

EPIDEMIOLOGY

Cumulative loneliness and subsequent memory function and rate of decline among adults aged ≥ 50 in the United States, 1996-2016

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Email: xuexiny@umich.edu**Abstract**

Background: To investigate the association between the cumulative duration of loneliness and subsequent memory function and rate of decline over a 20-year period in middle aged and older adults.

Method: Data were from biennial interviews with 9,032 adults aged ≥ 50 in the population-based US Health and Retirement Study from 1996-2016. Loneliness status (yes vs. no) was assessed biennially from 1996-2004 and its duration over this period was categorized as never, 1 time point, 2 time points, and ≥ 3 time points. Episodic memory was assessed biennially from 2004-2016 as a composite of immediate and delayed recall trials combined with proxy-reported memory. We used multivariable-adjusted mixed effects regression to estimate the association between loneliness duration and subsequent memory function and decline. Three-way interaction terms were included to test effect modification by sex and age.

Result: Mean (SD) age at baseline was 64 (9) years, 63% of the sample was female (5,646/9,032), and the median follow-up time was 10 years, contributing 46,890 observations from 2004-2016. A total of 1,624 adults (18%) experienced loneliness at one time point, 825 (9%) experienced loneliness at two time points, and 1,069 (12%) experienced loneliness at ≥ 3 time points. Annual memory decline among non-lonely adults was 0.08 standard deviation (SD) units (95% CI: -0.08, -0.07) per year. A longer duration of loneliness was associated with a faster rate of memory decline (1 time point: 0.01 SD additional annual decline, 95% CI: -0.01, -0.01; 2 time points: 0.02 SD additional annual decline, 95% CI: -0.02, -0.01; ≥ 3 time points: 0.03 SD additional annual decline, 95% CI: -0.03, -0.02; P trend < 0.001). The association was stronger among women than men (three-way interaction P trend < 0.001) and adults aged ≥ 65 years than those aged < 65 years (three-way interaction P trend = 0.01).

Conclusion: Long-term loneliness may be a salient risk factor for accelerated memory aging, especially among women aged 65 and over. Our findings could help rule out reverse causation between loneliness and memory outcomes, suggesting that loneliness could be part of a preclinical syndrome of Alzheimer's disease and related dementias.

Table 1. Multivariable-adjusted mixed effects linear regression analyses of the association between duration of loneliness from 1996-2004 and memory function and rate of decline from 2004-2016, the US Health and Retirement Study, N=9,032 (46,890 observations).

Characteristics	Model 1			Model 2			Model 3		
	β (95% CI)	<i>P</i>		β (95% CI)	<i>P</i>		β (95% CI)	<i>P</i>	
Year	-0.08 (-0.08 - -0.07)	<0.001		-0.08 (-0.08 - -0.07)	<0.001		-0.08 (-0.08 - -0.07)	<0.001	
Duration of loneliness									
Never	ref.			ref.			ref.		
One time point	0.01 (-0.03 - 0.04)	0.75		0.01 (-0.02 - 0.04)	0.44		0.02 (-0.02 - 0.05)	0.34	
Two time points	-0.01 (-0.05 - 0.04)	0.82		0.01 (-0.04 - 0.05)	0.79		0.01 (-0.03 - 0.05)	0.59	
≥Three time points	-0.03 (-0.07 - 0.01)	0.16		-0.01 (-0.05 - 0.03)	0.52		-0.01 (-0.04 - 0.04)	0.97	
<i>P</i> trend		0.24			0.75			0.77	
Year × Duration of loneliness									
One time point	-0.01 (-0.01 - -0.01)	<0.001		-0.01 (-0.01 - -0.01)	<0.001		-0.01 (-0.01 - -0.01)	<0.001	
Two time points	-0.02 (-0.02 - -0.01)	<0.001		-0.02 (-0.02 - -0.01)	<0.001		-0.02 (-0.02 - -0.01)	<0.001	
≥Three time points	-0.03 (-0.03 - -0.02)	<0.001		-0.03 (-0.03 - -0.02)	<0.001		-0.03 (-0.03 - -0.02)	<0.001	
<i>P</i> trend		<0.001			<0.001			<0.001	

Note:

Model 1 adjusted for baseline age, sex, race, marital status, education, employment status, and household wealth.

