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UNTIL TUESDAY, JULY 19, 2011, 7:30 AM CEST (1:30 am ET/USA)

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AAIC 2011 press room, July 16-21: +33 (0)1 57 25 20 35

**NEW GLOBAL MODEL OF ALZHEIMER'S RISK SUGGESTS A
25 PERCENT REDUCTION IN PRESUMED RISK FACTORS COULD
LOWER ALZHEIMER'S CASES BY 3 MILLION WORLDWIDE**

**- Mathematical Model Still Needs "Real World" Proof -
- Also, "Resilience Index" May Predict Successful Cognitive Aging -**

PARIS, July 19, 2011 – A new mathematical model of global Alzheimer's risk suggests that reducing the prevalence of well-known, lifestyle-based, chronic disease risk factors by 25 percent could potentially prevent 3 million cases of Alzheimer's worldwide, according to new research presented today at the Alzheimer's Association International Conference 2011 (AAIC 2011) in Paris.

Previous observational research has identified a number of potentially modifiable risk factors for Alzheimer's disease – including heart disease and its risk factors, levels of physical activity and mental stimulation, and diet – but it remains unclear whether changing these mostly lifestyle-based risk factors would result in fewer cases of Alzheimer's.

Scientists used mathematical modeling to calculate the percentage of Alzheimer's cases that may be attributable to diabetes, mid-life hypertension, mid-life obesity, smoking, depression, low educational attainment and physical inactivity. The researchers caution that these estimates make an important assumption that has not yet been proven – that there is a causal relationship between the risk factors examined and Alzheimer's disease, and that modifying the risk factors will lower Alzheimer's risk.

The researchers' new model suggests that half of worldwide Alzheimer's cases may be due to these modifiable lifestyle risk factors. They say the next step is to perform large-scale studies with people to discover whether changing these lifestyle factors will actually lower Alzheimer's risk over time.

In another study reported at AAIC 2011, researchers are investigating the characteristics of older adults who have maintained normal cognitive function to build an index of "resilient cognitive aging." Their goal is to identify a cluster of factors that predict cognitive stability in late life for use in clinical practice and research trials.

“Alzheimer’s disease is a global emergency, and we must accelerate the discovery of methods to detect and prevent it now,” said William Thies, PhD, Alzheimer’s Association Chief Medical and Scientific Officer. “Estimated worldwide costs of dementia are US\$604 billion -- \$183 billion in the U.S. alone. Deaths from Alzheimer’s disease are rising while those from other diseases are falling. In fact, Alzheimer’s is the only cause of death among the top 10 in the United States that cannot be prevented, cured or even slowed. The *World Alzheimer Report 2010* by Alzheimer’s Disease International says that dementia is significantly affecting every health and social care system in the world, and costs of dementia are set to soar.”

“On behalf of all those suffering with this devastating disease and their families, and the thousands of researchers at this conference, the Alzheimer’s Association calls for unprecedented global collaboration to better understand, diagnose, and treat Alzheimer’s disease with the goal of eliminating this worldwide epidemic,” Thies said.

Model Shows Lowering Risk Factors May Prevent Millions of Alzheimer’s Cases

Deborah Barnes, PhD, MPH, Associate Professor of Psychiatry at the University of California, San Francisco and Mental Health Research PI at the San Francisco Veterans Affairs Medical Center, and colleagues used mathematical modeling to calculate “population attributable risks” (PARs) for potentially modifiable Alzheimer’s risk factors to project the potential impact of risk factor reduction on Alzheimer’s prevalence in the U.S. and worldwide.

PARs are used to estimate the percentage of cases of a given disease that are potentially attributable to, or caused by, various risk factors. PARs take into consideration both the strength of the association between the risk factors and the disease as well as how common the risk factors are.

They found that roughly half of Alzheimer’s cases may potentially be attributable to modifiable risk factors. Together, seven modifiable risk factors contributed to as many as 17 million Alzheimer’s cases worldwide and nearly 3 million cases in the U.S.

