TDRA

TEMERTY FACULTY OF MEDICINE
UNIVERSITY OF TORONTO

Toronto Dementia Research Alliance

Advancement for Dementia Care Centre

9 November 2022

Baycrest camh Ontario Shores Centre for Mental Health Sciences Sunnybrook Health Sciences Centre UNITY HEALTH TORONTO UHN

Disclosures

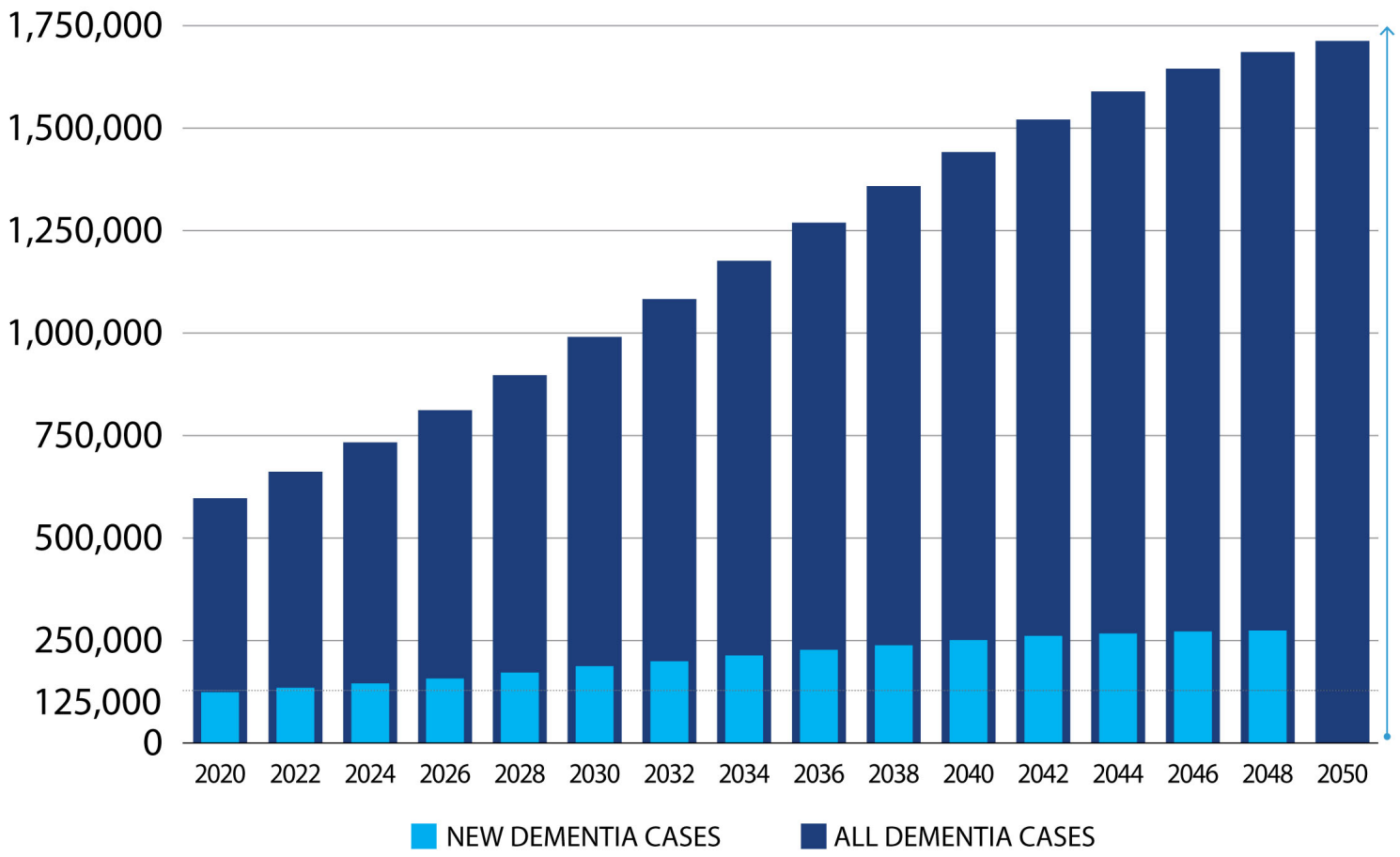
Funding:

- Brain Canada
- Brain and Behavior Research Foundation
- BrightFocus Foundation
- Canada Foundation for Innovation
- Canada Research Chair
- Canadian Institutes of Health Research
- Centre for Aging and Brain Health Innovation
- Ontario Ministry of Health and Long-Term Care
- Ontario Ministry of Research and Innovation
- US National Institutes of Health
- Weston Brain Institute

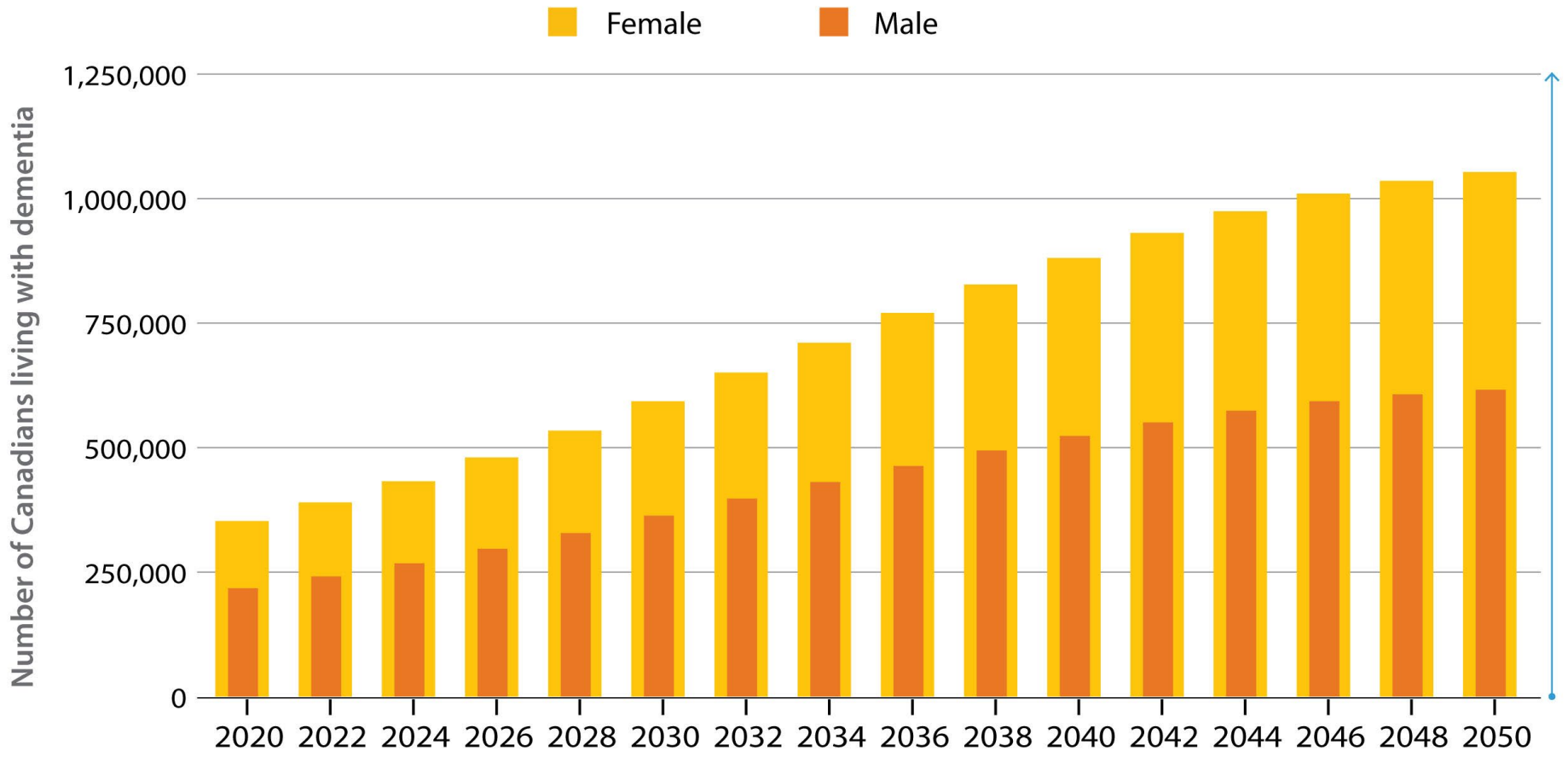
Relationships with Commercial Interests:

- In-kind equipment support from Newronika
- In-kind research online accounts from Scientific Brain Training Pro
- Participated in 2021 and 2022 in advisory board discussion for Biogen Canada Inc.
- United States Provisional Patent No. 17/396,030 that describes cell-based assays and kits for assessing serum cholinergic receptor activity

