treatment. Masked long-term follow-up of the ADAPT participant cohort will be essential.

O1-01-07 CAROTID ENDARTERECTOMY AND STROKE OR TIA ARE ASSOCIATED WITH AN INCREASED RISK OF MILD COGNITIVE IMPAIRMENT

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Background: Severe atherosclerosis in carotid arteries may cause cerebral hypoperfusion and ischemia. Alternately, cerebral ischemia during carotid endarterectomy or resulting from a stroke may contribute to mild cognitive impairment (MCI) and the subsequent development of dementia. **Objective(s):** To investigate the associations of carotid endarterectomy and stroke with MCI in a population-based case-control setting. **Methods:** A sampling frame of Olmsted County, MN, residents aged 70 to 89 years on 10/1/2004 was constructed using the records-linkage system of the Rochester Epidemiology Project. Random samples of persons within age and sex categories were invited to participate in the study. Participants were administered the Clinical Dementia Rating Scale, the Short Test of Mental Status, a neurologic examination, and psychometric testing (to assess memory, language, visuospatial, and executive function domains). A consensus panel of neurologists, neuropsychologists, and clinical nurses reviewed information on each participant to reach a diagnosis of normal cognition, MCI, or dementia. A history of carotid endarterectomy and stroke or transient ischemic attacks (TIA) was collected via a structured interview. **Results:** We identified 295 MCI cases and 590 age- and sex-matched controls with normal cognition (2 to 1 matching). The frequency of carotid endarterectomy was 13/295 (4.41%) in MCI cases and 12/590 (2.03%) in controls, and the frequency of stroke or TIA was 77 (26.10%) in MCI cases and 83 (14.07%) in controls. In conditional logistic regression models adjusted for years of education, the odds ratio (OR) of MCI was 2.21 (95% CI = 0.98, 4.99) in subjects with prior carotid endarterectomy compared to subjects without, and the OR was 2.15 (95% CI = 1.52, 3.06) in subjects with a history of stroke or TIA compared to subjects without. **Conclusions:** Our findings suggest that subjects who undergo carotid endarterectomy or have a stroke or TIA may be at increased risk of MCI or dementia.

O1-01-08 THE GINKGO IN EVALUATION OF MEMORY (GEM) STUDY DESIGN, RECRUITMENT, AND INCIDENT DEMENTIA RATES: A PRELIMINARY REPORT

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Background: There is scant experience in the conduct of large clinical trials for preventing Alzheimer's disease (AD) and other dementias. To avert the projected epidemic of AD over the next half century, effective preventions must be developed and tested utilizing large scale clinical trials such as the Ginkgo Evaluation of Memory Study (GEMS). **Objective(s):** To test in a randomized clinical trial the effectiveness of 120 mg BID of Ginkgo biloba (EGb761), a plant extract with powerful antioxidant activity and possible anti-amyloid activity, in preventing or delaying dementia/AD. Secondary outcomes included effects of Ginkgo on vascular disease, functional abilities, adverse events and mortality. **Methods:** 3071 elderly subjects (age 75+) were recruited at 4 sites in the US: Pittsburgh (University of Pittsburgh); Hagerstown, MD (Johns Hopkins); Sacramento, CA (UC Davis); and Winston Salem/Greensboro, NC (Wake Forest University). Subjects were screened with extensive medical and neuropsychological testing at baseline, including the Clinical Dementia Rating (CDR) performed with each participant's proxy. Those with normal cognition or mild cognitive impairment were randomized to either Ginkgo or identical appearing placebo. Assessments were performed every 6 months; pre-defined change in cognitive scores led to more extensive testing and evaluation for dementia. Dementia was determined by Consensus review of neurological evaluation records, including neuroimaging. **Results:** After low incidence rates of dementia for the first few years, the annual incident rate increased to over 4% per year. Over 350 of the projected 440 incident cases have thus far reached endpoint. Mortality and dropout were lower than expected; compliance and adherence were within acceptable range. **Conclusions:** Traditional prevention trial designs require long periods of time but can provide effective assessments of medications. Ginkgo was well tolerated by the elderly population. The study will reach endpoint in 2007 and results are expected to be published in 2008.

