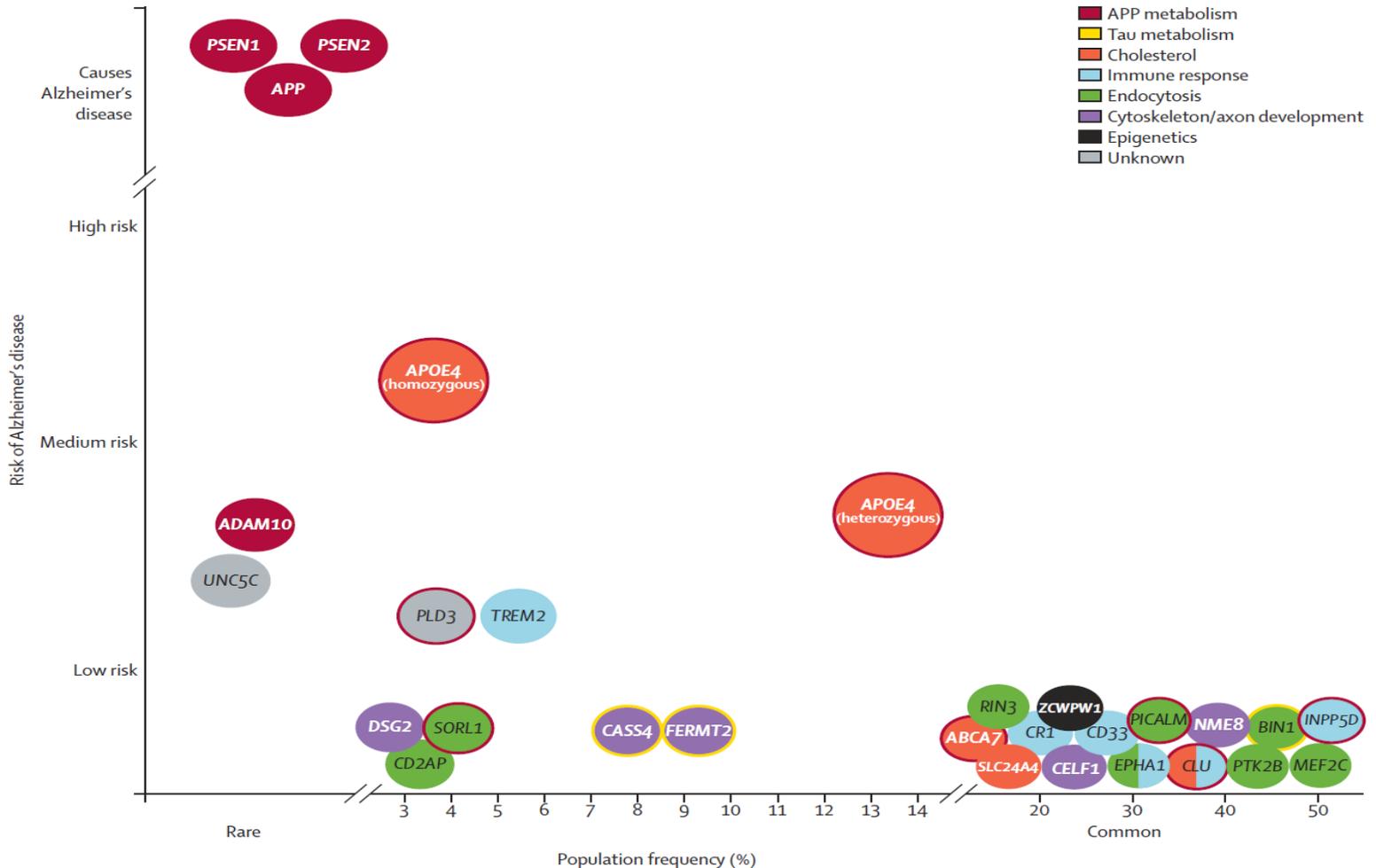
# Genetic analyses



- Whole blood samples are also sent to the **Clinical Genomics Centre** (Toronto, ON) for genetic analyses using Illumina's **Neuro Booster Array** (75,000 single nucleotide polymorphisms, or SNPs, important in investigating NDDs), centered on the backbone of the **Global Diversity Array** (>1.8M SNPs)

- Polygenic risk and hazard scores** for AD (83 genes) and PD will be generated from the data

- Genes of interest include:
  - TREM2** (inflammatory pathways, phagocytosis, microglial clustering)
  - TOMM40** (mitochondrial protein transport role)
  - APOE** (implicated in AD)
  - 390 other risk genes** for AD, PD, LBD, and FTD