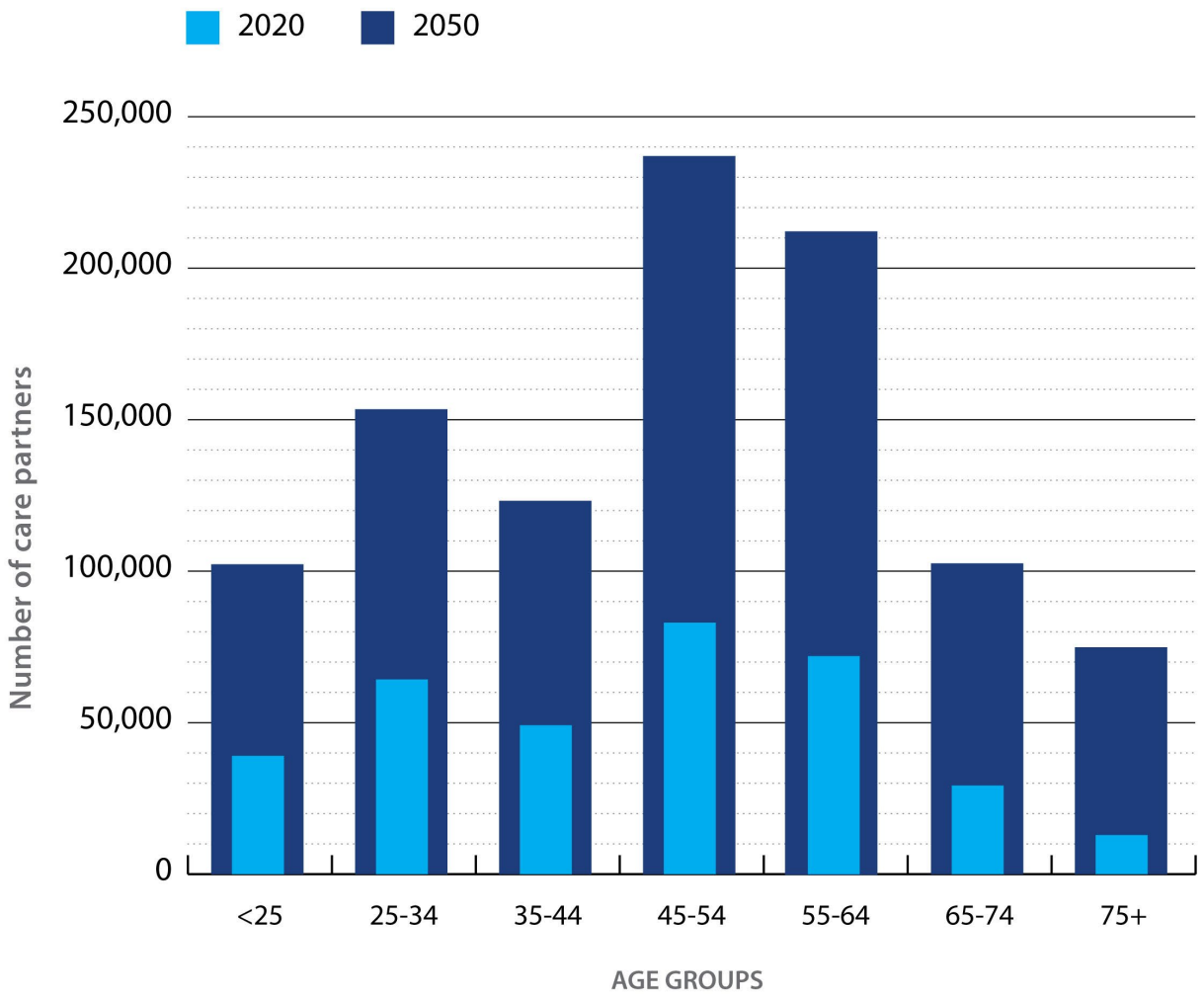
Number of People Living with Dementia and the Number of New Cases of Dementia per year in Canada, 2020 to 2050



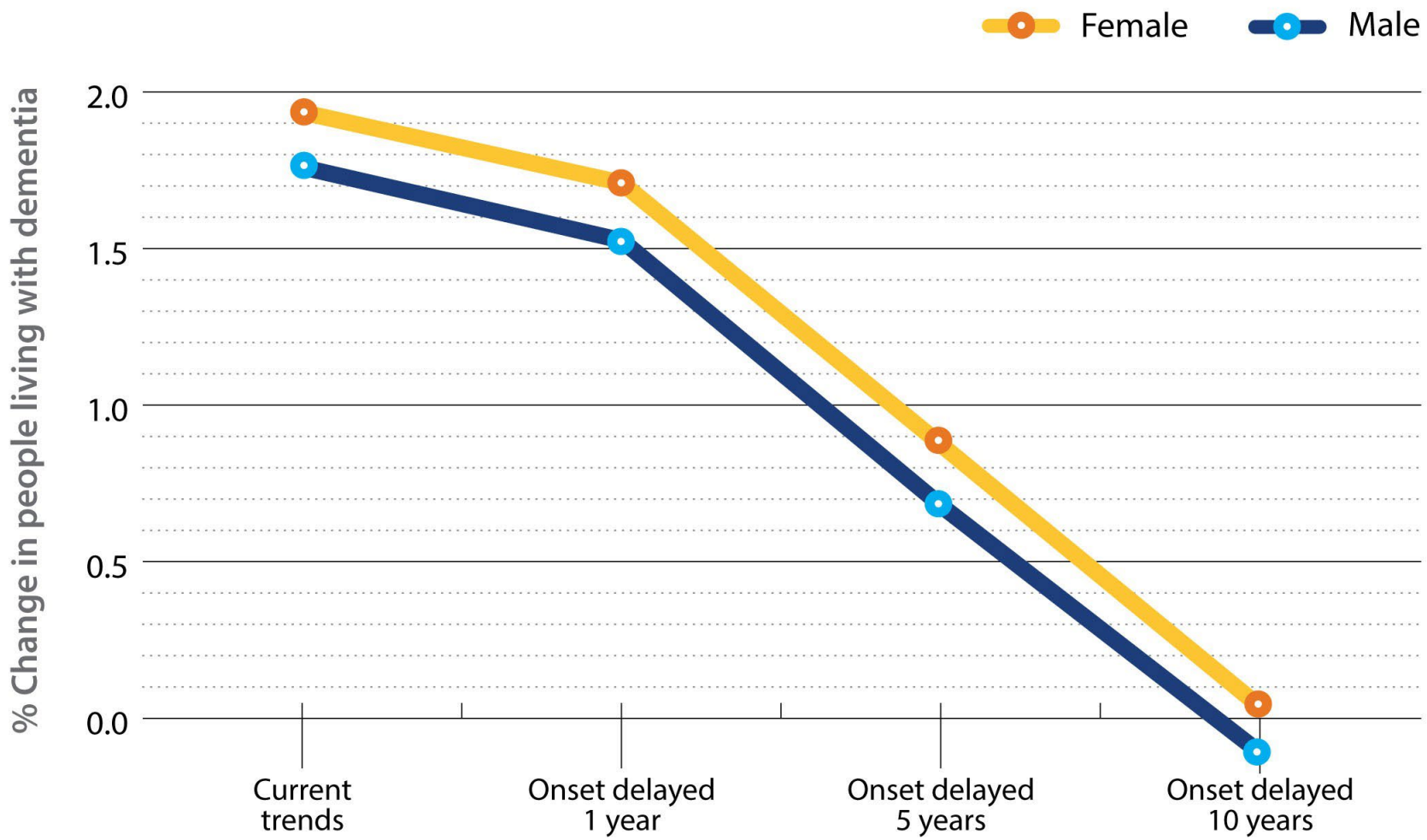
Number of People with Dementia in Canada by Sex, 2020 to 2050



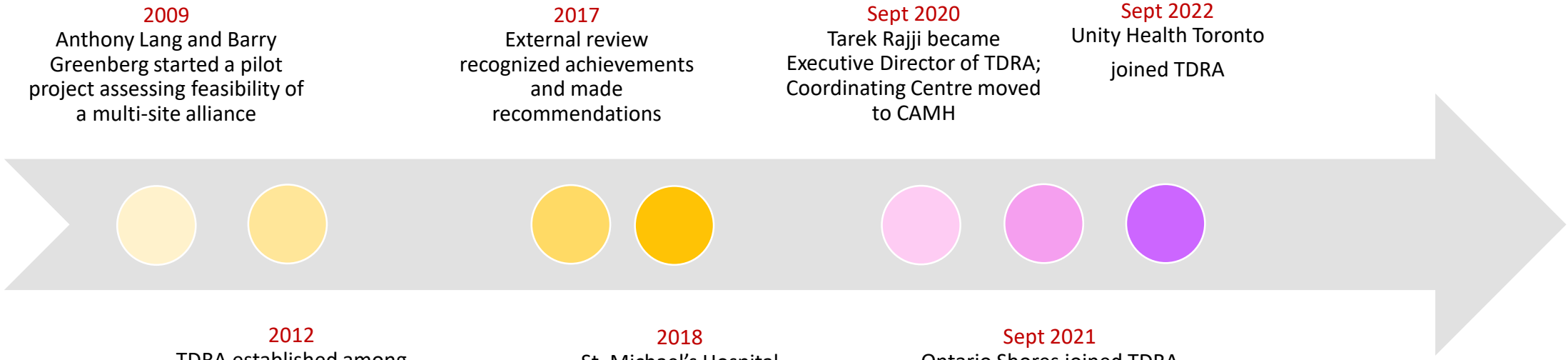
Age Distribution of Care Partners for People Living with Dementia in Canada, 2020 and 2050

