

## **EMBARGOED FOR RELEASE UNTIL MONDAY, JULY 17, 2017, 8 AM BST / 3 AM EDT**

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### **FROM THE ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE 2017**

#### **NEW AND EXPANDED RISK FACTORS FOR COGNITIVE DECLINE AND ALZHEIMER'S DISEASE**

*– Verbal and sensory skills, hospitalization may predict future cognitive function –*

**LONDON, July 17, 2017** – Detection of dementia at the earliest stages has become a worldwide scientific priority because drug treatments, prevention strategies and other interventions will likely be more effective very early in the disease process, before extensive brain damage has occurred. Research results reported at the Alzheimer's Association International Conference (AAIC) 2017 provide clues about associations between cognitive status in older people and several behavior and lifestyle factors, including verbal skill, hearing, and hospitalization.

“It is essential that we learn more about factors that indicate or impact risk for Alzheimer's disease and other dementias, especially lifestyle factors that we can change or treat,” said Maria C. Carrillo, PhD, Alzheimer's Association Chief Science Officer. “The Alzheimer's Association is committed to advancing scientific research to identify simple and accessible ways to spot the signs of cognitive decline.”

Having trouble with memory does not mean you have Alzheimer's. That said, the Alzheimer's Association says [early detection](#) allows people with dementia and their families:

- A better chance of benefiting from treatment.
- More time to plan for the future.
- Increased chances of participating in clinical drug trials, helping advance research.
- An opportunity to participate in decisions about care, living options, financial and legal matters.

#### **Hearing loss is associated with poor cognition and progression to mild cognitive impairment**

Taylor Fields, a doctoral student in the Neuroscience Training Program within the University of Wisconsin School of Medicine and Public Health, and colleagues examined the prevalence of hearing loss in late middle-aged adults with a family history of Alzheimer's, and the association between hearing loss and cognitive status and decline. The researchers found evidence for a link between hearing loss and mild cognitive impairment, a condition that can be a precursor to Alzheimer's disease.

The scientists used data collected from 783 people enrolled in the Wisconsin Registry for Alzheimer's Prevention (WRAP), a longitudinal study group of people with a parental history of Alzheimer's. Participants undergo periodic tests to evaluate their ability to remember, process, and learn information. Study volunteers self-reported whether they had been diagnosed with hearing loss. At the beginning of the study, all volunteers had normal test results for clinical tests of cognitive function, and all were assessed for progression to mild cognitive impairment.

Over the course of four years, 72 (9.2 percent) study participants reported being diagnosed with hearing loss. Relative to those who reported normal hearing, people in the study with hearing loss were:

- More likely to score significantly poorer on cognitive tests such as how quickly new information is processed, flexibility in thinking, and how the brain, eye, and hand coordinate during information processing.
- Roughly three times as likely to be characterized as having mild cognitive impairment.

“This study suggests that hearing loss could be an early indicator of worsening cognitive performance in older adults,” Fields said. “Identifying and treating hearing loss could have value for interventions aimed at reducing the burden of Alzheimer’s disease.”

### **Verbal fluency predicts cognitive health**

In another analysis of participants in WRAP, Kimberly Mueller, PhD, of the Wisconsin Alzheimer’s Institute, University of Wisconsin School of Medicine and Public Health, and colleagues investigated whether people with very early memory declines also show changes in their everyday speech. The researchers found that subtle changes in everyday speech, such as the use of short sentences, more pronouns, and pauses like “um” and “ah,” correlated with early Mild Cognitive Impairment (eMCI), which can be a precursor to Alzheimer’s disease.

In the study reported at AAIC 2017, the scientists analyzed two speech samples, taken two years apart, from 264 participants in WRAP. Of these participants, 64 were identified as having eMCI based on cognitive testing over 8-10 years. The speech samples, averaging one minute long, were collected by asking the participants to describe a simple picture.

Study participants with eMCI declined faster on two measures of speech: content and fluency. The content of their speech was less specific, with a higher proportion of pronouns to nouns (e.g., “she,” “it,” “them”). Their fluency was more disrupted (more hesitations, word repetitions, and filled pauses (“um,” “uh”)). Also, those with eMCI used less complex syntax and shorter sentences, and took more time to express the same amount of content as the cognitively healthy group.