- Alzheimer’s Disease International, in their *World Alzheimer Report 2010*, determined that there are 35.6 million cases of dementia worldwide.
- 5.4 million Americans are living with Alzheimer’s disease, according to the Alzheimer’s Association *2011 Alzheimer’s Disease Facts & Figures*.

The scientists calculated PARs for diabetes, mid-life hypertension, mid-life obesity, smoking, depression, low educational attainment and physical inactivity. (Dietary factors were not considered due to heterogeneity of definitions and lack of data on prevalence.) The researchers then estimated the total number of Alzheimer’s cases currently attributable to each risk factor individually and all seven risk factors combined in the U.S. and worldwide. Finally, they calculated the number of Alzheimer’s cases that could potentially be prevented by 10 percent and 25 percent reductions in prevalence of the risk factors.

At AAIC 2011, the researchers reported the proportion of Alzheimer's cases worldwide that are potentially attributable to each of the seven risk factors:

- low education 19 percent
- smoking 14 percent
- physical inactivity 13 percent
- depression 11 percent
- mid-life hypertension 5 percent
- mid-life obesity 2 percent
- diabetes 2 percent

And specifically in the U.S.:

- physical inactivity 21 percent
- depression 15 percent
- smoking 11 percent
- mid-life hypertension 8 percent
- mid-life obesity 7 percent
- low education 7 percent
- diabetes 3 percent

Together, the seven potentially modifiable risk factors contributed to roughly 50 percent of Alzheimer's cases worldwide (51 percent, 17.2 million) and in the U.S. (54 percent, 2.9 million).

“We were surprised that lifestyle factors such as physical inactivity and smoking appear to contribute to a larger number of Alzheimer's cases than cardiovascular diseases in our model,” said Barnes. “But this suggests that relatively simple lifestyle changes such as increasing physical activity and quitting smoking could have a dramatic impact on the number of Alzheimer's cases over time.”

According to Barnes' calculations, a 10 percent reduction in all seven risk factors could potentially prevent 1.1 million Alzheimer's cases worldwide and 184,000 cases in the U.S. over time. A 25 percent reduction in all seven risk factors could potentially prevent more than 3 million Alzheimer's cases worldwide and 492,000 cases in the U.S. over time.

“In our study, what mattered most was how common the risk factors were in the population,” said Barnes. “For example, in the U.S., about one third of the population is sedentary, so a large number of Alzheimer's cases are potentially attributable to physical inactivity. Worldwide, low education was more important because literacy rates are lower or people are not educated beyond elementary school. Smoking also contributed to a large percentage of cases because it is unfortunately still very common.”

Barnes says the estimates make an important assumption – that there is a causal relationship between the risk factors examined and Alzheimer's disease. “The next step is to perform large-scale intervention studies to really find out whether changing these risk factors will lower the risk of developing Alzheimer's over time,” Barnes said. The study results will be published online today in *Lancet Neurology*.

Study Begins to Identify Characteristics of “Resilient Cognitive Aging”

Identifying characteristics and encouraging behaviors that promote healthy cognitive aging would complement the effort to reduce risk factors to prevent Alzheimer’s and other types of dementia.

Susanne Steinberg, MD, of the Perelman School of Medicine, University of Pennsylvania, Philadelphia, and colleagues sought to investigate predictors of resilient cognition in 136 adults age 65 or over living independently in the community without evidence of memory impairment, and to test the association between their measures of cognitive function and known Alzheimer’s risk factors. The researchers defined cognitive resilience as stable cognitive performance, quantified as less than two percent change over 3 years.

At AAIC 2011, Steinberg reported results from the baseline visit where the study participants completed assessments of stress, anxiety, depression, personality traits, and a computerized evaluation of cognition. In addition, the researchers noted participants’ demographics, took a detailed medical history, and performed a brief physical exam focused on heart health and metabolic parameters.

The sample was well educated (mean number of years of education=16) and successful (primarily professionals or administrators, 93 percent). The racial distribution reflected the population in the Delaware Valley (Black: 13 percent; White: 85 percent). Women were overrepresented (61 percent). The majority were married (60 percent). The mean body mass index was in the overweight range (mean BMI=27.5).

