Effect of a Purpose in Life on Risk of Incident Alzheimer Disease and Mild Cognitive Impairment in Community-Dwelling Older Persons

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Context: Emerging data suggest that psychological and experiential factors are associated with risk of Alzheimer disease (AD), but the association of purpose in life with incident AD is unknown.

Objective: To test the hypothesis that greater purpose in life is associated with a reduced risk of AD.

Design: Prospective, longitudinal epidemiologic study of aging.

Setting: Senior housing facilities and residences across the greater Chicago metropolitan area.

Participants: More than 900 community-dwelling older persons without dementia from the Rush Memory and Aging Project.

Main Outcome Measures: Participants underwent baseline evaluations of purpose in life and up to 7 years of detailed annual follow-up clinical evaluations to document incident AD. In subsequent analyses, we examined the association of purpose in life with the precursor to AD, mild cognitive impairment (MCI), and the rate of change in cognitive function.

Results: During up to 7 years of follow-up (mean, 4.0 years), 155 of 951 persons (16.3%) developed AD. In a proportional hazards model adjusted for age, sex, and education, greater purpose in life was associated with a substantially reduced risk of AD (hazard ratio, 0.48; 95% confidence interval, 0.33-0.69; P < .001). Thus, a person with a high score on the purpose in life measure (score = 4.2, 90th percentile) was approximately 2.4 times more likely to remain free of AD than was a person with a low score (score = 3.0, 10th percentile). This association did not vary along demographic lines and persisted after the addition of terms for depressive symptoms, neuroticism, social network size, and number of chronic medical conditions. In subsequent models, purpose in life also was associated with a reduced risk of MCI (hazard ratio, 0.71; 95% confidence interval, 0.53-0.95; P = .02) and a slower rate of cognitive decline (mean [SE] global cognition estimate, 0.03 [0.01]; P < .01).

Conclusion: Greater purpose in life is associated with a reduced risk of AD and MCI in community-dwelling older persons.

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Alzheimer disease (AD) is one of the most dreaded consequences of aging, and the identification of modifiable factors associated with the risk of AD is a top public health priority for the 21st century, particularly given the large and rapidly increasing aging population. Although relatively few such risk factors have been identified, emerging data suggest that a variety of potentially modifiable psychological factors (eg, conscientiousness, extraversion, and neuroticism) and experiential factors (eg, social networks) are associated with risk of AD. Purpose in life, the psychological tendency to derive meaning from life’s experiences and to possess a sense of intentionality and goal directedness that guides behavior, has long been hypothesized to protect against adverse health outcomes. Indeed, purpose in life has been linked to positive outcomes, including better mental health and happiness, and it was recently reported that purpose in life is associated with longevity. However, the association of purpose in life with the risk of AD remains unknown.

In this study, we tested the hypothesis that greater purpose in life is associated with a reduced risk of incident AD using data from more than 900 participants in a large community-based epidemiologic study of aging, the Rush Memory and Aging Project. In subsequent analyses, we examined whether these associations persisted after adjustment for several potential confounders. Next, we examined the association of purpose in life with the development of mild cognitive impairment.
(MCI), the precursor to AD. Finally, we examined the association of purpose in life with the rate of change in cognitive function in older persons.

**METHODS**

**PARTICIPANTS**

Participants are from the Rush Memory and Aging Project, a longitudinal clinicopathologic study of common chronic conditions of aging approved by the institutional review board of Rush University Medical Center, Chicago, Illinois. Participants are older persons recruited from approximately 40 continuous care retirement communities and senior subsidized housing facilities in and around the Chicago metropolitan area. Study participation required agreeing to detailed annual clinical evaluations and organ donation at the time of death, and all participants provided written consent. Between 1997 and 2008, more than 1,200 older persons enrolled in the study. The purpose in life measure was added to the interview in 2001.