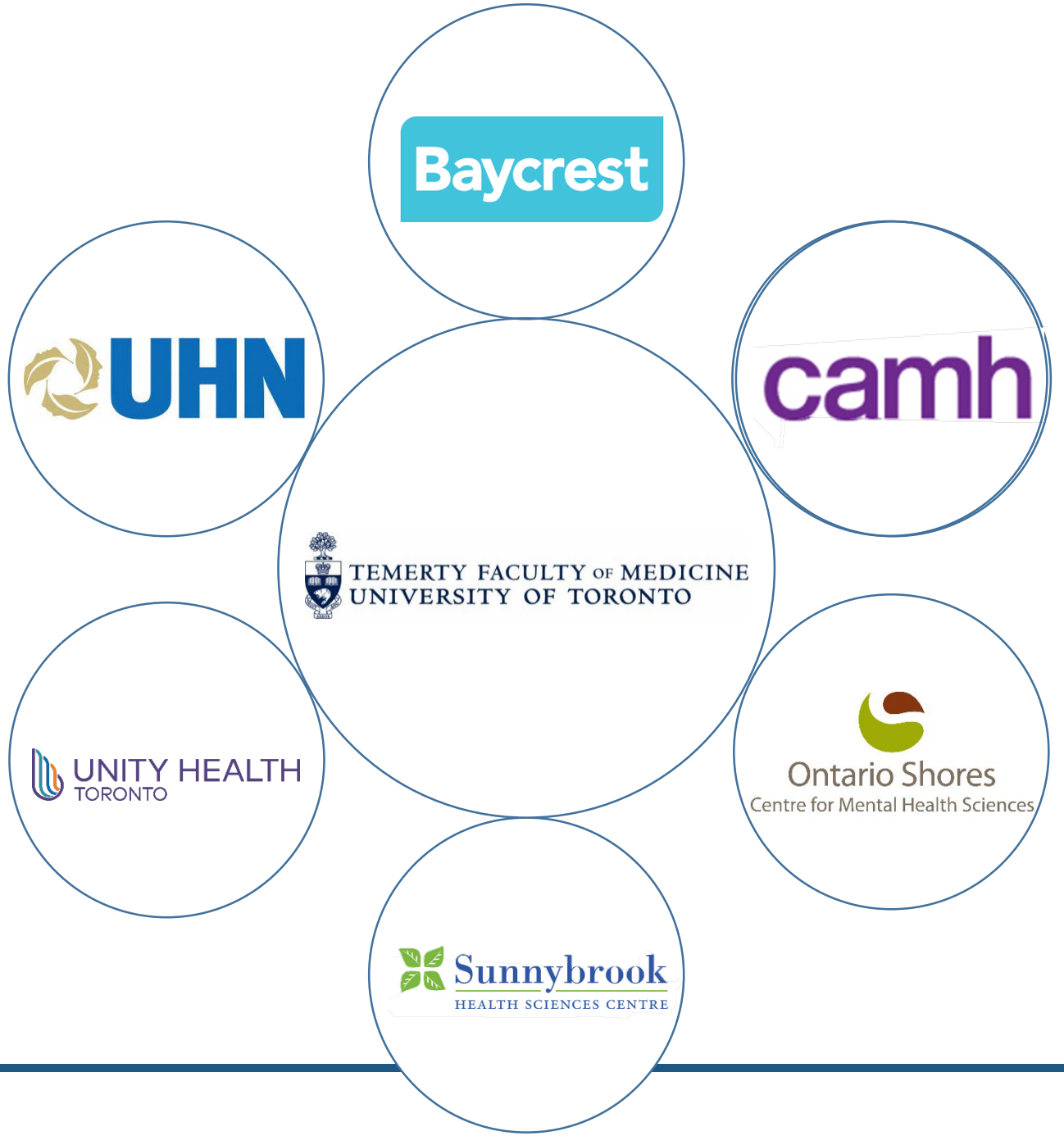


Impact of Delaying Dementia Onset on the Projected Number of People with Dementia in Canada in 2050



ALZHEIMER SOCIETY OF CANADA / THE LANDMARK STUDY: PATH (2022)


2009
Anthony Lang and Barry Greenberg started a pilot project assessing feasibility of a multi-site alliance
2012
TDRA established among U of T and five academic health centres with Sandra Black as Executive Director
2017
External review recognized achievements and made recommendations
2018
St. Michael's Hospital opted for observership status
Sept 2020
Tarek Rajji became Executive Director of TDRA; Coordinating Centre moved to CAMH
Sept 2021
Ontario Shores joined TDRA
Sept 2022
Unity Health Toronto joined TDRA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UHN
camh
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UNITY HEALTH
TORONTO
Ontario Shores
Centre for Mental Health Sciences
Sunnybrook
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Sarah Downey

Trevor Young

Executive Committee

Donald Weaver

David Bogart

Sanjeev Kumar

Carmela Tartaglia

Scientific Advisory Committee

Research Operations Committee

Patient/Family Advisory Council

Basic Science

EEG

Genetics

Memory Clinics

Neuro-pathology

Neuro-technology

Caregiver

Fluid Biomarkers

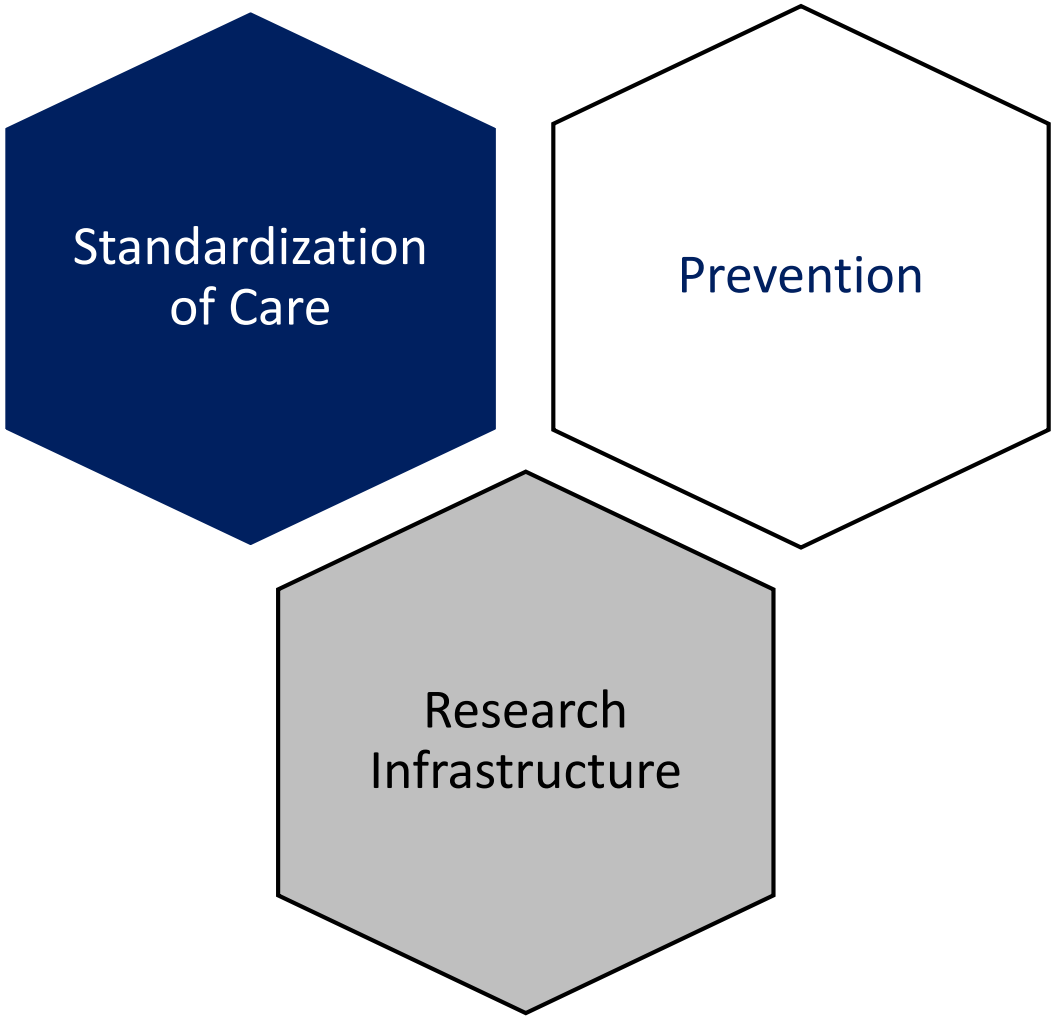
Long-term Care

Neuro-imaging

Neuro-stimulation

Open Science

TDRA


Standardization of Care
Prevention
Research Infrastructure

Memory Clinics Standardization

Standardization of Care

Sandra Black
(Sunnybrook)

