# Poster Presentations at the 8th Canadian Conference on Dementia (CCD), Ottawa, October 2015

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## POSTER ABSTRACTS

### Good Ideas: Non-Pharmacological Ideas and Tools Helpful in the Management of BPSD

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With the current push towards using fewer antipsychotics and more non-pharmacological interventions in long-term care, it has become increasingly important for knowledge and best-practice sharing across the province. The "Good Ideas" project began in 2001 in the context of my work as a Royal Ottawa geriatric psychiatry behavioural support outreach nurse to long-term-care facilities in Ottawa. A toolkit was begun as various ideas and tools were found to be useful in the management of behavioural challenges in the care of long term care residents. These non-pharmacological tools can have a significant impact on the management of behavioural challenges. Some were discovered via "out-of-the-box" thinking, some as a result of exploring possibilities on the Web, others were shared with me by colleagues in various roles and settings. I have worked in geriatric psychiatry in various capacities as a nurse at The Royal Ottawa Health Care Group since 1986, and have had the opportunity to accumulate several "good ideas" over time. I found myself carrying various articles, pamphlets, booklets, photos in my workbag and noticed I was being contacted more frequently over time on how to obtain certain items. When these non-pharmacological approaches were implemented, and successful, a common response would be: "what a good idea!" Thus, the name given to the project came to be. Good Ideas has grown over the years as the information has been shared with outreach team members and utilized in their own practice. All contacts are encouraged to share any new "good ideas" they encounter so those too can be added. Originally a hardcopy handout with a list and the resources to outsource items was created and distributed. This evolved into a PowerPoint presentation explaining the usefulness of each tool in specific target behaviours and how to obtain the tool, as well as photos. Later a poster was made and a second version was produced more recently. Currently the project is in the process of being translated to French for our bilingual Ottawa area. The project has circulated among my teammates to be used in education sessions in their long-term-care facilities or as an adjunct to larger full day education sessions on the topic of dementia care. A large colorful hatbox also contains some sample items to add to the hard copies. Good Ideas has been presented at the Regional Geriatric Program Annual Meeting poster presentation Oct 12, 2013, with very positive feedback from participants. Good Ideas is a project in perpetuity, with no stop date planned. It is my hope it will continue to grow long after my retirement date. It promotes the concept of creative thinking about behavioural challenges in dementia care, while supporting that pharmacological intervention should most often be as a last resort.

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### 'She Can't Walk, But She Is Not Weak''— a Rare Case of Tauopathy

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An 82 year lady came to my office, with a 2- year history of difficulty in walking. The referring geriatrician/memory clinic specialist called me saying that the patient couldn't walk, though she had good strength. She simply couldn't make her arms and legs do what she wanted them to do. The family said that it was almost like forgetting to walk. Patient had difficulty with dressing, using crockeries and cutleries, writing, and in combing her hair. She also said that her right arm often goes into odd positions. There was no significant past history or family history of any neurodegenerative disorder. Neurological examination showed an alert, cooperative woman who scored 27 on Mini-Mental State. She couldn't draw intersecting pentagons or write a sentence. She showed severe right upper limb apraxia, and couldn't even hold the pen in her hand. While examining her, the right lower extremity showed Alien-limb phenomenon, and right upper extremity showed occasional myoclonus. She showed evidence of Balint's syndrome while reaching for

objects. Extraocular movements showed jerky pursuits and delayed saccades. She had difficulty turning her head side to side, suggesting axial apraxia. Both lower limbs showed apraxia, and foot-tapping was practically impossible. It needed the assistance of two people for her to stand up, and she couldn't initiate a step, suggesting severe gait apraxia. She had no postural reflexes, and had rigidity and paratonia in all the four extremities, but worse on the right side. She had absent proprioception in her toes, a positive Babinski on the right foot, and also showed perseveration on clap test and impersistence in motor acts. These dysfunctions were out of proportion to the speech and cognitive disturbance. MRI scan of the brain showed anterior temporal atrophy with sparing of the mesial temporal structures and posterior frontal and parietal atrophy. A diagnosis of Corticobasal syndrome, a form of tauopathy, was made. A year after this diagnosis, the patient died. An autopsy was not done. Corticobasal degeneration is rare form of tauopathy characterized predominantly by asymmetric rigidity, limb dystonia, myoclonus, gait apraxia, alien-limb syndrome, ideational and ideomotor apraxia, and frontal lobe dementia syndrome. A high index of suspicion should be observed in patients with frontal lobe dementia syndrome, asymmetric levodopa-nonresponsive Parkinsonian syndrome, and in patients who are unable to perform movements in the absence of motor deficit. Early diagnosis could avoid unnecessary hospitalizations and investigations and would help family prepare for prognostication planning and placement options.

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**Service Coordination for System Navigation While Living With a Neurological Condition in Maniotba**

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The complex nature of living with a neurological condition often requires accessing a multitude of services across different agencies and disciplines. However, research indicates that people living with neurological conditions face unique challenges in the process of accessing and managing these services. Based on a review of the literature, system navigation is a major priority for these groups and can be improved through service coordination. As a result, the purpose of this thesis is to explore the diverse experiences of accessing care and services when living with a neurological condition in Manitoba. Using qualitative methodologies, and the framework of interpretive description, I conducted 15 in-depth, semi-structured interviews with adults living with a neurological condition in Manitoba. Recommendations to future service coordinators and government on possible initiatives to improve the daily experiences of individuals living with neurological conditions are also provided.

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**Capacity Building: Intergenerational Global Dementia Solutions**

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***Background:*** Capacity building for global health issues related to dementia is necessary to bridge the generation gap in the search for global dementia solutions. It is important that all generations, including younger less established ones, are engaged to strengthen their understanding of dementia related issues. We are at a pivotal moment, the entire global population is aging and the incidences of dementia are estimated to skyrocket. Currently, the numbers are estimated at 36 million in 2010. These numbers are doubling every 20 years to 66 million by 2030 and to 135 million by 2050. We need to harness the momentum for change and impact found in the energy and innovation from younger generations.

***Objectives:*** 1. To discuss global health dementia initiatives and show the importance of younger generations leadership and understanding of dementia as a social, economic and public health issue. 2. To encourage practitioners and researchers to make room for the voices of younger, less established generations in discussions surrounding the search for global dementia solutions.

***Overview:*** The first G8 Summit on Dementia took place in London, England in December 2013. This event spurred a commitment to dementia from all attending nations and their delegates, including an obligation to participate in four subsequent G7 Legacy events (England, Canada-France, Japan, USA). These four legacy events provided an opportunity for more specific dialogue from world leaders in dementia. In parallel with these Global Action Against Dementia Legacy Events, young local leaders were given the opportunity to develop innovative ideas to support the ongoing work of the World Dementia Council, and to create a sustainable global network which will continue to address the challenges presented by dementia.

***Results:*** The 120 selected Young Leaders in Dementia met in London, Ottawa, Tokyo, and Washington D.C., to discuss innovative ideas to address dementia. Young Leaders in Dementia were also represented in Geneva at the First Ministerial Conference on Dementia where they brought their recommendations to the World Dementia Council.

***Conclusion:*** Youth are the leaders of our future, and their full participation and understanding of the global health issue surrounding dementia is required to support the aging population. Capacity building, sustainability and innovation will guide the next generation in its solutions for public health issue of dementia.

## Hippocampal Atrophy in Semantic Dementia and Alzheimer's Disease : a Meta-Analysis

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***Background/Objectives:*** Imaging studies show a relationship between episodic memory impairment in Alzheimer's disease (AD) patients and hippocampal atrophy, which is present in most cases. On the other hand, semantic dementia (SD) patients manifest impairment in semantic memory due to a deterioration of the anterior temporal lobes. Many studies on SD also show similar hippocampal atrophy found in AD patients. It is therefore substantial to compare and clarify our knowledge regarding these two pathologies in order to guide their clinical diagnoses and help direct the different intervention methods available. One could hypothesize that different parts (anterior vs. posterior) of the hippocampus are affected in both diseases, as previous findings (La Joie et al., 2014) showed a relationship between the anterior part of the hippocampus and semantic memory, as well as between the posterior part of this structure and episodic memory, in healthy subjects.

***Methods/Overview:*** A meta-analysis was conducted using GingerAle software to verify if previous findings showed a differential hippocampal atrophy in AD and SD.

***Results:*** Results of data analysis show atrophy in the anterior part of hippocampus in SD patients, whereas an atrophy in both parts (anterior and posterior) in AD patients. Also, anterior atrophy found in SD was greater than that of AD.

***Conclusion:*** These results show a possible association between the etiology of both pathologies and the location of the atrophy.

## Platelet Derived Extracellular Vesicles (PL-EVS) Are Carriers of Alzheimer's Disease-Associated Proteins

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***Background/Objectives:*** Platelets (aka thrombocytes) are the smallest of the three major types of blood cells. They are produced from very large bone marrow cells called megakaryocytes and contribute to hemostasis. During their lifetime they release small vesicular particles, so called extracellular vesicles (EV) which make up till 90% of the circulating EVs in the bloodstream. These PL-EVs are involved in various cellular processes like autoimmunity, chronic inflammation, and neurodegeneration.

***Methods/Overview:*** After 5 days standard blood banking, PL-EVs were isolated by filtration and differential gradient ultracentrifugation into five subfractions and platelet exosomes (PL-EXs). Followed by further characterization: Nanoparticle Tracking Analysis, Flow Cytometry and proteomic/ lipidomic mass spectrometry.

***Results/Conclusions:*** PL-EVs showed overlapping particle mean sizes of 180–260 nm, but different proteomic and lipidomic composition. The amyloid precursor protein APP, the hallmark protein of Alzheimer's disease, is enriched in distinct platelet fractions, while the Apolipoprotein E, the highest risk factor for late onset Alzheimer's disease is located in late subfractions of PL-EVs. This result indicates an important role of PL-EVs and platelet function in the regulation and biogenesis of Alzheimer's disease.

## Dementia in the Waiting Room—Training Primary Care Receptionists To Identify and Respond to Early Signs of Dementia and Respond to Behavioural and Associated Behaviours

E. Danieli. Mount Sinai Hospital.

Primary Care receptionists can play an important role in the provision of dementia care and often have a high level of interaction with the patients and their families.(1) According to the OCFP and PIECES Canada,(2,3) only 50% of cases of dementia are specifically diagnosed, mostly at the moderate–severe stage of the disease, despite many red flags that can be identified in the clinical settings, such as missing appointments, showing up on the wrong day, etc.(2) In many cases it is the receptionist that witnesses these types of behaviours and, unless he/she reports them, the physician may not be aware that these behaviours are occurring. In addition, receptionists often find themselves caught in conflict situations that they have no formal training or support to manage.(4,5) In this presentation we will discuss a newly developed training and a service that was designed to train receptionists in identifying early signs of cognitive decline, as well as how to better respond to behavioural and psychological symptoms of dementia as they welcome patients into the clinic.

1. Carnegie MA, Gomel MK, Saunders JB, *et al*. (1996). General practice receptionists' attitudes and beliefs towards preventative medicine before and after training and supports intervention.

2. Ontario College of Family Physicians and PIECES Canada. (2009). Behavioural and psychological symptoms of dementia toolkit for family physicians. Available at: http://www.sagelink.ca/behavioural_and_psychological_symptoms_of_dementia
3. Aminzadeh F, Molnar WB, Dalziel WB, et al. (2012). A scoping interpretive review of literature on perspectives and practices of primary care physicians " vis " diagnosis and management of community living older persons with dementia, regional geriatric program of eastern ontario. Available at: http://www.cgjonline.ca/cgj/templates/images/RGPEOFullReport.pdf
4. Stewart TV, Loskutova N, Galliher JM, *et al*. Practice patterns, beliefs, and perceived barriers to care regarding dementia: a report from the American Academy of Family Physicians (AAFP) National Research Network. *J Am Board Fam Med*. 2014;27(2):275–83.
5. Dixon C, Tompkins C, Allgar VL. abusive behaviours experienced by primary care receptionists: a cross sectional survey. *Fam Pract*. 2004;21(2):137–39.

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**Behaviour Support in Primary Care**

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Family doctors/primary care practitioners are often the first point of contact for patients who are looking for assistance and the professionals most consulted by people with dementia (PWD). Thus, they are in a critical and strategic position to provide care for this population (Aminzadeh et al, 2012). Dementia is perhaps the most complex of all chronic diseases, characterized by an interaction of cognitive, functional, behavioural, and psychological symptoms that negatively impact various dimensions of health and quality of life of both the person with dementia (PWD) and his/her caregivers (Kales HC, et al., 2015). International studies show that dementia is associated with two to five times higher rates of health services utilization, including emergency services, alternate level of care hospital services, home care services and Long Term Care facilities (Aminzadeh et al, 2012; Thomas et al. 2014). However, there continues to be significant challenges in the provision of dementia care in the primary care sector, such as under recognition and diagnosis; under disclosure and under management. This is due to barriers to care, identified by primary care practitioners as complex biomedical, psychological and ethical nature of the disease; gaps in knowledge; skills and attitudes across the sector; and system structural barriers to care — in addition to experts calling for systematic approaches to strengthen primary dementia care (Aminzadeh et al, 2012). The Psychogeriatric Resource Consultant for Primary Care (PRC-PC) is a role initiated as part of the Toronto Central LHIN Behavioural Support for Seniors Program. The PRC-PC's role is to support primary care practitioners in building capacity for the care of older adults with psychogeriatric conditions and their families. In particular, the role focuses on building capacity for the care of older adults with dementia and responsive behaviours. This presentation will discuss the development and services of the PRC-PC role in the TC-LHIN and demonstrate the implementation of a systematic approach to the management of behavioural and psychological symptoms of dementia in primary care through clinical cases.

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**I-See-U: a Framework To Identify and Support Caregivers of People with Dementia in the Community**

E. Danieli, R. Feldman. Mount Sinai Hospital.

Family caregivers are vital in ensuring the health and quality of life of a patient with dementia, but caregiving comes with risks of declining health and wellbeing for the caregiver themselves. Health-care providers are challenged to balance the needs of both members of the dyad in providing care to the identified patient. The new framework called I-SEE-U guides practitioners to include the caregiver as part of the care team and bring them out of the role of the shadow patient. Although initially developed for primary care (PC), it is applicable in multiple sectors. I-SEE-U stands for Include, Screen, Educate, Extra Support, and Understand. It is an innovative collaboration between the Psychogeriatric Resource Consultant to Primary Care and the High Risk Caregiver Program at the Reitman Centre at Mt. Sinai Hospital.

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**Recall Consistency in Adults with Amnestic Mild Cognitive Impairment and Typically Aging Adults**

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***Background:*** Amnestic mild cognitive impairment (MCI) is characterized by memory impairment with preserved daily functioning (Petersen, 2004). Individuals with MCI show poor encoding, retention, and consolidation of new information. However, little research has investigated the relationship between recall consistency and memory performance in MCI. Recall consistency refers to the ability to recall the same items consistently across repeated learning trials. Inconsistent recall is typically associated with frontal lobe dysfunction (Luria, 1981).

***Objective:*** The objective of this study was to investigate recall consistency between individuals with MCI and healthy older adults with no cognitive impairment (No CI) on a commonly-used verbal memory test (i.e., CVLT-II).

***Method:*** Thirty-two MCI and 103 No CI cases were drawn from a population-based study. All participants completed

the California Verbal Learning Test- II. This memory test contains 5 repeated learning trials, as well as brief 20-minute delayed recall trials. Percentage of recall consistency was calculated using the number of target words recalled once on each of the first four learning trials that are also recalled on the very next learning trial. Independent *t*-tests were used to assess differences in recall consistency between groups. Correlations between recall consistency and recall measures were used to investigate the relationship between recall consistency and delayed memory performance (i.e., memory retention). A stepwise regression using demographic variables (e.g., age, education, & gender (step 1)) and other cognitive tests (e.g., digit forward, digit span backward, TMT A, TMT B, Boston Naming, FAS and animal fluency, & 3MS scores (step 2)) were used to predict recall consistency in both groups combined.

***Results:*** The MCI group had poorer performance on all recall trials than the No CI group (e.g., CVLT-II Total Recall Trials 1-5: No CI = 36.7 c.f. MCI = 25.3, $t$=6.9, $p$<.001; CVLT Long Delay: No CI = 8.0 c.f. MCI = 2.8, $t$=11.8, $p$<.001). As well, the MCI group (i.e., 62.0%) showed significantly lower recall consistency than the No CI group (i.e., 70.4%; $t$=2.34, df=40.1, $p$=.025). Correlations in No CI group showed that higher recall consistency was strongly associated with better immediate ($r$=0.59, $p$<.001) and delayed recall (Short Delay: $r$=0.40, $p$<.001; Long Delay: $r$=0.36, $p$<.001). Recall consistency was not associated with memory performance for the MCI group. The time to complete TMT B and the number of errors on TMT B entered the stepwise regression model to significantly predict recall consistency (F (1,115) = 11.73, $p$<.001, $R^2$ = 16%).

***Conclusions:*** Higher recall consistency was associated with better encoding and retention of new information in the No CI group. Recall consistency was reduced in the MCI group relative to No CI group. Inconsistent recall was associated with reduced performance on tests of executive functioning suggesting degradation in networks sub-serving frontal brain regions leading to more disorganized encoding strategies.

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**Depressive Symptom Trajectories in Older Adults with Dementia and Associated Risk of Functional Decline**

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***Background/Objectives:*** Despite the dynamic nature of depressive symptoms, most studies have relied on assessment of depressive symptoms at a single point in time, thus limiting our understanding of the burden, course and outcomes of depression among vulnerable populations such as those with dementia. We examined the course of depressive symptoms and associated risk of functional decline over 1-year among a large sample of older home care (HC) clients in Ontario with a diagnosis of Alzheimer's disease or related dementia.

***Methods:*** Longitudinal clinical data from the Resident Assessment Instrument for Home Care (RAI-HC) were linked to provincial administrative health databases at the Institute for Clinical Evaluative Sciences (ICES). We examined assessments performed by trained case managers among all Ontario HC clients between 2006 and 2009. The sample was restricted to clients (mean age 82 yrs; 73% female) with dementia and 3 consecutive assessments who remained alive during the year post-3rd assessment (n=16,597). Clinically important depressive symptoms were captured by the RAI-HC depression rating scale (DRS score 3+) and categorized as no symptoms (no DRS score of 3+ at any point), baseline-only, new onset (at 1st or 2nd reassessment but not at baseline), or persistent (at baseline and 1st or 2nd follow-up assessment). Associations between depressive symptom change and functional decline (i.e., decline in ADL scores assessed at the 4th consecutive RAI-HC and/or admission to long-term care) over 1-year were examined with multivariable logistic regression models adjusted for relevant confounders.

***Results:*** The estimates for baseline-only, new-onset, and persistent depressive symptoms were 5.1%, 9.5%, and 9.5%, respectively. An estimated 38.4% (n=6,375) clients with dementia experienced functional decline during the 1-year follow-up and estimates were higher among those with new onset or persistent depressive symptoms (47.7% and 42.6%, respectively) than among those with no (36.9%) or baseline only (36.7%) symptoms. In models adjusted for baseline characteristics including age, sex, antidepressant use, cognitive and functional impairment, co-existing neurological and chronic health conditions and previous acute care use, clients with new onset depressive symptoms were significantly more likely than those with no symptoms to exhibit functional decline [adj. OR=1.39, 95%CI 1.25–1.55]. Clients with persistent depressive symptoms showed a marginally increased risk of functional decline [adj. OR=1.14, 95%CI 1.02–1.28], whereas those with baseline only symptoms showed no increase in risk. To explore the impact of excluding deaths during follow-up, we examined the association between the dynamic depressive symptom measure and mortality and found comparable findings to those observed for functional decline (with the highest mortality risk among those with new onset symptoms).

***Conclusion:*** Our findings demonstrate that the adverse health outcomes of depression in dementia are not necessarily restricted to those with persistent symptoms as we observed the greatest risk of functional decline among clients experiencing new depressive symptoms. This work illustrates the need for

coordinated efforts among HC staff and mental health-care providers to improve the timely identification and effective management of emerging depressive symptoms among vulnerable persons with dementia in community settings.

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**Simultaneous Temporal Trends in Dementia Incidence and Prevalence, 2005-2013: A Population-Based Retrospective Cohort Study in Saskatchewan, Canada**

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***Background:*** Original studies published over the last decade concerning time trends in dementia epidemiology report mixed results. Discrepancies in the direction and magnitude of change over time may be partly due to differences in methodological approaches, observation periods, and population characteristics. Importantly, however, only one other original study of simultaneous trends in recent dementia incidence and prevalence has been published within the last 10 years. The present study used linked administrative health data for the province of Saskatchewan for the period 2005/06 to 2012/13 to: (1) examine simultaneous temporal trends in annual age- and sex-specific dementia incidence and prevalence among individuals aged 45 and older, and (2) stratify the changes in incidence over time by database of identification.

***Methods:*** A population-based retrospective cohort study design was employed. Data were extracted from seven administrative health databases for the province of Saskatchewan, linked by a unique anonymized identification number. Individuals 45 years and older at their first identification of dementia between April 1, 2005 and March 31, 2013 constituted the cohort, based on a case definition algorithm applied to four of the administrative health databases (hospital discharge abstracts, physician service claims, prescription drug, and RAI-MDS, i.e., long-term care).

***Results:*** Between 2005/06 and 2012/13, the 12-month age-standardized incidence rate of dementia decreased by 11.07% and the 12-month age-standardized prevalence rate increased by 30.54%. Despite an increase of 11.38% in the population at risk (PAR), the absolute number of incident cases dropped by 3.51% from 3,389 to 3,270, and the age-standardized incidence rate dropped from 8.41 to 7.48 per 1,000 PAR. The decline in the incidence rate was observed in every database of identification. The absolute number of prevalent cases rose by 47.95% from 8,795 to 13,012 against an increase of 12.16% in the PAR, and the age-standardized prevalence rate increased from 21.35% to 27.87% per 1,000 PAR. The largest share of the prevalence rate increase took place in the first four years of the study period, with the upward trend slowing between 2009/10 and 2012/13.

***Conclusions:*** A simultaneous trend of decreasing incidence and increasing prevalence of dementia in the province of Saskatchewan was observed, over a relatively short 7-year period from 2005/06 to 2012/13. Possible explanations for a diminished incidence rate of dementia include rising education levels, increased uptake of healthy behaviours, and improved treatment of vascular risks. Increased survival time with dementia may reflect improved health services (possibly including earlier diagnosis) and institutional care. Continued observation of these time trends is warranted given the short study period.

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**Innovation in Geriatric Medicine —Geriatric Medically Complex Clinic**

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The Geriatric Medically Complex Clinic is a one year demonstration project whose overarching goal is to improve medical care and patient/caregiver experience of the geriatric medically complex Patient post hospital discharge (ED or Admission) and proactively optimize the health of the medically complex older adult in the community. The aim is for urgent referrals seen within 72 hours. GMCC reduces system health-care costs while providing quality medical care. Several specific indicators/targets were developed for the project including: identification of preventable ADR and suboptimal prescribing and ED/admission avoidance. In fact, GMCC has 39 hospital admissions avoided, 165 ED visits avoided, the identification of 72 preventable adverse drug reactions, and 456 suboptimal prescribing identified. The inter-professional team included partnerships with St. Mary's General Hospital, Grand River Hospital, Geriatric Associates, Waterloo Wellington Community Care Access Center, and Specialized Geriatric Services. The development of the GMCC inter-professional team leveraged existing local experts in Geriatrics, strengthened professional and inter-organizational collaboration, built up capacity of primary care providers in the management of frail medically complex older adults, and increased system integration. The GMCC's innovative team includes: Geriatric Specialized Nurse Practitioners from SMGH (both inpatient and clinic/outreach), Geriatric Clinical Nurse Specialist (CNS), Geriatricians, Primary Care Physician with Elderly specialty, Project Lead seconded from WWCCAC, Geriatric Psychiatry specialized SW seconded from Cambridge Memorial Hospital, experienced geriatric focused Clinical Pharmacy resource from

SMGH, Social work Community Care Coordinator seconded from WWCCAC, and a dedicated Administrative Professional from SMGH. The team further forged relationships with Geriatric Emergency Medicine (GEM) Nurses at local EDs, local memory clinics, community support programs (including adult day programs, elder abuse and community support connections), Integrated Geriatric Service Worker program, Rapid Response Nurses and Care Coordination through CCAC and its service providers, elder abuse team, retirement homes, respite and shelter services, primary care and Health Links team, to better support patient transition and ongoing care for the Medically Complex Patient. As part of the team's ongoing commitment to quality improvements, periodic reviews of team roles were conducted. The project found stronger linkages to pharmacy, Geriatric Psychiatry and WWCCAC Community Care Coordinators also were an essential component of the medical management of complex patients. The flexibility built in to the model allows team members to assess and follow-up (in person or by phone) with Medically Complex Geriatric patients in the most appropriate setting for the patient and may include the Emergency Department, Hospital in-patient, their home setting or at the GMCC clinic, thereby ensuring the transition for patients are supportive. The GMCC engaged with patients and caregivers for the development of clinic workflow, referral pattern, and information sharing to verify processes meet the needs of patients and caregivers. The clinic has electronic methods for real-time communication and has been designed to be a paperless clinic. The patient survey evidenced the value of the clinic for older adults with complex needs. One hundred percent of respondents reported the health-care providers listening skills, explanations, and patient involvement was good or very good.

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**Clinico-Pathological Correlation of Neurodegenerative Cases in a Dementia Unit**

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The importance of brain autopsy and brain banking for neuropathological confirmation of disease diagnosis is well-recognized. Neuropathological examination has great potential in several areas, including effecting change in clinical diagnosis, guiding treatment, providing quality assurance about diagnosis and management, and as the starting point for research opportunities. Critical self-analysis of post-mortem cases can add valuable information to clinical practice. 61 cases submitted to the Maritime Brain Tissue Bank by a single physician between January 2002 and December 2013 were analyzed. These cases were derived from a single dementia unit at a long-term care facility in Halifax, Nova Scotia, Canada. The accuracy of clinical diagnosis as compared to neuropathological diagnosis was evaluated. Discordant cases are highlighted here. Partial or complete agreement between clinical and pathological diagnosis was confirmed in 77% of the cases, affirming the relative accuracy of clinical diagnosis but highlighting the need for more refined diagnostic techniques in this challenging area.