Eligibility for these analyses required a valid baseline score on the purpose in life measure, absence of dementia at the baseline evaluation, and at least 1 follow-up clinical evaluation. At the time of these analyses, 1,151 persons had undergone their baseline clinical evaluation and completed the purpose in life measure. Of those, we excluded 75 with dementia at baseline and an additional 125 because they had not yet reached or had died before the first follow-up. This left 951 eligible persons; analyses are based on this group. At baseline, the mean (SD) age of participants was 80.4 (7.4) years, their mean (SD) years of education was 14.5 (3.0), and they had a mean (SD) score of 27.9 (2.2) on the Mini-Mental State Examination; 74.9% of education was 14.5 (3.0), and they had a mean (SD) score of 27.9 (2.2) on the Mini-Mental State Examination, but these scores are used only to describe the cohort. Scores on 19 tests are used to create summary indices of global cognitive function and 5 specific cognitive domains: episodic memory, semantic memory, working memory, perceptual speed, and visuospatial ability. Episodic memory is assessed via 7 tests: immediate and delayed recall of story A from Logical Memory, immediate and delayed recall of the East Boston Story, Word List Memory, Word List Recall, and Word List Recognition. Semantic memory is assessed via 3 tests: a 15-item version of the Boston Naming Test, Verbal Fluency, and a 15-item reading test. Working memory is assessed via 3 tests: Digit Span Forward, Digit Span Backward, and Digit Ordering. Perceptual speed is assessed via 4 tests: Symbol Digit Modalities Test, Number Comparison, and 2 indices from a modified version of the Stroop Neuropsychological Screening Test. Visuospatial ability is assessed via 2 tests: a 15-item version of Judgment of Line Orientation and a 16-item version of Standard Progressive Matrices. One additional test, Complex Ideational Material, is used for diagnostic classification purposes only.

To compute the composite measure of global cognitive function, raw scores on each of the individual tests are converted to z scores using the baseline mean (SD) of the entire cohort, and the z scores of all 19 tests are averaged. Summary scores for the 5 cognitive domains (ie, episodic memory, semantic memory, working memory, perceptual speed, and visuospatial ability) also are derived by converting raw scores on each of the individual tests to z scores using the mean (SD) of the entire cohort and then averaging the z scores from tests in a specific domain. Psychometric information on these summary scores, including factor analytic support for the 5 domains, is contained in previous publications.

**ASSESSMENT OF COGNITION**

Cognitive function is assessed annually via a battery of 21 tests, as previously described. This battery includes the Mini-Mental State Examination, but these scores are used only to describe the cohort. Scores on 19 tests are used to create summary indices of global cognitive function and 5 specific cognitive domains: episodic memory, semantic memory, working memory, perceptual speed, and visuospatial ability. Episodic memory is assessed via 7 tests: immediate and delayed recall of story A from Logical Memory, immediate and delayed recall of the East Boston Story, Word List Memory, Word List Recall, and Word List Recognition. Semantic memory is assessed via 3 tests: a 15-item version of the Boston Naming Test, Verbal Fluency, and a 15-item reading test. Working memory is assessed via 3 tests: Digit Span Forward, Digit Span Backward, and Digit Ordering. Perceptual speed is assessed via 4 tests: Symbol Digit Modalities Test, Number Comparison, and 2 indices from a modified version of the Stroop Neuropsychological Screening Test. Visuospatial ability is assessed via 2 tests: a 15-item version of Judgment of Line Orientation and a 16-item version of Standard Progressive Matrices. One additional test, Complex Ideational Material, is used for diagnostic classification purposes only.

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**ASSESSMENT OF PURPOSE IN LIFE**

Purpose in life is a psychological construct that refers to the tendency to derive meaning from life’s experiences and to possess a sense of intentionality and goal directedness that guides behavior. Purpose in life was assessed using a 10-item scale derived from Ryff’s Scales of Psychological Well-Being (Table 1). Although the original scale included 20 items designed to measure purpose in life, several shortened versions (ranging from 3 to 14 questions) have been developed and evaluated psychometrically. For each of the 10 items, participants rated their level of agreement using a 5-point scale, as previously described. Scoring for the negatively worded items was flipped, and item scores were averaged to yield a total score for each participant, with higher scores indicating greater purpose in life. As previously reported, the Cronbach coefficient was 0.80.
distinct psychological construct that has predictive validity for covariates; these data suggest that purpose in life is a relatively passive symptoms, neuroticism, and disability, and purpose in life to moderate correlations between purpose in life and depression.

Social network size was quantified using standard questions regarding the number of children, family, and friends that participants had and how often they interacted with them. Social network size was the number of these individuals seen at least once a month, as reported elsewhere.23 The mean (SD) score was 15.1 (7.1) (range, 0-44).

