Title: Learning to Cope: Examining Effects of Self and Caregiver Education on the Link between Cognitive Impairment and Depression

Key words: Aging; Alzheimer's disease; Mental health; Education; Caregiving

Background: The burden of Alzheimer's disease includes not only the catastrophic degenerative effects of the illness itself, but also the disruptive effects of the illness on other aspects of individuals' lives, relationships, and communities. For example, cognitive impairment has been linked to higher incidence and severity of comorbid health conditions, especially mental illnesses like depression. Although the link between cognitive impairment and depression has been well-established, prior research has not considered how social and economic factors may help to mitigate the secondary mental health consequences of cognitive decline. This study examines the relationship between cognitive impairment and development of depressive symptoms during the longitudinal onset of Alzheimer's disease in late adulthood. First, I examine whether or not older adults' education moderates the impact of cognitive impairment on depression. Second, I identify circumstances in which a caregiver's education has a similar protective effect for participants.

Data and Measures: This paper uses data collected at the Indiana Alzheimer's Disease Center (IADC). IADC is a NIH-sponsored research facility housed within the Indiana University School of Medicine. IADC recruits and clinically assesses voluntary research participants who return to the clinic at approximately 12-month intervals for follow-up study. At each participant's annual IADC appointment, IADC conducts a diagnostic assessment and a battery of cognition-related tests. Participants are older adults (average age = 71) diagnosed with normal cognition (65%), mild cognitive impairment (20%), or dementia (15%). The first IADC visits were collected in 1990; follow-up visits and new enrollments have continued through 2018. Altogether, the sample analyzed in this study includes 1,802 observations of 691 IADC participants.

As a condition for enrollment, research participants at IADC are required to provide a study partner to serve as an informant for research center staff. This is a serious commitment that requires accompanying the participant throughout a 4-hour IADC appointment, completing several interviews and questionnaires, and discussing of sensitive health topics related to the participant. In most cases and especially among more impaired participants, the study partner is the sole or primary caregiver for the participant. About two thirds of IADC participants in the present study selected a spouse, and spouses become more common as impairment progresses.

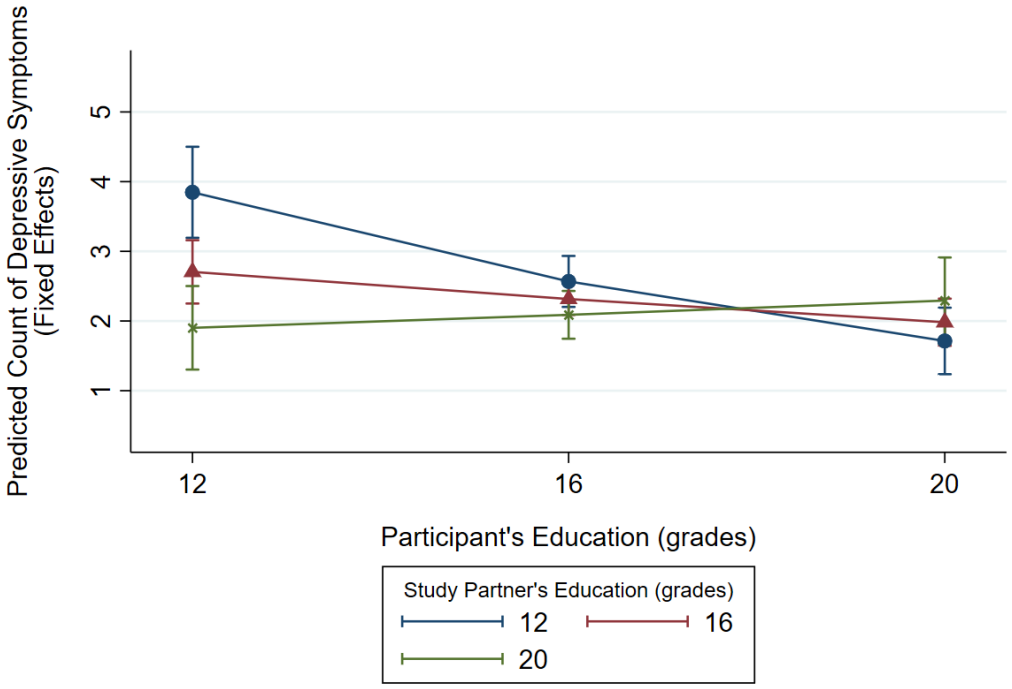
The main dependent variable for this study is a 15-item geriatric depression scale measured at each time point. Cognitive impairment was assessed using the widely known Mini-Mental State Exam, a composite scale summarizing cognitive function across multiple cognitive domains. The full set of participant and study partner variables are summarized in Table 1.

Methods: My analyses proceed in several steps. First, I use mixed effects negative binomial regression models to examine the direct association between cognitive impairment and depressive symptoms. Second, I identify direct effects of both participant and study partner characteristics on depressive symptoms. Third, I use interaction terms to examine whether or not relationship characteristics moderate the impact of cognitive impairment on depressive symptoms. Table 2 displays a portion of these results.

Results: Cognitive impairment is strongly associated with the occurrence of depressive symptoms among older adults coping with the onset of Alzheimer's disease. Both a participant's own educational attainment and that of the study partner have a protective effect on the development of depressive symptoms. However, results from interaction models suggest that the link between cognitive impairment and depression is conditional. Higher study partner education is associated with fewer depressive symptoms, but only among less educated or more impaired participants. In other words, the link between cognitive impairment and depression may be more contextual and relational than previously believed.