Model 2 adjusted for baseline age, sex, race, marital status, education, employment status, household wealth, and objective social isolation index.

Model 3 adjusted for baseline age, sex, race, marital status, education, employment status, household wealth, objective social isolation index, CES-D scores, and ADL scores.

Table 2. Sex- and age- specific subgroup multivariable mixed effect linear regression analyses of the association between duration of loneliness from 1996-2004 and memory scores and rate of decline from 2004-2016, the US Health and Retirement Study

Characteristics	Model 1			Model 2			Model 3			
	β (95% CI)	<i>P</i>		β (95% CI)	<i>P</i>		β (95% CI)	<i>P</i>		
Male (n=3,386)										
Year × Duration of loneliness										
One time point	-0.01 (-0.01 - -0.01)	0.03		-0.01 (-0.01 - -0.01)	0.04		-0.01 (-0.01 - -0.01)	0.03		
Two time points	-0.01 (-0.02 - -0.01)	0.01		-0.01 (-0.02 - -0.01)	0.02		-0.01 (-0.02 - -0.01)	0.02		
≥Three time points	-0.02 (-0.02 - -0.01)	<0.001		-0.01 (-0.02 - -0.01)	<0.001		-0.01 (-0.02 - -0.01)	<0.001		
<i>P</i> trend		<0.001			<0.001			<0.001		
Female (n=5,646)										
Year × Duration of loneliness										
One time point	-0.01 (-0.02 - -0.01)	<0.001		-0.01 (-0.02 - -0.01)	<0.001		-0.01 (-0.02 - -0.01)	<0.001		
Two time points	-0.02 (-0.03 - -0.02)	<0.001		-0.02 (-0.03 - -0.01)	<0.001		-0.02 (-0.03 - -0.01)	<0.001		
≥Three time points	-0.03 (-0.03 - -0.02)	<0.001		-0.03 (-0.03 - -0.02)	<0.001		-0.03 (-0.03 - -0.02)	<0.001		
<i>P</i> trend		<0.001			<0.001			<0.001		
<i>P</i> trend (Year × Duration of loneliness × Sex)*		<0.001			<0.001			<0.001		
Baseline age ≥65 (n=3,217)										
Year × Duration of loneliness										
One time point	-0.02 (-0.02 - -0.01)	<0.001		-0.02 (-0.02 - -0.01)	<0.001		-0.02 (-0.02 - -0.01)	<0.001		
Two time points	-0.03 (-0.04 - -0.02)	<0.001		-0.03 (-0.04 - -0.02)	<0.001		-0.03 (-0.04 - -0.02)	<0.001		
≥Three time points	-0.03 (-0.04 - -0.02)	<0.001		-0.03 (-0.04 - -0.02)	<0.001		-0.03 (-0.04 - -0.02)	<0.001		
<i>P</i> trend		<0.001			<0.001			<0.001		
Baseline age 50-64 (n=5,761)										
Year × Duration of loneliness										
One time point	-0.01 (-0.01 - -0.01)	<0.001		-0.01 (-0.01 - -0.01)	<0.001		-0.01 (-0.01 - -0.01)	<0.001		
Two time points	-0.01 (-0.02 - -0.01)	<0.001		-0.01 (-0.02 - -0.01)	<0.001		-0.01 (-0.02 - -0.01)	<0.001		
≥Three time points	-0.02 (-0.02 - -0.02)	<0.001		-0.02 (-0.02 - -0.02)	<0.001		-0.02 (-0.02 - -0.02)	<0.001		
<i>P</i> trend		<0.001			<0.001			<0.001		
<i>P</i> trend (Year × Duration of loneliness × Baseline age ≥65)*		0.02			0.01			0.01		

Note:*Three-way interaction *p* value was derived from pooled models.

Model 1 adjusted for baseline age, sex, race, marital status, education, employment status, and household wealth.

Model 2 adjusted for baseline age, sex, race, marital status, education, employment status, household wealth, and objective social isolation index.

Model 3 adjusted for baseline age, sex, race, marital status, education, employment status, household wealth, objective social isolation index, CES-D scores, and ADL scores.