Bradley Bushsbaum
(Baycrest)

Howard Chertkow
(Baycrest)

Daniel Felsky
(CAMH)

Corinne Fischer
(Unity Health Toronto)

Morris Freedman
(Baycrest)

Sean Hill
(CAMH)

Sanjeev Kumar
(CAMH)

Ekaterina Rogaeva
(U of T)

Stephen Strother
(Baycrest)

David Tang-Wai
(UHN)

Carmela Tartaglia
(UHN)

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Memory Clinics Standardization

Standardization of Care

- Standardized assessments
  - Toronto Cognitive Assessment (TorCA) -> Arabic, French, Italian, Romanian, Russian, Ukrainian
    - Modularization and digitization of TorCA and BNA-SF
  - Clinical Intake Form

- Patients share data for research
  - >2000 participants in Brain-CODE

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Memory Clinics Standardization

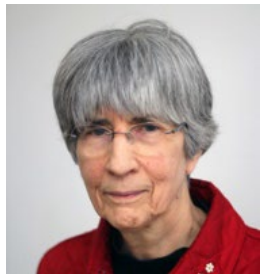
Standardization of Care

New Projects

Title	Funding	Description
Artificial Intelligence in the Memory Clinic	$1.68 million	Develop AI-based approaches to support the triage of referrals
Hybrid-Virtual Cognitive Program	$450,000	This study will develop a novel model of care for efficient and brief diagnosis of cognitive impairment applicable to tertiary memory clinic settings and that can be applied virtually or in-person
Virtual Assessment of Praxis as a Predictor of Basic Activities of Daily Living	$99,932	Explore whether virtual assessments of praxis are more informative than traditional questionnaires to assess impairments in activities of daily living.

Standardized Clinical Cognition MRI Protocol

Standardization of Care



Sandra Black
(Sunnybrook)

Corinne Fischer
(UHT)

Chinthaka Heyn
(Sunnybrook)

David Kim
(CAMH)

Sanjeev Kumar
(CAMH)

Paula Alcaide Leon
(UHN)

Amy Lin
(UHT)

Walter Montanera
(UHT)

Alan Moody
(Sunnybrook)

Christopher Scott
(Sunnybrook)

Carmela Tartaglia
(UHN)

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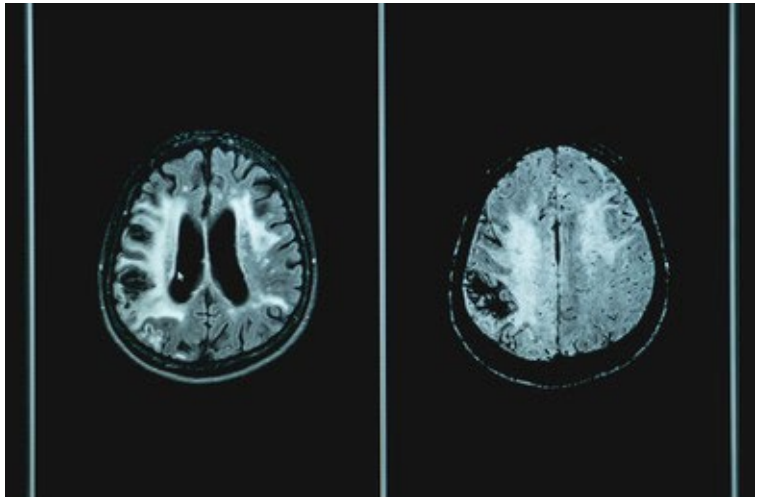
Standardized Clinical Cognition MRI Protocol

Standardization of Care

- Implemented in 2021 at Sunnybrook, Unity Health Toronto (UHT), and the University Health Network (UHN)
- CME-accredited course led by Paula Alcaide Leon and Carmela Tartaglia in early 2023

Site	Number of Scans
Sunnybrook	418
UHT	71
UHN	280
Total	**769**



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Long-Term Care Standardization

Standardization of Care

Amer Burhan
(Ontario Shores)

Peter Derkach
(West Park Healthcare)

Anuroop Duggal
(PFAC)

Corinne Fischer
(Unity Health Toronto)

Morris Freedman
(Baycrest)

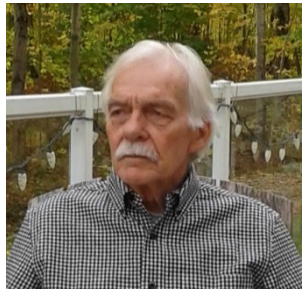
Sean Hill
(CAMH)

Andrea Iaboni
(UHN)

Sanjeev Kumar
(CAMH)

Krista Lanctôt
(Sunnybrook)

Clement Ma
(CAMH)



Frank Palmer
(PFAC)

Gillian Strudwick
(CAMH)

Baycrest

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Long-Term Care Standardization

Standardization of Care

- Received external funding ($200,000) to develop a clinical intake that allows embedding research into care

- Developed standardized intake form for patients with dementia in long-term care homes, with a focus on behavioural and psychological symptoms in dementia (BPSD)

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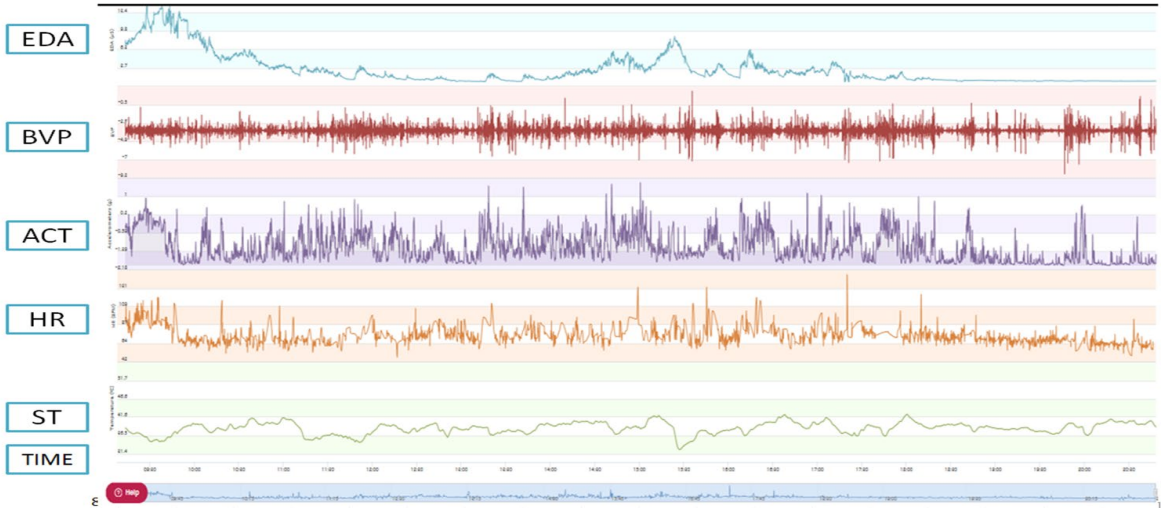
Physiological Signature of Emotional Distress in Persons with Dementia

Multi-sensory Devices and Deep learning to Facilitate **Personalized Management of Agitation**: Amer Burhan and collaborators from Sunnybrook, CAMH, TRI, and Ontario Tech) (will be discussed this PM)

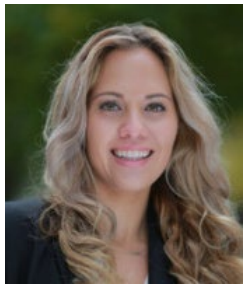


Dementia Caregivers Skills Training Through Virtual Reality Simulation (VR-SIM CARERS)

Amer Burhan
(Ontario Shores)

Ron Beleno
(AGE-WELL)

Mary Chiu
(Ontario Shores)



Kristina Kokorelias
(UHN)

CIHR IRSC Institute of Aging Institut du vieillissement

Canada NRC-CNRC

Person wearing virtual reality goggles. She is facing a computer screen that shows an artificial intelligence avatar.