Neuroticism, the personality trait that refers to the tendency to experience psychological distress, was measured using the neuroticism subscale of the NEO Five-Factor Inventory to constitute Inc, Cary, North Carolina).25

RESULTS

PSYCHOMETRIC PROPERTIES OF PURPOSE IN LIFE

Baseline scores on the measure of purpose in life ranged from 2 to 5 (mean [SD], 3.6 [0.5]), with higher scores indicating greater purpose in life. In unadjusted analyses, purpose in life was associated with age (r = -0.25) and education (r = 0.26) (P < .001 for both); women reported lower purpose in life compared with men (P = .02).

PURPOSE IN LIFE AND RISK OF AD

During up to 7 years of follow-up (mean, 4.0 years), 155 of 951 persons (16.3%) developed AD; mean follow-up was similar in those who did (mean, 4.5 years) vs those who did not (mean, 4.0 years) develop AD. Those who developed AD were older and reported lower purpose in life than did those who did not (Table 2). In addition, those who developed AD reported higher baseline levels of neuroticism and fewer chronic medical conditions.

We constructed a proportional hazards model to test the hypothesized association of purpose in life with risk

Abbreviations: AD, Alzheimer disease; MMSE, Mini-Mental State Examination.

Other variables used in the analyses included age (based on date of birth), sex, and education (years of schooling completed).13 Depressive symptoms were assessed using a 10-item version of the Center for Epidemiologic Studies Depression Scale, as previously described.13 Persons were asked whether they had experienced each of 10 symptoms in the past week, and the score was the number of symptoms reported. The mean (SD) score on the Center for Epidemiologic Studies Depression Scale was 1.3 (1.8) (range, 0-9).

Neuroticism score, mean (SD) 14.8 (7.0) 16.8 (7.2) .002

Social network size, mean (SD) 6.8 (6.0) 5.8 (4.8) .08

No. of medical conditions, mean (SD) 1.3 (1.1) 1.2 (1.1) .03

MMSE score, mean (SD) 28.3 (1.8) 26.3 (3.2) <.001

Abbreviations: AD, Alzheimer disease; MMSE, Mini-Mental State Examination.

aStatistical significance is based on t tests or χ2 tests, as appropriate.
of AD; this core model and all subsequent models adjusted for age, sex, and education. In this analysis, greater purpose in life was associated with a substantially reduced risk of AD (hazard ratio [HR], 0.48; 95% confidence interval [CI], 0.33-0.69; \( P < .001 \)) (model 1 in Table 3). Thus, a person with a high score on the purpose in life measure (score = 4.2, 90th percentile) was approximately 2.4 times more likely to remain free of AD than was a person with a low score (score = 3.0, 10th percentile) (Figure 1).

Next, because the association of purpose in life with AD may vary along demographic lines, we repeated the analysis described previously herein with additional terms for the interactions of age, sex, and education with purpose in life in separate models. No interactions were found (data not shown). In addition, because negative affect (ie, depressive symptoms), neuroticism, social networks, and chronic medical conditions may affect the association of purpose in life with AD, we repeated the core model described previously herein with additional terms to control for these important covariates. The association of purpose in life with AD persisted even after adjustment for all the covariates together in a single model (HR, 0.60; 95% CI, 0.39-0.92; \( P = .02 \)).

Because it is possible that the inclusion of persons with mild, undiagnosed AD could have affected the findings reported previously herein, we repeated the core analysis 3 times after sequentially excluding persons who developed AD during each of the first 3 years of follow-up. In each case, and with as few as 62 cases of incident AD, purpose in life remained associated with the risk of AD (models 2-4 in Table 3).

**Purpose in Life and Risk of MCI**

It is widely recognized that AD has a long preclinical phase during which most persons transition through a stage referred to as MCI, when cognitive deficits are present but of insufficient severity to warrant a diagnosis of AD. To ensure that the present findings were not due to the inclusion of persons with early preclinical AD, we examined the relation of purpose in life with risk of MCI. In these models, persons with MCI at the baseline evaluation were excluded, leaving a final sample of 698 persons without cognitive deficits. During up to 7 years of follow-up, 285 of 698 persons (40.8%) developed MCI. Those who developed MCI were older and reported lower purpose in life and a higher number of depressive symptoms compared with those who did not develop MCI (Table 4).

