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## **CHILDHOOD SCHOOL PERFORMANCE AND TYPE 1 DIABETES IDENTIFIED AS RISK FACTORS FOR ALZHEIMER'S DISEASE, DEMENTIA**

*Loneliness and High TV Viewing also Linked to Lower Cognitive Function, According to Reports  
from the Alzheimer's Association International Conference 2015*

**WASHINGTON, DC, July 20, 2015** – The first study of dementia risk, including Alzheimer's disease, in older adults with type 1 diabetes (T1D) was reported today at the Alzheimer's Association International Conference® 2015 (AAIC® 2015) in Washington, D.C. People in the study with T1D were 93% more likely to get dementia (73% after adjustment for heart health risk factors) compared with people without diabetes.

Two studies presented at AAIC 2015 suggest an association between childhood school performance (age 9-10) and late life dementia. Other research reports identified loneliness, low physical activity and high TV viewing as risk factors for cognitive decline and dementia.

“Evidence is growing that there are lifestyle habits that you can adopt to maintain or potentially improve your health – including your brain health – as you age,” said Maria Carrillo, PhD, Alzheimer's Association Chief Science Officer. “Many of the habits are familiar. Often, the same healthful practices that are good for your overall health are also good for your brain. These actions and activities – controlling your heart health numbers, getting formal education, being physically and socially active – can help keep your brain and body healthy and potentially reduce your risk of cognitive decline. It's never too late or too early to start.”

Given the growing evidence that people can reduce their risk of cognitive decline, the Alzheimer's Association recently shared *10 Ways to Love Your Brain*, tips that may help lessen the chance of cognitive decline as we age. The suggestions include engaging in regular cardiovascular exercise that elevates your heart rate, getting more formal education, and quitting smoking. The complete list can be found at [alz.org](http://alz.org).

### **First Study of Type 1 Diabetes and Risk of Dementia in Late Life**

Type 1 diabetes (T1D) is a chronic condition where the pancreas produces little or no insulin, which is a hormone that regulates the movement of sugar into your cells. It is usually diagnosed in children and young adults. In type 2 diabetes (T2D), the body either resists the effects of insulin or doesn't produce enough insulin to maintain a normal glucose level. It is more common in adults, and is the most common form of diabetes, affecting 90 to 95% of Americans with diabetes.

Studies have shown that T2D is associated with a greater risk of dementia, including Alzheimer's disease; however, little is known about how T1D affects cognitive aging and dementia risk. At AAIC 2015, Rachel Whitmer, PhD, Kaiser Permanente Division of Research, Oakland CA, and colleagues reported results from first study of dementia in elderly adults with T1D.

“Elderly people with type 1 diabetes are a population that is unique from elderly people with type 2 diabetes,” Whitmer said. “They have a much younger age of diabetes onset, continuous insulin treatment, more frequent severe hypoglycemic episodes, but less vascular risk factors.”

The researchers followed the health histories of 490,344 people over 60 years old with no prior dementia who are in the Kaiser Permanente Northern California health system, tracking them over 12 years for new dementia diagnoses. 334 individuals had T1D. Analyses compared the T1D group with two control groups: one with T2D and one without diabetes, taking into account differences in gender, race, stroke, peripheral arterial disease and hypertension.

Results presented at AAIC 2015 show that 16% of those with T1D in the study were diagnosed with dementia during the follow-up period while 12% of those without T1D developed dementia. In other words, people in the study with T1D were 83% more likely to get dementia compared with people who did not have T1D; 61% more likely after adjustment for stroke, peripheral arterial disease and hypertension. The magnitude of T1D on dementia risk was larger when people with T2D were excluded for the comparison group (93% more likely; 73% after adjustment).

“Both type 1 and type 2 diabetes are rapidly increasing worldwide, and people with type 1 are living longer than ever before,” Whitmer said. “Since management of type 1 diabetes requires vigilance and constant self-care, cognitive impairment poses a particular threat to this vulnerable population. More research is needed to identify risk and protective factors for Alzheimer’s and other dementias in this group that is newly entering the aging population.”

