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CONTACT: Alzheimer's Association International Conf. Press Office, +44 (0) 20-7069-6000, media@alz.org
Niles Frantz, Alzheimer's Association, + 1 312-335-5777, nfrantz@alz.org
Emily Head, Press Officer, *The Lancet*, +44 (0) 207 424 4249, emily.head@lancet.com

FROM THE ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE 2017

***THE LANCET* COMMISSION: ONE THIRD OF DEMENTIA MAY BE PREVENTABLE**

**- *The Lancet* releases International Commission on Dementia Prevention, Intervention and Care -
- U.S. NIA shares inaugural research grants on health disparities in Alzheimer's -**

LONDON, July 20, 2017 – In a report presented today at the Alzheimer's Association International Conference 2017 (AAIC 2017) in London, *The Lancet* International Commission on Dementia Prevention, Intervention and Care reported that more than one third of global dementia cases may be preventable through addressing lifestyle factors that impact an individual's risk. These potentially modifiable risk factors have been identified at multiple phases across the life-span, not just in old age.

The Lancet Commission's report was simultaneously published in *The Lancet* and presented at AAIC 2017.

Also at AAIC 2017, the U.S. National Institute on Aging (NIA) announced inaugural research grants to investigate health disparities in Alzheimer's disease.

"Today's findings are extremely hopeful," said Maria Carrillo, PhD, chief science officer at the Alzheimer's Association. "At an individual level, many people have the potential to reduce their risk of cognitive decline, and perhaps dementia, through simple, healthful behavior changes. At a public health level, interventions based on this evidence could be extremely powerful in managing the global human and economic costs of Alzheimer's disease and other dementias."

The Alzheimer's Association offers [10 Ways to Love Your Brain](#), including practical guidance to reduce your dementia risk based on the latest research.

***The Lancet* International Commission on Dementia Prevention, Intervention and Care**

The Lancet Commission brings together 24 international experts to consolidate the huge strides that have been made in our knowledge and understanding of dementia risk factors, treatment and care, and the emerging knowledge as to what we should do to prevent and manage dementia. The Commission conducted a new review and meta-analysis; based on which they extended current models of risk by including hearing loss and social isolation. Incorporating potentially modifiable risk factors from across the life-span, they proposed a novel life-course model of risk, highlighting the opportunity for prevention.

Among their key recommendations are:

- Be ambitious about prevention. Interventions for established risk factors may have the potential to delay or prevent one third of dementias.
- Treat cognitive symptoms. To maximize cognition, people with Alzheimer's dementia or dementia with Lewy bodies should be offered cholinesterase inhibitors at all stages, or memantine for severe dementia.
- Individualize dementia care. Good dementia care spans medical, social and supportive care; and should be tailored to unique individual and cultural needs, preferences, and priorities.
- Care for family carers. Family carers are at high risk of depression. Effective interventions reduce the risk and treat the symptoms, and should be made available.
- Plan for the future. People with dementia and their families value discussions about the future and important upcoming decisions.
- Manage neuropsychiatric symptoms. Management of the neuropsychiatric symptoms of dementia - including agitation, low mood or psychosis - is usually psychological, social, and environmental, with drug treatment reserved for more severe symptoms.
- Consider end of life. A third of older people die with dementia, so it is essential that professionals working in end-of-life care consider whether a patient has dementia as they may be unable to make decisions about their care or express their needs and wishes.

Focus on Prevention

The Lancet Commission launched a novel life-span-based model of dementia risk, showing interventions that may maximize cognition, decrease distressing associated symptoms, reduce crises, and improve quality of life. The team estimate the contribution of each of the risk factors to the overall incidence of dementia, at the population level. The combined evidence to date shows that roughly 35 percent of all cases of dementia are attributable to nine potentially modifiable risk factors. Many of the risk factors occur at particular life stages but some, such as smoking and hypertension, are likely to make a difference at all life stages. The nine modifiable risk factors include:

- Early life - Education to a maximum of age 15
- Mid-life - Hypertension; Obesity; Hearing loss
- Later life - Depression; Diabetes; Physical inactivity; Smoking; Low social contact

Risk factors that are more common account for a higher percentage of population risk. For instance, the authors estimate that eight percent (8%) of all dementia cases could be associated with poor early school education; and five percent (5%) could be associated with smoking. While the mechanism linking education, hypertension, diabetes and smoking to dementia is relatively well understood, the recognition of hearing loss as a potential risk factor is still new, and the research is at an earlier stage.