“Our study is the largest prospective, longitudinal study of spontaneous speech samples in a study group of this kind,” Mueller said. “We don’t know whether the eMCI group will go on to develop Alzheimer’s, so we will continue to follow them, and our next step is to repeat these analyses with participants who have other biomarker evidence, such as amyloid plaques and neurofibrillary tangles as seen on PET scans. Speech analysis may be a valuable cognitive marker to add to clinical assessments of cognitive function in the future.”

### **Emergency and urgent hospitalizations, but not elective admissions, are related to accelerated cognitive decline in older people**

Research shows that older adults are at high risk for memory and other cognitive problems after being hospitalized, not only transient delirium but also long-term changes in cognition. However, it is unknown whether elective hospitalizations, such as for scheduled surgery, put older individuals at the same risk for faster cognitive decline as emergency or urgent admissions (nonelective hospitalizations).

In research reported at AAIC 2017, Bryan James, Ph.D., of the Rush Alzheimer’s Disease Center at Rush University Medical Center in Chicago, Illinois, USA, and colleagues found that nonelective hospitalizations were associated with acceleration in cognitive decline from prehospital rates, but elective hospitalizations were not associated with a change in the rate of cognitive decline. Data came from 930 older adults (75% female, mean age of 81 years old) enrolled in the Rush Memory and Aging Project (MAP) in Chicago. The study involved annual cognitive assessments, as well as clinical evaluations. Information on hospitalizations was acquired by linking 1999-2010 Medicare claims records for these participants to their MAP data. All hospital admissions were designated as elective, emergency, or urgent (the latter two combined as nonelective for analysis).

Of the 930 participants, 613 were hospitalized at least once over an average of almost five years of observation. Of those who were hospitalized, 260 (28%) had at least one elective hospital admission, and 553 (60%) had at least one nonelective hospital admission; 200 participants (22%) had both types of hospitalizations. In a model adjusted for age, sex, education, self-reported chronic medical conditions, length of stay, surgeries, intensive care unit stays, and comorbidities, nonelective hospitalizations were associated with acceleration in the rate of cognitive decline from before hospitalization, while elective hospitalizations were not. Nonelective hospitalizations were associated with an approximately 60% acceleration in the rate of decline.

“We saw a clear distinction: nonelective admissions drive the association between hospitalization and long-term changes in cognitive function in later life, while elective admissions do not necessarily carry the same risk of negative cognitive outcomes,” James said. “These findings have important implications for the medical decision making and care of older adults. While recognizing that all medical procedures carry some degree of risk, this study implies that planned hospital encounters may not be as dangerous to the cognitive health of older persons as emergency or urgent situations.”

While the U.S. Congress has recently provided additional funding for Alzheimer’s research at the National Institutes of Health, the commitment continues to fall far short of the need. In 2017, for every \$100 the NIH spends on Alzheimer’s research, Medicare and Medicaid will spend \$12,500 caring for those with the disease. Congress must continue its commitment to Alzheimer’s and other dementias by increasing funding for Alzheimer’s research by at least an additional \$414 million in fiscal year 2018.

**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/](http://www.alz.org/aaic/)

AAIC 2017 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 +1 800.272.3900.

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- Taylor Fields, et al. Self-Reported Hearing Loss, Cognitive Performance, and Risk of MCI: Findings from the Wisconsin Registry for Alzheimer’s Prevention. (Funder(s): University of Wisconsin at Madison Neuroscience Training Program)
- Kimberly Mueller, Ph.D., et al. Signs of Early Cognitive Decline within Connected Speech: Evidence from the Wisconsin Registry for Alzheimer’s Prevention (WRAP). (Funder(s): U.S. National Institutes of Health)
- Bryan James, Ph.D., et al. Cognitive Decline after Elective and Nonelective Hospitalization in Community-Dwelling Older Adults. (Funder(s): National Institute on Aging)