### **How School Grades, Formal Education, and Work Complexity Impact Dementia Risk**

There is considerable variation among people diagnosed with dementia, including Alzheimer’s disease, in the amount of amyloid plaques, tau tangles, inflammation and other damage in the brain. “Cognitive reserve” is a concept developed to explain the gap between the amount of brain damage and the level of memory and thinking symptoms the person experiences. It has been proposed that the greater the level of cognitive reserve, the higher the brain’s ability to adapt to injury like that which causes dementia, and the more damage – and more time – required for cognitive function to decline far enough to be considered dementia. Formal education and occupational complexity have been viewed as the main contributors to cognitive reserve.

To further investigate and understand this notion, Serhiy Dekhtyar, PhD, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden and colleagues followed 7,574 individuals aged 65+ from the Uppsala Birth Cohort Study (Sweden) for more than 20 years to detect their new cases of dementia. In addition to conventional measures of cognitive reserve, such as education and occupational attainment, they also collected data on childhood cognitive ability – school grades around age 10.

“We ended up with a full life-course model of cognitive reserve in dementia, with childhood cognitive ability, early-adulthood education, and mid-life occupational attainment, which has never been tested before,” Dekhtyar said.

Dementia was diagnosed in 950 individuals. According to study results reported at AAIC 2015:

- Dementia risk was elevated 21% in people who were in the lowest 20% of childhood school grades in this population. Importantly, high occupational complexity could not compensate for the effect of low childhood school marks.
- Dementia risk was reduced 23% among individuals in occupations characterized by high complexity with data and numbers.
- Lowest dementia risk (39% reduction) was found in the group who had both higher childhood school performance and high occupational complexity with data.

“Our findings highlight the importance of early-life cognitive performance for the late-life risk of dementia. It appears that baseline cognitive ability – even at age 10 – may provide the foundation for successful cognitive aging much later in life,” said Dekhtyar. “Formation of cognitive reserve is a process that apparently begins early in life.”

Dekhtyar noted that these findings are corroborated in a smaller clinical study of dementia also conducted in Sweden. (*See the next description.*)

### **School Performance, Education and Occupational Complexity: Corroboration**

At AAIC 2015, Hui-Xin Wang, PhD and colleagues from the Aging Research Center and Department of Clinical Neuroscience, Karolinska Institutet & Stockholm University, Stockholm, Sweden reported their study on the role of childhood school performance, education and the complexity of a person’s job on the risk of dementia. The investigators used data from 440 men and women age 75 and older who started the study with good cognitive functioning in the Kungsholmen project, a multifaceted research program to gather information about aging and dementia.

163 people (37%) developed dementia during a nine-year follow up period. The results were cross-referenced with school grades in five elementary school subjects (mathematics, reading, geography, history, and writing) from when the participants were nine or 10 years old. The researchers also had collected information on the participants’ formal education and occupational complexity.

The researchers found several significant correlations between grades and dementia risk:

- Dementia risk was elevated more than 50% in individuals over 75 with the lowest 20% of early-life school grades, even if they had more formal education or a job requiring significant complexity.
- Individuals who completed secondary education had a lower risk of dementia compared to individuals with only elementary education (28% lower risk).
- Women in the study who had an occupation with high complexity with people (e.g., high demands on negotiating, instructing, and supervising) were at 60% lower risk of developing dementia compared to those who had an occupation with low complexity with people.

“These findings suggest that early-life cognitive ability may be an important predictor of dementia in late life,” said Wang.

### **Low Physical Activity and High TV Viewing are Associated with Worse Cognitive Function**

Physical activity in later life is generally considered a protective factor against cognitive decline and possibly Alzheimer’s and other dementias, but little is known about the role of physical activity in early adulthood.

“Understanding this relationship in early adulthood may be particularly important because global data suggests that levels of physical inactivity and sedentary behavior are increasing,” said Tina Hoang, MSPH, of the Northern California Institute of Research and Education (NCIRE), San Francisco, with her mentor, Kristine Yaffe, MD, of the University of California, San Francisco.

Yaffe, Hoang and colleagues investigated the association of long-term patterns of low physical activity and high television viewing time over 25 years with cognitive function at mid-life. The study population included more than 3,200 black and white adults, 18-30 years old, in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Physical activity and television viewing were assessed at repeated visits (≥3 assessments) over 25 years. Low physical activity was defined as activity below 300 kcal/50 min session, 3 times per week; high television viewing was defined as more than 4 hours per day.