John Rubinstein
(U of T)

Joel Sadavoy
(Sinai)

Adriana Schnall
(Baycrest)

Michael Smith
(NRC)

Jeanie Zabukovec
(Ontario Shores)

Lynn Zhu
(Ontario Shores)

- **One of Three** Projects funded by NRC-CIHR Aging in Place Challenge
- **$546,204 in funding**

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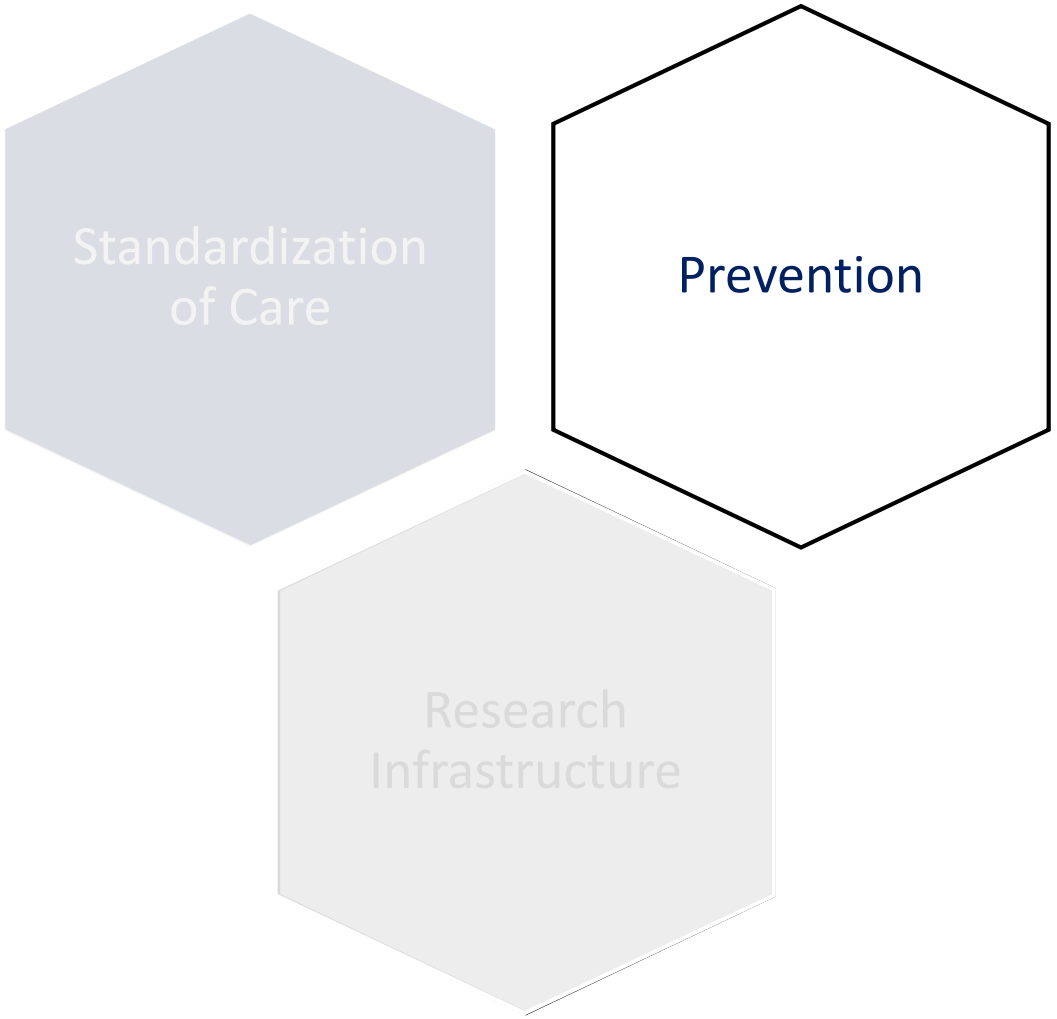
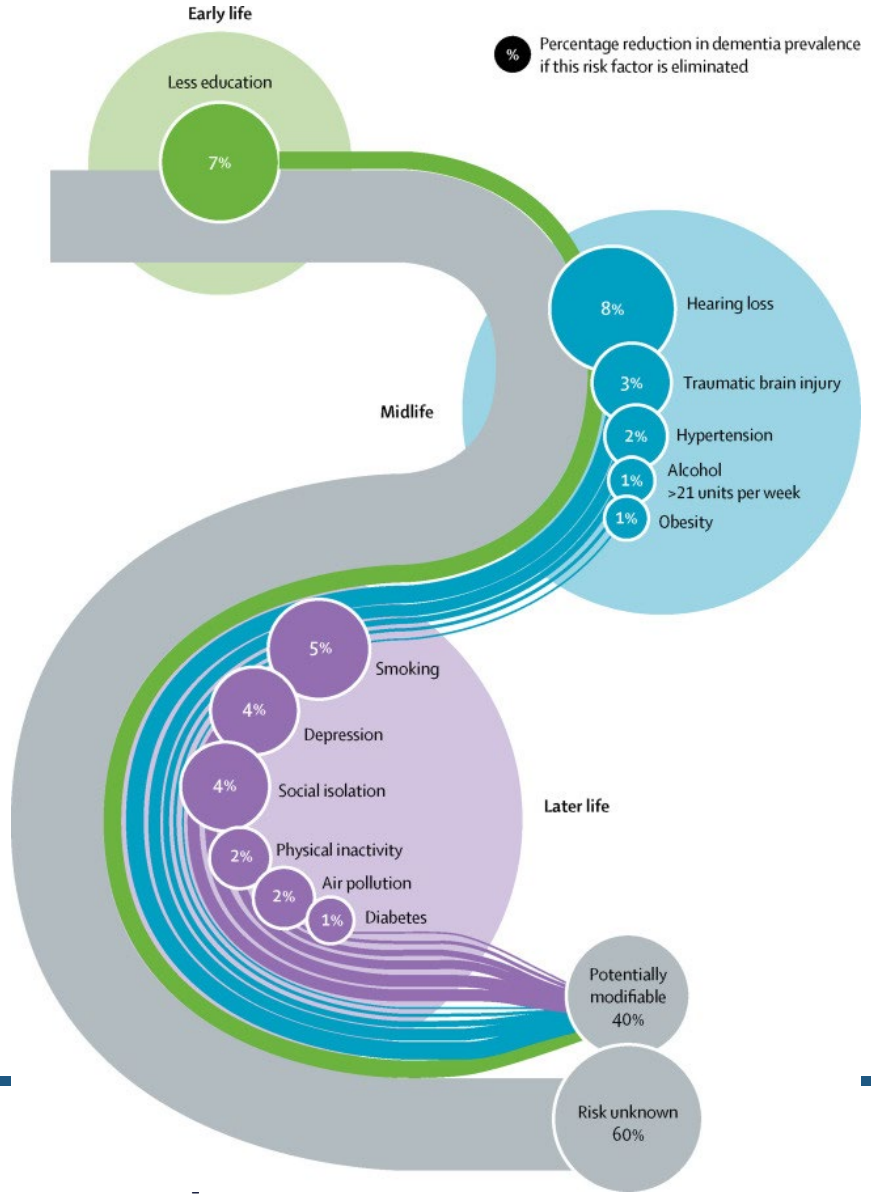

Standardization of Care
Prevention
Research Infrastructure

Temerty-Tanz-TDRA Initiative

Prevention



Modifiable Risk Factors

Social Determinants

Low Education (7%)

Social Isolation (4%)

Air Pollution (2%)

Primary Care

Hearing Loss (8%)

Smoking (5%)

Specialty Clinics

Depression (4%)

Traumatic Brain Injury (3%)

Hypertension (2%)

Physical Inactivity (2%)

Alcohol (1%)

Diabetes (1%)

Obesity (1%)

Three elements:

1. Seed funding (Awarded for 2021)
2. Research Fellowships
3. Workshop (Delayed to 2022)

The Lancet Commission on Dementia, 2020

Temerty-Tanz-TDRA Initiative - Fellowships

Prevention

1. Brain Medicine Research Fellowship

Dr. Iryna Palamarchuk
Started March 2022 (CAMH + Sunnybrook)
Project: Assessing the use of transcranial alternating current stimulation and focused ultrasound to enhance prefrontal cortical functions in older adults with depression or MCI

2. Brain Medicine Research Fellowship

Dr. Adrian Espiritu
Started July 2022 (**Ontario Shores** + UHN)
Project: Using repetitive transcranial magnetic stimulation as a novel intervention for treatment-resistant late-life depression and motor-cognitive risk syndrome

3. Post-Doc Fellowship

Dr. Samar Elsheikh
Starting Date TBD
Currently selecting a research project

Temerty-Tanz-TDRA Initiative - Seed Funding
3 Projects launched in 2022

Prevention

Impact of lipopolysaccaride on immune response and cerebral amyloid deposition in older adults with a history of major depressive disorder

- PIs: Damien Gallagher, Ariel Graff-Guerrero
- Updates: The laboratory work for the study has been completed, initial analyses conducted, first draft of paper circulated

The contribution of cerebrovascular disease to depression in patients with and without AD

- PIs: Angela Golas, Carmela Tartaglia
- Updates: The project is in its analysis stage.

Assessment of heart rate variability in older adults with lifetime history of depression or mild cognitive impairment

- PIs: Jean Chen, Linda Mah
- Update: A research student has joined the team to lead the project starting fall 2022.