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**Abstract 18732 / Proposal ID P2-457**

Diagnosis and Prognosis: Neuropsychology  
Posters Monday, July 17, 2017: 9:30 AM

**Signs of Early Cognitive Decline within Connected Speech: Evidence from the Wisconsin Registry for Alzheimer's Prevention (WRAP)**

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**Background:** Alzheimer's disease (AD) is primarily characterized by early memory impairment; however, many patients show deficits in language across all stages of AD. Typical language testing is insensitive to early language problems that may manifest in discourse. We examined connected speech longitudinally in a group of late-middle-aged adults at risk for AD. We hypothesized that those with early Mild Cognitive Impairment (eMCI) would show decline in connected speech over time compared to cognitively healthy (CH) adults.

**Methods:** First, we submitted connected speech measures from a picture description task to exploratory and confirmatory factor analyses (EFA, CFA) from a subgroup of cognitively healthy WRAP participants (n=399; mean age=60±7, 67% female). Next, we examined resulting factor scores as outcomes in a subset of participants with speech samples obtained at 2 time points (n=219), using a linear mixed effects model (LME), with fixed effects of time point and baseline cognitive status (CH/eMCI), and a random effect of intercept nested within subjects. Secondary analyses used logistic regression to investigate the effect of speech factors on cognitive status at latest visit.

**Results:** The EFA/CFA factor structure (Fig 1, Table 1) met goodness-of-fit criteria. Participant characteristics for longitudinal analyses are presented in Table 2. Cognitive status at time 1 was a significant predictor of Semantic ( $p = .007$ ) and Syntax ( $p < .001$ ) factors, with a significant interaction of time and cognitive status for the Semantic factor ( $p = .04$ ) (Table 3, Fig.2). Syntax was a significant predictor of eMCI ( $p < .0001$ ), as was change in Fluency ( $p = .01$ ) (Table 4).

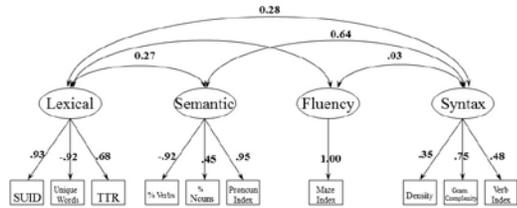
**Conclusions:** This is the first study to demonstrate a confirmed factor structure of connected speech measures in a prospective AD-risk-enriched cohort. Evident are baseline differences between eMCI and CH in syntax complexity. Baseline syntax and change in Fluency were significant predictors of eMCI at the latest visit. Unexpectedly, participants with eMCI performed higher on the Semantic factor at baseline; however, they declined more steeply than the CH group over time. Future analyses will continue to examine longitudinal relationships among speech factors and subtypes of cognitive impairment (memory, executive function, language), which may contribute to early identification of and intervention for AD.

**Abstract 18732 / Proposal ID P2-457**

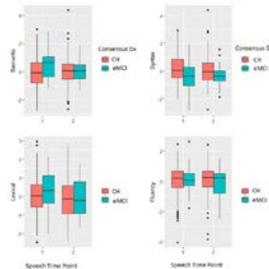
Diagnosis and Prognosis: Neuropsychology  
Posters Monday, July 17, 2017: 9:30 AM

**Signs of Early Cognitive Decline within Connected Speech: Evidence from the Wisconsin Registry for Alzheimer's Prevention (WRAP)**

Tables and Figures:



**Figure 1.** Conceptual model submitted to confirmatory factor analysis using the cross-validation subsample (N=149). Note: CFA met the following satisfactory fit indices:  $\chi^2=15.43$ , CFI = .99, RMSEA=.04, 90% confidence interval=.00-.08, GFI=.98, AGFI=.97, SRMR = .07. Definitions: SUID is Semantic Unit Idea Density (number of information units/total words); Type-tokens ratio: number of unique words/total words; Pronoun index: total pronouns divided by nouns + pronouns; Maze Index: total number of revisions, repetitions, and filled pauses/total words; Verb Index: total number of verbs/utterances; Grammatical complexity: The number of grammatical relations that mark syntactic embeddings divided by the total number of grammatical relations; Density: ratio of the prepositions corresponding to verbs, adjectives, adverbs, prepositions and conjunctions to the total number of words (excluding repetitions and fillers).