A long-term pattern of each behavior was defined as meeting these cutoffs for more than two-thirds of visits. 17% of participants reported a long-term pattern of low physical activity, 11% a long-term pattern of high television viewing, and 3% reported both. At year 25 of the study, participants were assessed for memory, executive function and processing speed using well-established tests.

At AAIC 2015, Yaffe, Hoang and colleagues reported that study participants with low levels of physical activity over 25 years had significantly worse cognition in mid-life, adjusting for age, race, sex, education, smoking, alcohol, BMI, and hypertension. Similarly, participants with high levels of TV watching over 25 years also had significantly worse mid-life cognitive function. Study participants with both long-term low physical activity and high television viewing were almost two times more likely to have poor cognitive function in mid-life.

“Our findings demonstrate that even early- and mid-adulthood may be critical periods for promotion of physical activity for healthy cognitive aging,” Hoang said. “Sedentary behaviors, like TV viewing, could be especially relevant for future generations of adults due to the growing use of screen-based technologies. Because research indicates that Alzheimer’s and other dementias develop over several decades, increasing physical activity and reducing sedentary behavior beginning in early adulthood may have a significant public health impact.”

### **Loneliness is Associated with Worse Cognitive Function in a Study of Older U.S. Adults**

Research suggests that late-life depression is associated with future incidence of Alzheimer's in some older adults. In general, less is known about individual aspects of, or causative factors for, depression and their relationship to Alzheimer's/dementia risk. One component, loneliness, has been associated with functional decline and increased progression to dementia.

To examine the relationship between loneliness and cognitive function in older adults, Nancy J. Donovan, MD, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, and colleagues examined data from more than 8,300 adults age 65 and older participating in the U.S. Health and Retirement Study from 1998 to 2010. Participants in that study had assessments of their loneliness, depression, cognitive function and memory, health status, and social network characteristics every two years. Seventeen percent (17%) of participants reported loneliness at the beginning of the study with approximately half of the lonely individuals reporting clinically significant depression.

At AAIC 2015, the researchers reported that the loneliest people in the study experienced accelerated cognitive decline – approximately 20% faster over 12 years – than people who were not lonely, regardless of demographic factors, social network, health conditions and baseline depression. Similarly, people reporting depression at baseline experienced significantly faster cognitive decline during the study. However, looking in the other direction, the researchers found lower cognitive function does not lead to worsening loneliness.

“Our study suggests that even one or two depressive symptoms – particularly loneliness – is associated with an increased rate of cognitive decline over 12 years,” Donovan said. “We found that lonely people decline cognitively at a faster rate than people who report more satisfying social networks and connections. Although loneliness and depression appear closely linked, loneliness may, by itself, have effects on cognitive decline. This is important to know as we develop treatments to enhance cognitive health and quality of life for older adults.”

### **About AAIC**

The Alzheimer’s Association International Conference (AAIC) is the world’s largest gathering of leading 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 2015 home page: [www.alz.org/aaic/](http://www.alz.org/aaic/)

AAIC 2015 newsroom: [www.alz.org/aaic/press.asp](http://www.alz.org/aaic/press.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](http://alz.org) or call 800.272.3900.

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- Rachel Whitmer, PhD, et al. Type 1 Diabetes and Risk of Dementia in Late Life: The Kaiser Diabetes & Cognitive Aging Study. (Funder: U.S. National Institute on Aging)
- Serhiy Dekhtyar, PhD, et al. A Life-Course Study of Cognitive Reserve in Dementia. Dementia Incidence in Inpatient Registers and MMSE Test Scores in a Clinical Study in Sweden. (Funders: Swedish Research Council for Health, Working Life and Welfare (FORTE), Swedish Research Council (VR))
- Hui-Xin Wang, PhD, et al. Childhood School Performance, Education, and Occupational Complexity. A Life Course Study from the Kungsholmen Project. (Funders: Swedish Research Council, Swedish Council for Working Life and Social Research, Swedish Brain Power, Konung Gustaf V:s och Drottning Victorias Frimurare foundation, Gun and Bertil Stohnes foundation, Gamla Tjänarinnor foundation, Dementia Association, Alzheimer Foundation Sweden, and U.S. National Institute on Aging)
- Tina Hoang, MSPH, et al. Early Adult Patterns of Physical Activity and Television Watching and Mid-Life Cognitive Function. (Funder: National Heart, Lung, and Blood Institute, NIH)
- Nancy Donovan, MD, et al. Reciprocal Relations of Loneliness and Cognitive Function in Older U.S. Adults. (Funders: U.A. National Institute on Aging; The Dupont-Warren/Livingston Fellowships, Harvard Medical School; the Muriel Silberstein Alzheimer's Disease Fund)

