Alzheimer’s disease (AD) is the 5th leading cause of death in the USA. With nearly 300 failed therapeutic trials to date, lifestyle modifications have been shown to reduce AD risk by as much as 50%. Preceding the FINGER Study by nearly a decade, the BrainSavers Brain+Body Total Fitness program was developed by an interdisciplinary team to reduce the risk of AD / all-cause dementia and promote healthy aging via education, exercise, and engagement. This evidence-based program utilizes the principles of neuroplasticity and cognitive reserve. Pre-Covid, BrainSavers was delivered live, led by certified instructors. Two years of curriculum were developed, comprised of six lifestyle components: cognitive exercise, physical exercise, healthful nutrition, socialization, stress reduction, and sleep hygiene. Results of a six month beta trial documented self-rated improvements in memory and general cognitive performance, quality of life, socialization, nutritional status, and physical fitness. Quantitative results showed statistically significant differences in physical fitness measures including cardio-respiratory endurance, lower body strength, balance, speed, and agility. Trends were seen in six of nine cognitive skills. During Covid the program was transformed into an online format as BrainSavers Synapse: Staying Connected, which has been enthusiastically received. Future research will compare longer-term outcomes of both formats. Based on results to date and extensive peer-reviewed literature on lifestyle as a modifier of dementia risk, we predict this program will contribute to better individual and societal outcomes, including substantial improvements in cognitive and overall health, and a significant reduction in healthcare costs.

ANALYSIS OF SURVIVAL DATA WITH COMPETING RISKS IN ADRD (ALZHEIMER’S DISEASE AND RELATED DEMENTIAS) RESEARCH
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Competing risk is an event that precludes the occurrence of the primary event of interest. For example, when studying risk factors associated with dementia, death before the onset of dementia serve as a competing event. A subject who dies is no longer at risk of dementia. This issue play more important role in ADRD research given the elderly population. Conventional methods for survival analysis assume independent censoring and ignore the competing events. However, there are some challenge issues using those conventional methods in the presence of competing risks. First, no one-to-one link between hazard function and cumulative incidence function (CIF), and Kaplan-Meier approach overestimates the cumulative incidence of the event of interest. Second, the effect of covariates on hazard rate cannot be directly linked to the effect of cumulative incidence (the risk). We will discuss two types of analyses in the presence of competing risk: Cause-specific hazard model and Fine-Gray subdistribution hazard model. Cause-specific hazard model directly quantify the cause-specific hazard among subjects who are at risk of developing the event of interest, while Fine-Gray subdistribution hazard model directly model the effects of covariates on the cumulative incidence function.

The type of research questions (Association vs. Prediction) may guide the choice of different statistical approaches. We will illustrate those two competing risk analyses using the large national dataset from National Alzheimer’s Coordinating Center (NACC). We will analyze the association between baseline diabetes status and the incidence of dementia, in which death before the onset of dementia is a competing event.

ARE DRUGS THAT CAUSE DYSBIOSIS LONGITUDINALLY ASSOCIATED WITH COGNITIVE SCORES, COGNITIVE IMPAIRMENT, & DEMENTIA?
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Recent research has examined how the microbiome may influence cognitive outcomes; however, there is a paucity of research understanding how medication associated with dysbiosis may be associated with cognitive changes. This study used data from the Health and Retirement Study and the Prescription Drug Study subset for adults 51 and older (n=3,898). Continuous (0-27) and categorical (cognitively normal=12-27; cognitive impairment=7-11; and dementia=0-6) cognitive outcomes were used. Prescriptions utilized were proton pump inhibitors, antibiotics, selective serotonin reuptake inhibitors, tricyclic antidepressants, antipsychotics, antihistamines, and a summed dose-response measure. Linear mixed models (LMM) and generalized linear mixed models (GLMM) were used for continuous and binary outcomes. For the LMM model, the main effect for those taking one medication was insignificant; however, the interaction with time showed a significant decrease over time (β: -0.07; 95% confidence interval (CI): -0.14, 0.01). The mean cognitive score was lower for those taking two or more medications (β: -1.48; 95% CI: -2.70, -0.25), although the interaction with time was insignificant. GLMM results showed those taking two or medications had odds that are 612% larger (odds ratio (OR): 7.12; 95% CI: 3.03, 16.71) of going from cognitively healthy to dementia but the interaction with time showed decreased odds over time (OR: 0.92; 95% CI 0.86, 0.97). For cognitive impairment, those who took two or more medications had odds that were 45% larger (OR: 1.45; 95% CI: 1.05, 2.00) of going from cognitively healthy to cognitively impaired. This study indicated a dose-response aspect to taking medications on cognitive outcomes.

ASSOCIATION BETWEEN BODY WEIGHT CHANGE IN LATE LIFE AND RISK OF DEMENTIA: A POPULATION-BASED COHORT STUDY
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Background: Adiposity in midlife is a modifiable risk factor for dementia. However, the effect of adiposity in late-life on dementia remains unclear. We investigated the association of body mass index (BMI) and weight changes after age 60 with the incident dementia.