**Figure 2.** Boxplots of Connected Speech Factor by Visit and Consensus Diagnosis at Speech Time 1 (unadjusted means).

**Table 1.** Relative and absolute reliability indices of connected speech factors in a subset of cognitively stable individuals at 2 time points.

Factor	Time 1		Time 2		ICC	Mean Diff (Bias)	SD Diff (Bias)	t	p-value*	95%CI	95%CI	Within subject variance	SEM*	CR*		
	Mean	SD	Mean	SD												
Lexical	4.62	1.86	8.07	1.55	0.77	0.81	0.76	0.39	0.88	-1.15	0.25	-0.26	0.37	0.37	0.68	0.37
Semantic	6.65	1.64	4.82	1.61	8.50	0.53	0.19	0.82	1.19	0.17	0.86	4.21	0.25	0.71	0.13	0.82
Stroke	4.05	1.62	8.01	1.62	8.49	0.32	0.49	0.87	1.19	-0.59	0.56	-0.29	0.16	0.79	0.13	0.82
Fluency	8.26	1.66	8.06	1.63	8.89	0.52	0.40	0.29	1.93	2.82	0.95	0.00	0.40	0.55	0.16	0.29

\*t-value was computed as a Bonferroni-corrected t-test of ICCs. 95% Confidence Interval, lower bound; 95% Confidence Interval, upper bound; Standard error of the mean; Coefficient of Repeatability, t, 27758M.

**Table 2.** Participant Demographics and Cognitive Characteristics of Linear Mixed-effects Regression Sample.

Variable	Total Sample	Cognitively Healthy	Early MCI	p-value
N	715	184 (86%)	75 (10%)	
% N				
Age at Speech Sample 1	62.7 (6.5)	62.3 (6.4)	64.6 (5.4)	0.05
Age at Speech Sample 2	63.8 (6.4)	63.4 (6.4)	65.7 (5.4)	0.05
Sex (Male: %)	142/72 (16%)	136/17 (16%)	17/16 (48%)	0.11*
APOE $\epsilon 4$ allele (n/total)	94/126 (48%)	79/105 (41%)	14/20 (41%)	0.47
Family History (any/total)	18/74 (8%)	15/68 (8%)	3/5 (30%)	0.64
WRAP 1 Reading	1562 (3.4)	136 (3.4)	1562 (3.4)	0.64
WRAP 2 Total Score	364 (3.4)	32.3 (3.4)	364 (3.4)	<.0001**
Speed of Verbal		29 (1.5)	29 (1.5)	<.0001**
Working Memory		14 (1.0)	14 (1.0)	<.0001**
Verbal Learning & Memory		14 (1.0)	14 (1.0)	<.0001**
Immediate Memory		17 (1.1)	17 (1.1)	<.0001**

Reading Fluency, Working Memory, Verbal Learning & Memory, and Immediate Memory are a factor scores as described in Devilbiss et al., 2016.  
\*Statistically significant at p < .05. \*\*Statistically significant at p < .001.