The Commission's report delivered recommendations for targeted public health strategies that the researchers expect will significantly lower the global burden of Alzheimer's and other dementias. For example:

- The authors strongly recommend vigorously treating hypertension in middle aged and older people without dementia to reduce dementia incidence.
- Other recommended interventions include more childhood education, getting regular exercise, maintaining social engagement, stopping smoking, and management of hearing loss, depression, diabetes, and obesity.

The authors stated that, due to lack of data, the study did not include dietary factors, alcohol use, visual impairment, air pollution and sleep.

“While public health interventions will not prevent, or cure all potentially modifiable dementia, intervention for cardiovascular risk factors, mental health, and hearing may push back the onset of many people for years,” said Professor Gill Livingston, MD, from University College London and lead author of *The Lancet* Commission. “Even if some of this promise is realized, it could make a huge difference and we have already seen in some populations that dementia is being delayed for years. Dementia prevalence could be halved if its onset were delayed by five years.”

According to the Commission's report, worldwide dementia prevalence could be reduced by more than 1 million cases with a 10 percent reduction in the prevalence of seven principal health and lifestyle factors. An intervention that delayed dementia by a year might decrease the number of people living with dementia globally by 9 million in 2050.

“Overall, there is good potential for prevention and, once someone develops dementia, for care to be high-quality, accessible, and give value to an underserved, growing population. Effective dementia prevention and care could transform the future for society and vastly improve living and dying for individuals with dementia and their families. Acting now on what we already know can make this difference happen,” said Lon Schneider, MD, from the University of Southern California and co-author of the Commission.

Advancing health disparities research in Alzheimer's - National Institute on Aging inaugural grants

According to the Alzheimer's Association 2017 [Alzheimer's Disease Facts and Figures](#), African-Americans are about twice as likely to have Alzheimer's or other dementias as older whites, and Hispanics are about one and one-half times as likely to have Alzheimer's or other dementias as older whites. Yet, these populations are underrepresented in Alzheimer's and dementia research.

The NIA has identified a clear need to diversify research cohorts and improve methods and tools for conducting health disparities research related to Alzheimer's disease and other dementias. Two funding opportunities were created to encourage research that examines disparities in Alzheimer's disease using diverse cohorts of subjects. At AAIC 2017, NIA will announce the inaugural grant recipients and their projects, and highlight the new information expected to be generated because of these awards.

“Aging research using a framework that incorporate factors at multiple levels needs to be conducted with study populations that have robust demographic diversity,” said Carl V. Hill, PhD, MPH, Director of the NIA Office of Special Populations. “When cohorts are diverse, new pathways that link environmental, sociocultural, behavioral and biological factors can be identified. This is our hope for these research awards.”

According to the funding opportunity announcements, health disparities populations include: Blacks/African Americans, Hispanics/Latinos, American Indians/Alaskan Natives, Asian Americans, Native Hawaiians and Other Pacific Islanders, Socioeconomically Disadvantaged Populations, and Rural Populations. Additional populations may include: Disability Populations, and Sex and Gender Minorities.

About Alzheimer's Association International Conference (AAIC)

The Alzheimer's Association International Conference (AAIC) is the world's largest gathering of researchers from around the world focused on Alzheimer's and other dementias. 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.

AAIC 2017 home page: www.alz.org/aaic/

AAIC 2017 newsroom: www.alz.org/aaic/pressroom.asp

About the Alzheimer's Association

The Alzheimer's Association is the leading voluntary health organization in Alzheimer's 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 alz.org or call +1 800.272.3900.

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- Gill Livingston, MBChB, Lon S. Schneider, MD, MS. The Lancet International Commission on Dementia Prevention and Care. (Funder(s): University College London, Alzheimer's Society UK, Economic and Social Research Council, Alzheimer's Research UK)
 - www.thelancet.com/commissions/dementia-2017 [available once the news embargo lifts]
- Carl V. Hill, PhD, MPH and Rachel Whitmer, PhD, chairs. Advancing Health Disparities Research with the National Institute on Aging (NIA). (Funder: U.S. National Institute on Aging)

Abstract 19550 / Proposal ID FTS5-01-01

Diagnosis and Prognosis: The Lancet International Commission on Dementia Prevention and Care
Focused Topic Session: July 20, 2017: 8:30-10:00 AM