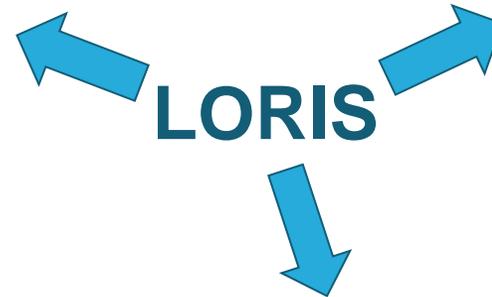
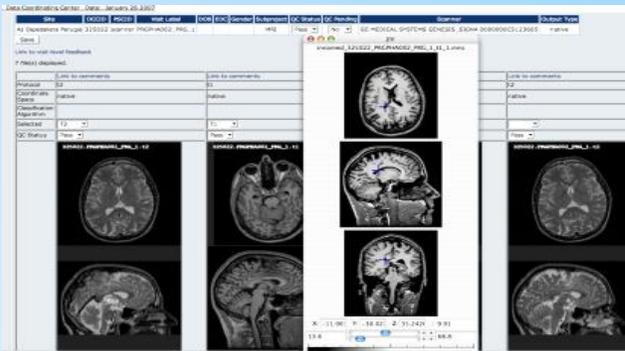
# LORIS database



- 80 personnel-years of development
- Web-based, secure data transfer of multi-site data
- Generalized, open-source MYSQL architecture – flexible, extensible
- Applications in development, neurodegeneration (US, Europe, Asia)

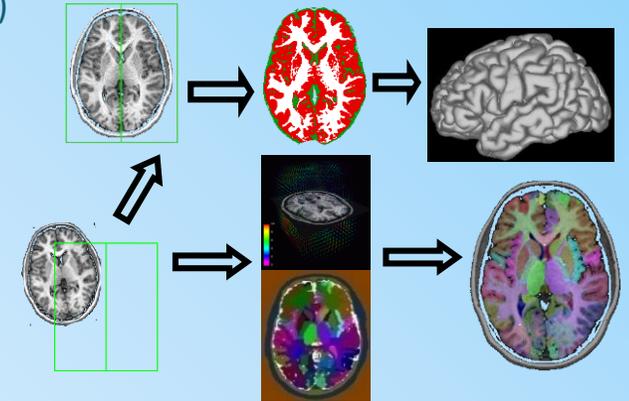
## Acquisition management

- Project management tools
- Double data entry/ range checking
- Automated 3D image QC
- Java-based remote 3D image QC
- 150 behavioral instruments
- MANTIS bug-tracking



## Analysis pipelines

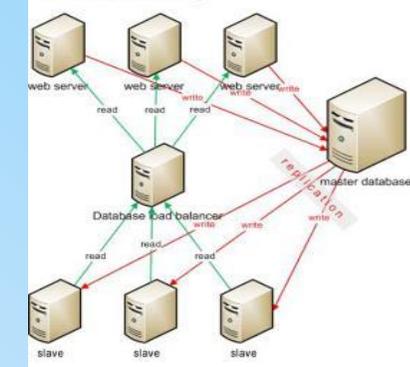
- External pipelines for analysis (MNI, SPM, FSL, LONI, AFNI). Integrated with grid-computing networks (CBRAIN, NeuGrid)



## Repository /download

- Data types: behavior, clinical, imaging, genetic
- On-line remote MRI browser
- Data querying GUI (volumes, surfaces, behavior)
- e.g. NIH database of normal brain development