O2-03-06 -- Oral session, Monday, July 20, 2-3:30 pm, #146

Theme Selection: Public Health and Psychosocial

Topic Selection: Epidemiology: Cardio Metabolic Factors, Cognitive Decline and Dementia

**Type 1 Diabetes and Risk of Dementia in Late Life: The Kaiser Diabetes & Cognitive Aging Study**

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Background: Though type 2 diabetes (T2D) is associated with a two-fold greater risk of dementia little is known regarding how type 1 diabetes (T1D) impacts cognitive aging. Individuals with T1D are living longer than ever before, and compared to T2D, have a much younger age of onset and, consequently, longer diabetes duration, continuous insulin treatment and more severe hypoglycemic episodes, but less vascular risk factors. The goal of our study was to determine if older individuals with T1D are at higher risk of dementia compared to those without T1D.

Methods: All member of Kaiser Permanente Northern California ( KPNC) age > 60 on January 1, 2002 (N=490,344) with no prior dementia were followed through July 1, 2014 for dementia diagnoses made in primary care, neurology and psychiatry. T1D status was determined using information from the KPNC Diabetes registry (ICD 9 code 250.01). Cox proportional hazard models using age as the time scale were constructed to evaluate the association between T1D and risk of dementia with censoring for death and health plan memberships gaps of > 90 days. Models were additionally adjusted for gender, race, stroke, peripheral arterial disease (PAD), and hypertension. Models were run both with and without T2D in the reference group.

Results: 230 individuals had T1D and of these 16% were diagnosed with dementia during the follow-up while 12% of those without T1D developed dementia. Compared to those without T1D those with T1D were 83% more likely to get dementia (Hazard Ratio {HR} 1.83, 95% Confidence Interval {CI} 1.3, 2.5) and 61% more likely after adjustment for stroke, PAD and hypertension. When excluding those with T2D from the reference group, the magnitude of T1D on dementia risk was larger (HR=1.93, 95% CI,1.3,2.6; fully adjusted HR 1.73, 95% CI 1.3,2.3).

Conclusions: This is the first study of dementia in elderly adults with T1D. Those with T1D were 80% more likely to get dementia than those without T1D. Since management of T1D requires vigilance and constant self-care; cognitive impairment poses a threat to this vulnerable population. Future studies need to identify risk and protective factors for dementia in this group newly entering the aging population.

O2-11-04 -- Oral session, Monday, July 20, 4:15-5:45 pm, #146

Theme Selection: Public Health and Psychosocial

Epidemiology: Cognitive Reserve, Education and Long-Term Effect on Cognitive Change and Dementia Incidence

**A Life-Course Study of Cognitive Reserve in Dementia. Dementia Incidence in Inpatient Registers and MMSE Test Scores in a Clinical Study in Sweden**

**Serhiy Dekhtyar, PhD**

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Background: Cognitive reserve helps mitigate the impact of pathology on the clinical expression of dementia. Education and occupational complexity are considered as contributors to reserve, although it has been argued that cognitive reserve is likely formed over the life-course. A life-course model of cognitive reserve in dementia risk has not yet been tested. We apply a life-course model and examine if school grades around age 10, formal educational attainment, and lifetime occupational complexity affect dementia incidence in inpatient registers. Effects of early-life school performance are then re-examined in a clinical study of population that underwent Mini-Mental State Examination.

Methods: For the incidence study of dementia, 7,574 subjects aged 65+ from the UBCOstudy were followed for 21 years. Information on school performance, education, and occupational attainment was collected from archives and censuses. Dementia diagnosis was extracted from inpatient registers. Discrete-time PH-models were estimated. For the clinical study on school grades and MMSE, 142 non-demented subjects aged 75+ in 1987 who enrolled in the Kungsholmen Project were back-traced until age 10, and their elementary grades were extracted from the archives. MMSE was administered at baseline.