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**Correlating Quantitative Tractography at 3T MRI and General Cognitive Tests in Healthy Older Adults**

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***Background/Aims***: This study used diffusion tensor imaging tractography at 3T MRI to relate cognitive function to specific white matter tracts in the brain.

***Methods:*** Brain T2 fluid attenuated inversion recovery-weighted and diffusion tensor 3T MRI scans were acquired in thirty-six healthy participants without mild cognitive impairment or dementia. They completed a battery of neuropsychological tests including the MoCA, Stroop test, Trail Making Test B, Wechsler Memory Scale-III Longest span forward, Wechsler Memory Scale-III Longest span backward, Mattis Dementia Rating Scale, California Verbal Learning Test Version II Long Delay Free Recall, Letter Number Sequencing. Tractography was generated by the Fiber Assignment by Continuous Tracking method. The corpus callosum, cingulum, long association fibers, corticospinal/bulbar tracts, thalamic projection fibers, superior cerebellar peduncle, middle cerebellar peduncle, and inferior cerebellar peduncle were manually segmented. The fractional anisotropy (FA) and mean diffusivity (MD) of these tracts were quantified. We studied the association between cognitive test scores and the MD and FA of tracts while controlling for age and total white matter hyperintensities volume.

***Results:*** The age of participants ranged from 44 to 89 years. Worse scores on the Stroop test was associated with increased FA of the corpus callosum (coefficient: 134, $p$=.022), corticospinal/bulbar tract (coefficient: 105, $p$=.045), and thalamic projection tracts (coefficient: 81.5, $p$=.048). Scores on the other cognitive tests were not associated with either the FA or MD of measured tracts.

***Conclusion:*** This study demonstrates the utility of quantitative tractography in clarifying structure-function relationships between white matter tracts and cognitive function. In healthy persons, the Stroop test appears to be a better predictor of the microstructural integrity of white matter tracts measured by DTI than the MoCA.

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**Level of Care Needs Before Hospital Admission Impacts Inpatient Geriatric Rehabilitation Outcomes Among Older Adult with Dementia**

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***Background:*** While research has demonstrated cognitive impairment is a risk factor for functional decline and may affect rehabilitation outcomes compared to the cognitively intact, the characteristics that lead to rehabilitation success in people with dementia have not been evaluated. Our objective was to determine the association between level of care/place of residence on functional gains among older adults with dementia during inpatient geriatric rehabilitation.

***Methods:*** Retrospective cohort study. Consecutive subjects admitted to an inpatient geriatric rehabilitation unit with a dementia diagnosis (n=175, age 83.1±7.2 y, 55.4% female) had mobility, cognitive and demographic data collected at admission and discharge. The Functional Independence Measure motor function subscale (FIM-motor) was used to estimate level of mobility. Gains in motor function were the difference between FIM-motor scores at admission and discharge. Multivariable linear regression evaluated the association between level of care/place of residence and mobility gains during rehabilitation.

***Results:*** Mobility gains were smaller, with increasing care among pre-admission residence settings. The mean gain in mobility was 48.9% for "home without services", 44.6% for "home with services", 38.0% for "assisted living", and -4.9% for "residential care". In regression analysis, compared to "home without services", average FIM-motor gains were lower by 4 points for "home with services" ($p$=.042), 5.6 points for "assisted living" ($p$=.029) and 23.2 points for "residential care" ($p$<.001).

***Conclusion:*** Pre-admission residence and care needs were associated with mobility gains during inpatient geriatric rehabilitation. More research is needed on the association between pre-admission function and loss of function prior to inpatient rehabilitation on functional outcomes to refine positive prognostic factors associated with residence setting.

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**Objective Assessment of Risk Factors in Alzheimer's Disease (AD): a Novel Study Based on Artificial Neural Network**

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***Background:*** Alzheimer's disease (AD) is one of the major causes of dementia, representing about 60% of total incidences of dementia. In recent statistics report, AD ranks 6th of the leading causes of death in North America and Europe. AD is a chronic neurodegenerative disease identified by the gradual atrophy of various brain regions. There are no medications or cure for AD. Existing medications are mainly to ease, or treat cognitive and behavioral symptoms. Thus, there arises a pressing need for early diagnosis methods. Identification of risk factors of AD is one of if not the most important prerequisites for an efficient diagnosis system. In this work, a novel evaluation framework is proposed to assess the risk scores of various medical variables based on an automatic diagnosis system.

***Objective:*** This paper explores how different variables contribute to the diagnosis of AD in an automatic diagnosis system based on artificial neural network (ANN). In particular, variable risk level is assessed in terms of the corresponding impact on the diagnosis accuracy.

***Methodology:*** The Alzheimer's Disease Neuroimaging Initiative (ADNI) database was utilized in our study. The neuroimaging and biological data from 822 ADNI participants (229 normal patient, 405 MCI patients, and 188 AD patients) are adopted in this work. The neuroimaging data are processed by FreeSurfer to measure cortical thickness and volume of neuroanatomical structures. Experiment subjects have multiple visits to the trial site, resulting in multiple high dimensional vectors of medical records. Excluding invalid records (e.g., with missing entries), there are a total of 2158 feature vectors, 586 normal records, 1006 MCI records, and 416 AD. An artificial neural network (ANN) is trained to classify the patient as AD, MCI, or Normal (i.e., automatic diagnosis). Level of risk for various variables is defined as how much the system performance changes if the specific variable is ruled out. The same ANN based automatic diagnosis system is used for analysis. Two different approaches are utilized to study the performance change — i.e., with or without self-optimization. Extensive analysis is provided to show the risk level (or score) of different variables.

***Results:*** Variable risk score changes as we choose different algorithms for diagnosis. Overall, the top three most important variables are age, left hippocampus volume, and right hippocampus volume. However, with re-optimization, the

importance of hippocampus volumes drops dramatically. The resultant top three most important variables become age, volume for right temporal grey matter, and total white matter. This is because the missing information can be compensated by neighboring brain structures through a nonlinear system model.

***Conclusion:*** This study gives a general framework for variable risk assessment based on the corresponding impact on the diagnosis decision. Age is identified as the most important risk factor for AD, which is consistent with medical observations. However, hippocampus volume shows different performance in different experiment settings. This is due to the internal correlation between different brain volumes.

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**Apathy and Frontotemporal Dementia: a Meta-Analytic Examination of the Prevalence Rates**

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***Background/Objectives:*** Frontotemporal dementia (FTD) is associated with considerable morbidity and mortality as well as caregiver distress, and is one of the most common causes of dementia in patients under the age of 60. Apathy, a non-cognitive neuropsychiatric syndrome, distinct from depressive syndrome, presents across all stages of FTD and affects both prognosis and quality of life for patients and caregivers. This condition has been reported with mixed prevalence rates. Understanding the true prevalence allows for better management of neuropsychiatric syndromes and should eventually lead to better resource allocation. Hence, we have examined the reported prevalence rates for apathy in FTD in light of the moderating variables.

***Methods:*** PubMed was queried for the prevalence of apathy in FTD. Selection criteria were set *a priori* to include studies reporting on the apathy prevalence. No limitation was set for age, gender, or language of study. Studies were excluded if they reported on clinical trials, case-series or case reports. For each study, an event rate was generated to represent the prevalence rate. Using random effect model, an aggregate prevalence rate estimate was calculated with the comprehensive meta-analysis software. This analysis was subjected to bias, heterogeneity, and moderating variable analyses. Moderating variables included variants of FTD diagnosis, apathy assessment approach, age, sex, and global cognitive score.

***Results:*** A total of 175 possible studies emerged from the search of the literature and reviewing the studies. From these, 36 meet selection criteria, and 29 provided data for analysis. We obtained a 91% concordance rate between two independent raters (AAS and CH) of studies. The aggregate random effect point prevalence estimate was 0.752 [95%CI: 0.673–0.818], and it was heterogeneous [Q-value: 140.404; p-value<.001; I2: 80.058]. This includes 1099 FTD patients (behavioral, language, temporal variants, as a well as mixed, mutation carriers, and undifferentiated groups), with 810 having symptom of apathy. The prevalence estimate for behavioral/frontal variant was 0.787 [95%Ci: 0.633-0.887; Q-value: 89,846; p-value<.001; I2: 87.757; N=12]; and for undifferentiated FTD was 0.725 [95%CI: 0.592-0.828; Q-value: 30.544; I2:70.534; N=10]. Other FTD variants were reported with less than adequate samples (<3 studies) to be included for further analysis. Apathy was recorded by using chart data, clinician interview (i.e., Lund and Manchester 1994 criteria), using various scales (e.g., Neuropsychiatric inventory (NPI) of various versions, Middelheim Frontality Score-Item 8). Most studies reported prevalence using the NPI. For these the prevalence was 0.810 [95%CI: 0.702-0.885; Q-value: 85.316; p-value<.001; I2: 80.074; N=18]. All other scales were reported with minimal samples. Heterogeneity could not be explained by age, sex, or global cognition. There was no publication bias as quantitatively examined.

***Conclusions:*** To our knowledge, this is the first meta-analysis examining the prevalence of apathy in FTD and taking moderating factors into consideration. This study showed that apathy in FTD is highly prevalent in all variants. Future studies examining apathy in familial FTD are warranted. There is a substantial heterogeneity in the data that are not explained by demographic factors.

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**Utility of Actigraphy as an Agitation-Monitoring Tool in Advanced Dementia Patients: a Pilot Study**

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***Background:*** The numbers of older adults with dementia are increasing and neuropsychiatric symptoms (NPS), such as agitation or aggression, are common among older adults. Accurate measurement of NPS is necessary for diagnosis and management of these challenging behaviors. The use of actigraphy or electronic motion analysis to measure NPS in older adults with dementia may allow for a more accurate, detailed, and objective measures of NPS. Improvements in measurement of NPS may in turn facilitate better clinical outcomes through early detection of NPS and assessment of treatment response.

***Purpose:*** To evaluate the application of actigraphy to the measurement of NPS in older adults with dementia in geriatric psychiatry inpatient settings and assess the feasibility of using actigraphy to measure NPS in this population.

***Objectives:*** 1. To determine the actigraphic characteristics of individuals who have dementia with lower compared to higher severity of agitation using portable electronic actigraphs. 2. To evaluate whether specific patterns of motor activity recorded by actigraphy are correlated with agitation in older adults with dementia. 3. To determine key facilitators and barriers to the use of actigraphy for measuring agitation and other NPS.

***Methods:*** A total of 26 patients with advanced dementia were recruited from 2 inpatient geriatric psychiatry dementia units (London and Kingston, Ontario) and one LTC facility secure dementia unit (Kingston, Ontario). Actigraphic movement data (i.e., activity counts, physical activity intensity, body position, and minutes with or without movements) were collected using wGT3x+ Activities Monitors, ActiGraph LLC, Pensacola, Florida. Actigraphy sensors were attached to the non-dominant hand of participants with a wrist band and measured activity continuously from 1–7 days. Clinical and demographic characteristics, Global Deterioration Scale, MMSE, Clinical Global Impression Scale, CMAI, NPI, and Cornell Scale for Depression in Dementia were collected the same week of the Actigraphy monitoring. Cognitive impairment, agitation, and secondary measures of NPS were compared with data collected form wGT3x+ Activities Monitors. To test our hypothesis that higher levels of agitation will be correlated with higher daytime motor activity as measured by Actigraphy, participants were dichotomized into groups based on the severity of agitation using a cut off score of > 50 on the CMAI. *T*-tests or Wilcoxon rank-sum test for continuous variables and chi-squared tests for categorical variables were used to evaluate the differences in demographic characteristics, cognitive impairment, or neuropsychiatric symptoms between participants with high scores in agitation vs. those with low scores. All tests were two-sided, with a level of statistical significance set at $p \leq .05$.

***Results:*** The Actigraph sensor was well tolerated by participants. We were able to obtain a clear profile of motor activity for daytime, evening, and night time periods. Preliminary analysis showed that there is a strong correlation between rigorousness of the motor activity and scores on CMAI and scores on agitation related sub-items on the NPI.

***Conclusions:*** Actigraphy is a promising tool to monitor agitation in dementia and may offer an alternative to direct observation.

**How Well Does a Memory Clinic Support Patients in a Community?**

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***Background:*** Dementia is becoming increasingly more common as our population ages, with the prevalence of the disease anticipated to double within 20 years. There is increasing emphasis on families to continue caring for these individuals in their own homes for as long as possible, creating need for better outpatient care for these patients and their families by health-care teams. To this end, outpatient memory clinics have been developed in both specialty and primary care settings. The Outpatient Memory Clinic in Saint John, NB uses a unique model of care. It is a follow-up clinic that complements the care provided by the primary health-care provider for patients who have been previously diagnosed in the Geriatric Assessment Outpatient Clinic. A part-time nurse, with support from a geriatrician, follows patients living in the community (at home, in assisted living, or special care home) in an effort to provide the family and patient with ongoing support in managing the patient's cognitive, behavioural, functional, and social needs. We sought to describe patient demographics, physical and cognitive functioning at admission and discharge, emergency department utilization, acute care admissions to hospital, and reasons for discharge.

***Methods:*** The sample consisted of all consecutive discharges from the clinic over one year (January 1, 2013–December 31, 2013). The charts were reviewed retrospectively and ethical approval was obtained from the Research Ethics Board of Horizon Health Network.

***Results:*** There were 373 clinic visits provided to 308 patients in 2013. There were 122 discharges from the clinic. The average length of follow-up was 28.9 months with 3.8 visits to the clinic. The majority were female (69.6%) with a mean age of 85.0 years. Alzheimer's disease (68.6%) was the most common diagnosis. The largest group of patients was living at home with a spouse (32.4%). Less than half (43.1%) had paid homemaker services in the home for an average of 32.9 hours per week. The majority (85.3%) had been on at least one cholinesterase inhibitor. The initial average Mini-Mental State Exam (MMSE) score was 21.6 and declined to 17 on discharge. Function also declined, with 27.8% becoming more dependent in their activities of daily living (ADLs) and 40.5% becoming more dependent in their instrumental activities of daily living (IADLs). Just over half (54.9%) had 192 emergency department (ED) visits (0.62 visits/year per patient). There were 122 acute care hospitalizations of 65.7% of the sample (0.52 admissions/year per patient). The most common reasons for discharge from the memory clinic

were due to direct admissions to a nursing home (38.2%) or an admission to hospital resulting in an alternate level of care stay (20.6%); 19.6% of the sample died during follow-up.

***Conclusion:*** An outpatient based memory clinic focusing on follow-up for patients with dementia supports the patient and family to help them stay in the community for as long as their care needs and supports would allow. The majority transitioned to a nursing home directly from home. Many patients were supported at home until their death.

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**Clinical Utility of Amyloid Imaging in Differential Diagnosis of Atypical/Unclear Dementias and its Impact on Caregivers**

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***Background:*** Alzheimer's disease (AD) affects an increasing number of individuals in our societies. It is characterized by accumulation of fibrillary amyloid plaques in the brain. Recently, several studies have emphasized the role of positron emission tomography (PET) using amyloid biomarkers which allow *in vivo* visualization of plaques to distinguish AD pathology from other forms of protein accumulations leading to dementia. However, very few studies have investigated the role of amyloid imaging in the differential diagnosis of atypical/unclear cases that is complex dementia syndromes where even a comprehensive investigation yields no clear diagnosis. Moreover, no studies have investigated the impact of a correct diagnosis on caregivers and their perception of the process.

***Methods:*** Using a novel amyloid tracer (NAV4694), we scanned 20 patients with an atypical/unclear dementia syndrome as determined by an experienced behavioral neurologist from a tertiary care center. All patients had a full work-up (i.e., clinical, blood tests, neuropsychological evaluation, structural and functional imaging) yet no certain diagnosis. Amyloid-PETs were either positive or negative based on qualitative and quantitative reads by two independent readers. A questionnaire was given to the treating neurologist to determine whether amyloid imaging allowed a more accurate diagnosis and changed treatment plans. Caregivers were met one month after the revelation of the diagnosis and completed a questionnaire followed by a standardized interview designed to assess its impact.

***Results:*** A statistically significant increase in confidence levels amongst physicians who ordered amyloid imaging in such cases was found. Revelation of diagnosis to caregivers was associated with better acceptance of the disease, as well as a clearer view of future challenges.

***Conclusions:*** This study suggests that amyloid imaging is useful in the differential diagnosis of atypical/unclear dementias, and has a positive impact on caregivers. Amyloid-PET is indicated in the investigation of complex, atypical/unclear dementing disorders.

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**Dépistage Cognitif de Québec (DCQ): a Novel Cognitive Screening Test for Atypical Dementias**

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***Background:*** Recognition of the clinicoanatomical heterogeneity of dementing disorders has led to a major revision of their nosology in the last decade. With the potential emergence of disease-specific therapies, important efforts have been directed at correctly subtyping the patients among these newly described syndromes, mainly with neuroimaging tools. Conversely, cognitive screening tests have not kept the pace with this evolving nosology, being mainly targeted on diagnosing typical Alzheimer's disease (AD). As a result, while MMSE and MoCA are excellent tests for the screening and follow-up of typical AD, no validated screening tool truly helps clinicians in screening and subtyping atypical syndromes such as primary progressive aphasia or frontotemporal dementias. We present the Dépistage Cognitif de Québec (DCQ), a novel cognitive test aimed at improving the diagnosis of atypical/complex dementias in tertiary care memory clinics.

***Methods:*** Based on a systematic review of the literature on cognitive screening tools and focused groups with Canadian experts in dementia, we elaborated a tool based on five domains: 1) Memory, 2) Visuospatial, 3) Executive, 4) Language, and 5) Behaviour. We administered the DCQ and the MoCA to 180 normal aged individuals (age 50-90, mean 67 yr) to generate normative data and assess its psychometric properties.

***Results:*** The DCQ is a 30-min questionnaire that can easily be administered by a nurse. The questionnaire has adequate convergence validity with established measures of memory, visuospatial, executive and behavioural skills (Pearson coefficients between $r$=0.67 and $r$=0.95 $p$<.01). Cronbach's alpha is high at 0.82, suggesting good internal consistency. Test-retest reliability at 30 days in 30 participants is very high (0.89) and inter-rater reliability using three different clinicians is excellent (0.96). The DCQ currently exists only in French.

***Conclusions:*** The DCQ holds great promise for the screening and sub-typing of atypical dementia syndromes in tertiary care memory clinics.

**Assessment of Sex Analysis in Studies of Technology-Based Interventions To Alleviate Caregiver Burden Among Caregivers of Persons with Dementia**

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***Background:*** With an increase in the number of family caregivers for persons with dementia (PWD), caregiver burden is a major concern. Technology has been identified as an intervention to address this issue. However, to date, there is little consideration of sex differences among caregivers in the design and planning of these interventions.

***Objective:*** To systematically review the literature on technology-based interventions for caregivers of PWD and report the frequency and approaches of sex-based analysis.

***Methods:*** The literature was systematically searched for reviews of technology-based interventions for caregivers of PWD. All titles and abstracts of publications included in the retrieved reviews were screened using pre-determined inclusion and exclusion criteria. Full text articles that met the inclusion criteria were included for analysis.

***Results:*** Four reviews were identified and 19 articles representing 17 studies were retrieved. Among these studies, 16 included men and women caregivers; however, only four examined outcomes by sex. In the studies that examined outcomes by sex, three reported significant differences ($p<.05$) between men and women caregivers. While women caregivers were found to benefit more from technology in reducing caregiver burden, they had a lower rate of technology adoption when compared to men. In addition, women caregivers perceived companionship support as more important within technology-mediated support groups when compared to their male counterparts.

***Conclusions:*** There is currently a lack of (1) sex-based analyses, (2) inclusion of men, and (3) provision of sex-specific information in studies of technology-based interventions for caregivers of PWD.

**Unveil the Hidden Information Behind the Variables of Alzheimer's Disease (AD): a Systematic Comparison of Manifold Learning Algorithms in AD**

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***Background:*** Alzheimer's disease (AD) is a chronic neurodegenerative disease causing dementia, amnesia, and deficit in one or more cognitive functions, which affects an individual's ability to carry out activities of daily living (ADLs). Statistical estimation of whether an individual has AD involves the analysis of various physiological variables — e.g., images (magnetic resonance imaging (MRI), positron emission tomography (PET)), genomics, metabolism. Statistical AD diagnosis can be formulated as a multiple-class classification problem in machine learning. Much of the research in this area makes direct use of the raw values of variables in the statistical analyses, which are usually contaminated with noise and distortion. A manifold learning step can be introduced to remove noise and extract discriminant features (or variables) for the statistical analyses of AD.

***Objective:*** Despite the fact that various machine learning algorithms have been investigated for the automatic diagnosis of AD, limited attention has been put on the design of an optimal manifold (i.e., one which has the best discriminant ability). This study explores this property of various manifold learning algorithms in an automatic diagnosis framework.

***Methods:*** Evaluation tests are carried out using the neuroimaging and biological data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) in a three-class (normal, mild cognitive impairment, and AD) classification task using support vector machines (SVM). The imaging and biological data from 843 patients from ADNI are adopted for verification tests. The MRI images are registered to a unified brain model and transformed to stereotaxic space, followed by tissue classification and brain volume calculation using CIVET. Five different manifold learning algorithms were chosen for comparison: Locality Preserving Projection (LPP), Principal Component Analysis (PCA), Neighborhood Preserving Embedding (NPE), Stochastic Proximity Embedding (SPE) and Sammon mapping. Tenfold cross validation is utilized in our experiment setup.

***Results:*** In our randomized verification tests, manifold learning algorithms clearly improve the performance of the automatic diagnosis task. Without manifold learning, the SVM based automatic diagnosis system obtains an average diagnosis accuracy of 76.67% (optimal at 30 selected features), while all the manifold learning algorithms outperform the baseline by 2% to 17%. In particular, the Neighborhood Preserving Embedding (NPE) shows the best result, with 94.01% accuracy with only 18 features. Moreover, the optimal results are all from a subset of the entire variable set.

***Conclusions:*** Manifold learning is an effective way to remove noise and extract discriminant features for classification tasks (i.e., AD diagnosis). This can be a meaningful way to improve the performance of automatic diagnosis systems. Considerations should be given to which algorithm is more suitable for AD diagnosis. In addition, the experimental results show that there are strong correlations between different variables

utilized for AD diagnosis. Even a naïve dimension reduction approach can show some improvements.

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**Metabolic Syndrome and Inflammation on Cognitive Function in the International Mobility in Aging Study**

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***Objective:*** Many studies have suggested that Metabolic Syndrome (MetS) and inflammation affect cognitive function in old age. However, the association between MetS-inflammation and cognitive function does not seem to hold for all populations, especially in terms of sex/gender and levels of inflammation.

***Research Design & Methods:*** This is a cross-sectional analysis with 1700 participants of the longitudinal International Study of Mobility and Aging (IMIAS) from 5 different cities: Tirana (Albania), Manizales (Colombia), Natal (Brazil) Kingston, and Saint Hyacinthe (Canada) who were aged 65–74 years at baseline. Metabolic syndrome (according to the criteria of the Adult Panel Treatment III) high sensitive C-reactive protein (HS-CRP) and cognitive function were assessed. Cognitive function was assessed with the Leganés Cognitive Test (LCT), a screening test for dementia validated for population with low education. Sex–specific linear regressions were performed using log transformed cognitive function as outcome and HS-CRP and MetS as main exposures and potential interacting factors.

***Results:*** MetS prevalence ranges from a lowest 22.1% in Saint Hyacinthe (men) to a highest 63.1 % in Tirana (women) and were significantly different across sites for women ($p$<.001) but not for men ($p$<.1). Sex differences in prevalence of MetS were significant in Tirana and Natal. Sex differences in cognitive impairment indicative of dementia were only found in Tirana (LCT < 23: 4.7% for men vs. 11.7% for women). Means of HS-CRP were higher in women than in men at all sites. MetS was not related to cognitive function in men (beta=0.052 CI 95%: 0.04–0.145) adjusting by age, education and research city ($p$<.25). These results were homogeneous across sites and presence of inflammation did not change this finding. Presence of MetS, however, was associated with worse cognitive function in women (beta =0.11; CI 95%: 0.03–0.195) ($p$<.001 for sex-MetS interaction term) with the highest number of MeTS criteria associated with worse cognitive function. These results were homogeneous across sites and did not vary by inflammation level. Interaction terms between sex and components of MetS on cognitive function were significant for: systolic blood pressure ($p$=.001) high blood pressure, ($p$=.001), triglycerides ($p$=.02), glycosylated Hb levels (diabetes) ($p$=.037) meaning that individual components of MetS did not have the same effect in women and men on cognitive function.

***Conclusions:*** Our findings support an association between MetS and poor cognitive function in women but not in men, emphasizing the importance of aggressively targeting metabolic risk factors in women.

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**Vitamin D Receptor Gene Polymorphism Fok1 and Association with Spatial Working Memory**

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***Background:*** Vitamin D insufficiency has been associated with Alzheimer's disease (AD) and impaired cognition. Recent studies have also shown significant associations between vitamin D receptor (VDR) single nucleotide polymorphisms (SNPs), AD and cognitive decline. While Fok1 SNPs have not been directly implicated in AD, the TaubF haplotype (combined polymorphisms in Taq1, Apa1, Tru91, Bsm1, Fok1) has been. A recent study also revealed a significant association between Fok1 and global cognition. We hypothesized that working memory would differ among Fok1 SNPs and sought to examine the relationship between Fok1 genotype, vitamin D level, and cognitive functioning.

***Methods:*** Participants (n=78) were healthy adults, 54.7±13 yrs of age, with 14.7±3 yrs of education, 67.1% female and 62% with 25(OH)D levels <75 nmol/L living at a northern latitude (54N) and free of significant cognitive impairment, brain injury, brain tumour, and stroke. All participants were assessed during the winter months. Serum vitamin D (25OHD) levels were analyzed via liquid chromatography/tandem mass spectrometry. Cognitive testing consisted of the Symbol Digits Modalities Test, verbal (phonemic) fluency, digit span, and CANTAB battery, including a spatial working memory (SWM) task. Genotyping for Fok1 (rs2228570) was done by TaqMan assay (ABI3700).