Prevention: The First Line of Care

Karen Ritchie, PhD, (karen.ritchie@inserm.fr) INSERM, Montpellier, France

Over the past thirty years there has been an immense investment in population studies of dementia designed to identify risk factors and their modes of interaction. While the exact cause of the dementias remains unknown, these studies together suggest a complex interaction of exposures which contribute differentially to the probability and timing of disease onset. Surprisingly little has been done in public health terms to translate these findings into public health prevention programs which could in turn have a significant impact in reducing incidence and pushing back time of disease onset. Analyzing findings from prospective population studies it can be seen that a number of key risk factors are potentially reversible (notably insulin resistance, depression, hypertension, diet, activity). By modeling intervention scenarios it may be demonstrated that public health prevention strategies focusing on the most potent and potentially reversible risk factors could have a significant impact on dementia incidence over the coming decade with reductions estimated at around 30%. These findings have now been reproduced using prospective population studies in both Europe and the United Kingdom. The impact of prevention programs targeting the principal dementia risk factors is likely to be highly significant, with current epidemiological modelling suggesting it to be even more potent than modification of the principal genetic risk factor. Exposure to these risk factors occur, however, primarily in middle age suggesting firstly that strategies to delay dementia onset should be carried out much earlier than is currently the case. In this context a number of recent research initiatives and clinical trials are now targeting the long pre-clinical phase of Alzheimer's disease. Prevention strategies must start with a shift in public perceptions of the disorder from being a disease of old age characterized by dementia, to a clinically silent disease of middle-age characterized by underlying brain changes.

Abstract 19551 - A New Model of Potentially Modifiable Risk Factors for Dementia

Gill Livingston, MBChB, MD, University College London, London, United Kingdom

One way of considering risk in dementia is to calculate the Population Attributable Fraction (PAF), which is the percentage reduction in new cases over a given time if a particular risk factor were completely eliminated. The work to-date focuses on cardiovascular risk factors for dementia; and depression and low educational attainment. **Which modifiable risk factors?** We calculated a combined PAF for known modifiable risk factors for all-cause incident dementia listed in the UK National Institute of Health and Care Excellence and US National Institute of Health guidelines. We used data from meta-analyses. **PAF for modifiable risk factors** The attributable risk in a population depends on the prevalence of the risk factor and the strength of its association (relative risk) with the disease. While systematic reviews adjusted for many confounders, they could not adjust for all the risk factors in our total PAF calculation. We therefore calculated overall PAF by using a formula to adjust for communality when confounding has not been fully accounted for ($PAF = 1 - [(1 - PAF_1)(1 - PAF_2)(1 - PAF_3) \dots]$) allow calculation of each factor's unique risk. We found three principal component using this method, which explained 53% of the total variance between the nine risk factors, suggesting substantial overlap. We then calculated overall PAF from nine risk factors; education to age 11 or 12, midlife hypertension, midlife obesity, hearing loss, later-life depression, diabetes, physical inactivity, smoking and social isolation. We will present the new model of life course risk factors in the conference. There are additional factors which we do not have data to include in our calculations but may be important. These encompass, dietary factors, alcohol use, visual impairment, bilingualism, living near major roads and sleep disorders which have received some attention for their role in the development of cognitive impairment. We will discuss other limitations of the data at the conference. The general principle is that there is an important proportion of modifiable risk factors in dementia, which could translate into a large impact on the global burden of dementia which would then have huge implications for social and healthcare costs.

Abstract 19552 - Treatment of Cognition

Robert J Howard, MD, University College London, London, United Kingdom

Treatment with cholinesterase inhibitors modestly improves cognition, activities of daily living and global clinician rating of patients with mild, moderate and severe Alzheimer's disease (AD). Improvements are close to minimal clinically important values such that clinicians should not expect to be able to make decisions about response in an individual treated patient. Treatment decisions will often be influenced by experience of side-effects, in particular nausea, vomiting, diarrhea, vivid dreams and cramps. These drugs do not improve non-cognitive AD symptoms and there is no convincing evidence for additional cognitive or functional benefit with higher than standard (>10mg donepezil) dosing. Although most trials have been of short duration, treatment benefits appear to be sustained, even in severely affected individuals, and this should be considered in discontinuation decisions. Meta-analyses report cognitive benefits in patients with dementia with Lewy bodies and Parkinson's disease dementia. Although not recommended for patients with frontotemporal or vascular dementia, patients with mixed vascular and AD pathology may benefit from treatment. Memantine improves cognition, activities of daily living and global rating, but benefits are smaller than those seen with cholinesterase inhibitors, often not reaching clinically important levels and is often used for patients who cannot tolerate a cholinesterase inhibitor. Combination treatment with a cholinesterase inhibitor is associated with very small additional benefit compared to cholinesterase inhibitor alone. Cognitive stimulation therapy has better evidence to support claims for improving cognition in AD than cognitive training and cognitive rehabilitation. It is important to bear in mind that most cognitive intervention studies have not included active control interventions or strategies to blind outcome assessors that would allow meaningful comparison with the results of pharmaceutical trials. Finally, physical exercise may improve activities of daily living in AD, but reported effects on cognition have not been consistent. Together with the difficulties in interpretation of efficacy associated again with failure to include adequate control interventions or to blind outcome assessors, it is still unclear whether the intensity of prescribed exercise needs to exceed a threshold above which cognitive benefits can be demonstrated.