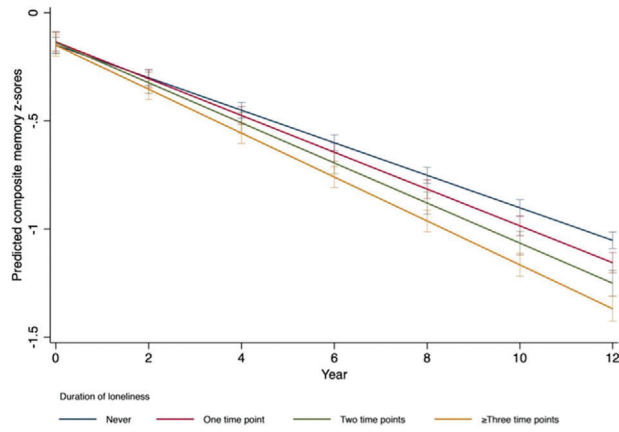


Figure 1 Predicted composite memory z-scores from 2004-2016 by duration of loneliness, the US Health and Retirement Study

Note: Composite memory z-scores are predicted by estimates in Model 3 in Table 2. Covariates in Model 3 were set to the following values: age 63 years, male, partnered, white, less than high school, 2nd quintile household wealth, objective social isolation index=1, CES-D score=1, and ADL score=1.

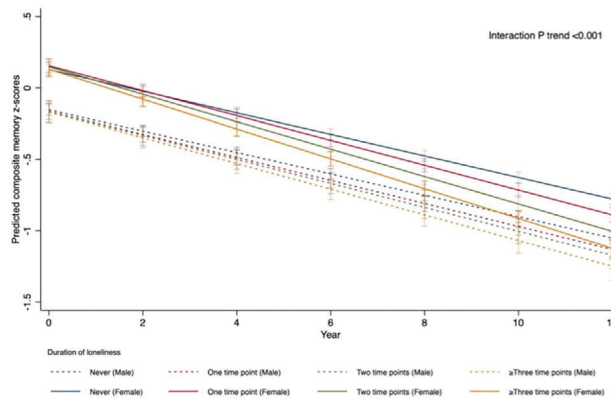


Figure 2 Predicted composite memory z-scores from 2004-2016 by duration of loneliness and sex, the US Health and Retirement Study

Note: Composite memory z-scores are predicted by estimates in fully adjusted pooled models with three-way interaction term between duration of loneliness, year, and sex. Covariates were set to the following values: age 63 years, partnered, white, less than high school, 2nd quintile household wealth, objective social isolation index=1, CES-D score=1, and ADL score=1.

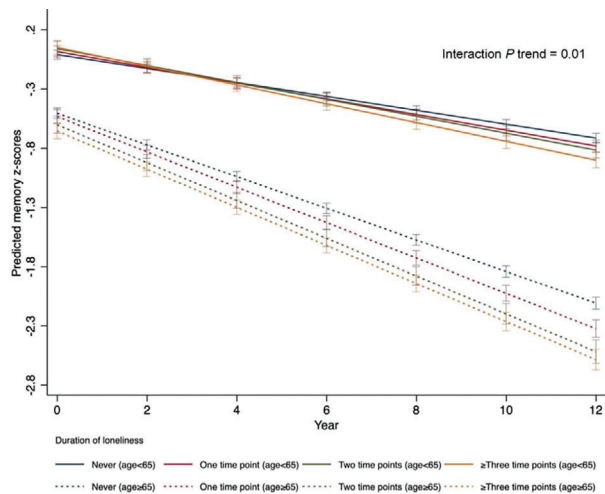


Figure 3 Predicted composite memory z-scores from 2004–2016 by duration of loneliness and baseline age, the US Health and Retirement Study

Note: Composite memory z-scores are predicted by estimates in fully adjusted pooled models with three-way interaction term between duration of loneliness, year, and baseline age (50–64 vs. ≥ 65). Covariates were set to the following values: baseline age (60 for age <65 group; 70 for age ≥ 65 group), male, partnered, white, less than high school, 2nd quintile household wealth, objective social isolation index=1, CES-D score=1, and ADL score=1.