***Results:*** Prevalence of Fok1 SNPs (AA, AG, GG) were in approximate Hardy Weinberg Equilibrium. Vitamin D levels, age, and sex did not differ significantly, but years of education was higher in the GG (16.8±4) versus AG (14.2±3) groups ($p$=.022). There was a significant difference among SNPs on both strategy, AA=28.3±8, AG=34.5±6, GG=32.5±7; F(2,75)=3.18, $p$=.047, and error measures, AA=15.4±16, 34.3±17, 28.2±19; F(2,75)=3.54, $p$=.034 of the SWM task, a test of nonverbal executive functioning. In particular, the AA group performed best and significantly better than the AG group (Bonferroni $p$'s <.05). Results did not change with

correction for years of education. There were no significant differences among SNPs on any of the other cognitive tests.

***Conclusions:*** Vitamin D receptor gene Fok1 polymorphism may contribute to differences in cognitive function, independently of vitamin D level and years of education. In particular, the SWM task differentiated between genotypes on two measures. This same task has previously been shown to differentiate between individuals with insufficient and sufficient levels of vitamin D. Our findings add to existing literature that Fok1 polymorphism is associated with nonverbal working memory/executive functioning performance in addition to global cognition. Given our small sample size, these preliminary results necessitate confirmation in a larger study.

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**Are Vitamin D Receptor Polymorphisms Associated with Vitamin D Levels and Alzheimer Disease?**

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***Background:*** Recent studies have suggested an association between low Vitamin D level and cognitive impairment and also between vitamin D receptor single nucleotide polymorphisms and cognitive decline. Some of the observed differences may be attributable to the affinity of the vitamin D receptor for the Vitamin D ligand. We hypothesized that polymorphisms in the Vitamin D receptor gene may influence our body response to Vitamin D, and may incur risk of Alzheimer disease. In the current study, we compared genotype frequencies in a cohort of patients with Alzheimer disease and controls in a Canadian population.

***Methods:*** We examined 8 single nucleotide polymorphisms in the Vitamin D receptor, including Fok1, Taq1, Apa1, Bsm1, Cdx, Tru91, rs7968585, and rs7976091. Prevalence of the single nucleotide polymorphisms was compared between 248 patients clinically diagnosed with probable Alzheimer disease (AD) enrolled through a dementia specialty clinic (AD group), and 78 cognitively intact subjects (NC group) who were enrolled in a study to screen for Vitamin D deficiency. All subjects were Canadians of European descent. Serum vitamin D [25(OH)D] levels were analyzed via liquid chromatography/tandem mass spectrometry. Genotyping was done by TaqMan assay (ABI3700). Associations were tested by chi-square, followed by logistic regression to adjust for the effect of APOE, sex, age, and multiple comparisons. We also examined the correlation between these polymorphisms and total vitamin D levels.

***Results:*** Vitamin D levels did not differ significantly between the AD (79.0±27 nmol/L) and NC groups (83±39 nmol/L); however, the AD patients were significantly older (mean=70.5 yrs) compared to the NC subjects (mean=57.0 yrs, $p<.001$). In the initial screening phase, we found association between Taq1 ($p=.04$) and Apa1 ($p=.015$) with AD, but not with the other polymorphisms. After adjusting for the effect of age, sex, and APOE genotype (e4 carriers vs. non-carriers), the effect of Taq1 disappeared, but the effect of Apa1 remained, suggesting that the CC allele is associated with an increased risk of AD. Interestingly, there was no significant association between this polymorphism and serum vitamin D levels. Bsm1 and Taq1 were the only single nucleotide polymorphisms significantly associated with vitamin D levels ($r=.15$, $p=.008$, and $r=.14$, $p=.011$, respectively).

***Conclusions:*** Previous studies involving Dutch, Turkish, and British populations have implicated Taq1 and Apa1 polymorphisms in cognitive decline and Alzheimer disease. Our study, which involved a Canadian population and controlled for APOE e4 status, extends these earlier findings and suggests that the vitamin D receptor polymorphism Apa1 is associated with an increased risk of AD. Interestingly, while Taq1 was significantly associated with vitamin D levels, Apa1 was not. Further analysis in a larger scale study is warranted to elucidate the role of Vitamin D as a risk of AD.

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**Examining the Role of Membrane-Lipid Metabolism in Neurodegeneration and Aging**

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As we age, the brain becomes more vulnerable to disease and injury. Patients with various types of dementia, such as Alzheimer's disease (AD) and vascular dementia, are susceptible to stroke injuries which can interact and cause synergistic damaging effects within the brain. Gangliosides, a type of membrane lipid, undergo metabolic changes during disease and injury that may be responsible, in part, for the propagation of neurodegeneration observed in these patients. MALDI mass spectrometry imaging (MSI) is able to overcome many of the challenges previously associated with the study of membrane-bound lipids and can provide new insight into their biological relevance in disease and injury. Deregulation of the homeostatic expression of gangliosides plays a mechanistic role in the process of neurodegeneration by increasing age-related vulnerability to injury and perpetuating neurodegeneration and can be visualized using MALDI IMS. Matrix-Assisted Laser Desorption/Ionization (MALDI) Imaging Mass Spectrometry (IMS) was used to acquire dynamic, high-resolution images, as well as mass spectrometry data, of ganglioside expression in the brain of both normal aged animals and animals undergoing a neurodegenerative injury of varying severity. A comorbid rat model of amyloid-beta toxicity (bilateral ICV injections) and endothelin-1 induced stroke (unilateral striatal injec-

tion) was used to examine ganglioside expression compared to either endothelin-1 alone, amyloid-beta toxicity alone, or controls at 3 and 21 days after injury to determine how ganglioside metabolism changes after a neurodegenerative insult of increasing severity. Embryonically-derived rat primary cortical neurons were used to further investigate the toxic properties of simple gangliosides GM2 and GM3. The homeostatic expression of certain ganglioside species was altered in aged rats compared to young rats such that the ratio of 20 carbon species to 18 carbon species was found to be elevated in a number of key anatomical regions including the striatum, ventricles, and hippocampus. An increase in potentially toxic simple species GM2 and GM3 was also observed in these areas, indicating a shift in the homeostatic expression profiles of ganglioside as a result of aging. In the neurodegeneration model, A-series ganglioside expression shifted after neurodegenerative injury such that an accumulation GM2 and GM3 was significantly elevated only in the comorbid amyloid-beta/endothelin-1 group (most severe injury) compared to the non-injured hemisphere at 3 days after injury and remained elevated 21 days after injury. Ganglioside GM3 induced apoptotic cell death when exogenously administered to rat embryonically-derived primary cortical neurons, while GM2 demonstrated minimal toxic effects. Gangliosides have been shown to play an important role in the pathogenesis of age-related diseases and injuries and are promising avenues of therapeutic intervention for patients suffering from dementia and dementia-related pathologies.

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**Delusions in Alzheimer's Disease Are Associated with Prefrontal and Cerebellar Atrophy**

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***Background/Objective:*** In additional to cognitive decline, many Alzheimer's disease (AD) patients experience delusions in the course of their disease. Delusions are estimated to affect a third of AD patients, and have been shown to be associated with increased cognitive and functional decline and increased caregiver burden. Functional and structural imaging studies largely suggest right frontal atrophy, but the neuroimaging correlates behind delusions remain inconclusive, as regions from virtually all the lobes have been implicated. Our previous cross-sectional study using data from 58 patients in the Alzheimer's Disease Neuroimaging Initiative (ADNI) database found right fronto-temporal grey matter atrophy in the delusional subset (n=29) compared to non-delusional AD controls (n=29). The current study aimed to continue this investigation by identifying regions of grey matter atrophy in association with delusions in a larger sample of AD patients.

***Methods/overview:*** Structural MRI scans of 59 delusional AD patients (AD+D) were compared to 78 non-delusional patients (AD-D) using voxel-based morphometry (VBM) to identify clusters of grey matter atrophy. All scans and clinical data were obtained from the National Alzheimer's Coordinating Center (NACC) database collected from September 2005 to May 2012. AD diagnosis was based on the NINCDS-ADRDA diagnostic criteria for probable AD, and delusions were identified by the NPI-Q completed by an informal informant. An independent two-sample *t*-test with unequal variances was used to test for regions of grey matter atrophy in the AD+D group compared to AD-D, adjusted for total intracranial volume (sum of grey matter, white matter, and cerebrospinal fluid). A Gaussian kernel of 5 mm FWHM, with the contrast 1(D-)>2 (D+) were used. A one-tailed significance was set at $p$ $\alpha$=0.001 with a voxel threshold of 50.

***Results:*** The AD+D and AD-D groups did not differ significantly on age, sex, handedness, age of disease onset, education, or MMSE scores. Mean age was 77.1±10.1 and mean MMSE was 20.0±9.0. 16 clusters of grey matter atrophy were identified in the AD+D compared to AD-D. These clusters included the bilateral superior frontal gyrus, left inferior frontal, bilateral middle frontal gyrus, bilateral cerebellar pyramis, and the left superior parietal lobule.

***Conclusions:*** Our findings support the growing body of literature in reporting frontal atrophy, although not lateralized, and suggest that atrophy of prefrontal-cerebellar networks may contribute to the development of delusions in patients with AD. We confirm our previous findings of frontal atrophy, but without temporal or asymmetric atrophy. The difference could be due to a larger sample and the inclusion of AD-only patients versus AD and mild cognitive impairment patients. The prefrontal cortex is responsible for integrating multimodal inputs with internal states to consequently produce a contextually appropriate output. The cerebellum makes vast connections with the prefrontal cortex and plays a role in higher order cognitive functions. Moreover, damage to the cerebellum has been shown to trigger psychosis in schizophrenic patients. Lastly, the superior parietal lobules have a role in deductive reasoning skills. Therefore, breakdown in these areas involved in sensory interpretation and reasoning may give rise to illogical conclusions based on the environment and consequently to delusions.

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**Atrophy in the Default Mode Network Following the Development of Delusions in Patients with Alzheimer's Disease**

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***Background/objectives:*** Delusions, estimated to affect 1/3 of patients with Alzheimer's disease (AD), are associated with increased cognitive and functional impairment, caregiver burden, a faster rate of cognitive decline, and a higher rate of institutional care. However, the neuroanatomical changes associated with delusions are poorly characterized, which limits our ability to treat this symptom. Neuroimaging studies have suggested that delusions are associated with frontal, medial temporal, and posterior atrophy, but the evidence remains mixed. The Default Mode Network (DMN), a resting state network, has shown abnormal connectivity in normal aging, as well as in mental disorders including AD. Disrupted connectivity within the DMN may not be simply a function of disease progression, but may also play a role in the expression of delusions. The current study aimed to identify regions of gray matter (GM) atrophy following the development of delusions in patients with AD. We hypothesized that regions of the DMN would show atrophy.

***Methods/Overview:*** We identified 19 patients from National Alzheimer's Coordinating Centre (NACC) database who fulfilled our criteria and who had pre- (D-) and post-delusional (D+) T1 MRIs. AD diagnosis was based on the NINCDS-ADRDA diagnostic criteria. Patients' last D- scans were compared to their first D+ MRIs using VBM analysis. The scans were on average 3.1 years apart. The NPI-Q delusional sub-score was used to identify the presence of delusions. A dependent two-sample *t*-test and an 8 mm FWHM Gaussian kernel was used. Multiple comparisons were corrected using False Discovery Rate with $\alpha$=0.05 with no masking, and significant cluster threshold was set at 50 voxels.

***Results:*** The mean (± standard deviation) age of the sample at baseline D- scan was 78.3±6.4, and 81.4±6.0 at the D+ scan with an average MMSE decline of 4.9 points. We identified 16 significant clusters of decreased GM in the D+ scan compared to the D- scan: bilateral insula, left amygdala, right cingulate gyrus, right superior temporal gyrus, left middle temporal gyrus, right inferior frontal gyrus, bilateral precentral gyrus, right medial frontal gyrus, left cuneus, left cerebellar culmen, and right anterior cingulate.

***Conclusions:*** Core regions of the DMN—including the ventral and dorsal mPFC, medial temporal cortex, and the precuneus—showed atrophy following the onset of delusions in AD patients. Several of the previously reported areas of atrophy associated with delusions may in fact reflect DMN atrophy. The dorsal and ventral mPFC are involved in integrating social and sensory cues, mentalizing about self and others, and assigning meanings to situations. Meanwhile, the cerebellum has extensive connections to the cerebrum and may play a much greater role in cognition than previously thought. Therefore, it is conceivable that breakdown in these areas could contribute to the development of delusions. Recently, the DMN has demonstrated significantly increased relevance to mental disorders, with abnormalities being reported in patients with AD, autism, schizophrenia, depression, and anxiety. A better understanding of the neuroanatomical correlates underlying delusions could pave the way to differential diagnosis and interventions targeting these brain regions. A limitation of this study is that we lacked a non-psychotic, severity-matched AD control for comparison.

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**What Happens to Alternate Level of Care Patients in Hospital? Is Dementia a Factor?**

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***Background:*** The Canadian population is aging. It is expected that 20% of the population will be 65 years of age and older by 2026. With aging comes an increased risk of chronic disease, functional decline, and dementia. This often translates into a need for assistance in the home or a move to a more supportive care environment, such as a nursing home (NH). This transition to a higher level of care is often precipitated by an acute medical event requiring hospitalization. Difficulties transitioning to community-based supportive care environments can mean that patients remain in hospital waiting. Patients waiting in hospital are referred to as alternate level of care (ALC) patients. The number of ALC patients in hospitals can contribute to overcrowding in the emergency department and increased wait times for surgery. Dementia is common in these patients. A better understanding of this population can assist in developing strategies that may be beneficial.

***Methods:*** A chart review of a stratified random sample of all patients identified in Horizon Health Network as ALC on February 9, 2012 was undertaken. Six months later, the patients' disposition was also collected. This study was approved by the Research Ethics Boards of Horizon Health Network and University of New Brunswick Saint John.

***Results:*** One-quarter (25.8%) of hospital beds were occupied by ALC patients. The median number of days in hospital, up until the date of data collection, was 141.7 days. The majority were female (59.3%), and only 36.2% were married. On average, they had 3.9 chronic illnesses and 49.3% had a diagnosis of dementia. The most common reason for admission to hospital was dementia-related (17.3%). Half (50.2%) were living with others prior to admission. Of those living at home, 74.1% had no paid homemaker supports. The majority (57.5%) were waiting for admission to a NH. Six months later, 36.7% of the total sample remained in hospital

with a median number of days in hospital of 437. Only 29.4% had been discharged to a NH with a median length of stay (LOS) of 213 days. Those who were discharged to NH were significantly older, less dependent in toileting, transferring, and ambulating, and needed less assistance with their bladder and bowels than those who remained in hospital. The frailty index did not differ between those who were discharged to NH versus those who remained in hospital. After 6 months, 14.5% of the sample had died.

***Conclusion:*** ALC patients occupy a significant amount of acute care hospital beds, the majority of whom are waiting for NH beds. Dementia is common and was one of the leading reasons for admission to hospital. These patients experience functional decline while waiting. Even after six months of follow-up, the majority were still in hospital. Those who were successfully discharged from hospital to NH were less impaired functionally. The frailty index was unable to predict who was successfully discharged and who remained in hospital. Many ALC patients die in hospital waiting for alternative living arrangements in the community.

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**Reducing the Utilization of Neuroleptics Without Indication (RUN)**

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***Background:*** Responsive behaviours are common in older adults affected by dementia and are a leading cause of caregiver stress. Management of such behaviours may result in the prescription of a neuroleptic. However, neuroleptic use in elderly patients affected by dementia is associated with a 1.6–1.7 times increased risk of all-cause mortality. There is also an increased risk of cerebrovascular accidents. In spite of an unclear benefit-to-risk ratio, older adults with dementia continue to be placed on neuroleptics without having an indication to warrant their use.

***Objective:*** This study is designed to evaluate the impact of an integrated knowledge translation (KT) approach on the use of neuroleptic medication in a complex continuing care (CCC) hospital where 10.06% of admitted inpatients in 2014 were taking a neuroleptic without an indicated diagnosis of psychosis.

***Methods:*** An Interrupted-Time-Series (ITS) design was used to evaluate the impact of a KT intervention on the prescription of neuroleptics without indication in patients 65 years of age or older who were admitted to the 102 CCC beds at Baycrest Centre for Geriatric Care in Toronto, Ontario. After a 3-month baseline assessment, the KT intervention was rolled out over 8 weeks. Outcome data were collected for a total of 5 months post-intervention. The primary outcome measure is the reduction in the use of neuroleptics without indication across the CCC units. We anticipate a 25% relative reduction at the end of the 5-month, post-intervention period.

***Results:*** The charts of 158 patients were reviewed from August 1, 2014 – May 31, 2015. The mean (SD) age of the patients was 77 (11) years, 57.3% were males and 96% were moderately-severely frail with a mean (SD) Case Mix Index (CMI) of 1.13 (0.20). Baseline data showed that of 111 patients admitted to the CCC units in the pre-intervention period, 24 (21.6%) were prescribed a neuroleptic. Of these, 19 (17.1%) patients were prescribed a neuroleptic without indication. Units receiving the intervention were able to reduce the use of neuroleptics without indication from 17.1% in the pre-intervention phase to 8.1% in the post-intervention phase. This corresponds to a 47.5% relative reduction in the use of neuroleptics without indication.

***Conclusion:*** KT strategies can be used effectively in a CCC setting to ensure neuroleptics are prescribed with indication in older adults. We hope that our strategy can be replicated across the health-care system so that best practice guidelines are followed and the highest standard of care is offered to the aging population. Future studies are needed to replicate our findings in other settings.

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**Treating Dementia with Cough Medicine: a Double-Blind Randomized Controlled Trial Repurposing Ambroxol as a Disease Modifying Treatment for Parkinson's Disease Dementia**

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***Background:*** Currently there are no disease-modifying treatments for cognitive impairment in Parkinson's disease dementia (PDD). Furthermore existing treatments for PD or PDD do not address the accumulation of pathological aggregates of α-synuclein, which presumably underlie neurodegeneration. To date, one of the strongest genetic risks for developing PD and PDD is to carry a single mutation in the gene for enzyme β-Glucocerebrosidase (GCase), the gene which causes the lysosomal storage disease Gaucher's disease. In animal and cell culture models, raising the levels of GCase reduces the level of α-synuclein. The goal of this study is to assess the safety and tolerability of Ambroxol as a disease modifying drug in PDD. Ambroxol is an expectorant with an excellent safety record sold over the counter throughout the world, but which is not available in North America. Ambroxol was discovered in a high throughput screen as a pharmacological chaperone GCase, which stabilizes and increased the levels of GCase. Ambroxol has no known drug interactions, no specific symptoms in overdose, and is safe

to administer intravenously to pregnant women to aid fetal lung maturation.

***Methods/Overview:*** In a double blind, placebo-controlled design, we will randomize 75 patients 1:1:1 to receive placebo or Ambroxol at 525 mg or 1050 mg for 1 year. The main inclusion criteria are 1) clearly established Parkinson's disease which has clearly developed more than 1 year before the onset of dementia; 2) dementia with MMSE $16 \leq 26$; 3) on stable doses of medications for mood, PD, and cognition. The main exclusion criteria are 1) clinical, imaging or laboratory evidence of clinically significant stroke or other neurological condition; 2) significant medical illness (e.g., cardiac, liver or renal disease) or cancer with metastatic potential in the last 5 years. The primary outcome measures will be the cognitive component of the Alzheimer's Disease Assessment Scale (ADAS-Cog), and the Alzheimer's Disease Cooperative Study Clinician's Global Impression of Change (ADCS-CGIC). Secondary outcome measures of cognition will include the Parkinson's Disease-Cognitive Rating Scale (PD-CRS), Neuropsychological Inventory (NPI), Clinical Dementia Rating Scale (CDR), and others. Parkinsonian symptoms will be followed using the UPDRS, timed up and go, and the Purdue Pegboard. We will examine biomarkers for disease progression in CSF including Aβ42, phospho-tau and α-synuclein, and neuroimaging measures of neurodegeneration including brain ventricular volume and hippocampal atrophy using volumetric MRI, and N-acetylaspartate from MR-spectroscopy. We will establish the pharmacokinetics and pharmacodynamics of Ambroxol by measuring the levels of Ambroxol and its effect on GCase levels in blood and cerebrospinal fluid.

***Conclusions:*** We hope that, by repurposing Ambroxol, we will greatly accelerate development of a therapy for PDD. If effective, this medication will also be useful for other diseases with α-synuclein aggregation, including Parkinson's disease and Lewy Body Dementia.

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**Development of a Novel PET Agent Targeting Cathepsin-D in Alzheimer's Disease Transgenic Mice**

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***Background:*** Currently there is no widely accepted test to diagnose Alzheimer's disease (AD). Without a laboratory standard for diagnosis, the development of clinical trials in early/ presymptomatic AD is difficult. This problem has taken on urgency, as several promising clinical trials may have failed because treatment was initiated too late in the disease, when irreversible synaptic and neuronal loss had already occurred. Although a number of imaging techniques are being developed to aid in the diagnosis of AD, including PET ligands to quantitate amyloid, tau, and volumetric assessment of cerebral atrophy by MRI, these all suffer from high patient-to-patient variability. The lysosomal enzyme Cathepsin D (CatD) is another possible biomarker for AD. CatD is an aspartyl lysosomal protease that has been shown to be over-expressed in the AD brain and cerebral spinal fluid (CSF), and recently found in significantly higher levels in neural-derived plasma exosomes reflecting AD pathology. We have previously developed a contrast agent (CA) to detect CatD activity *in vivo*. Our agent consists of a DOTA chelating moiety (to bind gadolinium or radioactive Gallium) conjugated to a peptide backbone containing a CatD cleavage sequence and HIV-1 Tat cell penetrating peptide (CPP). The CPP allows the agent to cross the blood–brain barrier both into and out of the brain. In the presence of elevated CatD levels in the brain, cleavage of the agent removes the Tat peptide, temporarily trapping the agent in the brain. We have previously shown that an optical near infra-red (NIR) fluorescence imaging version of this CatD targeting CA can identify Alzheimer's diseased mice. The purpose of this study was to characterize and test our novel CatD targeting CA *in vivo* using positron emission tomography (PET).

***Methods:*** The contrast agent was radiolabeled with Gallium-68 for PET detection. Alzheimer's disease 5XFAD transgenic mice (N=5-8) and non-transgenic littermates received the agent by intravenous tail administration at 2, 6, and 9 months of age. Mice were then scanned for up to 3 hours using an Inveon preclinical microPET system (Siemens Medical Solutions, Knoxville, TN, USA).

***Results:*** Using microPET, the transgenic and wild type mice showed no significant differences in CA uptake in vital organs. However, the 5XFAD mice demonstrated significantly higher relative uptake rate of the CatD targeting CA in the forebrain relative to hindbrain at 2, 6, and 9 months of age compared to controls.

***Conclusions:*** The prolonged retention of the CatD targeted CA in 5XFAD mice measured by PET is consistent with previous studies, and suggests this agent may be useful for AD detection.

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**Screening of Cognitive Disorders in Aging via Smart Homes: a Literature Review**

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***Background/Objectives:*** The aging of the world population is a reality that is likely to be accompanied by a substantial increase in elderly with dementia. New tools will have to be developed to screen quickly cognitive disorders and allow early intervention. In this context, smart home has many attractive advantages, including taking continuous measurements in the living environment of the elderly. The aim of this study is to investigate the effectiveness of smart homes for early screening of cognitive disorders in the elderly.

***Methods/Overview:*** The databases Medline, EMBASE, CINAHL, PsycINFO, Proquest, and Web of Science were screened, as well as the grey literature.

***Results:*** Six studies of two different experimental designs were included in the present review: time series (n=5) and cross-sectional (n=1). These have used, among other things, motion sensors for taking measures of various indicators of cognitive disorders, such as walking speed and performance in the activities of daily living. Various indicators of cognitive disorders allowed to highlight statistically significant differences between elderly with and without mild cognitive impairment.

***Conclusions:*** Despite technologic limitations, the smart home has an interesting potential for early screening of cognitive disorders in the elderly. Other studies will be needed to explore the clinical relevance of smart environments.

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**Adopting a Palliative Approach to Care**

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The growing demographic of persons with dementia is forecasted to reach epidemic proportions globally and is expected to affect over eighty million people by 2040 (Passmore et al., 2012). Patients with moderate to severe dementia often experience not only the burdens of behavioral and psychological symptoms of dementia (BPSD), unrecognized and undertreated pain, but, also futile and burdensome interventions as they near the end of life. A palliative approach to care that emphasizes preserving personhood and dignity, alleviating suffering, and enhancing the quality of life and the dying experience is a recent shift in focus that has not been well studied in this patient population (Parsons et al., 2010). A diverse inter-professional team at the University Health Network in Toronto working with patients with moderate to severe dementia took up the challenge to make this shift in care to meet the needs of patients and their families. A complex patient experience was the sentinel event that launched the team's initiative to explore a palliative approach to care for patients with moderate to severe dementia. An inter-professional palliative care working group was established with the goals of: facilitating end of life decision making, enhancing end-of-life care to patients and their families, and enhancing the team's confidence in providing evidence-based care at the end of life. A partnership was developed with an internal palliative care consult team. A variety of strategies were put in place over two years to build capacity in meeting the palliative care needs of our patients. We will provide a description of the strategies implemented, feedback received from the inter-professional team, and challenges identified in using a palliative approach to care with this patient population.

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**An Indo-Canadian Cross-Cultural Qualitative Study on Caregivers of Persons with Dementia**

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Epidemiological research has indicated that there are 7.7 million new cases of dementia each year. The majority of this increase is in low- and middle-income countries (LMIC) (Ferri, 2006). Caregivers from high and LMIC experience consequences to caring for persons with dementia (PwD). In high-income countries, multiple interventions have been implemented to reduce caregiver distress. (Pinquart, 2006; Smits, 2007; Brodaty, 2003; Lee, 2004; Spijker, 2008; Olazaran, 2010). PwD in LMIC, in contrast, have limited access to specialist services for diagnosis and treatment of dementia (WHO, 2012). Thus, care for PwD is primarily the responsibility of the family (Prince, 2012; Honyahiki, 2011; Dias, 2004). Given limited access to services in LMIC, we seek to understand if there is a relationship between access to services and caregiver knowledge in high-income countries (Vancouver, Canada) and LMIC (Mysore, India). From our knowledge, this is the first qualitative study to simultaneously examine the caregiver educational needs in different cultural and economic settings.