Abstract 19553 - Approach to Agitation and Other Psychiatric Syndromes/ Behaviors

Lon S Schneider, MD, MS, Keck School of Medicine of USC, Los Angeles, CA, USA

We will highlight the commission's approach to agitation and other psychiatric syndromes, behaviors. The goals are to recognize psychiatric symptoms, manage, protect, and individualize care over the long-term. Psychiatric symptoms in dementia are common, generally increasing with stage of dementia and affecting nearly everyone with dementia at some point. Many different symptoms co-occur and may cluster into affective, psychosis, apathy, and hyperactivity, highlighting the need for careful assessment and a management strategy, for example, the DICE approach. We will outline interventions with the best evidence for the assessment and management of agitation, including pleasant events and maximizing communication as prevention strategies, and providing good quality care. We will discuss management principles for agitation and their overlap with other symptoms (such as hallucinations, delusions, depression and apathy) which may co-occur. Indications for drug interventions including antipsychotics and antidepressants, harmful effects, and withdrawal will be outlined. Assessing and managing agitation might start with asking the person what is wrong and involve improving communication and person-centered care, consideration and management of physical causes (pain, infection, discomfort etc.) pleasant activities, social engagement, occupational interventions, caregiver interventions; before considering pharmacological treatments. For management of depressive symptoms it is important to consider risk for self-harm, self-neglect, underlying delirium, pain, and the need for tailored treatment to patient's needs and wishes. Substantial improvement in quality of life can be gained with considerate and personalized interventions for psychiatric symptoms including agitation.

Proposal ID FTS5-02-01

Public Health & Psychosocial: Advancing Health Disparities Research with the National Institute on Aging
Focused Topic Session, July 20, 2017: 11:45 AM-1:15 PM

The session will focus on the inaugural grantees of PAR15-349: Health Disparities and Alzheimer's Disease (R01) and PAR15-350: Emerging Directions for Addressing Health Disparities in Alzheimer's Disease (R03). This session will highlight the oncoming new information that will result because of the awards.

Chair - Carl Hill, Ph.D., M.P.H. (hillcv@mail.nih.gov), National Institutes of Health (NIH), Bethesda MD
Chair - Rachel Whitmer, PhD, Kaiser Permanente Division of Research, Oakland CA 94530

Abstract 19570: Racial Disparities in the Health of Caregivers for Persons with Alzheimer's Disease
Julie M Zissimopoulos, Ph.D, University of Southern California, Los Angeles, CA

Abstract 19571: Alzheimer's Disease & Related Dementias: Geography, Environments, and Mechanisms (ADRD-GEM)
Jiu-Chiuan Chen, MD, ScD, University of Southern California, Los Angeles, CA

Abstract 19572: Lifecourse Health, Cerebral Pathology and Ethnic Disparities in Dementia
Rachel A. Whitmer, PhD, University of California, San Francisco, San Francisco, CA, Kaiser Permanente Division of Research, Oakland, CA

Abstract 19573: Discussant
Elizabeth Rose Mayeda, PhD, MPH, University of California, San Francisco, San Francisco, CA

Abstract 19574: Offspring Study of Mechanisms for Racial in Alzheimer's Disease
Jennifer J Manly, PhD, Columbia University, New York, NY

Abstract 19575: Imaging and Health Disparities
Charles S DeCarli, MD, Department of Neurology, University of California at Davis, Davis, CA

Abstract 19576: Health Disparities in Alzheimer's Disease Among Mexican Americans
Sid O'Bryant, PhD, University of North Texas Health Science Center, Fort Worth, TX

Abstract 19577: Fitness and Lifestyle Affect Neural and Cognitive Risk Factors for Alzheimer's Disease in Older African Americans
Mark Gluck, Ph.D, Rutgers University - Newark, Newark, NJ

Abstract 19578: African American Fighting Alzheimer's in Midlife
Carey E. Gleason, PhD, Geriatric Research Education and Clinical Center, W.S. Middleton Memorial Veterans Hospital, Madison, WI

Abstract 19579: Discussant
Hector M Gonzalez, PhD, Michigan State University, East Lansing, MI

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