**Table 3.** Parameters resulting from linear mixed effects regression models.

Variable	Semantic		Syntax		Lexical		Fluency	
	B (SE)	95% CI	B (SE)	95% CI	B (SE)	95% CI	B (SE)	95% CI
Intercept	4.251 (3.20)	-3.3 to 7.5	48.289**	.88 to 1.09	19.1 (3.1)	-2.8 to 4.5	-136.221	-1.50 to -1.81
Age (months)	-0.001 (0.01)	-0.04 to 0.02	-0.01 (0.01)	-0.02 to 0.01	-0.002 (0.01)	-0.02 to 0.01	-0.01 (0.01)	-0.02 to 0.01
Sex (Female)	.06 (1.1)	-1.5 to 2.7	-.23 (1.1)	-.44 to 0.01	0.64 (1.1)	-1.8 to 2.6	4.11 (1.0)**	.39 to 6.0
WRAP 1 reading score	-.06 (4.6)	-17.7 to 0.6	2.91 (6.0)**	.88 to 4.9	-3.91 (6.0)**	-9.9 to 2.0	1.91 (6.0)**	-2.7 to 6.6
Speech Verb (1,2)	0.06 (1.06)	-0.8 to 1.7	-.08 (0.9)	-.24 to 0.06	-2.38 (0.7)**	-.57 to -1.2	-0.51 (0.7)	-.15 to 1.2
Consensus Diagnosis (MCI)	1.09 (4.9)**	0.3 to 1.8	-3.91 (5.0)**	-.81 to -1.4	-2.51 (5.1)	-.09 to 3.1	-0.56 (5.1)	-.33 to 2.4
Speech Verb (1,2) X Consensus								
Diagnosis			-4.91 (4.7)	-.64 to .58				

Intercepts: B, standard error (SE); Confidence Interval (CI); Consensus: Consensus Diagnosis; Age: age in months; Sex: sex; WRAP 1: WRAP 1 reading score; WRAP 2: WRAP 2 total score; Verb: WRAP 2 verb score; Consensus: Consensus Diagnosis; Verb: WRAP 2 verb score; Consensus: Consensus Diagnosis; Verb: WRAP 2 verb score.  
\*Statistically significant at p < .05. \*\*Statistically significant at p < .001.

**Table 4.** Speech factor predictors of Latest Consensus Diagnosis in logistic regression model.

Variable	Syntax		Semantic		Lexical	
	B	OR (95% CI)	B	OR (95% CI)	B	OR (95% CI)
Intercept	-2.32	1.78 (1.07-3.12)	1.96	3.77 (1.69-8.45)	-2.43	1.78 (1.07-3.12)
Age	-0.09	0.91 (0.87-0.95)	-0.09	0.91 (0.87-0.95)	-0.09	0.91 (0.87-0.95)
Age at Speech	0.04	1.04 (1.01-1.07)	0.04	1.04 (1.01-1.07)	0.04	1.04 (1.01-1.07)
WRAP 1 Reading	-.14	0.86 (0.81-0.91)	-.09	0.91 (0.87-0.95)	-.09	0.91 (0.87-0.95)
Factor Change	-.82	0.44 (0.31-0.61)	-.76**	0.47 (0.37-0.61)	-.74	0.47 (0.37-0.61)

Intercepts: WRAP 1: WRAP 1 reading score; WRAP 2: WRAP 2 total score; Factor Change: Change in factor scores from speech visit 1 to speech visit 2; Syntax: WRAP 2 verb score; Semantic: WRAP 2 total score; Lexical: WRAP 2 verb score.  
\*Statistically significant at p < .05. \*\*Statistically significant at p < .01.

**Abstract 15004 / Proposal ID P1-554**

Public Health and Psychosocial: Epidemiology  
Posters Sunday, July 16, 2017: 9:30 AM

**Self-Reported Hearing Loss, Cognitive Performance, and Risk of MCI: Findings from the Wisconsin Registry for Alzheimer's Prevention**

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**Background:** Auditory deficits are present in Alzheimer's disease dementia (AD) but it remains largely unknown whether they precede or are concomitant with the disease. The aim of this study was to determine the prevalence of hearing loss in a cohort of middle-aged adults at risk for AD, and evaluate whether hearing loss is associated with prospective cognitive decline and progression to mild cognitive impairment (MCI).

**Methods:** Seven hundred and eighty-three cognitively-normal adults (age=53.55±6.52 years, 71% women, and 42% with maternal history of AD) enrolled in the Wisconsin Registry for Alzheimer's Prevention participated in this study. Participants underwent serial cognitive and clinical assessments and self-reported whether they had ever been diagnosed with hearing loss as part of a medical history questionnaire. Diagnosis of MCI was rendered via a multidisciplinary consensus conference. Frequency distribution was used to assess prevalence of hearing loss. Covariate-adjusted linear regression was used to assess the relationship between hearing loss at initial assessment and cognitive performance at a subsequent visit four years later. Binary logistic regression was used to estimate risk of incident MCI as a function of prior hearing loss, after controlling for relevant covariates.