***Methods:*** We recruited 10 caregivers of PwD in Vancouver who were connected with the hospital or outpatient services. In Mysore, 15 caregivers of PwD were identified through MyNAH: Mysore Studies on Natal Effect of Ageing and Health (CSI Holdsworth Hospital). Semi-structured interviews were

conducted with each caregiver. These interviews consisted of the following general questions: current level of care, medical supports, caregiving supports, and educational needs. Interviews were audio-recorded and transcribed.

***Analysis:*** The constant comparison technique was used to identify data relevant to the research questions. The task of content coding included ordering the data in relation to the objectives of the study, categorizing answers, and examining the data for associations.

***Preliminary Results:*** Data analysis is currently under progress, but preliminary findings reveal the following themes: 1. Greater expression of caregiver distress in Vancouver as compared with Mysore. 2. Approval of educational needs in Mysore, but not deemed necessary as compared with high-income. 3. Specialist resources are deemed important in both geographical areas, but not seen as crucial in Mysore.

***Preliminary Discussion:*** In Mysore, both the levels of expressed caregiver distress and the perceived role of education in caregiving were diminished despite minimal medical services when compared to Vancouver. In Vancouver, education and medical services were utilized but, interestingly, the expression of distress was higher. The minimal expression of stress in LMIC by caregivers is likely due to social and cultural etiologies. Caregivers may not want to be viewed as disrespectful or unable to carry out roles assigned by extended families. The societal view on elders may find it unacceptable to express caregiver stress.

***Preliminary Conclusion:*** Models created in high-income countries may be inadequate to support caregivers in LMIC as they may not reflect caregiver's experience. There is a need to develop educational resources for caregivers of PwD that are culturally appropriate in LMIC. In high-income countries as well, being aware of economic/cultural context may also be important when working with caregivers from diverse cultural groups.

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**The Adapted Cohen-Mansfield Agitation Inventory (A-CMAI)**

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The gold standard measure of responsive behaviours or behavioural and psychological symptoms of dementia (BPSD) is arguably the Cohen-Mansfield Agitation Inventory (CMAI), based on its wide use both clinically and in research. This is a paper-based assessment that measures the frequency of 29 specific, observable behaviours (e.g., pacing, repetitious mannerisms, spitting) on a 7-point scale of frequency once every two weeks. This measure works well in many settings; however, when applied to an inpatient hospital unit specialized in treating responsive behaviours in persons with dementia, measurement of behaviour was limited by the bi-weekly assessment frequency. Accordingly, this poster focuses on an adaptation of the CMAI that was created to better suit the needs of clients with high frequency behaviours in the context of front-line staff that work 8-hour shifts. This adapted measure, named the Adapted CMAI (A-CMAI), measures the frequency or duration of the same behaviours as the original CMAI, plus additional behaviours that are common reasons for admission when treating clients with responsive behaviours (i.e., refusal or avoidance of care, hallucinations or delusions, drowsiness, sleep/naps, sleep disruption). The A-CMAI is completed every 8 hours by registered nursing staff who were trained on the measure, and scores are entered in Baycrest's integrated electronic health records system. Completion takes approximately 5 minutes. Data for each client are exported from client health records weekly by the unit psychologist and translated into graphical figures depicting behaviour frequency or duration over time. The graphs are reviewed by the interdisciplinary care team weekly, in a team conference, to provide baseline measurement of client behaviour, monitor client progress over time, inform treatment decisions, and evaluate treatment outcome. In trials of the measure over the past 1.5 years, the A-CMAI has been found to provide several benefits in the context of an inpatient unit that aims to treat intensive responsive behaviours. Similar to the CMAI, it: i) has encouraged clear reporting, as behaviour is specifically described (e.g., kicking) rather than vaguely termed (e.g., aggression); and ii) it has improved communication between team members, as staff learn the same language to discuss behaviours. In addition, the A-CMAI: i) has reduced the need to rely on retrospective recall through more frequent measurement of behaviours; ii) has allowed for measurement discrimination at a higher frequency of behaviour; iii) has three assessment periods each 24 hours, which have been used to identify clients circadian behavioural patterns; and using the data to graphically monitor client progress, iv) has helped to focus team meetings and improved communication. Moving forward, we plan to continue with use of the A-CMAI on our inpatient unit specialized in treating responsive behaviours, empirically validate the A-CMAI, disseminate the measure to similar behavioural units, extend training to health-care aides (i.e., personal support workers), and use this measure to assess treatment outcomes in research.

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**Neuropsychological Issues in the Diagnosis of Frontal Variant Frontotemporal Dementia (FV-FTD): Executive Function Error Interpretation May Be Useful for the Elusive Assessment of the Ventromedial/Orbitofrontal Prefrontal Circuits**

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***Background/Objectives:*** In a classic 1968 work, Mesulam described the difficulties of patients with clear day-to-day problems, but no cognitive impairment, even on tests of executive function. More recently, this phenomenon has been understood as the failure of most tests of executive function to measure the functioning of most of the prefrontal circuits. Most traditional executive function measures capture the integrity of the dorsolateral prefrontal circuit and, due in part to the structure required for standardized neuropsychological testing (see works by Burgess), do not reflect the functioning of the ventromedial or orbitofrontal prefrontal circuits. Tests of gambling (Iowa Gambling Test) or social cognition (theory of mind tests) have been demonstrated to be associated with ventromedial/orbitofrontal circuits, at least for those with clear lesions/developmental delays. Interpretation of errors on more traditional tests of executive function (such as trail making test, Stroop interference test, and card sorting tests from the Delis Kaplan Executive Functioning System (DKEFS)) and errors on memory tests in the context of intact encoding and consolidation (California Verbal Learning Test) have been suggested to also reflect ventromedial/orbitofrontal function (see the Modern Day Phineas Gage; Cato et al., 2004). In the diagnosis of fv-FTD, converging evidence from a collateral informant (we use the Frontal Behavioral Inventory (FBI) to guide the interview) or imaging (SPECT or PET), together with neuropsychological support, is helpful. Although not well studied in caregivers of persons with dementia, informant reports are known to be impacted by the psychological state of the informant, which makes converging support from neuropsychological testing or functional imaging for mild to moderate level behavioral changes reported on the FBI all the more important.

***Methods/Overview:*** Clinical impression from a series of case studies of persons diagnosed with fv-FTD, who demonstrated additional behavioral and neuropsychological evidence when followed prospectively.

***Results:*** Initial assessment data for a subset of these fv-FTD patients (some cases with and some without imaging support) suggested neuropsychological function was well within normal limits, but analysis of errors on DKEFS (trails, interference, and/or card sorting) with and CVLT intrusion/false positive errors in the context of average range immediate and delayed memory demonstrated variable impairments. These neuropsychological data supported the informant interview information, and more importantly, the prospective follow-up for the diagnosis of fv-FTD. We found the Iowa Gambling test and tests of social cognition from the Advanced Clinical Systems not to be useful for early stage fv-FTD.

***Conclusions:*** Although time consuming to score, the normed error analyses from the DKEFS may be useful for measuring the elusive functioning of the ventromedial/orbitofrontal prefrontal circuit and, therefore, useful as part of the converging evidence for the diagnosis of some patients with fv-FTD.

## Rural and Remote Memory Clinic: a One-Stop Memory Clinic Saves Travel Burden for Rural/Remote Families

L. Hofeld, M. O'Connell, D. Morgan, J. Kosteniuk, A. Kirk, N. Stewart, A. Cammer, K. Stevenson, R. Loepky, D. Minish. University of Saskatchewan.

***Background/Objectives:*** The Rural and Remote Memory Clinic (RRMC) in Saskatoon, SK was designed as an innovative clinic model to serve the needs of rural/remote SK residents. The aim of the clinic is to reduce travel burden and is, therefore, a one-stop assessment (PI Morgan). Patients arrive at the RRMC having completed comprehensive and up-to-date blood work and an EKG (for potential drug contraindications). Clinic days involve 2 patients/families; new patients and family caregivers provide consent for clinical service and for research (that is for de-identified data to be entered into a database). The clinic nurse (Holfeld) completes a medical history. The patient and caregiver then participate in a brief interdisciplinary interview with the clinical team. A neurological exam (Kirk) is performed. While the patient completes a brief 2-hour neuropsychological assessment (O'Connell neuropsychologist and supervisor, Minish psychometrist), additional collateral information is obtained from the caregiver which includes standardized scales (functional assessment questionnaire, neuropsychiatric inventory, and Zarit burden interview, among others). A registered dietitian (Cammer) also completes a caregiver interview. After a lunch break, patient and caregiver participate in a brief interview with a physical therapist (Stevenson/Loepky), and complete a physical therapy assessment. The patient completes standardized scales, including one of depressive symptoms (interpreted/followed up on by psychologist, O'Connell). A CT head scan is performed. The neurologist (Kirk) interprets blood work/CT head scan information in addition to neurological/interview. Finally, all interprofessional assessment data are shared at a team conference and a consensus regarding diagnosis and management is discussed. The findings are communicated with the patient and family at the end of the day. A written report from neurology and a brief neuropsychological report are provided to the referral source and primary care provider (if not overlapping). A physical therapy and dietitian report are provided on an as-needed basis. Follow-up is as clinically indicated (Kirk), and for the most part (depending on clinical presentation) occurs over telehealth videoconferencing to reduce travel burden.

***Methods/Overview:*** Descriptive analyses of all consecutive cases.

***Results:*** 412 patients seen ranged in age from 22 to 92 years (M = 71.4; SD = 11.66), and of these 20% had no evidence of cognitive impairment. Most were diagnosed with dementia

(61%; of these 62% were diagnosed with dementia due to Alzheimer disease). Some form of mild cognitive impairment (amnestic vs. non-amnestic/single domain vs. multi-domain) was diagnosed in 16%, while 3% were diagnosed with cognitive impairment not otherwise specified. This patient sample had to travel between 42 and 865 km one-way from home to the RRMC in Saskatoon (M = 267; SD = 123).

***Conclusions:*** This one-stop interdisciplinary memory clinic model reduces travel burden for rural patients and their families when compared with multiple trips to see multiple specialists, saving on average 267 km one-way travel to Saskatoon.

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**CCNA Team 20: Issues in Dementia Care for Rural and Indigenous Populations**

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***Mission:*** The mission of CCNA Team 20 Rural is to improve the quality of primary health care (PHC) for individuals with dementia in rural and remote communities. Team 20 Rural is one of 20 teams in the Canadian Consortium on Neurodegeneration in Aging (CCNA).

***Objectives:*** We are using a community-based participatory approach during a 5-yr study (2014–2019) by collaborating with decision-makers and PHC teams in one Saskatchewan health region (Sun Country). Our objectives are to: 1) identify gaps and strengths in current dementia care practices in rural PHC teams, 2) adapt, implement, and evaluate a PHC model for dementia in rural PHC teams based on best practices (e.g., multidisciplinary team, standard tools and protocols, education/support, regular patient follow-up), 3) investigate the facilitators/barriers of successful adaptation of a rural PHC model for dementia, and 4) sustain and spread a newly developed PHC model for dementia to rural PHC teams in additional SK health regions.

***Main Activities:*** Since the start of the study in 2014, we have pre-tested a baseline care pathway telephone questionnaire (a non-intervention health region) and conducted baseline telephone interviews regarding current dementia care strengths and gaps in Sun Country Health Region. Interview participants included PHC teams, patients, caregivers, and members of our Regional Advisory Council. We are currently collaborating with one of eight existing PHC teams in Sun Country, to develop a new model of PHC for dementia. We have also released a report that provides provincial level data on dementia services across SK, and dementia incidence and prevalence. Study activities are facilitated by a 13-member Sun Country Regional Advisory Council that includes health region management and the Alzheimer Society of Saskatchewan.

***Next Steps:*** In Year 2 of the study, we will identify quality indicators for rural dementia care, based on a literature review and collaboration with Sun Country Health Region. We also intend to scale up and spread our newly developed model of PHC for dementia to a second PHC team in Sun Country (enrolling 1 team/yr). Building on the report released in Year 1, we will undertake a comparison of dementia epidemiology in SK and ON, using administrative health data.

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**What Clinicians Should Know About Functional Performance Assessments in Individuals with Mild Cognitive Impairment**

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Although it is recognized that individuals with mild cognitive impairment (MCI) are independent in performing everyday tasks, they take more time, are less efficient, and make more errors. (Albert et al., 2011). However, errors in performance are very subtle, which makes it challenging for clinicians to differentiate between functional decline that is part of the normal aging process and pathological decline. In fact, we have conducted a Canadian national survey to ask clinicians about how they assess functional impairment in individuals with MCI. We have found no consensus among clinicians as they use different types of assessments which cover different functional domains, and most of the assessments have not yet been validated with this population. In order to gain a better understanding on the current functional criteria used in the literature and to provide guidance to clinicians, we have conducted three systematic reviews to evaluate the instruments which have been used in studies with the MCI population. Specifically, we examined the psychometric properties of each instrument (both performance-based and questionnaires) and the functional domains covered (e.g., shopping, finance management, etc.). We have found nine performance-based instruments and five questionnaires that have been validated with the population. Different functional domains have been assessed. Even though we cannot make specific recommendations to clinicians on the best assessment to use, we can provide clinicians with direction when conducting functional assessments. We will discuss each one in our presentation.

**Development of a Novel Neuronal Activity Biomarker for Alzheimer Disease Using Resting State-FMRI**

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***Background:*** Brain atrophy measured by MRI and cerebral glucose metabolism measured by the uptake of $^{18}$F-labeled fluorodeoxyglucose using positron emission tomography (PET) have been established as important biomarkers associated with disease progression and treatment response in Alzheimer disease. Cerebral glucose metabolism is a direct indicator of brain neuronal activity. However, neuronal activity can also be inferred from blood-oxygen-level-dependent (BOLD) contrast as exploited in functional magnetic resonance imaging (fMRI). More recently, resting-state (RS)-fMRI measures of spontaneous low frequency fluctuations (< 0.1 HZ) in the BOLD signal have been used to identify functionally connected brain regions (networks) without the performance of an overt task. In this study we defined a new metric for neuronal activity based on the standard deviation of the magnitude of the blood-oxygen-level dependent (BOLD) fluctuation. The purpose of this study was to determine whether this new metric could be used to accurately differentiate healthy individuals from people with Alzheimer disease (AD). Furthermore, we determined whether there was a linear correlation between the fluctuation magnitude of the neuronal derived RS-fMRI signal and FDG-PET.

***Methods:*** RS-fMRI and FDG-PET data were obtained from the Alzheimer disease neuroimaging initiative (ADNI) database for normal elderly controls (NEC, N=15), and AD patients (N=15). The brain extracted RS-fMRI data were preprocessed, aligned and co-registered to the Montreal Neurological Institute (MNI-152) space. An independent component analysis (ICA) method was applied to each dataset followed by a multiple-template matching technique and neuronality test to identify valid neuronal activity components using a support vector machine (SVM) classifier. Then, a brain activity map was constructed from the neuronal components, based on the variation in signal magnitude over time in each pixel, and was co-registered to the MNI-152 space to measure brain activity in several brain regions. The partial volume corrected FDG-PET image for each subject was also co-registered to the MNI-152 template. The glucose utilization standardized uptake value (SUV) of each brain region was measured relative to the cerebellum.

***Results:*** Our results showed that both the mean brain activity measured by RS-fMRI and FDG-PET measured glucose utilization was significantly lower ($p$<.05) in several brain regions including the amygdala and hippocampus in people with AD compared to healthy controls. The novel RS-fMRI brain activity biomarker was positively correlated with the Mini Mental State Examination (MMSE) score and Aβ1-42 cerebral spinal fluid levels. The greatest classification accuracy, sensitivity, and specificity were obtained when using measurements from the hippocampus for both modalities. There was also a significant linear correlation between the novel brain activity metric obtained using RS-fMRI and the rate of glucose metabolism measured using FDG-PET.

***Conclusion:*** The results from this study indicate that the newly defined RS-fMRI measured brain activity metric can differentiate subjects with Alzheimer disease from healthy elderly in a similar manner to that obtained when using FDG-PET measured glucose metabolism.

***Acknowledgement:*** Funding provided by the Canadian Institutes of Health Research.

**Transitioning from Independent to Assisted Living: Family Caregiver Experiences and Responsibilities**

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***Introduction:*** It is a relatively new trend for persons with dementia to move to assisted living prior to moving to long-term-care homes as their illness progresses. While research about the experience of moving to LTC indicates that caregiving responsibility continues through the process, little is known about the caregiver perspective on transition to assisted living.

***Objectives:*** To describe the tasks, responsibilities, and experiences of the primary caregiver associated with the transition of a person with dementia to an assisted living facility.

***Methods:*** This study is part of a longitudinal study of transitions in care. Semi-structured qualitative interviews were conducted with 12 caregivers and, where possible, persons with dementia at the time of the move. Descriptive content analysis was conducted. The caregiver mean age is 59.5 and the range is from 43 to 81. The PWD mean age is 83.3 and the range is 77 to 91. Three caregivers are spouses, 1 is a sibling, 7 are adult children, 1 is a niece. Nine caregivers are female. Eight PWD are female.

***Results:*** The transition into assisted living for a PWD fell into three stages, each of which brought different responsibilities and impacts for the caregiver. The first stage included the decision for the person with dementia to move into an assisted

living facility. Responsibilities for caregivers included visiting prospective facilities, and planning for and also preparing for the move. The task of preparing for the move and selling the person's home was stressful for caregivers. The second stage was the move itself. Responsibilities at this stage included moving items, setting up the new space, taking care of phone, mail, and bills, and helping the person with dementia adjust on the first day in the new space. Several caregivers had assistance from other family members during this stage. The final stage was the settling in and adjustment of the PWD to their new home. Caregiver responsibilities included visiting, reassuring, and providing emotional support; monitoring and negotiating services in the new home; promoting health and well-being; doing errands and assisting with IADLs; and communicating with other relatives. For many caregivers, this stage brought about relief from worries about the PWD's safety and well-being.

***Discussion:*** This study adds to the scant literature about persons with dementia transitioning to assisted living. Similar to research about transition to long-term-care homes, caregivers had significant responsibilities, even after the move. Future research should examine this experience in more detail, with a larger sample.

***Conclusion:*** In this study, caregivers played a crucial role in the transition of a person with dementia into an assisted-living facility. Through each phase of the transition, the caregivers' responsibilities influenced the quality of life of both the person with dementia and the caregiver.

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**Investigating Risky Driving and Turning Errors in Patients with Amnestic and Multiple-Domain Mild Cognitive Impairment**

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***Background:*** Across major governing bodies, including the Canadian Medical Association, there is an absence of concrete guidelines specifying when patients with mild cognitive impairment (MCI) require a formal driving assessment. The results of on-road and simulator assessments remain inconsistent, with some studies reporting that patients with MCI exhibit driving impairment, whereas others report that patients with MCI retain the ability to drive safely. As a result, there are limited tools and guidelines available to assist health-care professionals in assessing the driving fitness of patients with MCI.

***Objectives:*** Given the heterogeneous presentation of MCI, this study aimed to investigate the driving performance of patients with amnestic MCI, single-domain (aMCI), and multiple-domain MCI (mdMCI). It was hypothesized that MCI patients would exhibit increased risky driving errors (i.e., collisions, centre line crossings, road edge excursions) compared to healthy controls and that patients with mdMCI would exhibit greater driving impairment.

***Methods:*** The current study used driving simulator technology (STISIM) to compare the driving performance of 17 patients with MCI (7 patients classified with aMCI and 10 patients with mdMCI) and 13 healthy age- and education-matched control drivers. Patients and controls completed several driving tasks that increased in complexity, from routine right and left turns to more cognitively demanding left turns with traffic, where most real-world accidents occur.

***Results:*** Overall, patients with MCI committed over three times as many risky driving errors (12.1 vs. 3.4 errors, $p$=.031) and demonstrated an increased rate of turning errors (0.15 vs. 0.07 errors per turn, $p$=.017) compared to healthy controls. Patients with mdMCI tended to commit more risky errors than healthy controls (17.2 vs. 3.4, $p$=.036), and patients with aMCI committed a similar number of risky errors as control drivers (4.9 vs. 3.4, $p$=.157). Both mdMCI and aMCI patients performed similar to controls during routine right and left turns without traffic; however, patients with mdMCI committed significantly more errors than control participants during left turns with traffic (0.24 vs. 0.04 errors per turn, $p$=.006). Patients with aMCI performed similar to controls during left turns with traffic (0.05 vs. 0.04, $p$=.877).

***Conclusions:*** Results suggest that, in general, patients with MCI may be at an increased risk of driving impairment. Although patients with mdMCI may maintain driving performance during more routine aspects of driving (e.g., right and left turns), deficits may become apparent during more demanding aspects of driving (e.g., left turns with traffic), which require integration of multiple cognitive functions (i.e., visuospatial ability, executive function, attention). In contrast, individuals with aMCI may be able to maintain driving performance at a behaviourally equivalent level to controls across various driving conditions. The results suggest that differentiating between various subtypes of MCI may be important when evaluating driving fitness. Future large-scale research is required to better characterize the driving impairments associated with the various sub-types of MCI (e.g., executive, amnestic, single-domain, multiple-domain) and to develop objective assessment tools that can help determine when patients with MCI may be unsafe to drive.

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**Best Practices Regarding Nutritional Care of Urban and Rural Long-Term Care Residents with Dementia**

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Dementia is recognized as a public health priority; worldwide prevalence of dementia is projected to double to 65.7 million by 2030. Dementia is the top chronic condition necessitating placement in long-term care (LTC), and residents with dementia require more direct-care time. Physiological changes can negatively impact nutritional intake, while behavior changes can increase nutritional needs, contributing to a higher risk for malnutrition and adverse health outcomes such as muscle wasting, infection, poor wound healing, loss of sensory function, and reduced quality of life. Nutritional health of LTC residents with dementia is, therefore, central to quality care, as optimizing nutritional status can reduce disease co-morbidity and prevent accelerated decline. The role for registered dietitians (RDs) in LTC is increasing; however, the majority of resident care is provided by aides with limited training in both nutrition and dementia who rely on task-specific nutrition care. Staff report difficulty in food provision to residents with dementia, yet current standards for nutrition care in LTC do not address dementia. Rural LTC facilities may be further disadvantaged due to limited access to specialists such as RDs. Examination of best practices and staff perspectives of nutrition care for residents with dementia in rural LTC is timely, with opportunity to significantly improve dietetic practice and resident care. Under an evidence-based practice framework, three interrelated studies will be undertaken to examine nutrition care best practices for LTC residents with dementia in urban and rural areas.

***Project 1:*** Systematic Review of Nutritional Care for persons with dementia in long-term-care homes. This review will identify peer-reviewed, published literature addressing the best practices pertaining to nutrition care for persons with dementia living in the LTC home setting, with particular attention to interventions and practices found effective in the rural LTC setting.

***Project 2:*** Examination of nutrition care for persons with dementia in urban and rural LTC homes from the perspective of RDs. In-depth interviews will be used to gain an understanding of the role of the RD in providing nutrition care to residents with dementia in urban and rural LTC homes, identify the strengths and barriers experienced by RDs working in the field of LTC dementia care, and determine if there is a relationship between these factors and rural/urban practice location.

***Project 3:*** Examination of nutrition care for persons with dementia in urban and rural LTC homes from the perspective of care aides. This qualitative study will use multiple focus group discussions with care aides to examine nutrition care practices and principles of nutritional care for persons with dementia from the perspective of care aides and determine whether there is a difference in the principles identified and considered by care aides within urban and rural LTC homes. By understanding both the best practice evidence and the implementation of nutrition care for residents with dementia from the perspective of RDs and care aides, we can more effectively design system-wide nutrition care policies and practices to improve the quality of person-centered nutrition care, which will enhance resident health outcomes.

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**Systemic Review of RCTs of Interventions for Vascular Cognitive Impairment**

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***Background:*** As part of the Canadian Consortium on Neurodegeneration in Aging (CCNA) strategy to reduce the burden of vascular cognitive impairment, the Vascular Illness sub-team is systematically reviewing all prior randomized controlled trials (RCTs) for vascular cognitive impairment and dementia.

***Methods:*** On July 1, 2015, the ALOIS database (www.medicine.ox.ac.uk/alois) was searched using seven synonyms for vascular cognitive impairment or cereberovascular disease. ALOIS is an ongoing, open access, searchable database of all RCTs for treatment or prevention of cognitive impairment and dementia, maintained by the Cochrane Dementia and Cognitive Improvement Group of the Cochrane collaboration. Source data include PubMed, EMBASE, and PsychINFO, as well as conference proceedings and trial registries, such as clinicaltrials.gov.

***Results:*** A total of 559 RCTs were identified, of which 463 had been published in a journal, 2 in a book, 28 as conference proceedings only, and 58 as trial registries only. There were 507 completed trials, 41 ongoing trials or protocol publications, 2 trials terminated early, and 9 were of unclear status. Trial start dates ranged from 1960 to 2015. There was a trend toward more RCTs in more recent years. Trial populations studied included vascular dementia (262), mixed dementia (57), stroke or vascular diseases (276), and vascular mild cognitive impairment (MCI)/cognitively impaired not demented (CIND) (2). Most trials (446/559) described pharmacological interventions; commonly studied drugs included cholinesterase inhibitors (28), citicoline (13), ginkgo biloba (33), hydergine (22) nimodipine (19), antithrombotics (11), and antihypertensives (39). Three-quarters of the trials had fewer than 150 participants, and half had fewer than 60.

***Conclusions:*** We identified a large number of previously published RCTs in VCI. However, small trial sizes may have contributed to inconclusive results, resulting in the current

lack of evidence-based treatments for VCI. There were few studies of vascular MCI or vascular CIND. In future work, we plan to systematically assess study quality, meta-analyze results where appropriate, and analyze for publication bias.