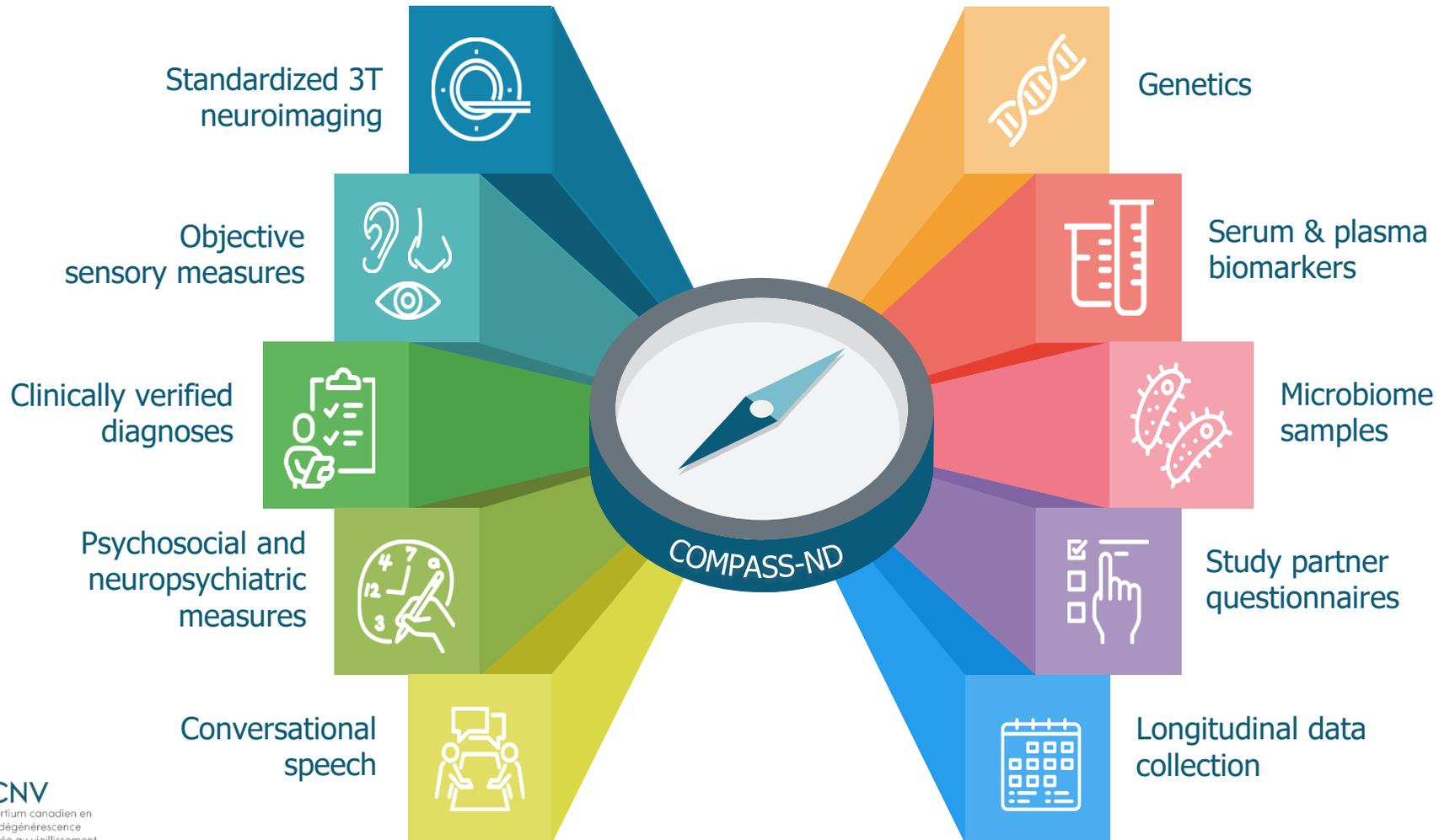
### Traditional Clustering



# Big data on dementia: COMPASS-ND



In addition to the wealth of deeply-phenotyped **clinical**, **cognitive**, and **neuropsychological** data across multiple cohorts, our study encompasses:



# Big data on dementia: COMPASS-ND



- COMPASS-ND data is now available to CCNA researchers
- To date, the data have generated 32 journal articles (11 in the past year) and several graduate theses
- Data will be available to international researchers in Autumn 2024
- Data from deeply-phenotyped subjects, “usual” dementia subjects
- Access to data and samples coming

# Acknowledgements



**Canadian Journal of  
Neurological Sciences**

## The Comprehensive Assessment of Neurodegeneration and Dementia: Canadian Cohort Study

Published online by Cambridge University Press: 16 July 2019

Howard Chertkow, Michael Borrie, Victor Whitehead, Sandra E. Black, Howard H. Feldman, Serge Gauthier, David B. Hogan, Mario Masellis, Katherine McGilton, Kenneth Rockwood, Mary C. Tierney, Melissa Andrew, Ging-Yuek R. Hsiung, Richard Camicioli, Eric E. Smith, Jennifer Fogarty, Joseph Lindsay, Sarah Best, Alan Evans, Samir Das, Zia Mohaddes, Randi Pilon, Judes Poirier, Natalie A. Phillips, Elizabeth MacNamara, Roger A. Dixon, Simon Duchesne, Ian MacKenzie and R. Jane Rylett

### Steering Committee & Platform 1 Implementation Team

Michael Borrie, Howard Chertkow, Natalie Phillips, Randi Pilon, Victor Whitehead, Jennifer Fogarty, Sarah Best, Nimi Bassi, Joseph Lindsay

### LORIS Database Team

### Neuroimaging Group

### Brain Donation Program

The Canadian Consortium on Neurodegeneration in Aging, and the COMPASS-ND study are supported by grants (CAN-137794, CAN-163902, BDO-148341) from the Canadian Institutes of Health Research with funding from several partners.

### Monitoring and Data Validation Teams

Celine Fouquet, Jonathan Beuk, Ana Stirbu, Logane Gnassi, Afra Tucker, Turaç Aydoğan, Julianna Gajraj, Renée Kaminski, Panayiota Ventura, Maegan Harvison, Kevin Ablett, Jakub Qazi, Patricia Giurca, Sophie Duval, Clément Conil, Cynthia Di Prospero, Mina Xie, as well as staff and students from Parkwood Institute (Dr. M. Borrie), University of Alberta (Dr. R. Camicioli), and the Phillips' lab (Dr. N. Phillips)

All the principal investigators, coordinators, psychometricians, physicians, nurses, clinicians, research assistants, and other site staff at 32 COMPASS-ND study sites across Canada

Our participants – a big THANK YOU!