Implications: This research demonstrates the importance of education for managing the onset of Alzheimer's disease and mitigating some of its disruptive secondary consequences. Specifically, I find evidence that educational and social resources moderate the relationship between cognitive decline and depressive symptoms. However, the protective effect of a caregiver's education only emerges when an older adult may not be up to the challenge of coping on their own. Among these most vulnerable older adults, access to a more educated caregiver essentially eliminates the health penalty reported by less educated adults relative to their more educated peers.

Figure 1. Predicted Count of Participants' Depressive Symptoms based on Interaction between Participant Education and Study Partner Education



Note: Based on fixed effects from Table 4.2, Model 5

Table 1. Descriptive Statistics for All Variables, with Tests for Mean Differences over Levels of Cognitive Impairment (Source: IADC 1990-2018).

	Between-person Statistics for All Participants			**Comparison of Diagnostic Categories using All Observations**			
				Cognitively Normal	*Mild Cognitive Impairment*	*Dementia*	
Variables	Mean (%)	SD	Range	Mean (%)	Mean (%)	Mean (%)	Test[1]
Dependent variable							
Geriatric depression scale	2.38	2.81	0, 14	1.46	3.25	3.41	121.04***
Participant variables							
Age at enrollment	64.37	12.68	30.12, 100.41	61.88	66.17	67.55	46.16***
Cognition scale (std.)	0.14	0.98	-2.98, 1.09	0.66	0.32	-0.87	-
Education (grades)	15.74	2.73	12, 20	16.25	15.68	14.89	44.61***
Sex							81.09***
Female	(53.77)			(64.04)	(41.69)	(43.71)	
Male (ref.)	(46.23)			(35.96)	(58.31)	(56.29)	
Marital status at enroll.							13.74**
Married (ref.)	(75.19)			(72.46)	(75.80)	(79.55)	
Widowed, Divorced, or Separated	(21.09)			(22.57)	(21.87)	(18.01)	
Never married	(3.72)			(22.57)	(21.87)	(18.01)	
Siblings at enrollment	2.77	2.58	0, 12	2.73	2.58	2.97	3.00*
Children at enrollment	2.36	1.60	0, 8	2.18	2.44	2.63	14.98***
Study partner variables							
Education (grades)	15.41	2.48	12, 20	15.77	15.19	14.92	21.31***
Sex							43.01***
Female	(64.37)			(57.34)	(74.64)	(69.98)	
Male (ref.)	(35.63)			(42.66)	(25.36)	(30.02)	
IADC visits	3.09	1.49	1, 10	3.50	2.92	2.47	30.18***
How long known (years)	40.66	15.83	1, 80	38.84	40.50	43.93	16.59***
How often see							56.30***
Daily (ref.)	(74.53)			(67.93)	(77.84)	(83.86)	
Weekly	(14.98)			(18.47)	(11.95)	(10.88)	
2-3x Monthly	(6.60)			(7.88)	(8.16)	(3.38)	
Yearly/less	(3.88)			(5.72)	(2.04)	(1.88)	
N	691			926	343	533	

Note: 1802 total longitudinal observations of 691 participants. [1]The test statistic is *F* from one-way ANOVA for continuous variables. The test statistic is X^2 for categorical variables. These statistics are calculated on the full sample of Level 1 observations.

Table 2. Longitudinal Mixed Effects Negative Binomial Regression Model Predicting Count of Depressive Symptoms using Participant and Study Partner Covariates, including Educational Attainment (Source = IADC 1990-2018, *N* = 1802).

	(1) Education & Cognition		(2) Education Interaction	
Fixed Effects	**IRR**	**95% CIs**	**IRR**	**95% CIs**
Time in study (years)	0.972***	(0.958,0.986)	0.973***	(0.959,0.987)
Education variables				
Participant education	0.947**	(0.917,0.979)	0.750***	(0.640,0.878)
Study partner education	0.969*	(0.941,0.997)	0.760***	(0.645,0.895)
Participant Education * Study Partner Ed.			1.016**	(1.005,1.026)
Participant variables				
Age at enrollment	0.989**	(0.982,0.996)	0.989**	(0.982,0.997)
Cognition scale (std.)	0.885***	(0.830,0.943)	0.885***	(0.831,0.943)
Sex (Male)				
Female	0.889	(0.732,1.080)	0.902	(0.743,1.095)
Marital (Married)				
Widowed/Div./Sep.	1.167	(1.000,1.000)	1.162	(0.933,1.448)
Never married	0.644+	(0.405,1.026)	0.640+	(0.403,1.017)
Siblings at enrollment	0.993	(0.962,1.026)	0.992	(0.961,1.024)
Children at enrollment	1.049+	(0.995,1.107)	1.050+	(0.996,1.107)
Study partner variables				
Sex (Male)				
Female	1.127	(0.962,1.321)	1.119	(0.956,1.310)
IADC visits	0.996	(0.978,1.014)	0.996	(0.978,1.014)
How long known (yrs)	1.001	(0.996,1.006)	1.000	(0.996,1.005)
How often see (Daily)				
Weekly	1.081	(0.903,1.294)	1.090	(0.911,1.305)
2-3x Monthly	0.864	(0.695,1.075)	0.864	(0.695,1.075)
Yearly/less	0.667**	(0.504,0.883)	0.676**	(0.511,0.895)
Constant	2.212***	(1.939,2.523)	2.193***	(1.925,2.498)
ln(alpha)	0.041***	(0.017,0.097)	0.040***	(0.017,0.096)
BIC	6790.110		6788.832	

Notes: *** p<0.001, ** p<0.01, * p<0.05 + p<0.10. Exponentiated coefficients (Incidence Rate Ratios). Random intercept not shown.