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**The Canadian Consortium for Neurodegeneration in Aging (CCNA): Overview of the Neuropsychology Battery**

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***Background/Objectives:*** The CCNA is a $31.5 million research initiative funded by the Canadian Institute of Health Research (CIHR) and partners. It is aimed at understanding the mechanisms of neurodegenerative illness, its prevention, treatment, and improving the quality of life of those with dementia. Neuropsychological assessment is a crucial component of the diagnosis of dementia and the specification of its various etiological subtypes.

***Methods/Overview:*** Following a comprehensive background interview and physical examination, all 1600 participants in the CCNA will undergo a comprehensive assessment of cognitive function, and will also have imaging of their brain and blood drawn. In this presentation, we will provide an overview of the neuropsychology test battery for the CCNA. The assessment of cognitive function will play two roles in the CCNA. First, certain measures of general cognitive function, memory, cognitive complaints, and activities of daily living will contribute to the clinical ascertainment and diagnosis of participants who will form the participant groups of the CCNA Clinical Platform (e.g., those with subjective cognitive impairment, mild cognitive impairment (MCI), vascular MCI, Alzheimer's disease, vascular dementia, mixed dementia, fronto-temporal lobar dementia, Parkinson's disease/Lewy body dementia). Second, an independent and more comprehensive test battery, consisting of both clinical and experimental measures, will assess a broad range of cognitive function (e.g., verbal and non-verbal learning and memory, executive function, attention/concentration, language, processing speed, perceptual abilities). Performance on these tests, together with imaging and medical data, will be used to clinically characterize the groups and to provide research data.

***Discussion/Conclusions:*** We will describe the rationale for and the goals of the battery, the process of its development (including parallel versions in both English and French), its current content, and its alignment with other neurodegeneration research initiatives in Canada. The plans for research staff training, data monitoring, quality control using the Longitudinal Online Research and Imaging System (LORIS) software system, and normative development will also be described.

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**Behavioural Neurology Assessment—Revised: Normative Data and Test Reliability**

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***Background:*** The original Behavioural Neurology Assessment (BNA) was published in 2005 as a brief mental status examination that assessed the major cognitive domains and provided quantitative and qualitative information. Although the BNA demonstrated 93% sensitivity and specificity for detection of dementia, it is less sensitive for detection of mild cognitive impairment (MCI). Therefore, the BNA was revised to enhance its sensitivity and specificity for detection of MCI. The BNA-Revised (BNA-R) is an in-depth assessment that is intermediate between short screening tests (e.g., MoCA and MMSE) and lengthy neuropsychological assessments, and can be administered by any health professional in both ambulatory and inpatient settings. It is comprised of subtests within 7 cognitive domains: orientation (12 points), immediate verbal recall (30 points), delayed verbal and visual recall (27 points), delayed verbal and visual recognition (21 points), visuospatial function (32 points), working memory/attention/executive control (123 points), and language (85 points), with a total score of 330.

***Objectives:*** To develop a normative database on the BNA-R and to determine test reliability and test-retest stability.

***Methods:*** Three hundred normal community volunteers between ages 50–89 years were tested on the BNA-R, with

75 subjects per decade (men=104, women=196; mean years of education=15.3 + 2.6, range=8 to 20 years). To assess test stability, 29 subjects were tested on two separate occasions. Internal consistency was determined by calculating Cronbach's alpha for the 7 domain and total scores.

***Results:*** Median time to complete the BNA-R was 34 minutes (range 25–63). Mean total BNA-R score was 292.6 (SD=18.6) with age having a significant effect; F(3, 296)=6.06, $p$=.001. There was a significant, but small, effect size for sex with women scoring a mean of 6.2 (SED=2.2) points higher than men; F(1,298)=7.59, $p$=.006, Cohen's d=.32. Age and education were weakly, but significantly, correlated with the total score (both $r$s=0.21, $p$<.001). Test scores remained relatively stable over a median of 73 days (range 28–120 days) with a stability coefficient of $r$=.85 and mean increase of only 4.1 points; t(27)=2.37, $p$=.025. Reliability of the 7 domain scores ranged from 0.20 (orientation) to 0.81 (immediate recall); the Total score yielded a reliability of 0.73.

***Conclusions:*** Overall performance on the BNA-R was characterized by a small effect size for age. Assessment of test-retest reliability demonstrated good stability with only a modest increase in test scores. Internal reliability of the total score was found to be adequate and reflected the diverse natures of the cognitive abilities assessed. The BNA-R was found to yield a relatively quick and reliable assessment of multiple cognitive domains in a sample of 300 normal, community-dwelling volunteers between the ages of 50–89 years. Normative data will be presented that characterizes performance across 4 decades from ages 50–89 for each cognitive domain and total test score. The BNA-R is currently being validated for the detection of amnestic MCI. An iPad version has been developed and is currently being evaluated for equivalence to the paper format.

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**Outcome from a Randomized Controlled Trial on Music Therapy in Alzheimer Disease**

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***Background:*** Numerous case series suggest that music therapy (MT) may be beneficial for patients at various stages of dementia, but objective quantitative evidence are limited. We hypothesize that MT can improve behavioural symptoms in patients with AD. In the current study, we examined the behavioural, cognitive, and biological outcomes of 10 weeks of MT in subjects with moderate AD.

***Methods:*** We conducted a randomized controlled assessor-blinded trial with a delay-start cross-over paradigm to assess the effects of MT on subjects with AD with behavioural symptoms in an out-patient setting. The inclusion criteria include: 1) a clinical diagnosis of AD, 2) no previous musical expertise, 3) normal hearing abilities, and 4) NPI score of 5 or more. MT was applied by an accredited music therapist following a standardized structured protocol (Clair & Bernstein 1990). A total of 27 subjects were randomized;12 received immediate MT for 10 times 60 min sessions over 10–12 weeks, followed by another 12-week period of waiting; while 15 waited for 12 weeks before they received their MT. Primary outcome were change in NPI and CGIC during MT compared to the waiting period. Secondary outcomes include the ADAS-Cog, CMAI, GDS, morning salivary cortisol, and QOL-AD for subject and caregiver. We used a linear mixed model to assess for the change in each measure within each subject between test conditions, including sequence effect.

***Results:*** We found a significant drop in NPI after MT (-2.6) compared to an increase during the waiting period (+5.9, $p$=.037), but no significant differences in C-GIC ($p$=.23). There was also a significant lowering of morning salivary cortisol level (-0.15 ug/dL) during MT compared to the waiting period (+2.7, 0.039). No significant differences were observed in the ADAS-Cog, CMAI, GDS, or QOL-AD for the subject or the caregiver. There is a significant sequence effect, suggesting some carry-over benefits in the immediate group compared to the delay-start group.

***Conclusion:*** Our findings suggest that MT has beneficial effect on managing behavioural symptoms in patients with AD and decreasing stress as measured by morning cortisol level. It can be a safe alternative to pharmacological treatment in managing AD patients with behavioural symptoms.

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**Differential Response in FMRI of Patients with Alzheimer Disease Listening to Familiar vs. Unfamiliar Music**

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***Background:*** Music therapy has been proposed as a safe and effective treatment for patients with Alzheimer disease (AD). Studies have measured the effectiveness of music therapy through behavioural assessment and observations, but few have examined the neural basis of these changes. We hypothesized that the activation pattern of the brain during the music processing of familiar and unfamiliar music would be different in AD patients compared to controls.

***Methods:*** Ten AD subjects were compared to 10 healthy age-matched controls. Each subject was exposed to auditory stimuli of familiar music and unfamiliar music by the

same composer with white noise as the control condition in randomized order of blocks. Each block involved playing a 75-second auditory stimulus preceded by 30 seconds of white noise. Functional MRI images were acquired with a 3T Philips scanner and analyzed with general linear model (GLM) for blocked designs in SPM8. GLM analyses were applied after the images were realigned, normalized to MNI space, and spatially smoothed. At the subject level analysis, the smoothed fMRI time courses corresponding to each block of stimulus were convolved with canonical HRF and activation values were found for each stimuli. Random effect group analysis was then performed on the resulting beta estimates from each subject's first-level analysis. Significant regions were then identified by family-wise error (FWE) ratios with $p<.005$ and a minimum cluster size of 8 voxels.

***Results:*** AD patients have significantly greater activation with familiar music in the superior and middle temporal gyrus, pars triangularis, right insula, right inferior frontal gyrus, and left supplementary motor area, but deactivation with unfamiliar music in the middle temporal gyrus and temporopolar area (BA38), whereas unfamiliar music generated more overall activation than familiar music in controls.

***Conclusion:*** AD subjects have a greater area of brain activation when listening to familiar music, while control subjects showed greater activation with unfamiliar music. This may suggest that control subjects are more interested in and pay more attention to novel music, while AD subjects pay more attention to familiar music. This difference in activation pattern may have implication to the practice of music therapy.

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**Locating Dementia in the Indigenous Worldview**

K. Jacklin. Northern Ontario School of Medicine.

***Background:*** In recent years there has been a rise in the incidence and prevalence of dementia in Indigenous populations in Canada. This stands in contrast to just 15 years prior, when a diagnosis of dementia in Indigenous communities was unusual. The relative rarity of the illness in this population in the past coupled with the high and increasing rates in the present, has led to the recognition of dementia as an emerging illness in Indigenous populations. In this presentation, I explore the findings from our multi-site qualitative study concerning knowledge, attitudes, perceptions, and cultural values concerning dementia in diverse Indigenous communities in Ontario. Specifically, I explore Indigenous understandings and perceptions of dementia as they are currently being constructed against a backdrop of the changing epidemiological profile of the illness, and offer a definition of dementia based on a collective narrative analysis.

***Methods:*** The research has been driven by Indigenous community research partners who became concerned with a noticeable increase in the number of elderly requiring care for dementia. Our approach combines anthropological theory and methods with Indigenous knowledge within a community-based participatory research model. Participant observation, focus groups (n=48) and in-depth interviews (n=120) were carried out with people with dementia, caregivers, health-care providers, elders, and traditional healers at six geographically and culturally diverse Indigenous research sites in Ontario, Canada.

***Results:*** The majority of all participant groups agree that dementia as an illness is a new phenomenon in their communities. The narratives of the people with dementia, seniors and caregivers reveal an Indigenous-specific interpretation of dementia that differs from the more commonly held views of other Canadians. These participants most often interpreted the symptoms of dementia as something that is natural and normal and congruent with their understandings of the circle of life and their spiritual beliefs and worldview. In seeking explanations for the present-day prevalence of the illness in their communities, participants most often offered explanations related to disruptions to cultural continuity resulting from colonialism.

***Conclusions:*** Stark contrasts in the understandings of dementia held by Indigenous people compared to those held by the biomedical community may hinder or limit access to health-care resources and impact the effectiveness of provider communication with patients and families and health promotion resources. As health-care systems seek to respond to the increasing dementia care needs of the aging Canadian population, our findings suggest that specific and appropriate strategies need to be in place to effectively address dementia needs in Indigenous communities.

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**Developing a Community-Based Approach to Understanding Issues in Dementia Care for Indigenous Populations in Canada**

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***Background:*** The Canadian Consortium on Neurodegeneration in Aging (CCNA) has been established to undertake

research that will address the increasing rates of age-related neurodegeneration affecting cognition in the Canadian population. The consortium brings together 340 top Canadian researchers who conduct research within the three identified research themes: Primary Prevention, Secondary Prevention, and Quality of Life. This paper outlines the research concerning Indigenous populations in Canada that will be undertaken the CCNA's Team 20. Our research team is the only team within the CCNA investigating neurodegenerative diseases in Indigenous populations. We are focused on research that can contribute to improving quality of life for Indigenous people with dementia and their caregivers. Our goal is to identify culturally appropriate approaches to dementia diagnosis, care, and health education.

***Methods:*** Our research program will work with First Nations to better understand their needs and support the creation of community-driven appropriate programs and services to enhance quality of life for Aboriginal people with dementia and their caregivers. Our projects involve seven First Nations community partners on Manitoulin Island, Ontario, and the File Hills Qu'Appelle Tribal Council, Saskatchewan. Our approach to the research combines Indigenous knowledge approaches with multi-disciplinary academic theories within a community-based participatory methodology. Our team is guided by two project Elders and an advisory group from each region.

***Results:*** The Team 20 research platform involves two core projects, activities aimed at capacity building, a synergistic project with Team 14, and three additional leveraged projects, all concerned with improved quality of life for Indigenous people with dementia and their caregivers. During the first year of our work within the CCNA we have used community-based approaches to successfully complete most of the local procedural process to formally begin data collection.

***Conclusions:*** Our previous work found that there is an Indigenous specific view of dementia that presents many opportunities for the development of culturally grounded strength-based approaches to dementia care for Indigenous people. We hypothesize that cultural approaches to care for Indigenous people with dementia and their care-givers hold the potential to slow the progression of a cognitive decline and improve outcomes in dementia care for Indigenous people.

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**Volunteers for Research Guide: Improving Capacity of Local Alzheimer Offices To Assist Volunteers Wishing To Participate in Clinical Trials and Studies**

L. Chambers[1], M. Harris[2], L. Lusk[2], D. Benczkowski[1], M. Lowi-Young[1]. [1]Alzheimer Society of Canada; [2]Gestaltcollective.

***Background:*** New drugs, care practice interventions, and diagnostic tools need rigorous testing. Canada's recent sharp increase in funding for dementia research has created a crisis in recruitment of numerous and diverse volunteers to participate in clinical trials and studies, especially people with early cognitive impairment.

***Objective:*** The Alzheimer Society objective is to improve ways its offices in its 60 provincial and local Societies assist persons with dementia and their caregivers to participate in clinical trials and studies.

***Methods/Overview:*** Review of literature, environmental scan of Society offices across Canada, consultations with researchers and other charitable societies were conducted to determine the content of "Research Recruitment: A Guide to Get Started". It acknowledges that there is no standard approach on how a Society should organize to support study volunteer recruitment. The Guide is designed to help Societies generate discussion and each to determine its own recruitment plan. The Guide was piloted in eight "early adopter" Society offices across Canada. The pilot is informing the roll-out of the Guide in a further 25 Society offices.

***Results:*** Two of the eight offices that piloted the Guide were located in communities without Academic Health Centers. All pilot Society offices reported:

- Using the processes in the Guide to convene discussion with staff about recruitment of volunteers.
- That the Guide steps and worksheets encouraged them to take an approach that best fits their context.
- That they liked the six scenarios illustrating how recruitment could be supported (as opposed to guidelines). At least one scenario was particularly relevant for each Society.

Recommended revisions to the Guide were included in the roll-out to the 25 additional Society offices across Canada. These have included:

- Changing title from 'clinical trials and studies' to 'research',
- Keeping the six scenarios to convey what research recruitment might entail,
- Clarifying researcher's role in volunteer recruitment,
- Including annotated table of contents,
- Including easier instructions for what volunteers should ask, and
- Providing follow-up staff orientation on research processes, Society office collaboration with researchers, and inter-office learning.

Experience with Guide implementation also reinforces the need for promotion of research by the Society offices that

focuses on putting in place processes and structures at an organizational level to sustain relationships between Societies and researchers or research institutes. These aim to: 1) promote productive relationships between Societies and researchers, that is, enabling local Society staff to connect with researchers or research organizations in their geographic area to develop mutual awareness, appraise opportunities to work together and apply knowledge of each other in productive ways; and, 2) create an engaged body of research partners through developing and maintaining the processes required to identify and enable interested individuals to either contribute to research as a volunteer participant and/or as partners in the research process.

***Conclusion:*** Charitable organizations that raise funds for research also have a role in promoting research recruitment of persons with dementia and their caregivers. Use of the Guide facilitates organizational change to both create a positive research culture as well as practical solutions that can help organizations achieve this goal.

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**Event-Related Potentials Elicited During Cognitive Tasks: Biomarkers for Mild Cognitive Impairment**

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***Background:*** Mild cognitive impairment (MCI) is an intermediate condition between healthy aging and dementia, where memory loss is greater than expected for the person's age and education. In the context of growing interest in biomarkers of early cognitive change, event-related potentials (ERPs) are garnering attention as potential physiological indicators of dysfunction in patients with cognitive decline. ERPs are derived from electroencephalograms (EEG) and measure the brain's response to cognitive events. A number of studies have shown that ERPs can distinguish between groups of patients with MCI and healthy controls. In this study we investigate if ERPs elicited during working memory, inhibitory controls, and semantic memory tasks could accurately identify individuals with MCI.

***Methods:*** A total of 15 MCI participants were recruited from the Bruyère Memory Program; 17 healthy controls (HC) were recruited from the community. After cognitive testing, all classifications of MCI and HC were confirmed by a clinical committee. MCI participants consisted of seven males and eight females. They had a mean age of 75.7 years old and a mean education of 14.7 years. There were six male and eleven female HC participants. They had a mean age of 72.4 years old and a mean education of 15.6 years. The two groups did not differ significantly in age or education. EEGs were measured using NeuroScan NuAmps 4.3 and analysed using Brain Analyzer 2.1. Participants performed n-back, go/no-go, and verbal recognition tasks while an EEG was recorded. The P200, P300, and N400 ERP components were analyzed. Receiver operating characteristics (ROC curves) were performed on ERP component amplitudes and latencies to determine which best distinguish between groups.

***Results:*** During the n-back test, the P200 latency in the 1-back condition at Pz site had a sensitivity of 86.7% and specificity of 82.4%. During the go/no-go test, the P300 amplitude in the go condition at FCz site had a sensitivity of 80.0% and specificity of 76.5%. During the verbal recognition test, the N400 amplitude in the NRW condition at CPz site had a sensitivity of 80.0% and specificity of 71.6%. The discriminant potential of the P200 latency was good with an AUC of .85 ($p$<.01). In contrast, the AUC for the P300 and N400 amplitudes were .74 ($p$=.022), and .79 ($p$=.005), respectively, which are considered fair.

***Discussion:*** To our knowledge, this is the first comparison of these three ERP parameters in terms of their diagnostic utility. In this study, the ERP P200 latency for the n-back task demonstrated the best diagnostic accuracy. This may be due to the fact that the n-back assesses working memory, whereas the go/no-go and verbal recognition tests assess inhibition and semantic memory, respectively. EEG changes may predate cognitive changes in the clinic, which may make it a valuable bio-marker. This work needs to be repeated with a larger sample size. Other future research should further compare ERP data from various cognitive paradigms, evaluating their utility in different populations with cognitive decline and which paradigm or set of paradigms provides the best sensitivity and specificity.

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**Mild Cognitive Impairment: Cognitive Testing and EEG Changes With Go-NoGo**

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***Background:*** In recent decades there has been an increased interest in electroencephalogram (EEG) and its potential role in assessing cognition, because it measures brain changes to the level of milliseconds. In cognitive paradigms, the EEG signals associated with a cognitive task are averaged to yield an "event-related potential" (ERP). A number of studies have shown that ERP wave-forms generated from groups of patients with mild cognitive impairment (MCI) differ from those generated from healthy controls (HC). One cognitive function that helps memory acquisition is the inhibition of low priority information. This inhibition can be tested with a

"Go-NoGo" paradigm. In this paradigm, the participants hit a computer key each time they see a particular letter on the screen (Go), but do not hit the key when they see the distractor (NoGo). The Go and NoGo stimuli typically represent 80% and 20% of the stimuli, respectively. This study compares the results of traditional cognitive testing to ERP Go-NoGo testing in participants with MCI and the HC group.

***Methods:*** Thirteen patients with MCI were recruited from the Bruyère Memory Program, and thirteen HCs were recruited from the general population. Cognition was tested using the MoCA, RBANS subtests, and Trail Making Tests A & B. A clinical committee reviewed the results to confirm the clinical diagnoses of MCI and HC. EEGs were measured using NeuroScan NuAmps 4.3 and analysed using Brain Analyzer 2.0. Analyses were performed on midline electrodes with special interest in ERP signal components N200 and P300. Participants performed Go-NoGo cognitive tests to elicit ERPs.

***Results:*** The MCI group consisted of 7 females and 6 males with the average age of 75.8 (SD=6.6) years and average education of 14.5 (SD=3.0) years. The HC group consisted of 9 females and 4 males, with the average age of the group being 72.7 (SD=6.5) years ($p$=.241) and an average education of 16.9 (SD=1.8) years ($p$=.022). As expected, there were significant differences between MCI and HC groups in psychometric testing with lower performance seen in the MCI group. In addition, MCI participants performed with lower accuracy than controls in the NoGo condition with a mean of 78.6% (SD=9.9%) for the MCI group and 90.7% (SD=8.9%) for the HC ($p$=.009). There were no differences found between groups in response time. Finally, P300 mean amplitudes were significantly smaller in MCI participants when compared to controls in both the Go and NoGo conditions ($p$=.03).

***Discussion:*** In this sample, ERP behavioural and electrophysiological elements followed the same clinical pattern of separation between the MCI and HC groups as did cognitive testing. Clinically, these Go-NoGo results could suggest that people with MCI have problems with mechanisms of inhibitory control, which are an important part of memory formation. In addition, ERPs could be of interest as a potential bio-marker for cognitive decline as they directly measure brain function. This work needs to be repeated with a larger sample, and other paradigms should be considered to determine if ERPs could be helpful in diagnosing cognitive decline.

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**Assessing Subcortical Atrophy in Mild Cognitive Impairment and Alzheimer's Disease Using Normative Data**

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***Background:*** Normative data for volumetric estimates of brain structures based on age and sex are necessary in order to qualify and quantify brain atrophy in any given individual, for example those with suspected mild cognitive impairment (MCI) or Alzheimer's disease (AD). Although many studies have described atrophy using structural neuroimaging, most have used matched cohorts of limited size, and further employed manual or proprietary automated segmentation techniques that were not readily accessible, reducing the possibility for reproducibility and comparability. We produced norms for volumetric estimates of sub-cortical brain structures from MRI using a large sample of cognitively healthy adults and a free, widely available automated segmentation technique. Our objective was to assess anatomical differences in MCI and AD individuals using these norms.

***Methods:*** We merged T1-weighted MRI data from 16 samples provided by 15 independent research groups to gather a normative sample of 2,143 healthy adults (1,062 women) aged 18 to 94 year old (mean 49.5, SD: 20.9). Images were acquired with either Siemens (54.6%), Philips (34.7%), or GE (10.7%) scanners with 3T (55.9%) or 1.5T (44.1%) magnetic field strength using various 3D protocols, but identically processed using FreeSurfer (version 5.3.0) to produce subcortical volumes. We generated linear models for each subcortical volume with age, sex, total intracranial volume (TIV), manufacturer, and magnetic field strength as predictors, as well as interactions between predictors and quadratic and cubic terms for age and intracranial volume. Models were built using SAS 9.4 PROC GLMSELECT with a 10-fold cross-validation procedure as selection criterion. Predicting formulas were validated using three independent samples of older adults randomly selected from the ADNI2 cohort: healthy controls (n = 50), MCI (n = 50), and AD (n = 50).

***Results:*** Models predicting sub-cortical volumes had a mean explained variance of 48%. For most regions, age, sex, and TIV explained most of the volume variance, while manufacturer, magnetic field strength, and interactions explained a limited amount. Using the normative data on the independent samples revealed, as expected, that individuals with AD had significantly smaller hippocampi and larger inferior lateral ventricles as a group, and effect sizes showed that the distribution of individuals' atrophy on these areas was clearly different from that of healthy controls. Unsurprisingly, MCIs were between the controls and AD.

***Conclusions:*** By using these structural neuroimaging normative data based on a large sample of healthy older adults with brain volumes generated by FreeSurfer, researchers can easily measure the magnitude of potential brain atrophy according to the individual's characteristics and the characteristics of the scanner. The large set of normative data, coupled with the use of readily available software, should ease the comparison of data and studies.

## Eliciting Dementia Research Priorities From Canadians

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***Background:*** In health research, there is recognition of the need to incorporate the experiences and insights gained from persons living with the health condition being studied. For example, the Canadian Institutes of Health Research (CIHR) Strategy for Patient Oriented Research (SPOR) promotes patient engagement in research; in particular, those with personal experience of a health problem and their caregivers, including family and friends, should be involved with researchers, health-care providers, and decision-makers in the processes of research (including governance, priority-setting, conduct of research, and knowledge translation). Recognizing the importance of this patient partnership, the Alzheimer Society of Canada is collaborating with the Canadian Consortium on Neurodegeneration in Aging (CCNA) on a process to elicit dementia research priorities from Canadians.

***Objective:*** The objective of the Canadian dementia priority-setting partnership is to identify the top ten dementia research priorities from Canadians with dementia, their caregivers, health and social care providers, and the public, and to ensure that this information be used to influence dementia researchers and research funders. Through such mechanisms, more research will be conducted in these priorities areas, ultimately leading to better prevention, care, treatment, and quality of life in dementia.

***Methods/Overview:*** This priority-setting project will employ the methods of the James Lind Alliance (JLA), a non-profit initiative of the UK National Institute for Health Research and Medical Research Council. The project is being overseen by a Steering Group which includes people with dementia, caregivers, and clinicians. The methods include a cross-Canada survey, in collaboration with national, provincial, and local Alzheimer Societies, seeking to engage a broad representation of people in different stages of dementia, their caregivers, and health and social care providers, and the public. This survey questionnaire was developed from the JLA template, and from reviewing published and ongoing JLA studies to date, consultation with international advisors (researchers who had carried out a JLA project), and soliciting feedback from partners (for example, Alzheimer Society). The research questions generated by this survey will be refined, systematically checked against current research evidence, and then prioritized through a two-stage process (including a final in-person workshop).

***Results:*** The survey questionnaire has four sections. The first outlines the objectives of the survey for prospective participants to make an informed decision to participate in the survey The second asks the respondent to list their own research questions as priorities for research (under headings: prevention, diagnosis, symptoms, care, quality of life, treatment, and other). The third section asks for information about the respondent, including demographic information and role in relation to dementia (e.g., person with dementia, health or social care provider). The fourth section asks for the respondent's contact information, but only if they would like to participate in the subsequent research questions prioritization stage. The survey questionnaire will be translated from English to French and other languages.

***Conclusions:*** The JLA priority-setting partnership methods, including the survey questionnaire, are being adapted to the context of the project, including with jurisdiction-specific requirements and input from partners and advisors.