2022 Competition: 7 LOIs received, full applications were due Oct 14, PFAC members involved in review process

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Temerty-Tanz-TDRA Initiative - Inaugural Workshop

Prevention

- Wednesday, November 30th, 2022; 8am -5pm
- Hart House, University of Toronto
- Key note speakers, presentations & moderated discussion periods
- $4,000 in sponsorship funding from the Ontario Brain Institute
- CME-accreditation in process

Keynote Speakers

Olusola Ajilore
(University of Illinois at Chicago)

Stafford Lightman
(University of Bristol)

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KCNI-Tanz-TDRA Project

Prevention

Daniel Felsky
(CAMH/KCNI)

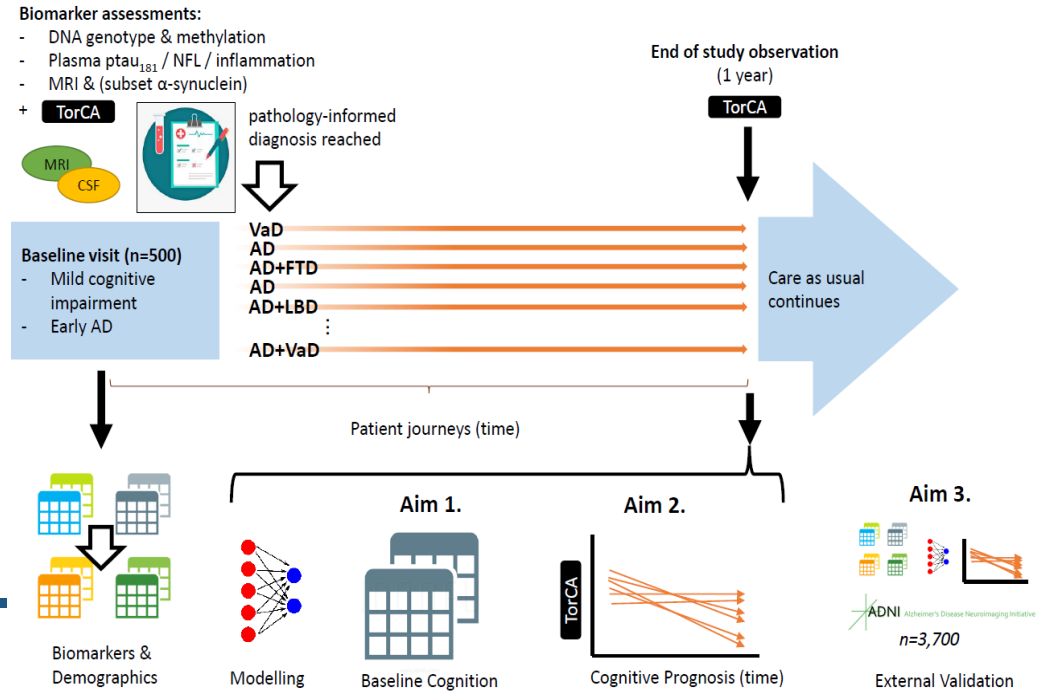
Morris Freedman
(Baycrest)

Ekaterina Rogaeva
(UHN/Tanz)

David Tang-Wai
(UHN)

Carmela Tartaglia
(UHN)

- Secured funding ($600,000)
- Develop non-invasive prognostic algorithms – based on biomarkers and supported by AI – in older individuals presenting with cognitive complaints
- A protocol has been developed and is undergoing REB review



Optimization of Prefrontal Theta-Burst Stimulation to Treat Depression: A Bench to First-in-Human Study

Prevention

Tarek Rajji
(Overall PI & Clinical)

Graham Collingridge
(PI Preclinical)

Evelyn Lambe
(PI Preclinical)

Sanjeev Sockalingam
(PI iKT)

Integrated KT

Advisory Committee | Community of Practice | Dissemination

Ex Vivo

- Identify optimal **spacing** for a 3-episode TBS in prefrontal cortex of wild-type mice
- Identify optimal number of **episodes** for the optimally spaced TBS in wild-type mice
- Refine number of episodes in "depressed" mouse → *ex vivo* **spaced-TBS** protocol
- Compare in "depressed" mouse spaced-TBS to 20-episode compressed-TBS, i.e. the currently used protocol for patients with depression

In Vivo

- Refine spacing and number of episodes of *ex vivo* spaced-TBS protocol in freely moving "depressed" mice → final **spaced-TBS**
- Compare in freely moving "depressed" mouse final spaced-TBS to 20-episode compressed-TBS

In Human

- Compare in patients with depression spaced-TBS to 20-episode compressed-TBS on DLPFC plasticity
- Assess relationships between DLPFC plasticity and depressive symptoms

***Ex vivo & in vivo* mechanistic studies**

PKA, Rolipram | CP-AMPAR, Protein Synthesis | SK channels, Fluoxetine

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Bell Let's Talk

Fondation Brain Canada Foundation

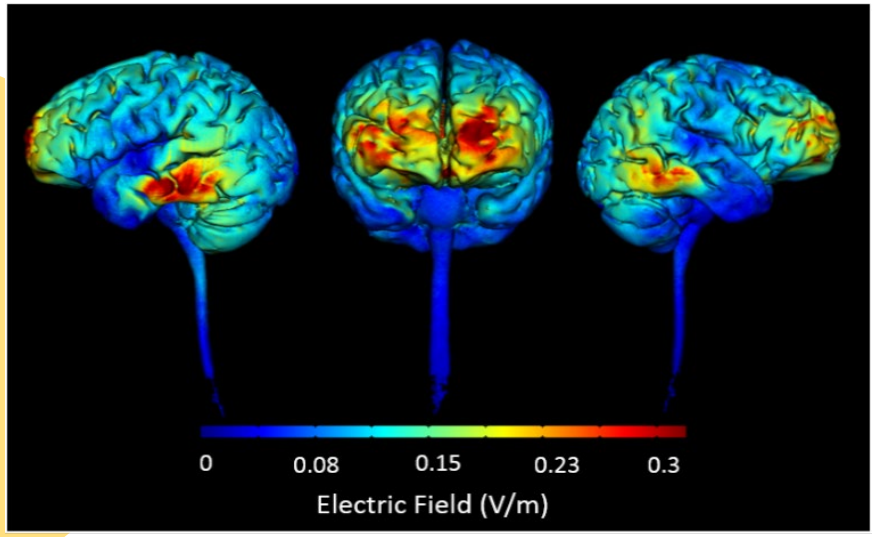
Secured funding of $950,000

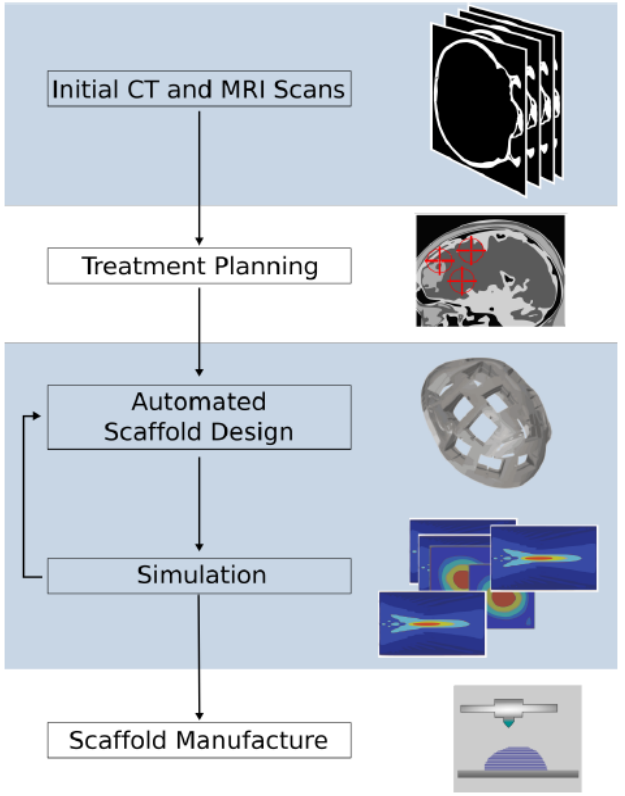
tACS-FUS Project

Prevention

- Collaborative project securing external funding of $500,000
- Focus on examining feasibility of combining two non-invasive stimulation methods, to enhance working memory in older adults
- Project in the process of obtaining REB and Health Canada approval

Transcranial alternating current stimulation (tACS)





Focused Ultrasound (FUS)

Investment in Learners

Past TDRA Clinical Fellows (2019-2021)

Dr. Eslam Abdellah
(2019-2020)

Neuropsychiatry, University of Ain Shams, Egypt

TDRA Fellowship: Cognitive and Behavioral Neurology

Baycrest

Dr. Carly Scramstad
(2019-2020)

Neurology, University of Manitoba, Canada

TDRA Fellowship: Cognitive Neurology

Sunnybrook

Dr. Mehrdad Maboudi
(2019-2020)

Neurology, Tabriz University of Medical Sciences, Iran

TDRA Fellowship: Cognitive Neurology

UHN

Dr. Fatemeh Bahari
(2020-2021)