In this group, the researchers found that the most significant factors related to maintaining healthy cognition included low scores on measures of stress, anxiety, depression and trauma – despite participants’ experiencing life-threatening illnesses, violence, or living with addicted parents and spouses. The investigators hypothesize that resilience in the face of distressing life events is likely related to positive coping styles and the personality trait of “conscientiousness.” A positive coping style is defined as developing a strategy, remaining positive, getting advice, and taking action. Conscientiousness, as measured by the NEO-Five Factor Inventory, includes competence, sound judgment, order, dutifulness, achievement striving and self-discipline.

On the other hand, for the people in this study group, experiencing physical neglect in childhood or scoring less well on a suicide subscale was significantly correlated with poorer cognitive performance.

At AAIC 2011, Steinberg will report additional data on the impact of contributors to “meaning in life,” such as “clear values and goals,” “being well reconciled with the past,” and “presence of emotional support.” The researchers are developing a quick, non-invasive composite score of cardiovascular risk factors that can be calculated during a physician’s office visit. The score will include: arterial pressure, body mass index, waist/hip ratio and depression; plus histories of smoking, drinking, diabetes, dyslipidemia, cardiac disease, transient ischemic attack, and thyroid conditions.

“These findings represent the initial steps in the development of a ‘Resilience Index’ that may allow early interventions to promote the maintenance of cognitive stability,” Steinberg said.

About AAIC

The Alzheimer's Association International Conference (AAIC) is the world's largest conference of its kind, bringing together researchers from around the world to report and discuss groundbreaking research and information on the cause, diagnosis, treatment and prevention of Alzheimer's disease and related disorders. As a part of the Alzheimer's Association's research program, AAIC serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community.

About the Alzheimer's Association

The Alzheimer's Association is the leading voluntary health organization in Alzheimer care, support and research. Our mission is to eliminate Alzheimer's disease through the advancement of research, to provide and enhance care and support for all affected, and to reduce the risk of dementia through the promotion of brain health. Our vision is a world without Alzheimer's. Visit www.alz.org or call 800-272-3900.

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- Deborah Barnes, PhD, MPH, et al. The Projected Impact of Risk Factor Reduction on Alzheimer's Disease Prevalence. (Funders: Alzheimer's Association, U.S. National Institutes of Health, NARSAD, University of California San Francisco School of Medicine)
- Susanne Steinberg, MD, et al. Predictors of Resilient Cognitive Aging: Baseline Characteristics. (Funders: Marian S. Ware Alzheimer Program, U.S. National Institutes of Health)

All materials to be presented at the Alzheimer's Association International Conference on Alzheimer's Disease 2011 are embargoed for publication and broadcast until the date and time of presentation at the conference, unless the Alzheimer's Association provides advance written notice of change of date and/or time.

12561

Session: O3-06 Prevalence and Trends in Society (Epidemiology II)

Presentation: O3-06-06: Speaking time: Tuesday, 7-19-11, 4:15-4:30 pm

The Projected Impact of Risk Factor Reduction on Alzheimer's Disease Prevalence

Presenting author: Deborah Barnes, PhD, MPH, University of California, San Francisco

Contact e-mail: deborah.barnes@ucsf.edu

Background: Observational studies have identified a large number of potentially modifiable risk factors for Alzheimer's disease (AD), but it remains unclear whether risk factor modification would result in fewer AD cases. The goal of our study was to calculate population attributable risks (PARs) for potentially modifiable risk factors to project the potential impact of risk factor reduction on AD prevalence.

Methods: PARs were calculated for seven potentially modifiable risk factors (diabetes, mid-life hypertension, obesity, smoking, depression, low educational attainment and physical inactivity) for which estimates of both risk factor prevalence and relative risk of AD were available. Dietary factors were not considered due to heterogeneity of definitions and lack of data on prevalence. Risk factor prevalence was determined for the US and worldwide. Relative risks were determined from recent meta-analyses. We also estimated the total number of AD cases currently attributable to each risk factor individually and all risk factors combined (accounting for correlation between risk factors) as well as the number of cases that could potentially be prevented by 10% or 25% reductions in risk factor prevalence.