## Magnitude 0f Delay in Aβ-Related Memory Decline in Apoeε4 Non-Carriers

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***Background:*** In cognitively normal (CN) older adults, abnormal levels of amyloid (Aβ+) and apolipoprotein E (APOE) ε4 carriage each increase risk for Alzheimer's disease (AD). The extent to which Aβ+ and ε4 carriage contribute independently to cognitive decline in preclinical AD is unclear. Compared to Aβ- CN ε4 non-carriers, Aβ+ CN ε4 carriers show substantial cognitive decline, particularly in episodic memory. However, these studies have not observed cognitive decline in Aβ+ CN ε4 non-carriers, suggesting that by themselves, neither Aβ+ or ε4 carriage are sufficient for cognitive decline to occur in preclinical AD. The study aimed to characterize the rate of Aβ-related cognitive decline over a 72-month period in CN older adults and in older adults with MCI who were ε4 carriers and non-carriers. We hypothesized that compared to Aβ- CN ε4 non-carriers and Aβ+ CN ε4 non-carriers, Aβ+ CN ε4 carriers would show greater cognitive decline and higher rates of progression to MCI over 72-months. We further expected that compared to Aβ+ MCI ε4 non-carriers, Aβ+ MCI ε4 carriers would show greater cognitive decline over 72-months.

***Methods:*** CN older adults (n=423) underwent Aβ imaging with PET, and APOE genotyping. Participants completed the Cogstate Brief Battery at baseline, and at 18-, 36-, 54-, and

72-months follow-up visits. Rates of change for the Cognigram composite scores were compared between groups using linear mixed model. A criterion for clinically meaningful memory impairment was defined as performance 1.5 standard deviation units below the mean of the amyloid negative CN older adults.

***Results:*** Relative to Aβ- CN ε4 non-carriers, both Aβ+ CN ε4 carriers and non-carriers showed significantly faster decline in memory, executive function, and language. However, the rate of decline in memory was significantly more pronounced in Aβ+ CN ε4 carriers than in Aβ+ CN ε4 non-carriers. The rate of memory decline in Aβ+ CN ε4 carriers indicated that a criterion for clinically significant impairment would be met in 10 years, as opposed to 27 years in Aβ+ CN ε4 non-carriers.

***Conclusions:*** In CN older adults, Aβ+ is associated with memory decline in ε4 non-carriers; however, the rate of this decline is much slower than that observed in ε4 carriers. Aβ-related memory decline is unaffected by ε4 carriage in MCI groups. These results suggest that the effect of Aβ and ε4 on memory decline in preclinical AD may be ideal targets for therapies that moderate neuro-degeneration arising from the interaction between Aβ+ and ε4. They also suggest strongly that clinical trials in preclinical AD should stratify samples according to APOE ε4 carriage.

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**Cognitive Decline, Hippocampal Atrophy, and Amyloid Accumulation in Preclinical and Prodromal AD**

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***Background:*** Few studies have examined directly the relationship between rates of memory decline and neurodegeneration and Aβ accumulation across the preclinical and prodromal periods of Alzheimer's disease (AD). The aim of this study was to characterize the magnitude and variance of episodic memory decline, hippocampal atrophy and Aβ accumulation in preclinical and prodromal AD.

***Design:*** A cohort of 178 healthy adults (HA) and 56 adults with mild cognitive impairment (MCI) from the Australian, Imaging, Biomarkers and Lifestyle (AIBL) study underwent assessment at a baseline, 18 and 36 month visit using positron emission tomography neuroimaging with Pittsburgh Compound B, magnetic resonance imaging of the hippocampus and neuropsychological assessment using the Cogstate Brief Battery and a set of paper and pencil cognitive assessments.

***Results:*** In preclinical AD, the rate of Aβ accumulation over 36 months (~1 Standard deviation (SD) unit) was greater than the rate of memory decline (Cognigram learning working memory composite (~ 0.5 SD units), verbal memory composite ~0.48 SD units)) which was in turn greater than the rate of hippocampal atrophy (~ 0.2SD units). In prodromal AD, the rate the rate of Aβ accumulation over 36 months (~ 1 SD unit) remained greater than the rate of memory decline (Cognigram learning working memory composite (~ 0.5 SD units), verbal memory composite ~ 0.52 SD units)) which was equivalent to the rate of hippocampal atrophy (~ 0.5 SD units). Analysis of the interrelationships between these characteristics of early AD in the high Aβ HA and MCI groups combined indicated that the rate of Aβ accumulation was associated with the rate of hippocampal atrophy, which was in turn associated independently with the rate of decline episodic memory.

***Conclusions:*** In the preclinical stages of AD there is substantial decline in episodic memory, and accumulation of Aβ. In the prodromal phase, hippocampal atrophy also becomes evident. The estimates of change and their related error presented here can be used to inform questions of statistical power the design of clinical trials of amyloid active drugs.

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**Factors Associated with Dementia Diagnosis in a Mild Cognitive Impairment Clinic**

C. Millikin, L. Koven. University of Manitoba.

***Background/Objectives:*** The Early Cognitive Change Clinic for Older Adults (ECCCOA), a service of the Winnipeg Regional Health Authority Department of Clinical Health Psychology, seeks to identify people with mild cognitive impairment (MCI) and provide them and their family members ("program partners") with a psychoeducational group intervention. Patients undergo a brief neuropsychological assessment with a clinical neuropsychologist, while program partners are interviewed by a clinical geropsychologist to obtain information about their family member's functioning and about their own level of mood disturbance and stress. Although ECCCOA's goal is to identify people with MCI, a significant percentage of patients present with dementia. The present study aimed to determine what factors are associated with dementia diagnosis in this setting. Dementia diagnosis was expected to be associated with older age, lower education, family physician (vs. specialist physician) referral, and lower screening test scores.

***Methods/Overview:*** Demographic and referral source data were evaluated for patients who completed ECCCOA assessments and were diagnosed with MCI or dementia. Diagnosis was based on neuropsychological tests, behavioural

observations, and collateral information from program partners. Patients who did not complete testing or who received a diagnosis other than MCI or dementia (e.g., normal cognition, PTSD) were excluded. MCI and dementia groups were compared with respect to demographic variables (age, sex, years of education), referral source (family medicine (family physician/nurse practitioner) vs. specialist physician (neurologist/psychiatrist/geriatrician) with other referral sources excluded), and MMSE and/or MOCA scores provided by referral sources. Analyses used independent groups *t*-tests for continuous variables and $\chi$-square tests for dichotomous variables. Results with $p<.05$ were considered significant.

***Results:*** Of 78 patients assessed between October 2013 and July 2015, 29 were diagnosed with MCI (37.2%) and 30 with dementia (38.5%, various types). Compared to patients with dementia, MCI patients were more likely to be female ($p<.05$), but the groups did not differ in age or years of education. MCI patients were equally likely to have been referred by family medicine and specialist physicians (10 vs. 10), while patients with dementia were nearly 3 times as likely to have been referred by family medicine (17 vs. 7) (this difference was not statistically significant). Mean MMSE did not differ (MCI: 27.2 [N=20], dementia: 26.8 [n=19]). Among patients with MOCA scores (n=12 in each group), patients with MCI performed better (23.7 vs. 21.1) than those with dementia. In those with both MMSE and MOCA (n=11 in each group), the difference score (MMSE-MOCA) was significantly higher among patients with dementia (6.1) vs. MCI (3.0).

***Conclusions:*** ECCCOA's goal is to identify patients 60 and older with mild cognitive impairment, but many patients who meet screening criteria are diagnosed with dementia. Though not statistically significant, the finding that dementia patients are disproportionately referred by family medicine physicians suggests a need for continuing medical education regarding diagnosis of MCI vs. dementia. MMSE did not distinguish MCI and dementia patients, but MOCA, and the disparity between MMSE and MOCA, did. The disparity score may be useful for identifying individuals with early stage dementia.

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**Is Development of Psychosis a Risk Factor for Attrition in Longitudinal Studies of Dementia?**

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***Background/Objectives:*** Attrition/dropout is a challenging issue for longitudinal studies of dementia. To date, several risk factors for attrition have been identified among participants in longitudinal dementia studies, including baseline cognitive status, white matter lesion volume, depression, patient-caregiver relationship, and caregiver burden. Development of psychotic symptoms (delusions and/or hallucinations) is associated with many negative outcomes for patients with dementia, such as more rapid cognitive and functional decline, increased caregiver stress, and earlier institutionalization. The present study sought to evaluate whether participants with Alzheimer's disease (AD) at baseline who develop psychosis have fewer study visits and less neuroimaging data compared to those who do not develop psychotic symptoms.

***Methods/Overview:*** The present study used data from the first phase of the Alzheimer Disease Neuroimaging Initiative (ADNI-1), a longitudinal study of biomarkers across the spectrum from normal aging to probable Alzheimer's disease. We examined participants diagnosed with probable AD at baseline who had at least one follow-up visit. Participants with delusions or hallucinations at baseline were excluded. Psychotic symptoms were measured with the Neuropsychiatric Inventory Questionnaire (NPI-Q) completed by an informant. Participants who developed delusions (N=18), hallucinations (N=14), or both (N=6) were compared to participants (N=118) who did not develop psychotic symptoms during study participation. The following variables were examined: number of study visits, number of months in study, visit frequency, number of MRI scans, number of FDG-PET scans. Analyses were conducted using independent samples *t*-tests with $p<.05$ accepted for statistical significance.

***Results:*** Compared to those who did not develop psychosis (AD-P), participants who developed any psychotic symptom (AD+P) had more study visits (mean=0.43) and more months in the study (mean=4). The subgroup that developed delusions had more months in ADNI-1 (mean=4.28). Participants who developed hallucinations had more study visits (mean=0.59) and more months in the study (mean=4.66). There were trends toward more frequent study visits in the participants who developed psychosis ($p=.079$) and more study visits in those who developed delusions ($p=.080$). There were no significant differences with respect to number of MRI or FDG-PET scans completed. The modal number of study visits post-symptom onset was 0 (N=8) or 1 (N=9) following development of delusions and 0 (N=10) or 1 (N=7) following development of hallucinations.

***Conclusions:*** ADNI-1 participants who developed psychotic symptoms had more study visits and more months of study participation. In no case was a study participation variable significantly lower among participants who developed delusions, hallucinations, or both. In contrast, examination of number of study visits post-symptom onset suggests that the majority of participants who develop psychosis complete

study participation shortly after onset of delusions or hallucinations. Overall, our results do not support a role for psychosis in attrition in longitudinal studies of dementia. However, further study is required, including replication in a larger sample with a higher rate of neuropsychiatric symptoms and longer study duration.

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**Touch Screen Applications for People with Dementia (INTOUCH): Indicators of Learning and Engagement**

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***Background:*** In dementia care, there is growing attention to clients' quality of life, including provision of pleasant and meaningful activities for clients who wish to engage independently rather than relying on a caregiver. There is also growing evidence that tablets are accessible computers for people living with dementia. Identifying independent activities that are stimulating and enjoyable would be of great benefit for both the individual and their carergivers.

***Objectives:*** Here we explore whether pre-existing iPad games can provide an avenue for engaging and meaningful activity for people with dementia.

***Methods:*** Sixteen participants with a dementia diagnosis were invited to play one of the following pre-selected games: Bubble Explode - a strategic game, or Jigty Puzzle - a creative, familiar rule based game, on three separate occasions. Each session was video-recorded and concluded with a simple questionnaire. We examined their ability to play over time and engagement by analyzing face-view and screen-view videos using Observer.

***Results:*** Games play over 3 days showed that people with dementia were able to learn both the mechanics of using the touch screen and the game rules. Participants spent more time with neutral expressions than positive or negative, and more time looking at the screen than away or at the researcher. All participants stated they enjoyed playing and found playing engaging in the post play questionnaire.

***Conclusions:*** People with a dementia diagnosis are keen to try one-player iPad games and are able to learn both the mechanics and rules required to play. In addition the predominance of neutral facial expressions and fixed eye gaze indicate that people with dementia concentrate on game play in the same way as people without dementia. The findings suggest that tablet games can provide an opportunity for engaging, independent activity for people living with dementia.

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**Tau Modulates BDNF Expression and Mediates Aβ-Induced BDNF Down-Regulation in Animal and Cellular Models of Alzheimer's Disease**

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***Background/Objectives:*** In Alzheimer's disease, soluble tau is hyperphosphorylated and some of this population accumulates and deposits as neurofibrillary tangles and/or neuropil threads. Although many theories exist, a precise toxic mechanism of tau pathology is not well understood. We hypothesized that soluble tau-induced neurotoxicity is due to its ability to decrease trophic support for affected neurons. Specifically, our goal was to determine if over-expression of wild-type tau could down-regulate brain-derived neurotrophic factor (BDNF), a pro-survival peptide that is decreased in Alzheimer's disease, tauopathies, and in several relevant animal and cellular models of Alzheimer's disease.

***Methods/Overview:*** Two transgenic mouse models of wild-type human tau over-expression and wild-type human tau (hTau40)-transfected human neuroblastoma (SH-SY5Y) cells were used to examine the effect of excess tau on BDNF expression. 8c-het mice over-express wild-type human tau on a heterozygous mouse tau background, and while they exhibit increased tau phosphorylation and altered tau isoform expression compared to wild-type mice, they do not develop neurofibrillary tangles. On the other hand, hTau mice, which over-express wild-type human tau on a null mouse tau background, exhibit neurofibrillary tangle-like pathology similar to that found in human Alzheimer's disease and tauopathies. BDNF expression was quantified by qRT-PCR in murine cortical tissue and in differentiated cells.

***Results:*** Both human tau over-expressing transgenic mouse models, as well as human neuroblastoma cells over-expressing wild-type human tau, significantly down-regulated BDNF mRNA compared to controls. Similarly, an established mouse model of amyloid-β over-expression, the APP23 mouse, was also found to significantly down-regulate BDNF expression. However, when crossed with tau knockout (TauKO) mice, the resulting APP23xTauKO animals exhibited BDNF levels that were not statistically different from wild-type mice.

***Conclusions:*** These results demonstrate that excess tau alone is capable of down-regulating BDNF and show that neither a mutation in tau nor the presence of neurofibrillary tangles is required for toxicity. Moreover, our findings suggest that tau is at least partially responsible for mediating amyloid-β-induced BDNF down-regulation.

## Design of the Sartan-AD Trial: a Randomized, Open Label, Proof of Concept Study of Telmisartan vs. Perindopril in Hypertensive Mild-Moderate Alzheimer's Disease Patients

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***Background:*** Over the last 20 years, epidemiological studies have consistently identified hypertension as a potent risk factor for heart attacks and stroke, but also for Alzheimer's disease (AD) (Skoog & Gustafson, 2006). Cross-sectionally, in normal elders, hypertension was associated with reduced cortical thickness on MRI in areas vulnerable to AD (Leritz, 2011). The Syst-Eur Study showed that treating hypertension prevented decline to dementia over four years (Forette, 1998, 2002), but other anti-hypertensive studies have been equivocal. Hypertension trials comparing angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (sartans) have generally not shown differences in emergent dementia, but sample sizes were insufficient to be definitive. Preclinical evidence provides a rationale to pursue such comparison. Centrally penetrating ACEIs stimulate cholinergic function (Tota, 2012; Yang, 2013) and have been linked to functional (O'Caoimh, 2014) and cognitive (Sink, 2009; Gao, 2013) benefits to AD patients, but since ACE catabolizes amyloid-beta (Aβ) 40-42, ACE inhibitors may accelerate amyloid deposition in AD (Kehoe & Passmore, 2012). Centrally-penetrating sartans, however, increase insulin degrading enzyme, which increases Aβ breakdown (Wang, 2007). They also facilitate long-term potentiation and memory (Ashby & Kehoe, 2013) and may have other neuroprotective effects. For example, telmisartan activates PPAR-γ and may improve neuronal glucose uptake (Wang, 2014; Saavedra, 2012). Recent studies suggested treatment with sartans versus other antihypertensive drug classes reduced emergent dementia in a veteran population (Li, 2012), and resulted in less premorbid cognitive decline and less AD pathology in an autopsy series (Hajjar, 2012). Hence a head-to-head trial of a centrally-acting ACEI and a centrally-acting sartan is warranted to determine comparative efficacy in slowing progression of AD.

***Objectives:*** 1) To conduct a proof-of-concept study comparing the efficacy and safety of an ACEI (perindopril) vs. a sartan (telmisartan) in reducing progression of brain atrophy (indexed by ventricular volume expansion on 3T MRI at 12 months), in hypertensive AD patients. Both drugs demonstrate equal cardiovascular protection and blood pressure control and are thought to be best in their class for CNS effects. 2) To compare treatment responsiveness of other cognitive (e.g., ADAS-Cog), neurobehavioural (e.g., NPI), functional and caregiver burden measures and multi-modal MRI measures.

***Study Design:*** 240 patients with probable AD (McKhann, 2011) and treated hypertension (age ≥ 55, MMSE 16–27, on a stable dose of a cholinesterase inhibitor and/or memantine for 3 months) will be recruited. Key exclusions include treatment with a sartan in the past 12 months, intolerance/contraindication to study medications or MRI, significant systemic or nervous system illness that could affect outcome measures and compliance. Patients will be randomized to telmisartan (40–80 mg/day) or perindopril (2–8 mg/day) and titrated appropriately, with protocols for adjustment to maintain target pressures. The study is open-label but rater-blinded for the primary outcome measure.

***Results:*** Results will include ventricular volume change at 1 year and cognitive, behavioural, functional, and caregiver measures (baseline, 6 and 12 months). Cortical thickness, microstructural integrity, and resting state functional MRI measures will also be analyzed. Positive results could have implications for clinical practice. (Funded by ADDF Canada and Weston Brain Institute.)

## Application of Spatially Targeted Optical Micro-Proteomics in Alzheimers and Related Dementias

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***Background:*** Fronto-temporal dementia (FTD) and amyotrophic lateral sclerosis (ALS) are neurodegenerative diseases caused by the progressive loss of cortical or motor neurons. Although clinically distinct, there is increasing evidence that these two diseases belong to a common disease spectrum, as they share clinical, neuropathological and genetic features. Since the majority of cases (90%) are without obvious genetic etiology, environmental components such as stress have long been suspected as a contributing factor in FTD/ALS pathogenesis. In response to environmental stress, cells form stress granules (SGs) which are cytoplasmic domains containing translationally arrested mRNAs. SG assembly and disassembly are dynamic processes mediated by a number of proteins. One of such proteins is TDP-43, an RNA binding

protein pathologically and genetically associated with FTD/ALS. The loss of SG regulation is predicted to yield cytoplasmic aggregates/inclusions reminiscent of what is observed in FTD/ALS neurons. How TDP-43 mutations impact the *in vivo* response to stress in neurons is disease-relevant and remains to be explored. We hypothesize that TDP-43 regulates SG composition and disease-causing mutations alter this process, rendering disease-relevant cell types more vulnerable to degeneration. We aim to define how endogenous TDP-43 and FTD/ALS-causing TDP-43 mutations impact the proteome and transcriptome of SG using a novel approach.

***Methods:*** Traditional proteomic methods cannot be used to determine SG composition due to difficulty in SG purification and their small size and transient nature. We will determine the proteomic and transcriptomic composition of SG using our method called spatially targeted optical microproteomics (STOMP). This technique allows us to directly label and isolate SG and elucidate their protein and RNA composition. In STOMP, the sample is first stained for a region of interest (ROI). It is then soaked in a solution of a benzophenone-linked hexahistidine peptide. Confocal images of the ROI are used to generate a mask to guide and target a 2-photon laser to specifically excite the benzophenone, covalently linking the hexahistidine peptide to proteins and RNAs in the ROI. The hexahistidine-linked compounds are then affinity purified and identified by mass spectrometry (MS) and RNA sequencing.

***Results:*** As proof-of-principle, we have used STOMP to determine the proteomic composition of amyloid plaques from brain sections of a transgenic mouse model of AD and a human case of severe AD. Thioflavin S was used to stain the ROI (amyloid plaques) and generate the mask and the MS results successfully identified proteins known to be in amyloid plaques, such as Aβ, along with several other proteins. To identify components of SG using STOMP, the mask is generated by subtracting a nuclear stain (7AAD) from the SG+Nuclear marker HuR. We have confirmed the successful labeling of SG proteins by the hexahistidine peptide using immunofluorescence. Samples have been submitted for MS analysis and pending results.

***Conclusions:*** The role of cellular stress signaling is an emerging concept in FTD/ALS research. Using our novel method, we will be able to determine SG compositional differences at both the protein and transcriptomic level in both transformed cell lines and in disease-relevant cell types responding to FTD/ALS-relevant stress-stimuli.

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**Assessing Neuropsychiatric Symptoms in Long-Term Care: Comparing the NPI-NH and CMAI Scales Across the Circadian Cycle**

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***Background:*** Tools that assess neuropsychiatric symptoms (NPS) in individuals with dementia are important in clinical research, and their validity is of paramount importance in evaluating clinical interventions. In the absence of a gold standard in NPS diagnosis, it is essential to evaluate construct validity across different tools designed to assess the same clinical reality. The Neuropsychiatric Inventory (NPI) and Cohen-Mansfield Agitation Inventory (CMAI) are two of the instruments widely used in clinical research for NPS evaluation; yet few studies have employed them simultaneously and compared their convergent/discriminant validity. Moreover, the construct validity of these two tools across the circadian cycle has not yet been assessed.

***Objectives:*** To investigate the agreement between the NPI nursing home version (NPI-NH) and CMAI in evaluating NPS among long-term care (LTC) residents with dementia across the circadian cycle.

***Method:*** NPS in 97 LTC residents with dementia, over a 2-week period, were assessed via interviews with nursing staff providing their care during day, evening and night shifts. Both the NPI-NH and the CMAI were used to assess NPS in the same resident. Of the 97 residents, 82 were evaluated by the nursing staff from the day shift, 72 by the evening and 84 by the night shift staff. We assessed the concordance between the two tools regarding NPS prevalence both overall and for specific CMAI factors (aggressive, physically nonaggressive, and verbally agitated behaviors) and NPI-NH symptom groups (psychotic, affective, hyperactive).

***Results:*** NPS prevalence was 69.5% (day), 70.8% (evening), and 44.0% (night) when assessed with the NPI-NH (considering the 10 symptoms common to both tools, excluding appetite and sleep disturbances), as compared with 52.4%, 61.1%, and 44.0%, respectively, when assessed by the CMAI. The overall concordance between the two tools was poor

during the day shift (kappa=0.25; total agreement 63.4%), and improved during evening (kappa=0.48; total agreement 76.4%) and night shifts (kappa=0.47; total agreement 73.8%). We observed significant associations between CMAI aggressive behaviors and NPI-NH hyperactive symptoms, as well as between verbally agitated behaviors and affective symptoms consistently in each shift. Also, CMAI aggressive behaviors were significantly associated with NPI-NH affective symptoms during the day and evening shifts and with psychotic symptoms only during the evening and night shifts. Verbal agitation was significantly associated with NPI-NH psychotic symptoms during the evening and night shifts, and with hyperactivity only during the day. CMAI physically nonaggressive behaviors presented a heterogeneous pattern across the circadian cycle: they were significantly associated with NPI-NH psychotic symptoms during the day, with all symptom categories in the evening and only with hyperactive symptoms at night.

***Conclusions:*** Our results indicate that NPI-NH and CMAI scales have acceptable convergent validity only when considering specific factors/symptom types, and that the time of day during which symptoms are evaluated may influence their agreement. These findings suggest that studies using these tools to measure outcomes of clinical interventions should consider specific neuropsychiatric symptoms or factors as measures of interest, and not the total scores of these scales.

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**Using the Path Model to Detect, Diagnose, and Direct Dementia Care**

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***Objective:*** Despite advances in diagnostic sensitivity, the prevalence of missed or delayed diagnoses of dementia remains high. In particular, symptoms of dementia often go unnoticed in frail older adults when more acute medical issues take priority during brief physician encounters. Nevertheless, recognition of dementia is important in acute care because it affects the risk-benefit trade of interventions and participation in decision-making. Routine evaluation of frailty stands to play a key role in identifying clinical vulnerability, including dementia. The Palliative and Therapeutic Harmonization (PATH) program provides a structured approach to evaluating frailty that helps to guide older adults facing complex medical and surgical decisions. Using an objective screen to measure and stage cognition, the PATH assessment model often identifies previously unrecognized cognitive impairment. This study examines the prevalence of undiagnosed dementia amongst the PATH population, the characteristics of the new diagnosis population, and the impact of the diagnosis on their subsequent decision-making and outcomes.

***Methods:*** Secondary analysis of a clinical database. PATH program patients undergo a standardized comprehensive geriatric assessment that incorporates validated cognitive and functional staging tools including the Mini-Mental State Exam (MMSE), the Brief Cognitive Rating Scale (BCRS), the Functional Assessment Staging Tool (FAST), and the Clinical Frailty Scale (CFS).

***Results:*** Data from the first 630 individuals completing the PATH program show that 57% of the total patients have a dementia diagnosis, and a further 19% were diagnosed during their PATH assessment. Of the undiagnosed population 56% were female; their mean age at diagnosis was 81.6 years, they had multiple comorbidities (mean = 8.5), and medications (mean = 9). Cognitive assessment found that the undiagnosed PATH population was frail (mean CFS 6.2) with mild–moderate impairment of memory and function (mean MMSE=20.3; mean BCRS= 4.2; mean FAST= 4.3). 61% were facing decisions regarding proposed medical or surgical procedures, while 14% were referred for advanced care planning. Of the 61% of patients facing decisions, 89% refused the proposed intervention based on the PATH team's recommendation (82% with the help of a substitute decision maker (SDM)). When outcomes were compared, 12.7% of undiagnosed patients opted to forego proposed interventions due to risks associated with their dementia, whereas only 1.6% of previously diagnosed patients did the same. Outcomes associated with undiagnosed PATH dementia patients include that 9.3% are alive and living with reduced symptoms, 10.1% are alive but significantly worse, 14.4% died from another unrelated health issue, and 0.8% died directly as a result of the central health issue.

***Conclusions:*** Our results found that overall there is a high degree of undiagnosed dementia amongst the patients referred to the PATH program. These findings have specific implications for promoting structured cognitive screening for frail older adults. Significantly, of the patients with new diagnoses facing decisions regarding proposed interventions, 82% had a change from directing their own medical care to having an SDM. When dementia is recognized, it often has a direct impact on the care plan. Further efforts are required to implement standardized dementia screening protocols for health-care teams serving this population.