Methods: Within the Swedish National Study on Aging and Care-Kungsholmen, 1,673 dementia-free participants
with data on BMI/weight both at baseline and the 6-year follow-up were followed to detect subsequent incident dementia cases. BMI change was assessed as the percentage of the difference between BMI at baseline and the initial 6-year follow-up and categorized into large (>10%) or moderate (5–10%) loss, stable (≤5%), and moderate (5–10%) or large (>10%) gain. Weight change (difference between weight at baseline and the 6-year follow-up) was categorized into large (>7.5 kg) or moderate (2.5–7.5 kg) loss, stable (≤2.5 kg), and moderate (2.5–7.5 kg) or large (> 7.5 kg) gain. Dementia was diagnosed following the DSM-IV criteria. Data were analyzed using Cox regression models.

Results: During the follow-up (median 5.78 years), 102 incident dementia cases developed. BMI/weight change showed U-shaped associations with dementia. Compared with stable BMI, the hazard ratios (95% confidence intervals) of dementia were 2.93 (1.72–4.91) for large BMI loss and 2.61 (1.09–5.54) for large BMI gain. Similar results were observed for a large weight loss (2.92 [1.67–5.07]) or gain (2.95 [1.16–6.53]). These associations became stronger among participants carrying an ApoE ε4 allele.

Conclusion: Both large bodyweight loss and gain are associated with a higher risk of dementia, especially among ApoE ε4 carriers.

ASSOCIATION OF BLOOD CELL PARAMETERS OF PERIPHERAL INFLAMMATION WITH BRAIN IMAGING MEASURES

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Neutrophil to lymphocyte ratio (NLR), red cell distribution width (RDW), and mean platelet volume (MPV), are easily measured circulating blood cell parameters that reflect chronic peripheral inflammation which increases risk for dementia and Alzheimer’s disease (AD). We investigated the cross-sectional association between these blood cell parameters and brain MRI measures, including total cerebral brain volume (TCBV) as percentage of total intracranial volume (TCV) to correct for differences in head size, hippocampal volume (HPV) and log transformed white matter hyperintensity (WMH) volume, in the Framingham Heart Study (FHS) cohorts. We identified 2882 FHS participants 25 to 92 years of age (mean 59 years), 53% women, who attended an exam that included a complete blood cell count sample and received a brain MRI within five years of blood draw. We used linear mixed effect models to examine associations, adjusting for age, age^2, sex, education, cohort, time between blood draw and MRI, prevalent cardiovascular disease, C-reactive protein, APOE-ε4 genotype and TCV for HPV and WMH, and accounting for familial correlation using a random effect. We observed significant (p<0.01) associations between higher RDW and smaller TCBV, and between elevated NLR and larger WMH volume. Analysis on an older subgroup (age ≥60 years, mean 71 years, n=1357) demonstrated larger effect sizes and additional significance between increased RDW with smaller HPV. We conclude that chronic peripheral inflammation as measured by NLR and RDW associates with MRI measures of brain aging (TCBV, HPV) and vascular brain injury (WMH) in FHS, with stronger impact in participants ≥60 years.

CHOOSING UNWISELY: DISSEMINATION NEEDS OF PRIMARY CARE PROVIDERS OF PATIENTS WITH ALZHEIMER’S DISEASE

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Choosing Wisely is a well-known campaign to disseminate evidence-based clinical practices to providers and patients to drive care decisions, with geriatrics recommendations released in 2013. In December 2019, we aimed to determine what the dissemination needs of primary care providers were towards these recommendations. We developed common clinical scenarios with follow-up survey questions, relative to the care of people with Alzheimer’s disease (AD) and utilizing Choosing Wisely geriatrics recommendations. The survey was distributed online to a national cohort of providers. Providers were also asked to rate their confidence level and rationale for clinical choices. Results were analyzed using mixed methodology, with constant comparative analysis utilized for qualitative responses. Nationally from 41/50 states, 211 providers responded, 72% female, with occupations of physician (36%, 77), advanced practice nurse (50%, 106) and physician assistant (13%, 28), with family practice (63%, 142) and internal medicine (20%, 43) the most prominent fields. Results revealed erroneous geriatric practices, including 1.) checking urinalysis for mental-status changes (53%, 116), 2.) treating asymptomatic bacteria with unnecessary antibiotics (59%, 124), 3.) placement of gastric tubes in end-stage dementia (11%, 23). Qualitative analysis of rationale for incorrect responses revealed knowledge misconceptions (e.g. feeding tube would help avoid aspiration). Confidence levels were high among providers as 75.9% rated themselves as above average, yet did not correlate to clinical errors. Choosing Wisely geriatrics recommendations are not being followed by some providers. Highly confident providers made errors similar to lower confident providers. New ways to disseminate geriatric recommendations are needed to improve the care of patients with AD.

DETECTING EARLY SIGNS OF ALZHEIMER’S DISEASE AND RELATED DEMENTIA ONSET FROM THE EHR

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As dementia is widely under-detected, a predictive model using electronic health records (EHR) could provide a method for early screening to implement preventive strategies. There