Results: Worldwide, the proportion of AD cases potentially attributable to these seven risk factors (in order of magnitude) was low education (21%), smoking (14%), physical inactivity (13%), depression (11%), mid-life hypertension (6%), obesity (6%), and diabetes (2%). In the US, PARs were physical inactivity (21%), obesity (17%), depression (15%), smoking (11%), mid-life hypertension (8%), low education (7%) and diabetes (3%). Together, these seven potentially modifiable risk factors contributed to more than 50% of AD cases worldwide (54%, 17.9 million) and in the US (59%, 3.1 million). A 10%-25% reduction in all seven risk factors could potentially prevent 1.1-3.1 million AD cases worldwide and 188,000-507,000 cases in the US.

Conclusions: More than half of AD cases may be attributable to potentially modifiable risk factors. RCTs are critically needed to determine whether multimodal risk factor reduction strategies can lower AD incidence and prevalence. Public health campaigns targeted at AD risk factor modification should be considered.

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Session: Tuesday, July 19, 2011 Posters

Presentation: P3-279; 12:30-3:00 pm

Predictors of Resilient Cognitive Aging: Baseline Characteristics

Presenting author: Susanne Steinberg, MD, University of Pennsylvania, Philadelphia

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Background: Objective: To investigate predictors of resilient cognition in older adults without evidence of memory impairment at enrollment.

Methods: Methods: 100 adults age 65 or over living independently in the community with a TIC score ≥ 27 and a MOCA ≤ 23 were enrolled into a prospective, observational, longitudinal study. We report results from the baseline visit when participants completed measures of stress, psychopathology and a computerized CogState exam. Demographics and a detailed medical history were recorded and a brief physical exam completed focusing on cardiac and metabolic parameters. Blood was drawn for APOE genotyping.

Results: The characteristics of the population follow. The mean age is 77.5 years, SD 6.84; range 66-95. The sample is well educated: mean number of years 16, SD .9 and range 6-20 years. As many as 39% ≥ 18 years in school. The cohort is successful: primarily professionals or administrators (93%). The racial distribution reflects the population in the Delaware Valley (Black: 13%; White: 85%). Women were overrepresented (61%) compared to men (37%). The majority were married (60%) with smaller groups of widowed (24%), divorced (10%) and single (6%). The mean body mass index was in the overweight range (27, SD 7.4). The "Resilience" population had low scores for 6 measures of stress, anxiety, depression and trauma. Compared with normative data, the "Resilience" population was found to be different for stress $p < 0.001$ (e.g. DASS) and personality traits subscales ($p < 0.001$) (NEO-FFI). On the MOS sleep scale, sleep adequacy, daytime somnolence and headache/shortness of breath was more frequent than in the US General Population. Linear regression was run to identify potential predictors of CogState outcome variables. Amongst the personality traits, only conscientiousness predicted performance on learning ($p = 0.035$), working memory simple ($p = 0.003$) and complex ($p = 0.008$), not unexpected in this well-educated successful population. Coping style affected performance on tasks of attention ($p = 0.025$) and verbal learning ($p = 0.05$). Sleep adequacy ($p = 0.001$), daytime somnolence ($p = 0.038$) and headache/shortness of breath ($p = 0.043$) affected executive function and delayed recall. History of medical conditions was associated with cognitive impairment. For example, those with a history of mTBI had differences in detection ($p = 0.027$), attention ($p = 0.034$), verbal learning ($p = 0.017$), executive function ($p = 0.008$) and visual processing ($p = 0.032$).

Conclusions: This late life population, despite high scores on cognitive screening tests, shows some evidence of impairment on CogState parameters. The presentation will focus on predictors of "resilient" aging.

Sponsored by the Marian S. Ware Alzheimer's Program.