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**The Psychological Impact of Adaptive Interaction Training on Nursing Staff in Advanced Dementia Care**

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***Background:*** Many people with very advanced dementia lose the ability to speak. This makes it very difficult for their needs

to be understood, but Adaptive Interaction (AI: Ellis & Astell, 2008) can equip caregivers with non-verbal communication skills to improve end of life interactions (Astell & Ellis, 2011). AI relies on the non-verbal fundamentals of communication including eye gaze, facial expressions, movement and vocalization. AI training permits caregivers to 'learn the language' of the people with dementia they care for to improve the quality of their interactions (Astell & Ellis, 2011).

***Objectives:*** This study examined the impact on nursing staff on a specialized geriatric dementia unit following AI Training, including staff self-reports of psychological empowerment, self-efficacy, and responses to clinical scenarios (vignettes).

***Methods:*** Six people with advanced dementia and six nursing staff were recruited from Ontario Shores' geriatric dementia unit (GDU). Each staff member was matched with one person with dementia for the duration of the training. Interactions between patient–staff dyads were video-recorded at baseline and four subsequent times and examined using Observer to compare interactions and patient's non-verbal communication repertoire during training.

***Results:*** Several changes in communication were seen. Following AI training, nursing staff reduced their reliance on verbal communication, sat more often in a face-to-face position, and engaged in more eye contact and touch when interacting with people with dementia. While most vocalizations were initiated by the staff prior to the training, as the training progressed, people with dementia were observed to initiate vocalizations and touch more often than in baseline interactions with their nurse. No change was found in self-efficacy or psychological empowerment. However, vignette analysis showed that, at the end of the training, the staff had a deeper understanding of non-verbal communication and strategies for communicating with non-verbal patients.
***Conclusions:*** Incorporation of AI training into psychiatric hospital care would provide caregivers the opportunity to learn how to recognize, interpret, and reciprocate non-verbal communication, supporting the development of therapeutic relationships with patients with minimal or no speech capacity.

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**Case Finding as a Recruitment Strategy for Subjective and Mild Cognitive Impairment Clinical Trials and Academic Studies**

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***Background:*** Clinical trials in mild to moderate Alzheimer's disease have failed to show a positive outcome to anti-amyloid therapies, including intravenous anti-amyloid therapies. Clinical trials testing the amyloid hypothesis are now designed to include those having mild cognitive impairment (MCI), subjective cognitive impairment (SCI), or participants with no cognitive complaints and positive amyloid bio-markers. People with early or no symptoms often have not discussed their memory concerns with their family physician and for that reason are not referred to specialists. This presents a recruitment challenge for these new clinical trials. For the last seven years, as a strategy for recruiting research participants with SCI or early MCI, we have used an approach that we call "case finding." Advertisements were posted during Alzheimer Awareness Month (January) and Senior's Awareness Month (June) for people 55 years and over who have memory concerns, are interested in research and have not had a stroke.

***Objectives:*** 1. To follow community members who are interested in research that have concerns about their memory and/or who may not normally have been referred to a memory clinic. 2. To evaluate the effectiveness of recruiting participants with cognitive concerns from this study population into clinical trials. 3. To perform a basic cost/benefit analysis of utilizing such a recruitment strategy

***Methods:*** Over the last 7 years a total of 238 people over 55 years responded to newspaper advertisements with self-reported memory concerns. Participants received cognitive screening tests using the standardized SMMSE, the MoCA, the 15-point GDS, the AD8, the Cornell Scale for Depression in Dementia, and the Lawton Brody Activities of Daily Living Scale. The test results were case conferenced with a geriatrician and a clinical suspicion of SCI, MCI, depressive symptoms, mixed picture, possible dementia or other was determined. All participants agreed for their test results to be sent to their family physician and follow-up offered.

***Results:*** Of the 238 participants, 93 returned for follow-up after one year, 61 after two years, 35 after 3 years, and 22 after 4 years. The most common clinical impressions of those seen were MCI (35.71%) and SCI (28.15%), the overall mean MoCA was 23.98 and the overall mean SMMSE was 27.62. Of the 238 participants seen at baseline in case finding, 36 have been recruited into a pharmaceutical clinical trial. When considering the cost to complete assessments in case finding, we have estimated that this cost would be covered within the study budget for 5 participants into pharmaceutical clinical trials over the 7 year period. Also, case finding has identified 22 participants who are anticipated to qualify for enrolment in the Comprehensive Assessment of Neurodegeneration and Dementia (COMPASS-ND) Study, part of the Canadian Consortium on Neurodegeneration and Aging.

***Conclusion:*** 1. The case finding method has been demonstrated to be an effective strategy for recruiting participants with MCI/SCI into clinical trials and academic studies. 2. Case finding is a cost effective strategy with the human resource needs covered by a small number of participants recruited into clinical trials.

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**Lysosomal Transport of APP by Macropinocytosis Is a New Pharmacological Target for Alzheimer's Disease**

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***Background:*** Alzheimer's disease (AD) is characterized by the deposition of Beta-Amyloid (Aβ) peptides in the brain. Aβ is produced by cleavage of the Amyloid Precursor Protein (APP) by beta- and gamma- secretase enzymes, and these cleavages are well documented to occur after APP is internalized from the cell surface. While most studies assume that the main pathway for APP is classical endocytosis to early endosomes, this has not been directly proven. We have found that APP and gamma-secretase proteins and activity are highly enriched in the lysosome, suggesting that this compartment could participate in the production of beta amyloid. We have recently demonstrated, in primary cultured mouse neurons and neuronal cell lines that, in addition to its well known classical internalization to early endosomes, APP can be internalized directly from the cell surface to lysosomes in a process called macropinocytosis. This transport is dependent upon the regulatory GTPase Arf6, and reduction of Arf6 activity significantly reduces both the transport of APP to lysosomes and Abeta production. While macropinocytosis is well described in immune cells, it is almost unheard of in neurons. RhoA and Rac1 are two regulatory GTPases that regulate actin cytoskeleton organization in macropinocytosis. Furthermore, RhoA and Rac1 have known pharmacological inhbitors, and have been implicated in Abeta production. The purpose of this study is to examine the function of Rac1 and RhoA in APP trafficking to lysosomes.

***Methods:*** To follow APP trafficking from the cell surface, neuronal N2A cells were transfected with APP constructs tagged with an N-terminal (extracellular) HA epitope tag, which allows for easy labeling of APP when it is at the cell surface. Intracellular compartments were identified by transfection with the marker proteins rab5 (early endosomes) and LAMP1 (lysosomes) fused to red fluorescent protein. Cells were treated with the Rac1 inhibitor EHT 1864, the RhoA/ROCKII inhibitor SR 3677, or control media containing DMSO alone. As a control, we also knocked down Rac1 and RhoA using small inhibitory RNAs (siRNA). To follow APP internalization, cells were put on ice for 30 minutes and cell surface APP was labeled with Alexa Fluor 633 fluorescent-labeled anti-HA antibody. Cells were then allowed to internalize at 37°, fixed, and imaged by confocal microscopy on a Zeiss LSM510 laser scanning confocal microscope. The colocalization of internalized APP and the compartment markers was quantitated using Imaris software (Bitplane). Beta-amyloid production was assessed by ELISA.

***Results:*** Here, we demonstrate that both EHT1864, and SR 3677 significantly reduced APP internalization to lysosomes by macropinocytosis, but these agents have no effect on classical endocytosis to endosomes. In addition, siRNA knockdown also reduces APP transport to lysosomes. Inhibition of Rac1 and RhoA also reduced production of Abeta 40 and 42 by half or more.

***Conclusions:*** We demonstrate that pharmacological inhibitors to RhoA and Rac1 can reduce the macropinocytosis of APP to lysosomes, and dramatically reduce Abeta production. This demonstrates that macropinocytosis of APP to lysosomes is a new potential therapeutic target for AD.

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**Predicting Medical Driving Assessment Outcomes in Seniors Using the KSCAdrive: an In-Office Screening Tool To Assist Clinicians in Deciding Whom To Refer for Driving Assessment**

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***Background:*** The issue of driving and the elderly is one that continues to receive attention in the research community and in the media. While driving is obviously a mode of transportation, it is often critical in remote areas and also offers independence and maximum flexibility for the driver. Dementia poses a particular risk for continued driving safety amongst seniors. It is estimated that by 2030 there will be nearly 100 000 licensed Ontario drivers who have developed a dementia (Hopkins R, et al., 2004). The responsibility to make a judgment about driving safety most often falls to the family physician or, if unclear, to then send the patient for a medical driving assessment at a cost of between $600–$1000 that is borne by the patient. The experience is stressful for many patients and often presents a considerable financial burden. That the CMA Determining Medical Fitness to Operate Motor Vehicles (8th Edition) guidelines recommend reassessment of driving safety every 6 months, once a dementia has been diagnosed, could mean several such driving assessments for a given individual. Typical in-office driving screens have had limited success with a "gold standard" tool yet to be identified.

***Objectives:*** The current study examines the utility of the Kingston Standardized Cognitive Assessment – revised

(KSCAr) ((Hopkins R, et al., 2004) to help identify those seniors who are in the "grey zone" of driving safety. This work builds on a pilot study looking at retrospective data examining cognitive patterns of patients referred for medical driving assessment (Kilik L & Dey A, 2011).

***Methods:*** In the present study, 29 individuals from London and Kingston with a diagnosis of MCI or dementia who had been referred for a driving assessment consented to participate in a study where they were given the KSCAr as part of a cognitive screening battery and also completed the DRIVEABLE medical driving assessment.

***Results:*** An 8-subtest sub-set of the KSCAr (KSCAdrive) was extracted from the full KSCAr that correctly predicted road test outcomes in 79.3% of cases. Suggested scores for "likely PASS", "likely FAIL" and "Recommend Medical Driving Assessment" decisions are offered.

***Conclusions:*** The KSCAdrive is offered as a promising tool to assist primary physicians and other clinicians in determining who should be sent for medical driving assessment.

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**White Matter Tract Integrity of the Default Mode Network in Alzheimer's Disease with Small Vessel Disease Burden**

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***Background:*** Subcortical white matter hyperintensities (WMH) on MRI are commonly observed biomarkers of cerebral small vessel disease (SVD) burden. WMH are common in Alzheimer`s disease (AD), and are considered an indicator of comorbid vasculopathy in AD. Decreased connectivity in the default mode network (DMN), the regions active when the brain is in an awake resting state, has been linked with increased cognitive impairment in AD. To our knowledge, the involvement of WMH on white matter tracts within the DMN network has yet to be explored.

***Purpose:*** To examine how changes in microstructural integrity in the white matter tracts of the DMN could be related to the co-existence of increased vascular burden in AD.

***Methods:*** AD participants (n=70) with diffusion tensor imaging (DTI) were dichotomized into AD high SVD (WMH: 3.5–5.6 cc, n=34) and AD low SVD (WMH: 0–3.5 cc, n=36) groups based on the median value of global WMH in this sample. Tract-Based Spatial Statistics (TBSS) was then used to compare fractional anisotropy (FA) between the two groups. Tracts were visualized with the John Hopkins University White-Matter Tractography Atlas as part of FSLView 4.0.1.

***Results:*** The FA of AD low SVD was significantly higher than the AD high SVD patients bilaterally in the cingulum tract, superior longitudinal fasciculus, inferior longitudinal fasciculus, anterior thalamic radiation, and inferior thalamic radiation ($p<.5$). FA was not significantly different between the two groups bilaterally for the corticospinal tracts, forceps major, and forceps minor.

***Discussion:*** The cingulum tract connecting the precuneus, posterior cingulate cortex and medial frontal cortex is important for DMN connectivity. Our findings indicating that high WMH volume was related to decreased white matter integrity, particularly in the cingulum tract, suggests that high WMH burden may be compromising microstructural integrity of tracts within the DMN. Future work will examine genotype (APOE), cognitive function, and other vascular risk factors to further understand these relationships. These findings suggest that WMH may need to be taken into account when assessing the DMN network connectivity of AD patient.

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**Study Design for Medical Imaging Trials Network of Canada (MITNEC) - Project C6—Amyloid and Glucose PET Imaging in Alzheimer and Vascular Cognitive Impairment Patients with Significant White Matter Disease**

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***Background:*** Alzheimer's Disease (AD) and stroke are major causes of dementia, and their prevalence doubles each decade over 65. The annual cost of dementia in Canada ($15B) is expected to increase to $150B annually, as dementia cases double to more than 1 million within a generation. Additionally, in population studies of persons over 65, "covert" cerebral small vessel disease (SVD) appears on MRI as silent lacunar infarcts in 25%, as microbleeds in 10%, and as focal or diffuse 'incidental' white

matter disease (WMD) in 95%. SVD is more common in dementia and stroke. It can manifest as periventricular white matter hyperintensities (pvWMH), can be extensive in 20% of the elderly, and resembles vasogenic edema. SVD independently contributes to cognitive decline and progression to dementia in the elderly. Most PET studies of amyloid have focused on subjects without significant WMH. Longitudinal amyloid PET imaging, however, opens a new avenue to understand the additive/interactive effects of SVD and AD. We hypothesize that collagenosis of the deep medullary veins can lead to difficulty clearing amyloid, contributing to the relentless pathological cascade of degeneration over time.

***Methods:*** The study design includes recruitment of two cohorts from 12 sites across Canada, including 75 mild cognitive impairment (MCI) and/or early AD subjects from memory clinics and 75 subjects with strokes/TIA from stroke prevention clinics. Inclusion criteria are the presence of moderate/extensive WMD, specifically Fazekas score of > 2 (with confluent pvWMH), as determined by previous MR or CT, ≥ 60 years of age, Mini-Mental State Exam scores ≥ 20. Subjects will undergo 3T MRI (including T1, PD/T2, FLAIR, GRE (or SWI when available), DTI, ASL, and resting state fMRI), $^{18}$F-FDG PET, $^{18}$F-florbetapir amyloid PET, cognitive testing, and blood sampling for ApoE ε4 analysis. Repeat MR and PET imaging and cognitive testing will be conducted at 24 months. The imaging protocols closely parallel the Alzheimer's Disease Neuroimaging Initiative (ADNI), permitting access to age and education matched comparisons to elders, MCI and AD subjects with minimal WMH. Recruitment is underway with several sites coming on-board in September-October 2015. Baseline recruitment is expected to be completed by April 2016.

***Hypotheses and Discussion:*** The primary objectives are to compare subjects with significant pvWMH at baseline and 2-year follow-up on uptake $^{18}$F-florbetapir, $^{18}$F-FDG, regional volumetric measures from MRI, and standardized cognitive testing. Specific hypotheses are that patients with high pvWMH volumes will show greater increase in amyloid deposition over two years, after accounting for appropriate covariates (e.g., baseline scores, age, education, ApoE-ε4 status), as well as decreased executive function, speed of processing, and instrumental ADLs. Greater cortical thinning and glucose hypometabolism in the signature areas of AD are also expected. 60%–85% of AD/MCI subjects are predicted to have "positive" amyloid scan (Am+), while only 20%–40% of stroke/TIA subjects will be Am+. Further subgroup analysis will aim to compare and contrast Am+ and Am- subjects from each cohort, as well as the ADNI subjects. This data will provide new insight into the role of pvWMH in amyloid accumulation.

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**Design and Implementation of a Collaborative Health Research Informatics System for Specialized Ambulatory Geriatric Care**

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***Background:*** In the fall of 2012, the Division of Geriatric Medicine at Western University in London Ontario and the Cognitive Clinical Trials Group at the Lawson Health Research Institute began the development of a longitudinal clinical research registry system for a specialized ambulatory geriatric cognition clinic.

***Methods:*** Through the use of different open source development platforms, as well as usability engineering techniques, the Collaborative Health Research Informatics System (CHRIS) was designed and implemented as a Masters in Health Informatics research project.

***Results:*** CHRIS uses an open approach to bridge the gap between clinical care and clinical research, fostering cooperation, and reducing compartmentalization. CHIS allows for the automatic generation of clinical dictations and visit summaries; visualization of clinical data at the point of care; data to be auto-completed and auto-saved; data to be extensively validated; and its system use to be tracked though an enhanced audit trail. Although CHRIS functions very much like a clinical documentation system, its primary focus is to allow for all clinical data to be used for clinical research.

***Conclusion:*** As the Canadian population is quickly ageing, the use of CHRIS could have many positive implications including greater access to medical information, greater practice efficiency, easier identification of patients for clinical trials, and advanced facilitation of longitudinal investigator initiated clinical research through the process of providing regular clinical care.

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**Venous Collagenosis: a Pathological Correlate of White Matter Hyperintensities**

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***Background:*** White matter hyperintensities (WMH) are biomarkers for small vessel disease and are prevalent on imaging

of the elderly and Alzheimer's (AD) patients. A review of imaging suggests that as WMH become larger and confluent, periventricular infarcts (PVIs) may form. Previous pathological correlates of WMH include activated microglia and clasmatodendrosis. However the exact pathogenic mechanism underlying WMH remains unclear. Although an association exists between WMH and cerebrovascular disease suggesting arteriolar pathology, previous findings of collagen in the deep medullary veins of elderly autopsy brains suggests that the veins may contribute to WMH pathogenesis.

***Purpose:*** To investigate the potential role of venous collagenosis in periventricular veins of all calibre in a WMH and PVI cohort.

***Methods:*** AD subjects were part of the longitudinal Sunnybrook Dementia Study which provided pre-mortem neuroimaging and formalin-fixed coronally sectioned archived brain tissue. The WMH cohort consisted of AD patients (n=22) with a mixed severity of WMH on imaging and controls (n=18) obtained from chart review with no neurodegenerative conditions present at autopsy. The Fazekas scale was used rate the WMH severity on imaging at 3 severity levels for each subject. Coronal WM blocks were sampled from the same 3 anatomic levels. Tissue blocks were paraffin embedded, cut into thin sections and stained with H&E/LFB and Gomori trichrome. The severity of venous collagenosis was quantitatively assessed in large veins (% stenosis) using trichrome staining and semi-qualitatively assessed in small and medium calibre veins according to a previously established method. Based on a review of imaging, 6 subjects with 12 PVIs were identified. In the PVI cohort (n=12), T1-weighted MR images were used to anatomically localize the PVIs in the formalin-fixed tissue. Tissue blocks were paraffin embedded and cut into 5Î¼ thin sections and stained with H&E/LFB, Masson's trichrome and immunohistochemistry for GFAP, CD68, and neurofilament. The presence and severity of venous collagenosis was assessed in a similar manner.

***Results:*** Collagen in the periventricular veins of all calibre was a common finding in the WMH cohort. On average, large veins had a 19.8% stenosis. WMH scores were significantly correlated with periventricular white matter pallor (rs(116)=0.252, *p*=.006), collagenosis scores of both small and medium calibre veins (rs(114)=0.268, *p*=.004, rs(114)=0.266, *p*=.004) and % laVS (rs(112)=0.377, *p*=.000). A multiple linear regression model revealed that percent stenosis in large veins was the strongest predictor of WMH (β=0.330, df=108, *p*=.000, with Bonferroni correction). Histological results in the PVI cohort revealed 3 infarcts, 4 dilated perivascular spaces, and 5 histological undetectable lesions. Small and large vein stenosis (> 30%) were common findings for histologically confirmed infarcts.

***Conclusion:*** Venous collagenosis of periventricular veins of all calibres may play a role in the pathogenesis of WMH, and may lead to venous infarction. Further study of this process is warranted and could be facilitated if venous collagenosis was rated in standard neuropathological exams, especially for subjects known to have significant WMH.

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**Personalized Games for People with Dementia**

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Many people living with dementia are under-stimulated and socially isolated. While there has been an increase in activities and programming based on occupational therapy, recreational therapy, music therapy, physiotherapy, and so on, such programs can cover only a fraction of the day for people with dementia. The result is that many people with dementia who are institutionalized are staying most of the day either in their rooms or wandering the hallways. A related problem is that people with dementia often have difficulty with social interactions and may become anxious or aggressive around people they don't recognize, or in situations they don't understand. Resulting behavioral disturbances may lead to over-medication and poor quality of life. Our goal is to reduce front-line caregiver distress by substituting disturbing behaviours and purposelessness with active and meaningful activities, distractions, and appropriate interventions. We are designing activities that provide physical, cognitive, and social stimulation, engaging and utilizing the strengths of residents with dementia with respect to current functioning, past interests, and current needs. We refer to these activities as ambient augmentation because they are ambient (available in the environment for easy access) and because they are designed to augment existing programming and activities by providing self-accessed and engaging interactions that may be used at any time. The overall goal of ambient augmentation in this case is to promote a 'state of calm' or 'well-being' in the resident. In the first generation of ambient augmentation activities (AAAs) that we have developed, there has been an emphasis on physical tasks such sorting objects by colour, or discovering objects by rotating a wheel to move sets of beads that are occluding photographs. We are currently implementing a second generation of AAAs that use interactions with screens and software to create more flexible interactions that can be personalized to meet the specific properties of each person. The first of these second generation AAAs is a whacamole task that we originally developed as a cognitive assessment tool for use in hospitals. Our research (Tong et al., 2015) demonstrates that cognitive assessment based on the Whacamole game delivered on a Tablet in an emergency setting is feasible, and that game performance correlates well with scores on standard assessments. We have found that patients in their seventies and eighties enjoy playing the

game in an emergency room setting. We are now adapting the game so that it retains its ability to assess cognitive status while also providing increased entertainment possibilities, and usability, for people with Alzheimer's. In this paper we present the results of the game with respect to its usability for elderly populations and its validity as a measure of cognitive status. We will also describe how the game is being redesigned and extended so as to create an effective AAA for people living with dementia.

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**Associations Between Sex and Perivascular Space Volumes in the Sunnybrook Dementia Study**

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***Introduction:*** Perivascular spaces are the channels that surround the brain's vasculature and are conduits for cerebrospinal and interstitial fluid, allowing for quick fluid transport within the parenchyma and likely playing an important role in toxic solute clearance. Enlarged perivascular spaces (PVS), visible on MRI, are more common with aging and neurodegenerative disorders such as Alzheimer's disease (AD) and vascular cognitive impairment (VCI). Several studies have found that men tend to have greater severity of PVS relative to women, although there are no theories to explain this recurring difference. The purpose of this study is to be the first to examine PVS sex differences in a large sample of various dementia subtypes.

***Methods:*** In this study we examined patients diagnosed with AD (N=270), VCI (N=89), frontotemporal dementia (FTD; N=110), dementia with Lewy bodies (DLB; N=74), and normal controls (NC; N=107). PVS were measured using a modified version of Lesion Explorer. PVS were segmented into basal ganglia (BG-PVS) and white matter (WM-PVS) semi-automatically using SABRE, followed by manual editing. The BG segmentation included: the caudate nucleus, lentiform nucleus, thalamus, internal capsule, and the substantia innominata. Sex/diagnosis interactions were examined using a Bonferroni corrected MANCOVA, examining regional PVS volumes, covarying for age, years of education (YOE), Mini-Mental State Examination (MMSE), total intracranial capacity (TIC), brain parenchymal fraction (BPF), white matter hyperintensity (WMH) volume, and stroke volume. Significant results were further analyzed with post hoc *t*-tests.

***Results/Discussion:*** Across the three PVS variables, MANCOVA revealed that PVS volumes are significantly associated with age ($F(3, 611)=5.01$, $p=.002$) and WMH ($F(3, 611)=13.02$, $p<.001$), both of which have been demonstrated in the literature. Sex alone was not significantly associated with PVS. However, the interaction of sex with diagnosis (sex*Dx) was significant ($F(24, 1839)=2.34$, $p<.001$), suggesting that diagnostic group appears to be an important modulating variable. Furthermore sex*age ($F(3, 611)=3.01$, $p=.028$) and sex*WMH ($F(3, 611)=3.22$, $p=.22$) were also significantly associated with PVS, indicating that sex may also be influencing the known relationships between aging/small vessel disease and PVS. Post hoc *t*-tests comparing men and women reveal significant differences for AD (total PVS, $p<.001$; WM-PVS, $p=.001$, BG-PVS, $p=.002$) and NC (total PVS, $p<.001$; WM-PVS, $p=.004$, BG-PVS, $p=.011$), with trending results for DLB (BG-PVS, $p=.053$).

***Conclusion:*** Men appear to be at a greater risk of PVS in AD, NC, and possibly DLB, potentially suggesting that mechanisms that increase perivascular enlargement (e.g., blockage or inflammation) may be operating more strongly in men. No sex differences were found for VCI and FTD, possibly due to greater PVS volumes in women relative to other diagnoses. Although interpretation is limited by uncertainty surrounding the mechanisms causing PVS enlargement, these findings underscore the importance of gender stratification in future PVS research.

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**Mindfulness-Based Cognitive Therapy for Depression Symptoms in Older Adults with Memory Difficulties and Caregivers of Family Members with Dementia**

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***Background/Objectives:*** Depression symptoms are common for older adults in the early stages of dementia and for family caregivers. Mindfulness-Based Cognitive Therapy (MBCT) reduces the risk of relapse in recurrent depression and also improves depression symptoms in various populations. Some MBCT studies provide evidence to suggest that improvements in mindfulness skills and self-compassion are related to reductions in depression. The main objective of the present study was to examine changes in depression symptoms, as well as associated changes in mindfulness facets, pre- to post-MBCT for both older adults experiencing memory difficulties and caregivers of family members with dementia.

***Methods/Overview:*** Two separate groups were recruited from the community to participate in the randomized controlled trial (RCT): older adults with self-reported memory difficulties (seniors) and family members caring for a loved one with dementia (caregivers). To be included in the study, seniors had to score 19–25 on the Montreal Cognitive Assessment and caregivers had to score > 26. A total of 36 participants were assessed for eligibility and 19 completed the study. Participants were randomized into either the MBCT intervention arm, one group for seniors (n=5) and one group for

caregivers (n=5), or the waitlist control arm (4 seniors and 5 caregivers). All participants completed the following battery of questionnaires before and after the intervention and waitlist period: Geriatric Depression Scale (GDS), Depression, Anxiety, and Stress Scale (DASS21), Five Facet Mindfulness Questionnaire (FFMQ), and the Self-Compassion Scale (SCS). An analysis of covariance was used with change score as the dependent variable, the pre-intervention score as the covariate, and group (senior or caregiver) as the independent variable. Planned correlations on outcome measures were also conducted for all seniors (n=8) and caregivers (n=7) who partook in the MBCT intervention, including crossover controls.