Results: In the incidence study, dementia risk was reduced in individuals with higher childhood grades (HR: 0.79;  $p < 0.05$ ) and among subjects in data-complex occupations (HR: 0.77;  $p < 0.05$ ). Professional/university education lowered dementia risk in minimally-adjusted models (HR: 0.74;  $p < 0.05$ ), although the effect faded with adjustment for occupational complexity. Lowest risk was found in those with both higher school grades and high occupational complexity with data (HR: 0.61;  $p < 0.001$ ). Data-complex occupations could not negate the effect of low grades. In contrast, dementia risk was reduced in those with higher grades, irrespective of complexity. In the clinical study on school grades and MMSE, a positive association was found between mean childhood performance and MMSE test score ( $p < 0.001$ ).

Conclusions: Higher childhood school performance is protective of dementia risk, particularly when preserved through complex work environments in adulthood. Formation of cognitive reserve in dementia risk appears to be a life-course process that begins early in life. Findings from the clinical study linking childhood grades and MMSE confirm the importance of early-life reserve.

O2-11-03 -- Oral session, Monday, July 20, 4:15-5:45 pm, #146

Theme Selection: Public Health and Psychosocial

Topic Selection: Epidemiology: Cognitive Reserve, Education and Long-Term Effect on Cognitive Change and Dementia Incidence

**Childhood School Performance, Education, and Occupational Complexity. A Life Course Study from the Kungsholmen Project**

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Background: Cognitive reserve has been shown to protect against dementia through stimulating life experiences, such as education and occupation. A previous study, based on inpatient registers, found that childhood school grades are associated with risk of dementia after adjustment for formal education and occupational complexity. It is, however, unclear if childhood school performance remains related to dementia when cases are ascertained during detailed clinical examination.

Methods: A cohort of 440 men and women aged 75+ from the Kungsholmen project was followed-up for nine years to detect incident dementia, identified as a result of detailed clinical examination in accordance with DSM III-R. To measure early-life contributors to cognitive reserve we used grades extracted from the school archives from when the KP participants were aged 9-10 years. Data on formal education and occupational complexity was collected at baseline and first follow-up examination. Cox proportional hazard models were used to estimate the relationship between life course cognitive reserve measures and dementia risk.

Results: Over the 9-year follow-up, 163 individuals (37%) developed dementia. Dementia risk was elevated (RR= 1.54, 95% CI: 1.03 to 2.29) in individuals with low early-life school grades (lowest 20%) even after adjustment for formal educational attainment and occupational complexity. Secondary education protected against dementia (RR=0.72, 95% CI: 0.50 to 1.03), whereas the effects of post-secondary and university degrees were indistinguishable from the baseline. Occupational complexity with data and things were weak predictors of dementia risk, although high complexity with people was found to be protective, albeit only in women (RR=0.25, 95% CI: 0.06 to 1.06). The pattern of results remained unchanged after genetic susceptibility (APOE\*ε4 status), comorbidities, and depressive symptoms were taken into account.

Conclusions: Early-life school performance appears to be a significant contributor to cognitive reserve irrespective of subsequent education and occupational complexity.

O2-11-02 -- Oral session, Monday, July 20, 4:15-5:45 PM, #146

Theme: Public Health and Psychosocial

Topic: Epidemiology: Cognitive Reserve, Education and Long-Term Effect on Cognitive Change and Dementia Incidence

**Early Adult Patterns of Physical Activity and Television Watching and Mid-Life Cognitive Function**

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Background: Physical activity and television viewing in early adulthood are critical risk factors for adverse health outcomes, but few studies have investigated whether these modifiable behaviors are associated with later life cognitive function. We examined the relationship between early to mid-life patterns of physical activity and television viewing with mid-life cognition.