Psychiatry, Mazandaran University, Iran

TDRA Fellowship: Geriatric Psychiatry

CAMH

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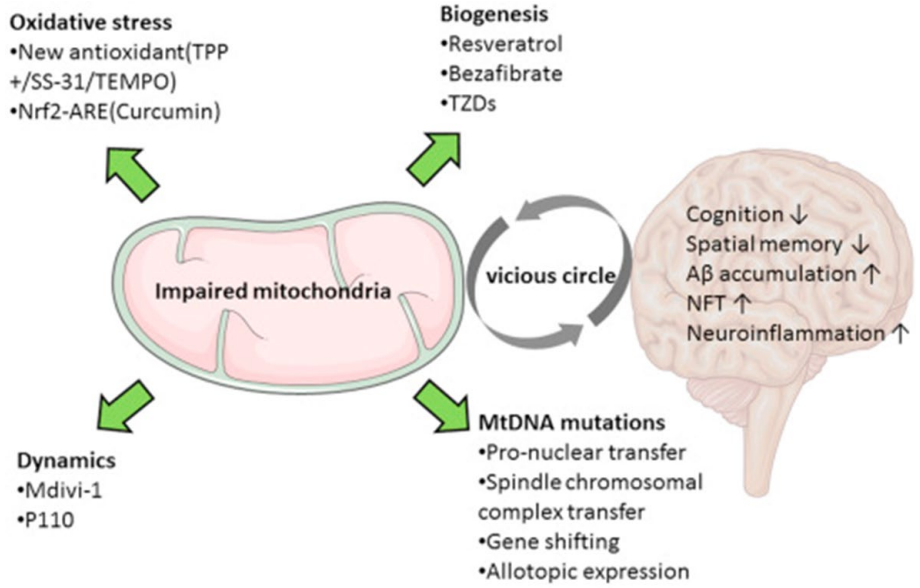
MITO2i-TDRA Fellowship

- Evidence for impaired mitochondrial function in dementia
- First Fellow: **Neda Rashidi-Ranjbar** under the supervision of **Tom Schweizer** and **Corinne Fischer** at Unity Health Toronto
- Studying the effect of photobiomodulation in treatment of mild cognitive impairment



1. CREMS Summer Medical Student
   - **2021:** Co-funded **Daksh Datta** who worked with **Krista Lanctôt** at Sunnybrook
   - **2022:** Co-funded **Elizabeth Boyd** who worked with **Krista Lanctôt** at Sunnybrook

   Examined data from the COMPASS-ND study for changes related to neuropsychiatric symptoms common across dementias

2. GDipHR Program Medical Student
   - **2022:** Co-funding of **Shreya Jha** who is working with **Sanjeev Kumar** at CAMH

   Examining abnormal cortical excitability in dementia and its association with brain metabolites and clinical symptoms using TMS-EEG and Magnetic Resonance spectroscopy

Sandra E. Black Award in Clinical Dementia Research

2021: Awarded to **Veronica Vuong**, who worked with **Claude Alain**

Focused on how music influences memory and neuroplasticity in people with MCI and early dementia, combining behavioural and cognitive measures and EEG

2022: Awarded to **Durjoy Lahiri** who is working with **Howard Chertkow**

Focused on investigating amyloid effects on clinical trajectory, brain imaging and biomarkers.

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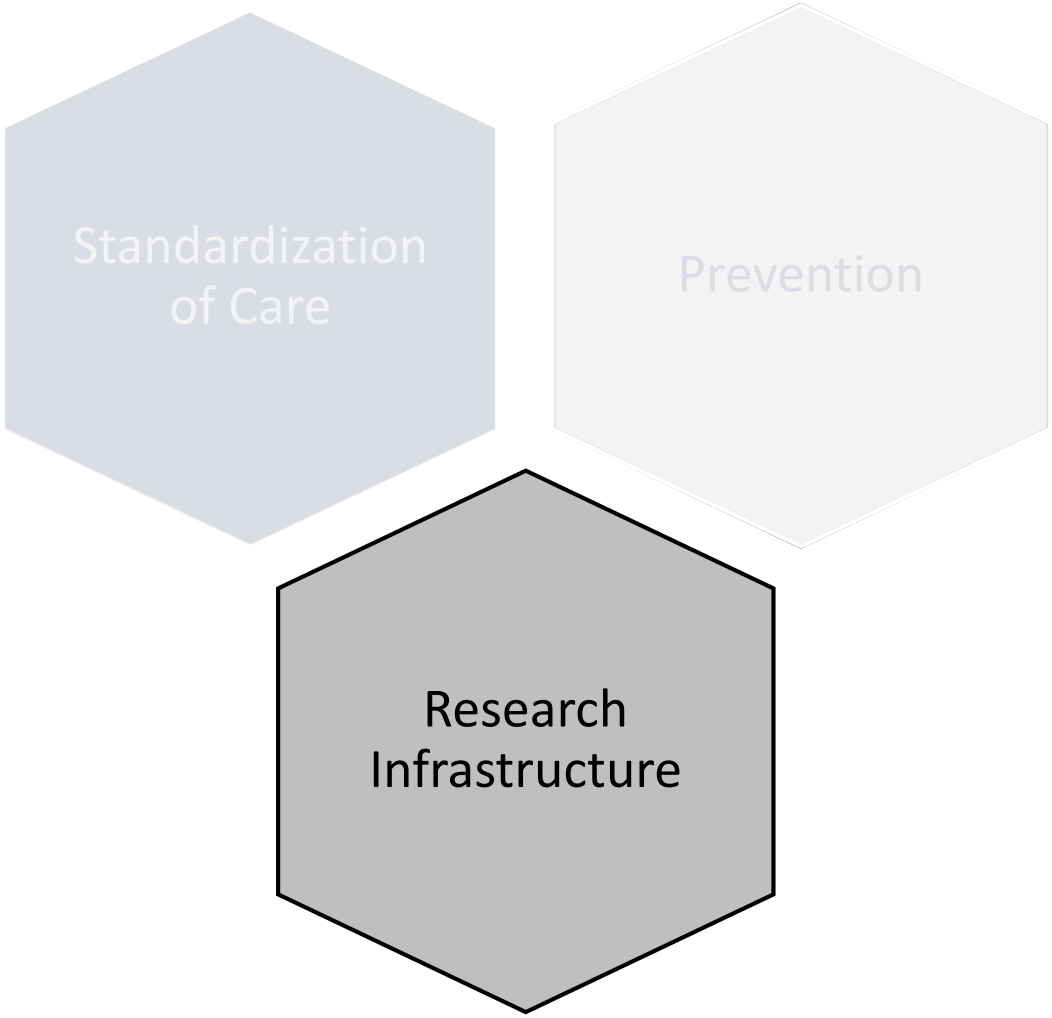
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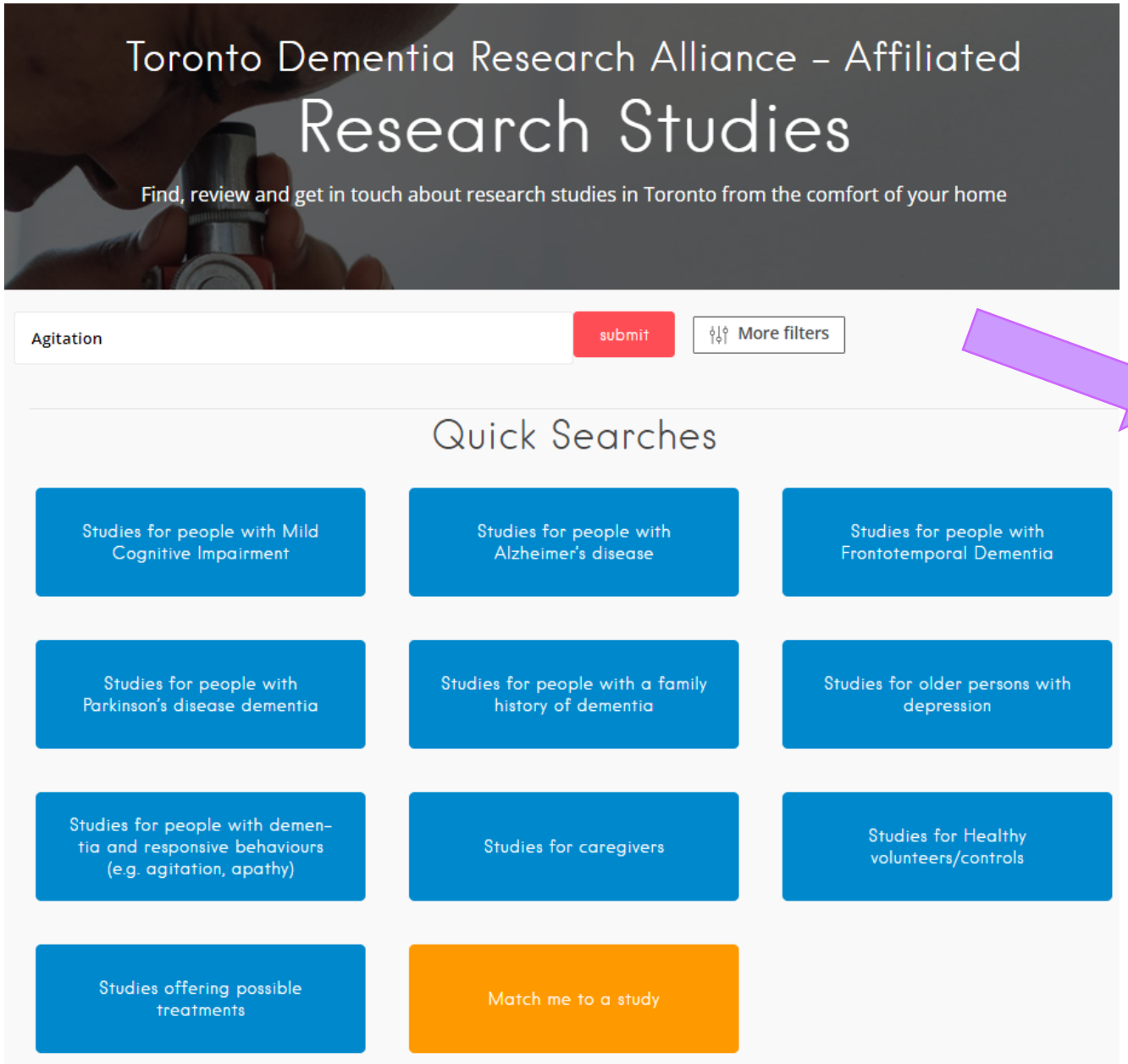

Research Infrastructure

Escitalopram for Agitation in Alzheimer's Disease (S-CitAD)

Interventional Study

Get in touch about this study

What is the study about?