***Results:*** Compared to respective waitlist control groups, there were no changes on any of the outcome measures for the senior or caregiver groups pre- to post-MBCT. For all participants who completed the MBCT intervention (seniors and caregivers; n=15), an increase in scores on the non-judging facet of the FFMQ were associated with a reduction in depression symptom scores on the GDS, r(14)=-.785, $p$=.001. Also, an increase in self-compassion scores on the SCS were associated with a reduction in depression symptoms scores on the GDS, r(14)=-.558, $p$=.031.

***Conclusions:*** Learning to view ones' inner experience non-judgmentally is a core skill taught in MBCT. Results from this study indicate that the ability to be non-judgmental and to be self-compassionate correspond with improvements in depression symptoms in seniors with memory difficulties and caregivers of family members with dementia. These findings are in line with research suggesting that improvements in mindfulness skills and self-compassion may be mechanisms underlying the reduced risk of relapse in people with recurrent depression. This pilot study could inform future RCTs designed to examine the effects of mindfulness training for depression symptoms in these populations.

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**Characterizing Sundowning Syndrome in Long-Term Care Residents with Dementia: the Role of Multiple Concurrent Neuropsychiatric Symptoms**

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***Background:*** Neuropsychiatric symptoms (NPS) are behavioural and non-cognitive expressions of dementia that are highly prevalent among residents in long-term care (LTC), increasing costs and burden of care for this vulnerable population. ''Sundowning syndrome'' is a poorly defined phenomenon that is generally characterized by the emergence or exacerbation of NPS in the late afternoon, evening or at night.

***Objective:*** To characterize the change in NPS experienced by LTC residents with dementia during the evening compared with during the day, as evaluated by front-line nursing staff who work during the day and evening shifts.

***Methods:*** As part of a larger study examining NPS prevalence and incidence, we assessed frequency and severity of symptoms in LTC residents using the Neuropsychiatric Inventory Nursing Home Version (NPI-NH) and the Cohen-Mansfield Agitation Inventory (CMAI) during the day (07:00–15:00) and evening (15:00–23:00). Individual symptoms were grouped as affective symptoms (dysphoria, anxiety, apathy), psychosis (delusions, hallucinations), hyperactivity (irritability, aggression, disinhibition), euphoria, and other symptoms (appetite, sleep, aberrant motor behaviour). Associations between resident clinical and demographic characteristics and changes in NPS during the evening were assessed.

***Results:*** A total of 97 residents were evaluated: 65 for whom evaluations were obtained during both the day and evening. The overall institutional prevalence of residents with any NPS did not increase significantly (64.6% day vs. 72.3% evening, $p$=.16). Within residents, however, an increase in both the number of individual symptoms (46.2% , $p$=.08) and symptom groups (50.8%, $p$<.01) during the evening (vs. day) was observed. Among residents who were symptom-free during the day, 74% developed symptoms during the evening ($p$=.02). Residents who experienced at least 2 symptoms during the day were at higher risk of experiencing more than 4 symptoms during the evening ($p$=.04). Symptom groups which were more predominant during the evening included hyperactive (34%), psychotic (14%), and other (30%) symptoms. Residents who developed psychotic behaviours in the evening were significantly more likely to also develop hyperactive symptoms in general (OR: 7.83; 95% CI: 1.6–38.2), or specifically to become aggressive during the evening (OR: 4.70; 95% CI: 1.0–22.0), but no significant association was found between evening psychotic symptoms and change in affective symptoms (OR: 2.03; 95% CI: 0.4–9.7). Increase in psychotic symptoms during the evening was associated with the Charlson Comorbidity Score (OR: 1.72; 95% CI: 1.1–2.7), but not with age, sex, Geriatric Comorbidity Score, or with

either current or ever use (since admission) of antipsychotics, antidepressants, or cholinesterase inhibitors.

***Conclusions:*** Although there exists much debate regarding how to define sundowning syndrome, our study has demonstrated an increase in either developing NPS or in experiencing multiple concurrent NPS, with psychotic and hyperactive symptoms likely to emerge concurrently during the evening. These findings should be verified in a larger cohort of LTC residents with dementia with an emphasis on identifying modifiable risk factors for sundowning in order to determine the most effective strategies for prevention.

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**Impact of the 'Artful Moments' Intervention on Persons with Dementia and Their Informal Caregivers**

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***Background:*** Engaging in creative activities has been shown to provide therapeutic benefits by relieving stress, improving creativity and increasing resilience. For persons with moderate to severe dementia, this can be a valuable intervention as the brain becomes increasingly affected over time. However, researchers believe that an individual can still experience the drive to be creative as a brain is being progressively affected by dementia. 'Artful Moments' is a collaborative project undertaken by the Art Gallery of Hamilton and St. Peter's Hospital in Hamilton that sought to develop and implement a program of arts-based activities for persons with moderate to severe dementia and their informal caregivers. Creative activities, such as art, are not only therapeutic to the person engaging in them, they are social activities that strengthen social ties among all members that participate, including family caregivers. In this study, we investigate whether the Artful Moments program facilitated positive engagement in the moment for persons with moderate to severe dementia. We also assess the impact on their informal caregivers.

***Methods:*** A qualitative descriptive design and purposive sampling were used in this study. The study population consisted of older adults with a diagnosis of moderate to severe dementia who are in-patients on the Behavioural Health Program (BHP) at St. Peter's Hospital, Hamilton. Participants were observed during multiple art sessions to evaluate their level of engagement in the program. In addition, informal caregivers completed a questionnaire at the end of each session describing their experience. Qualitative content analysis was used to identify themes related to positive engagement of persons with dementia in art activities, as well as the experiences of their family caregivers.

***Results:*** For persons with dementia, factors that promote continued interest and engagement in art include: caregiver involvement, group activities, opportunities to share opinions, validation of their personhood, and increased engagement over time. Informal caregivers cherished working together with their family members to participate in art and enjoyed seeing the creative side of their loved ones. They reported that Artful Moments enhanced communication with their family members and viewed the experience as an opportunity for building meaningful relationships with other program participants. Further, family caregivers reported that the program helped them to focus on accomplishing a task with their loved ones. They also reported experiencing reduced burden as a result of their participation in the program.

***Conclusions:*** Artful Moments promoted positive experiences in the moment for both persons with dementia and their informal caregivers. Overall, participating in art activities allows informal caregivers to shift their focus to the positive aspects of caregiving, such as the satisfaction gained in seeing their loved ones find renewed interest and joy in an activity.

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**The Cognitive Marker of Alzheimer's Disease**

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A comprehensive approach to the prevention of AD warrants a synergy across multiple domains and procedures. Whereas the study of biomarkers has mobilized major activity in the field, the development of cognitive markers is largely ignored despite their unique advantages. Cognitive markers are temporally distant predictors of illness present in the preclinical stage, resulting in detection of abnormal cognitive decline before diagnosis or even psychosocial impairment. The cost-effective implementation of cognitive markers makes them conducive as gatekeepers for more invasive, labor-intensive, and expensive procedures. In addition, since AD's prodromal phase produces subtle cognitive changes years and even decades before detection, the effective assessment of cognitive markers in midlife may assist preventive health care by bringing awareness of risks and, consequently, motivation for making lifestyle changes, and provide opportunities for early pharmacological intervention. This presentation addresses the theoretical, methodological, statistical, and pragmatic aspects of this prospect. From a theoretical perspective, the development of a cognitive marker for AD requires a shift in the neuropsychological paradigm—from detecting impairment to detecting abnormal changes in the absence of impairment. This conceptual change in practice presents several methodological challenges. For example, a new unit of measurement is introduced reflecting the magnitude of change, or observing difference among multiple scores

instead of a single score. Under the conventional model, measurement outcome is interpreted within the context of a normative sample, but the preventive model also detects abnormal decline intra-individually with the difference between the observed Δ and the mean score of an empirical Δ. The preventive screen needs to demonstrate high sensitivity to small departures from normal aging; however, the subtle decline in cognitive functioning over years would result in low power due to an unfavorable signal to noise ratio. One solution might be to increase the sample size of observations by anchoring the inception of screening in midlife, deeply within the pre-morbid period. Such implementation could occur during annual physical exams with an appropriately brief and self-administered computerized screen. Other strategies to be discussed include the use of modern statistical and other quantitative methods. Unlike the proposed model, conventional screens like the MMSE or MoCa determine impairment with cutoff scores lacking gradation of difficulty. This creates a significant ceiling effect resulting in undifferentiated performance across age groups, exceptionally low variance, and a high likelihood of failure to diagnose milder forms of dementia. For example, the MMSE misses approximately 80% of patients with MCI (Fox et al., 2014). In comparison, preventive screening offers cognitive challenges that assess maximal abilities with many alternative versions for repeated measurement. In doing so, abnormal decline is detected well before it would typically be considered clinically relevant from conventional screening. Cognitive markers can assess for pre-morbid though abnormal decline, and increase the awareness of risk in a manner that motivates health related behaviors. In this regard, the cognitive marker may play a major role in offsetting the epidemiological trajectory of AD through flagging risk early enough for alterations of lifestyle factors of midlife and providing an early window for intervention.

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**Preliminary Results from the Tapestry Caregiver Study**

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***Background:*** Health TAPESTRY (Teams Advancing Patient Experience: Strengthening Quality) is a primary health-care and research program that aims to foster optimal aging for at-risk older adults living at home. The study uses an interprofessional primary health care team delivery approach that centres on meeting a person's health goals with the support of trained community volunteers, system navigation, community engagement, and use of technology. An ongoing randomized control trial (RCT) is testing the effectiveness of the Health TAPESTRY approach. The burden of caregiving is increasingly recognized as having an impact on health and overall quality of life. As a sub-study of the Health TAPESTRY RCT, the TAP caring study aims to determine the impact of the TAPESTRY approach on the level of caregiver burden of TAPESTRY clients who self-identify as caregivers compared to those not receiving the TAPESTRY intervention.

***Methods:*** This is a sub-study of a design delay RCT with controls receiving the intervention after 6 months. Participants are age 70 years or older living at home and who self-identify as primary informal caregiver within the main RCT. They are from one of two sites of the McMaster Family Health Team. Participants in the intervention group received a visit with a pair of trained community volunteers who collected data on health goals, physical function, nutrition status, social connectedness, and other aspects of health, and facilitated use of a personal health record. Data were automatically collated into an electronic medical record that was sent to health-care teams who discussed the data at a team huddle and developed a care plan. Data collected included: caregiver burden (Zarit Burden Interview), Quality of life (EuroQOL five), social support (Duke Social Support Index), and demographics. Qualitative interviews were conducted to learn about the context of caregiving.

***Results:*** Of the 295 TAPESTRY patients who have completed the caregiver survey, 29% consider themselves as caregiver. Of these, 61% are female. They range in age from 70 to 95. Of those that are caregivers, 18% scored high with high caregiver burden. 60% of those scoring with high caregiver burden are female. Qualitative interview data identified that some caregivers in TAPESTRY experienced burden or stress when caring for their loved ones.

***Conclusions:*** There was evidence (both quantitative and qualitative) for the existence of caregiver burden among TAPESTRY participants who self-identified as primary informal caregivers. The ongoing TAP caring study can help identify factors contributing to high levels of burden among caregivers in primary care.

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**The TgCRND8 Mouse Model of Alzheimer's Disease Exhibits Sexual Dimorphisms in Behavioral Indices of Cognitive Reserve**

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Cognitive decline is sexually dimorphic in Alzheimer's disease (AD); however, it remains unclear why women phenoconvert more rapidly than men. Men are hypothesized to maintain greater brain and cognitive reserves than women despite comparable amyloid-β pathology. Currently, there is

no amyloid-β precursor protein transgenic mouse model that robustly recapitulates this phenotype without also exhibiting sex differences in amyloid-β deposition. Here, we report that, when TgCRND8 mice are placed on a C57Bl/6 background, both sexes exhibit equivalent aggressive increases in amyloid-β plaque number, yet the severity of behavioral impairment in the Morris Water Maze is greater in females than males. At 5.5 months of age, N4 and N5 TgCRND8 females show marked reductions in behavioral flexibility. They fail to overcome amyloid-β-associated stereotypic behaviors (i.e., hyperactive tight circling) and cannot efficiently adopt the alternative navigational search strategies required for spatial learning. By contrast, N4 and N5 TgCRND8 males show significantly higher behavioral indices of cognitive reserve. They can compensate for the same amyloid-β-associated stereotypy by switching between increasingly productive systemic and spatial search strategies until they effectively transition from systemic to spatial navigation trajectories indicative of spatial learning and memory. Together, these data identify a novel murine model that can be used for preclinical testing of interventions targeting sexual dimorphisms in cognitive reserve associated with risk of AD phenoconversion.

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**Parieto-Occipital Periventricular Hyperintensities Are Associated with Amyloid Accumulation**

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***Objectives:*** We sought to investigate the association between peri-ventricular white mater hyper-intensities (PVWMH) and biomarkers of cerebral amyloid-β (Aβ) accumulation in the Alzheimer Disease Neuroimaging Initiative, a large prospective multi-center observational study.

***Methods:*** Burden of frontal, parietal, and occipital PVWMH on 3T FLAIR MRI were evaluated in 435 mild cognitive impairment cases using novel semi-quantitative visual rating scales. Results were correlated with CSF-Aβ, florbetapir-PET, and fluorodeoxygluose (FDG)-PET.

***Results:*** Increasing burden of parietal and occipital, but not frontal, PVWMH were associated with cerebral amyloid accumulation evidenced by high florbetapir-PET signal ($p$=.001) and low CSF-Aβ ($p$=.001). In a logistic regression model, including PVWMH, age, APOE4 genotype, vascular risk factors, education, and race, both parietal and occipital PVWMH burden were independently associated with high florbetapir-PET signal and low CSF-Aβ (OR= 1.1–1.3 per millimeter or grade increase in PVWMH, $p$=.05). PVWMH were also associated with an Alzheimer disease (AD) pattern of cerebral hypometabolism on FDG-PET ($p$=.05). Inter-rater correlation for frontal, parietal and occipital PVWMH ratings was excellent (r/rho=0.7, $p$=.0001).

***Conclusions:*** PVWMH are associated with cerebral amyloid accumulation independent of age and APOE4 status, supportive of a synergistic interaction between small vessel cerebrovascular disease and AD. PVWMH are a marker of severity of cortical arterial disease which may promote Aβ deposition in AD by disruption of physiologic Aβ clearance mechanisms. Quantifying PVWMH using a visual scoring method may improve AD clinical trial design by identifying those at risk of accelerated amyloid accumulation who may benefit most from therapeutics targeting amyloid clearance.

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**An Overview of the Ontario Neurodegenerative Disease Research Initiative (ONDRI) Pipeline Development and Neuroinformatics for Quality Assurance and Quality Control of Magnetic Resonance Imaging Data**

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***Background:*** The global landscape of brain research is constantly evolving, both to face new challenges and to keep pace with new advancements. Although large-scale collaborative studies are the new norm, the tools and techniques that are employed for data quality control and assurance vary greatly from study to study, addressing different aspects of the many challenges faced when undertaking multi-site research. Since there is currently no consensus on the steps that should be undertaken to ensure high-quality data acquisition and management, sharing the processes of the Ontario Neurodegenerative Disease Research Initiative (ONDRI) project (part of the Ontario Brain Institute) will be beneficial to the broader imaging and neuroinformatics communities alike.

***Methods:*** ONDRI focuses on five critical areas of degenerative brain disease including amyotrophic lateral sclerosis (ALS, N=90), fronto-temporal dementia (FTD, N=60), Parkinson's disease (PD, N=150), vascular cognitive impairment (VCI, N=150) and Alzheimer's disease and mild cognitive impairment (AD/MCI, N=150). MRI is being performed at ten different 3 Tesla imaging sites across Ontario and includes six different acquisition sequences that are consistent with the ADNI standard and also the Canadian Dementia Imaging Protocol (CDIP): T1-weighted anatomical, proton density / T2-weighted, fluid attenuated inversion recovery (FLAIR), gradient echo, resting-state functional MRI, and diffusion tensor images (DTI). Monthly phantom acquisitions are also

required to assess scanner stability (fBIRN phantom) and geometric distortions (LEGO phantom). In order to ensure the highest caliber of data acquisition and storage, numerous procedures and pipelines have been developed, primarily centered around a neuro-informatics platform called BrainCODE (Centre for Ontario Data Exploration), utilizing an underlying framework including SPReD/XNAT (the Stroke Patient Recovery Research Database), OpenClinica, and REDCap. This abstract describes the quality control of MRI data using SPReD/XNAT after the site has been initiated and begun acquiring data for the study. Automatic pipelines are used to: monitor adherence to naming conventions and MRI protocol parameter settings; monitor signal-to-noise (SNR) and contrast-to-noise (CNR); monitor resting state fMRI scanner performance (using fBIRN tools for both subject and phantom acquisitions); monitor and correct MR scanner geometric gradient field distortions (using LEGO phantom). In addition, there is a standardized process for manual quality assessment for motion and other imaging artefacts, and a software tool for recording results in a standardized format. Additional pipelines are currently under development including an automatic phantom-based DTI data quality assessment pipeline.

***Discussion:*** These pipelines and procedures have been successfully implemented over the past 14 months, during which time more than 250 subject datasets have been acquired. These pipelines and procedures have assisted in the identification of protocol deviations and QC failures due to motion (8 failures identified, 7 subsequently reacquired successfully), allowing for timely interventions to remedy any issues and ensure the acquisition and databasing of quality data.

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**Identifying the Brain Activation Patterns of Patients with Mild Cognitive Impairment During Routine and Complex Driving Conditions**

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***Background:*** The ability to drive safely requires the integration of multiple cognitive domains and associated brain regions, including the visual, motor, parietal, and prefrontal areas. Mild cognitive impairment (MCI) can affect abilities such as attention, memory, processing speed, and executive functioning, all of which are critical for safe driving. Few studies have investigated the driving performance of patients with MCI and no study has investigated the underlying neural correlates of driving in MCI patients. Furthermore, there are no valid and reliable tools to help health-care professionals assess the driving fitness of patients with MCI. Understanding the neural underpinnings of impaired driving behaviour in patients with MCI represents an important first step in addressing this issue.

***Objective:*** The current study combined driving simulation and functional magnetic resonance imaging (fMRI) to identify the brain activation patterns of individuals with MCI while performing driving tasks that ranged in complexity, including both routine (e.g., right and left turns) and more cognitively demanding (e.g., left turns with traffic) driving conditions. It was hypothesized that patients with MCI would show a significant deviation in brain activation compared to healthy controls during various driving conditions and, specifically, increased activation in frontal regions involved in executive functioning.

***Methods:*** The brain activation patterns of 11 patients with MCI and 9 healthy age-matched control drivers were compared across right turns, left turns, and left turns with traffic using General Linear Model (GLM) analysis.

***Results:*** Both patients with MCI and healthy control participants showed reliable activation in the brain regions implicated in driving (i.e., occipital and parietal regions) previously observed in healthy young adults across all turning conditions. Patients with MCI showed a significant increase in brain activation in frontal regions compared to healthy controls during routine aspects of driving (i.e., right turns). Furthermore, MCI patients showed decreased activation in the precuneus compared to healthy controls during left turns with traffic; however, this result did not reach statistical significance.

***Discussion:*** Results suggest that patients with MCI demonstrate systematic differences in brain function compared to healthy controls across different driving conditions. Specifically, MCI patients recruit frontal areas significantly more during routine aspects of driving, such as right turns, compared to healthy controls. The observed increase in frontal activation resembles the network previously observed for young, healthy drivers during more cognitively demanding driving tasks, such as left turns with traffic and audio distraction. Patients with MCI may, therefore, recruit a more extensive set of brain regions, including regions involved in executive functioning, for even routine aspects of driving. The decreased activation observed in the precuneus for MCI patients during cognitively demanding left turns with traffic may have failed to reach statistical significance due to activation variability in patients with MCI during this driving condition. The results of this study provide strong preliminary evidence for the brain activation patterns of MCI patients during various driving conditions. A large-scale research study is required to better characterize these activation patterns as well as those associated with impaired driving performance.

**OPTIMAMED: First Results from an Intervention To Reduce Inappropriate Medication Use Among Long-Term Care Residents with Advanced Dementia**

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***Background:*** Most long-term care facility (LTCF) residents with advanced dementia receive multiple medications. With disease progression care goals shift to comfort care and consequently medications have to be reviewed, adjusted or discontinued because of reduced life-expectancy or changes in their harm-benefit ratio. Few interventions to achieve this goal have been performed.

***Objectives:*** To evaluate the feasibility and the effects of an inter-professional intervention to optimise medication use in LTCF residents with advanced dementia.

***Methods:*** Based on a scoping review and a multidisciplinary Delphi expert panel, lists of "mostly", "sometimes" or "exceptionally" appropriate medications and elements of successful interventions were identified. The lists were tailored for 3 Quebec LTCFs. In 2014, a 4-month intervention was implemented in 3 LTCFs: the families of participating residents received an information leaflet on optimal medication use in advanced dementia. Nurses, pharmacists, and physicians of the LTCF participated in two 90-minute continuing education (CE) sessions. The LTCF pharmacist performed a medication review for each study resident using the list of appropriate medications (as produced in our earlier study), and discussed recommendations with nurses and physicians. A study nurse recorded comfort and agitation levels of participants using the Cohen-Mansfield Agitation Inventory and the PACSLAC-F scales during the study period.

***Results:*** 93 residents were eligible and 48 participated; 3 residents died before follow-up and 45 were followed-up for study. 34 health professionals participated in the first and 23 in the second CE session. The study nurse was present during discussions concerning medication changes, and medication lists were well accepted. The number of medications used by the participants decreased significantly overall (from 422 to 389; $p$=.02) and for medications classified as "sometimes" appropriate (210 to 182; $p$<.05). During the study, 1 of 23 residents using antipsychotics, and 1 of 5 using cholinesterase inhibitors stopped these medications. Reductions made in medications classified as being "exceptionally" appropriate were not statistically significant. Levels of agitation and comfort did not change noticeably.

***Discussion:*** Our interdisciplinary LTCF intervention to optimise medication use in residents with severe dementia was feasible and reduced overall medication use. Families' and health professionals' comments provide opportunities to improve information material and the tailored lists. The three LTCF in Quebec City were interested in opportunities and tools facilitating improved medication use. Results from this pilot study need to be replicated in a larger trial; information to families and shared decision making should be a focus of the study.

***Conclusions:*** A scoping literature review and an expert consensus provided the elements for a feasible intervention to optimize medication use. A cluster randomized trial should validate medication outcomes, generalizability, and patient or family outcomes of this intervention.

**Robots Delivering Person-Centred Care?**

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***Introduction:*** The purpose of this paper is to critically reflect on the use of robotics for dementia care. It has been said that our society needs to re-think our current understanding of health care in order to meet the needs of our aging populations; are robotics a feasible option for the delivery of dementia care in Canada?

***Methods:*** This paper has opted for a discussion about the robotics presented at the Japanese Global Action Against Dementia Legacy Event and about whether Canada is ready to accept this level of gero-technology in the delivery of dementia care.

***Results:*** The paper provides insights about the cultural and inter-generational differences in the use of robotics in the delivery of care for older adults with dementia in both institutional and community dwelling settings. Japan is in a unique situation as a 'super-aging' country, where it has the oldest and the fastest aging population in all of Asia. Currently in Japan, one in four individuals is over the age of 65 and there are 4.6 million people (15% of the older adult population) already living with dementia. Japan's present actions for how persons with dementia are cared for, as well as how the challenges surrounding an aging population are met, sets the stage for other developed nations to follow in its footsteps.

***Conclusion:*** The author encourages the readers to remember the importance of cultural and context, with regards to the adoption of new technologies for dementia care. Technology is constantly reordering the way we live, and work and it is now restructuring how we may be able to deliver health care to those with dementia.

**Sex Differences in the Prevalence and Incidence of Mild Cognitive Impairment: a Systematic Review and Meta-Analysis**

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***Background/Objective:*** Mild cognitive impairment (MCI) is considered an intermediate stage between normal aging and dementia. An investigation of the sex distribution of prevalent and incident MCI may contribute to our understanding of the etiology of this condition, thereby potentially influencing sex-specific preventative strategies for MCI and its progression to dementia. However, epidemiological studies have reported conflicting findings on whether males or females have a higher prevalence or incidence of MCI. Thus, a systematic analysis on the prevalence and incidence of MCI in males and females is warranted. The aim of this systematic review and meta-analysis is to integrate results from the published international literature and to provide a quantitative index of the male-female ratio for both the prevalence and incidence of MCI.

***Methods:*** We performed a systematic search in 4 major databases (Medline, PubMed, Scopus, and PsychINFO) for cross-sectional and longitudinal population-based studies reporting prevalence or incidence of MCI in males and females. Independent reviewers screened titles and abstracts, extracted study data, and assessed quality of the studies. Publications that followed the Mayo Clinic or International Working Group criteria for MCI were selected. Publications that met eligibility criteria were analyzed using a random-effects model to provide pooled male vs. female risk and rate ratios for prevalent and incident MCI, respectively. Analyses were first conducted by combining all types of MCI, followed by subgroup analyses.

***Results:*** We identified 51 unique studies that met selection criteria. There was no statistically significant sex difference for the prevalence of all types of MCI combined ($p$=.986). However, there was a statistically higher prevalence of amnestic MCI among males ($p$=.024). There was no statistically significant sex difference for the incidence of combined MCI ($p$=.709). Results for the incidence of amnestic MCI, however, showed a marginally significant higher rate for males ($p$=.055). Additional planned sensitivity analyses will also be presented.

***Conclusions:*** Our results do not show sex differences in combined MCI for prevalence or incidence. However, our findings indicate a higher prevalence of amnestic MCI and also a trend towards a higher incidence of amnestic MCI among males compared to females. Thus, it is possible that analyses that combine subtypes of MCI (i.e., amnestic and non-amnestic MCI) may fail to distinguish sex-specific risk factors. It is possible that there may be different patterns and rates of cognitive impairment in males and females. This review suggests that further research examining sex and gender differences may advance our understanding of etiological factors in MCI.