SUNDAY, JUNE 10, 2007
ORAL
O1-02
PRIMARY PREVENTION AND RISK 2

O1-02-01 FORECASTING THE GLOBAL PREVALENCE AND BURDEN OF ALZHEIMER'S DISEASE

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Background: As the world population ages, additional resources will be required to adequately care for persons afflicted with Alzheimer's disease. Research is underway to develop interventions which both delay disease onset and slow disease progression. **Objective:** The goal was to forecast the global burden of Alzheimer's disease and evaluate the potential impact of interventions that delay disease onset or progression. **Methods:** A stochastic multistate model was used in conjunction with United Nations' worldwide population forecasts and data from epidemiological studies on the incidence and mortality of Alzheimer's disease. **Results:** In 2006, the worldwide prevalence of Alzheimer's disease was 26.6 million. Prevalence will quadruple by 2050, where worldwide 1 in 85 persons will be living with the disease. About 43% of prevalent cases are estimated to need a high level of care equivalent to that of a nursing home. Interventions that delay both disease onset and progression by a modest 1 year, would result in nearly 9.2 million fewer cases in 2050 with nearly all the decline attributable to decreases in persons requiring a high level of care. **Conclusions:** A global epidemic of Alzheimer's disease is on the horizon. Modest advances in therapeutic and preventive strategies that lead to even small delays in Alzheimer's disease onset and progression can significantly reduce the global burden of the disease.

O1-02-02 WORLDWIDE VARIATION IN THE DOUBLING TIME OF ALZHEIMER'S DISEASE INCIDENCE RATES

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Background: The doubling time is the age in years for the age-specific incidence rate to double. A systematic review of studies of Alzheimer's incidence rates was performed to estimate doubling times and to identify regional or gender relationships. Estimates of doubling times assist in understanding disease etiology and are essential to accurately forecast the

impact of the aging of the world's population on the future prevalence. **Objective:** To investigate regional and gender differences in the doubling of Alzheimer's disease age specific incidence rates. **Methods:** We identified all studies in the peer review literature that reported age specific incidence rates for Alzheimer's disease. We modeled the logarithm of the incidence rate as a polynomial in age. We used both fixed effects models and random effects models to account for inter-study variation. **Results:** Alzheimer's disease incidence rates exponentially increase with increasing age. The overall estimate of the doubling time was 5.7 years (95% confidence interval 4.2 to 9.0.) The doubling times from studies performed in North America, Europe, and other parts of the world were 6.0, 5.8, and 5.0 respectively, and were not significantly different (p=.3). No significant differences were detected by gender (6.7 years for males; 5.3 for females, p=0.12). **Conclusion:** Doubling times of Alzheimer's disease incidence rates are remarkably similar among populations throughout the world. The variation in absolute incidence rates could be due to methodological and diagnostic differences among studies or indicate different underlying, risk factors.

O1-02-03 ASSOCIATED CONDITIONS IMPACTING LIMITATIONS AMONG THE US POPULATION WITH LIMITATIONS DUE TO ALZHEIMER'S DISEASE

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Background: The majority of AD patients have other morbidities that contribute to the progression and course of their AD. To properly develop and allocate resources requires an understanding of the other factors limiting functional independence in this patient population. **Objective:** To characterize the activity limitation due to other conditions in the US population who have self (or proxy) reported limitations in activity due to AD. **Methods:** These data are from the National Health Interview Survey (NHIS). The NHIS is a representative sample of the US civilian, non-institutionalized population. Data from 2001 through 2005 were combined. Analyses were limited to the subset of family members aged 60 years or more who were reported to have activity limitations due to dementia, senility or Alzheimer's disease by the household's survey respondent. Data are weighted to reflect total in the population. **Results:** A total of 443 subjects with limitations due to dementia were identified. These subjects represent an annualized number of 105,336 persons in the United States aged 60 years or more. 35% of subjects are married, with a median age of 83 years, with 83% white and 11% African-American. A proxy responded for 58% of subjects. In addition to dementia, activity limitations were reported due to other conditions. The proportion of subjects with other conditions limiting activities is summarized in the following table:

Activity limitations due to	Percent reporting limitations
Arthritis/rheumatism	26%
Heart conditions	16%
Hypertension	12%
Diabetes	10%
Depression, anxiety or emotional problems	10%
Musculoskeletal/connective tissue problems	10%

Overall, 56% of subjects had limitations due to other conditions in addition to their dementia-related limitations. During the 30 days prior to the survey, psychiatric and emotional issues were assessed. 'Everything is an effort' was reported by 20% for 'most or all of the time,' while 12% felt sad, 12% felt worthless, and 11% felt hopelessness. A recent decline in health was reported by 45%. **Conclusions:** Persons with AD have substantial functional limitation and generally have other conditions contributing to the functional limitations. To improve or maintain functional independence in AD patients will likely require a multifaceted approach across several disease states. Additional research will assist to define the impact that AD has on the development and progression of functional limitations related to co-morbid conditions.

O1-02-04 HIGHER SELF-PERCEIVED RISK OF ALZHEIMER'S DISEASE IS ASSOCIATED WITH LOWER DROPOUT IN A STUDY DISCLOSING GENETIC SUSCEPTIBILITY

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Objective: To assess factors associated with dropout in the REVEAL (Risk Evaluation and Education for Alzheimer's) Study, a randomized clinical trial of risk assessment, including APOE disclosure, for first-degree relatives of persons with AD. **Design/Methods:** We analyzed data on 420 participants who were eligible for, and expressed interest in, genetic risk assessment through the REVEAL Study. We conducted a logistic regression analysis with dropout as the dependent variable. Age, gender, race (African American vs. White), and perceived risk of AD were independent variables. Perceived risk was assessed by agreement with the statement "I believe I will someday develop AD." **Results:** Please see Table 1 for details of demographics. Dropout was not associated with age, race, or gender. However, adjusting for these variables, high perceived risk of AD prior to disclosure was a significant predictor of lower dropout (odds ratio 0.5, 95% CI 0.3-0.8, p = 0.0047). **Conclusions:** Among those interested in genetic susceptibility testing, participants who believed prior to enrollment they will develop AD were more likely to remain in the study. Our results suggest that baseline illness perceptions are more predictive of follow-through with genetic testing for AD than demographic characteristics.

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Table 1
Demographics and Results of Dropouts in REVEAL Study Protocol

REVEAL	Dropouts	Non-Dropouts	Total	p value
Number (n)	148	272	420	
Age	59.3±11.1	58.0±10.6	58.4±10.8	0.44
Sex (% Female)	101 (73.2%)	191 (70.2%)	292 (71.2%)	0.45
Race (% African American)	50 (36.5%)	51 (18.9%)	101 (24.7%)	0.30
High Self Perceived Risk	94 (69.1%)	222 (81.6%)	316 (77.4%)	0.0047

O1-02-05 DNA EPITOPE VACCINE PREVENTS AD LIKE PATHOLOGY IN 3XTG-AD MICE AND PROTECTS THEM FROM COGNITIVE DECLINE

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Background: Development of a clinically successful AD vaccine requires a delicate balance between induction of anti-Aβ antibody responses sufficient for therapeutic benefit and complete avoidance of potentially autoimmune T cell responses. **Objective:** To achieve this goal, we have engineered an epitope vaccine to selectively initiate B cell responses toward an immunogenic self-epitope of Aβ, while T cell help is provided by a genetically-linked non-self T cell epitope synthesized in multiple antigenic peptide (MAP) format. However, because the MAP backbone is not suitable for human trials, we have adopted an alternative strategy and developed a chemokine-based DNA vaccine that encodes three copies of self-Aβ B cell epitope ($A\beta_{1\text{-}11}/3A\beta_{1\text{-}11}$) and a foreign promiscuous T cell