This study looks at the safety and effectiveness of the anti-depressant escitalopram in treating agitation in people with Alzheimer's disease. Participants and their caregiver(s) will receive psychosocial counselling to address agitation in Alzheimer's disease. Participants who do not show a response will be given, at random, either escitalopram or placebo.

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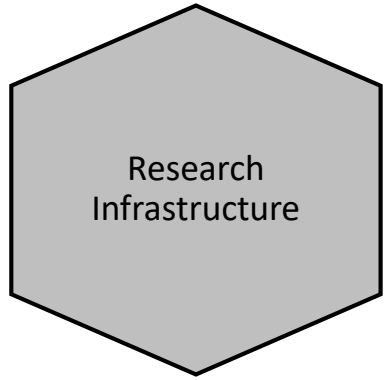
Recruitment Update through Toronto Dementia Network (TDN)



		Total		Specific		Non-specific	
	# Studies	# Referred	# Enrolled + Completed	# Referred	# Enrolled + Completed	# Referred	# Enrolled + Completed
BYC	9	10	0	3	0	7	0
CAMH	7	9	2	6	2	3	0
OSH	2	0	0	0	0	0	0
SBH	13	35	14	26	8	9	6
UHT	2	0	0	0	0	0	0
UHN	8	9	1	6	0	3	1
Total	41	63	17	41	10	22	7

Advances in Dementia Research Webinar Series

Research Infrastructure

Date	Topic	Speaker(s)	Attendees
14-Sep-21	Driving & Dementia	Dr. Mark Rapoport/Dr. Gary Naglie	45
17-Nov-21	Agitation in Dementia	Dr. Sanjeev Kumar	70
11-Jan-22	Diagnosis & Self-Care	Dr. Richard Swartz	50
24-Mar-22	Diversity in Risk & Protective Factors	Dr. Ho Yu	55
24-May-22	Non-Invasive Brain Stimulation	Dr. Tarek Rajji	43
12-Jul-22	Sleep, Cognitive Impairment & Stroke	Dr. Mark Boulos	36
27-Sept-22	Novel Drug Treatments for Agitation in Dementia	Dr. Krista Lanctot	68

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TDRA Alzheimer Society TORONTO

EDI Workshops

Research Infrastructure

- Presented by **Nicole Kaniki** - Director of Diversity, Equity, and Inclusion in Research and Innovation at the University of Toronto
- Hosted two workshops for TDRA investigators (June 2 and Sept 7, 2022)
- Slides and workshop recordings will be available on TDRA portal website

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Legal Research Working Group

Research Infrastructure

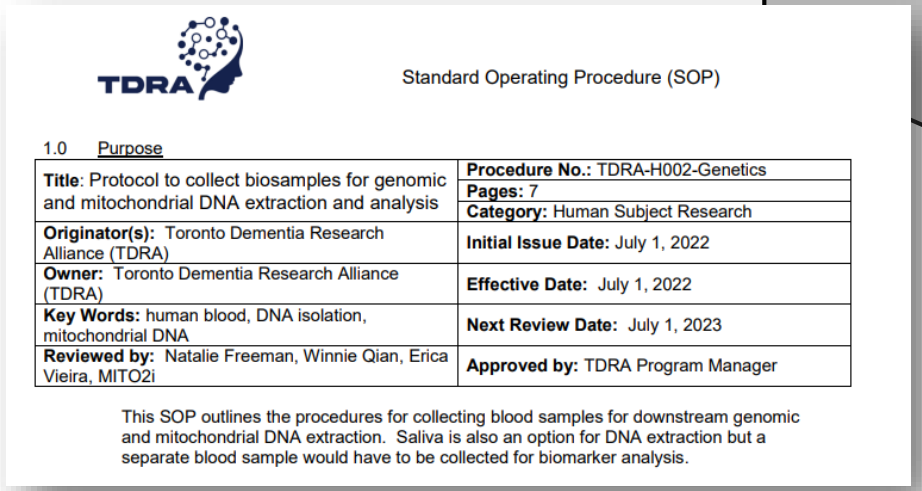
- TDRA has facilitated meetings with legal teams across partner sites allow them to interact directly on agreements.
- This novel model will allow them to gain awareness of projects on the horizon, address common issues more quickly, and create solutions that add efficiency to the contract negotiation process
- Licensing agreement for TorCA is in the final stages of review

SOPs and Virtual Biobank

Research Infrastructure

Available Resources

- SOPs for the collection, processing, and storage of biosamples:
  - TDRA-H001-Blood Separation
  - TDRA-H002-Genetics
- Virtual biobank and data repository
  - Help investigators find and access data and samples from other studies that are available for request. This will include not only studies in Toronto, but from national and international dementia research initiatives as well.



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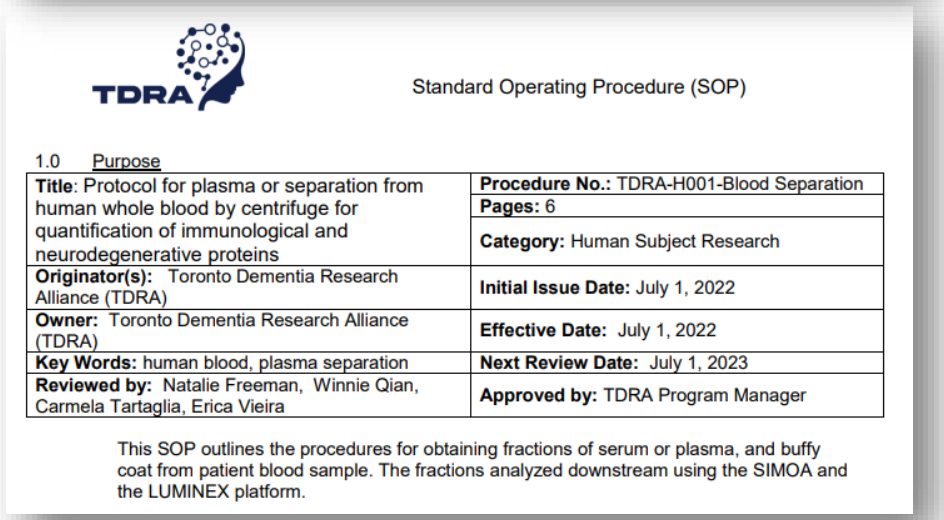
Standard Operating Procedure (SOP)

1.0 Purpose

Title: Protocol to collect biosamples for genomic and mitochondrial DNA extraction and analysis	**Procedure No.:** TDRA-H002-Genetics
	Pages: 7
	Category: Human Subject Research
Originator(s): Toronto Dementia Research Alliance (TDRA)	**Initial Issue Date:** July 1, 2022
Owner: Toronto Dementia Research Alliance (TDRA)	**Effective Date:** July 1, 2022
Key Words: human blood, DNA isolation, mitochondrial DNA	**Next Review Date:** July 1, 2023
Reviewed by: Natalie Freeman, Winnie Qian, Erica Vieira, MITO2i	**Approved by:** TDRA Program Manager

This SOP outlines the procedures for collecting blood samples for downstream genomic and mitochondrial DNA extraction. Saliva is also an option for DNA extraction but a separate blood sample would have to be collected for biomarker analysis.



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Standard Operating Procedure (SOP)

1.0 Purpose

Title: Protocol for plasma or separation from human whole blood by centrifuge for quantification of immunological and neurodegenerative proteins	**Procedure No.:** TDRA-H001-Blood Separation
	Pages: 6
	Category: Human Subject Research
Originator(s): Toronto Dementia Research Alliance (TDRA)	**Initial Issue Date:** July 1, 2022
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This SOP outlines the procedures for obtaining fractions of serum or plasma, and buffy coat from patient blood sample. The fractions analyzed downstream using the SIMOA and the LUMINEX platform.

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Thank You!

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