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**Table 3. Relation of Purpose in Life With AD in Sensitivity Analyses**

<table>
<thead>
<tr>
<th>Model (No. of Incident AD Cases)</th>
<th>Hazard Ratio (95% CI)(^a)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1: core model (n=155)</td>
<td>0.48 (0.33-0.69)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Model 2: excluding AD in year 1 (n=118)</td>
<td>0.52 (0.34-0.79)</td>
<td>.002</td>
</tr>
<tr>
<td>Model 3: excluding AD in years 1-2 (n=86)</td>
<td>0.45 (0.27-0.74)</td>
<td>.002</td>
</tr>
<tr>
<td>Model 4: excluding AD in years 1-3 (n=62)</td>
<td>0.30 (0.17-0.53)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: AD, Alzheimer disease; CI, confidence interval.

\( ^a \) Based on separate models; all models controlled for age, sex, and education.

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**Table 4. Baseline Characteristics of Participants Who Developed MCI vs Those Who Did Not**

<table>
<thead>
<tr>
<th>Characteristic(^a)</th>
<th>Did Not Develop MCI</th>
<th>Developed MCI</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>78.1 (7.3)</td>
<td>81.6 (6.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Female sex, %</td>
<td>78.8</td>
<td>75.4</td>
<td>.69</td>
</tr>
<tr>
<td>Race, white, non-Hispanic, %</td>
<td>89.4</td>
<td>92.6</td>
<td>.14</td>
</tr>
<tr>
<td>Education, mean (SD), y</td>
<td>14.5 (3.0)</td>
<td>14.7 (3.2)</td>
<td>.38</td>
</tr>
<tr>
<td>Purpose in life score, mean (SD)</td>
<td>3.7 (0.5)</td>
<td>3.6 (0.4)</td>
<td>.002</td>
</tr>
<tr>
<td>Depressive symptoms score, mean (SD)</td>
<td>1.1 (1.7)</td>
<td>1.4 (1.9)</td>
<td>.04</td>
</tr>
<tr>
<td>Neuroticism score, mean (SD)</td>
<td>14.3 (7.2)</td>
<td>15.1 (6.4)</td>
<td>.12</td>
</tr>
<tr>
<td>Social network size, mean (SD)</td>
<td>7.0 (6.3)</td>
<td>6.6 (6.1)</td>
<td>.25</td>
</tr>
<tr>
<td>No. of medical conditions, mean (SD)</td>
<td>1.4 (1.1)</td>
<td>1.2 (1.0)</td>
<td>.10</td>
</tr>
<tr>
<td>MMSE score, mean (SD)</td>
<td>28.7 (1.4)</td>
<td>28.2 (1.8)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination.

\( ^a \) Statistical significance is based on \( t \) tests, Wilcoxon rank sum tests, or \( \chi^2 \) tests, as appropriate.

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In a proportional hazards model adjusted for age, sex, and education, greater purpose in life at baseline was associated with a substantially reduced risk of MCI (HR, 0.71; 95% CI, 0.53-0.95; \( P = .02 \)). Thus, a person with a high score on the purpose in life measure (score = 4.2, 90th percentile) was approximately 1.5 times more likely to remain free of MCI than was a person with a low score (score = 3.1, 10th percentile) (Figure 2).

Next, because MCI does not uniformly progress to dementia or even persist,\(^19,20\) we examined the association of purpose in life with persistent MCI, defined as having MCI on 2 or more consecutive examinations (or MCI followed by dementia or death), as done in previous studies.\(^3\) Of 285 persons with incident MCI in the analyses described previously herein, 124 had MCI, dementia, or death at the next examination. In a proportional hazards model adjusted for age, sex, and education, purpose in life in the analyses described previously herein with additional terms to control for these important covariates. The association of purpose in life with persistent MCI, defined as having MCI on 2 or more consecutive examinations (or MCI followed by dementia or death), as done in previous studies.\(^3\) Of 285 persons with incident MCI in the analyses described previously herein, 124 had MCI, dementia, or death at the next examination; the remaining 161 were included in the reference group. In a proportional hazards model adjusted for age, sex, and education, purpose in life was associated with a reduced risk of MCI (HR, 0.65; 95% CI, 0.43-1.00; \( P = .05 \)). Although the association was stronger (ie, the point esti-
mate was lower), the CI included 1.0 due to reduced power from the smaller sample size.