**Results:** 72 (9.20%) participants reported having a diagnosed hearing loss whereas 711 (90.80%) participants reported having normal hearing. Relative to those who reported normal hearing, individuals who reported hearing loss scored significantly poorer on tests of processing speed and set switching (Trail Making Test parts A&B,  $p=.046$  and  $.025$ , respectively), cognitive flexibility (Stroop Color-Word Interference,  $p=.014$ ), psychomotor speed (WAIS-R Digit Symbol Substitution Test,  $p=.012$ ) and a composite measure of Speed and Flexibility ( $p=.030$ ) four years later. The odds of being characterized as having MCI at the latter visit were over three times higher for those who had reported hearing loss at the initial or intermediate visits (mean time interval=2.50±.47 years), relative to those who had not (OR=3.26  $p=.047$ , 95% CI 1.02-10.44).

**Conclusions:** In this cognitively-normal, at-risk cohort, self-reported hearing loss was prospectively associated with poorer cognitive performance and increased incidence of progression to MCI. Identification and treatment of hearing loss might be a viable approach to forestall the public health crisis posed by AD.

**Abstract 17960 / Proposal ID O2-06-05**

Epidemiology: Novel Risk Factors, Comorbidities and Biomarkers  
Oral session, Monday, July 17, 2017: 2:00-3:30 PM

**Cognitive Decline after Elective and Nonelective Hospitalization in Community-Dwelling Older Adults**

**Bryan D James, PhD (bryan\_james@rush.edu)**, Raj C Shah, MD, Robert S Wilson, PhD, Patricia A Boyle, PhD, Ana W. Capuano, Ph.D., Melissa Lamar, PhD, David A. Bennett, MD and Julie A. Schneider, M.D., M.S., Rush Alzheimer's Disease Center, Chicago, IL, USA

**Background:** Accelerated cognitive decline after hospitalization of older adults is widely recognized, but there is little data as to whether elective hospital admissions are associated with the same negative cognitive outcomes as nonelective (emergent or urgent) admissions. We tested the hypothesis that elective hospitalizations are associated with less acceleration in cognitive decline as compared to nonelective hospitalizations in older adults.

**Methods:** Data came from 930 older adults (74.5% female, mean age = 80.8 years) enrolled in the Rush Memory and Aging Project for which annual cognitive assessments (battery of 19 cognitive tests) were linked to over a decade of Medicare claims records. The MedPAR file codes all hospital admissions as elective, emergency, or urgent. We fit a series of mixed effects regression models with global cognitive function as the outcome with time-varying separate indicators for having elective or nonelective hospitalizations, and their interactions with time.

**Results:** Of the 930 participants, 613 were hospitalized at least once over an average of 4.8 (SD=2.6) years of follow-up; 260 (28.0%) had at least one elective hospital admission, and 553 (59.5%) had at least one nonelective hospital admission. Two hundred participants (21.5%) had both an elective and nonelective hospitalization. In separate models adjusted for age at baseline, sex, education, and self-reported chronic medical conditions, the rate of cognitive decline accelerated (as compared to rate of change with no hospitalization) after elective hospitalizations (estimate = -0.025,  $p < 0.001$ ) and the acceleration was almost twice as fast after nonelective hospitalizations (estimate = -0.043,  $P < 0.001$ ). When both types of hospitalizations were put in the same model, nonelective hospitalizations were related to faster cognitive decline (estimate = -0.042,  $p < 0.001$ ) but the association for elective hospitalizations was markedly attenuated and not significant (estimate = -0.002,  $p = 0.81$ ). Inferences were essentially unchanged after adding terms for mean length of stay, surgeries, ICU stays, and Charlson comorbidity index, a measure of seriousness of illness.

**Conclusions:** These data indicate that elective hospitalizations are not significantly related to acceleration in cognitive decline in older persons after accounting for nonelective hospitalizations.