Methods: In a prospective study of 3,247 adults, (18-30 years old) enrolled in the Coronary Artery Risk Development in Young Adults Study (1985-86), physical activity and television viewing were assessed at repeated visits ( $\geq 3$  assessments) over 25 years using a validated questionnaire. At each visit, low physical activity was defined as activity below the bottom quartile of baseline levels (approximately  $< 300$  kcal/50 min session 3 times/week), and high television viewing was defined as time above the top quartile of baseline levels ( $> 4$  hours/day). A long-term pattern of each behavior over 25 years was defined as meeting these cutoffs for  $> 2/3$  of visits. Cognitive function was assessed at Year 25 using the Digit Symbol Substitution Test (DSST), Stroop Interference Score, and Rey Auditory Verbal Learning Test (RAVLT).

Results: 17% of participants reported a long-term pattern of low physical activity, 11% a long-term pattern of high television viewing, and 3% reported both. Compared to participants with higher physical activity, those with low physical activity had an increased likelihood of low cognitive performance ( $> 1$  SD below the mean) on DSST (aOR=1.82, 95% CI 1.39-2.38) and Stroop (aOR=1.38, 95% CI 1.05-1.82) but not RAVLT after adjusting for age, race, sex, education, smoking, alcohol, body mass index, and hypertension. Results were similar for high television viewing (DSST: aOR=1.34, 95% CI 1.01-1.77; Stroop: aOR=1.61, 95% CI 1.20-2.14). Compared to participants with high physical activity and low television viewing, the odds of poor cognitive performance were more than two times higher for participants with low physical activity and high television viewing (DSST: aOR=2.45, 95% CI 1.53-3.93; Stroop: aOR=2.38, 95% CI 1.50-3.75).

Conclusions: Long-term patterns of low physical activity and high television viewing in early adulthood were associated with worse mid-life executive function and processing speed. These risk behaviors may be critical targets for prevention of cognitive aging.

O2-11-06 -- Oral session, Monday, July 20, 4:15-5:45 pm, #146

Theme Selection: Public Health and Psychosocial

Topic Selection: Epidemiology: Cognitive Reserve, Education and Long-Term Effect on Cognitive Change and Dementia Incidence

**Reciprocal Relations of Loneliness and Cognitive Function in Older U.S. Adults**

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Background: In older adults, loneliness has been associated with functional decline and increased progression to dementia. The objective of this study was to examine the reciprocal relations of loneliness and cognitive function in older adults, adjusting for sociodemographic and health-related factors, social network and depression.

Methods: The sample comprised 8,311 adults, ages 65 and older, participating in the U.S. Health and Retirement Study from 1998 to 2010. Participants underwent biennial assessments of loneliness (measured using a single binary question from the Center for Epidemiologic Studies Depression Scale (CES-D), 8-item version), depression (based on the remaining seven CES-D questions and classified as no, low (1-2) or high (3-7) depressive symptoms), global cognition, (using a composite score derived from the Telephone Interview for Cognitive Status, the Informant Questionnaire on Cognitive Decline in the Elderly and a word list memory task), health status and sociodemographic and social network characteristics. Repeated measures analyses were used to examine the reciprocal relations of loneliness and cognitive function over 12 years. In separate sets of regression models for baseline loneliness predicting cognitive function and for baseline cognition predicting loneliness, we controlled sequentially and cumulatively for (1) sociodemographic factors, (2) social network, (3) health conditions and (4) depression.

Results: Greater baseline loneliness was associated with accelerated cognitive decline over 12 years independent of sociodemographic factors, social network, health conditions and baseline depression (for loneliness interacting with time:  $b=-0.02$ ,  $p=0.002$ , indicating a rate of decline approximately 25% faster in the lonely compared to the non-lonely). In post-hoc models including interaction terms for depression and time, both low and high depression categories were significantly associated with faster cognitive decline ( $b=-0.01$ ,  $p=0.01$  and  $b=-0.02$ ,  $p=0.003$  respectively) and the estimated effect of loneliness on rate of cognitive decline became marginally significant ( $b=-0.01$ ,  $p=0.08$ ). Reciprocally, lower baseline cognitive score was associated with greater odds of loneliness at baseline and across time (OR=1.12,  $p=0.005$ ), but these associations were not significant when controlling for baseline depression.

Conclusions: Loneliness is a risk factor for accelerated cognitive decline in older individuals. Although loneliness and depression appear closely linked, loneliness may have independent effects on cognitive decline.

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