PURPOSE IN LIFE AND CHANGE IN COGNITIVE FUNCTION

Because the principal manifestation of AD is cognitive decline and because AD develops slowly across many years, we next examined the association of purpose in life with the rate of change in cognitive function. To make use of all the cognitive data, we began with the composite measure of global cognition and constructed a series of mixed-effect models that allowed us to estimate the association of purpose in life with rate of change in cognition while controlling for baseline level of cognition. The initial analyses included all persons without dementia at the baseline evaluation. In these analyses, purpose in life was related to baseline level of global cognition (estimate for purpose in life) \( \text{Table 5, column A} \) and to rate of global cognitive decline (estimate for purpose in life \( \times \) time) (Table 5, column A). This is illustrated in Figure 3, which shows the trajectories of cognitive decline for participants with high vs low purpose in life. Persons with greater purpose started at a higher level of cognition than did those with low purpose but declined less rapidly than did those with low purpose. Additional models examined 5 separate cognitive abilities starting with episodic memory, the hallmark of AD, and the 4 other measures, including semantic memory, working memory, perceptual speed, and visuospatial ability (Table 5). Purpose in life was related to baseline level of cognition in all 5 systems and was most strongly related to decline in semantic memory, followed by episodic memory, perceptual speed, and working memory.

Finally, we repeated the mixed-effects models just described after excluding persons with MCI at baseline to further clarify the relation of purpose in life with the level and rate of change in cognitive function. In these models, findings were similar; purpose in life was associated with a reduced rate of decline in global cognition, semantic memory, episodic memory, working memory, and perceptual speed (Table 5, column B).

We examined the association of purpose in life with risk of incident AD in more than 900 community-dwelling older persons. During up to 7 years of follow-up, greater purpose in life was associated with a substantially reduced risk of AD such that a person with a high score (90th percentile) on the purpose in life measure was approximately 2.4 times more likely to remain free of AD than was a person with a low score (10th percentile). The association of purpose in life with AD persisted after adjustment for several important covariates (ie, depres-
sive symptoms, neuroticism, social network size, and number of chronic medical conditions) and in sensitivity analyses in which we excluded persons who developed AD during the first 3 years of follow-up. Furthermore, in subsequent analyses, purpose in life was associated with a reduced risk of incident MCI, an early preclinical manifestation of AD. Finally, in models that controlled for baseline level of cognitive function, we found that purpose in life was associated with a less rapid rate of cognitive decline in persons without AD and in persons without AD or MCI. These findings suggest that the tendency to derive meaning from life's experiences and to possess a sense of intentionality and goal directedness are associated with a substantially reduced risk of AD and a less rapid rate of cognitive decline in old age.

Emerging data suggest that psychological and experiential factors are related to the risk of AD, with some (eg, neuroticism, loneliness, social isolation, and depressive symptoms) increasing risk and others (eg, conscientiousness, extraversion, and social integration) decreasing risk. Purpose in life is an indicator of human thriving that has long been hypothesized to buffer against adverse health outcomes. In recent years, purpose in life has been conceptualized as a component of psychological well-being, in this context, purpose in life has been shown in cross-sectional studies to be associated with psychological health, including happiness, satisfaction, personal growth, self-acceptance, and better sleep. Although prospective data on the association of purpose in life with health outcomes are limited, we recently reported that purpose in life was associated with a reduced risk of all-cause mortality in older persons from this cohort. We are not aware of any previous study that has examined the association of purpose in life with risk of AD.

The finding that purpose in life is associated with cognitive outcomes may have important public health implications. In particular, these findings may provide a new treatment target for interventions aimed at enhancing health and well-being in older adults. Purpose in life is a potentially modifiable factor that may be increased via specific behavioral strategies that help older persons identify personally meaningful activities and engage in goal-directed behaviors. Even small behavioral modifications ultimately may translate into an increased sense of intentionality, usefulness, and relevance. Furthermore, purpose in life may be modifiable, even in persons for whom participation in more effortful activities (ie, physical activity, volunteerism, and other activities involving travel outside the home or local area) may be limited because of underlying health problems. Thus, purpose in life may offer a new treatment focus and may represent a target accessible to most of the aging population. If true, the implications could be far reaching, and efforts to increase purpose in life may help reduce the rapidly increasing burden of cognitive impairment in old age. At present, the biological basis of the association of purpose in life with AD is unknown. Purpose in life is hypothesized to provide protective benefit in the face of illness or disease because it contributes to the optimal functioning of multiple physiologic systems. Although relatively few data are available on the association of purpose in life with physiologic measures, emerg-
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Author Contributions: Dr Boyle had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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