**Objective:** To examine whether reported age at onset of dementia symptoms among participants with Alzheimer disease (AD) is later for those with fewer years of education and, if so, to see if education is attributed to delayed detection of symptoms.

**Design:** Case series.

**Setting:** National Alzheimer’s Coordinating Center Minimum Data Set (N=21,880 participants) and Washington University Alzheimer’s Disease Research Center (N=1449 participants).

**Results:** Reported age at onset of dementia symptoms is slightly younger in participants with more education. Participants with fewer years of education show greater clinical severity of Alzheimer disease at first assessment.

**Conclusion:** Symptoms of Alzheimer disease are recognized later among those with less education.

**LOW EDUCATIONAL LEVEL IS A RISK FACTOR FOR INCIDENT ALZHEIMER DISEASE (AD).** However, among individuals with the E280A PS1 mutation, who would be expected to develop familial early-onset AD if they were to live long enough, we found that later-reported age at onset of dementia symptoms occurred in participants with lower education. Similar findings have been reported for most studies of individuals with clinical or autopsy-diagnosed sporadic AD. One investigation, using a regional sample of participants, reported that lower education was associated with both an older age at onset of symptoms and a greater severity of AD at presentation, as reflected in scores on the Blessed-Roth Dementia Rating scale. These results suggest that it is not the onset of AD that is delayed but rather that dementia symptoms are detected later among individuals with lower education. By using alternate measures of dementia severity, we sought to confirm these findings by examining whether age at onset of dementia symptoms and severity of dementia at first assessment were associated with education in 2 samples.

**METHODS**

**PARTICIPANTS**

One sample was composed of data from participants with a clinical diagnosis of AD enrolled in 30 Alzheimer disease centers (ADCs) across the United States and another comprised data from a single ADC. Inclusion criteria for both samples were (1) receiving a clinical diagnosis of AD at the most recent clinical assessment and having no missing data on (2) number of years of education or (3) age at onset of symptomatic AD (ie, dementia onset).

**NATIONAL ALZHEIMER’S COORDINATING CENTER SAMPLE**

The National Alzheimer’s Coordinating Center (NACC) sample was drawn from the 2003 Minimum Data Set, which contains information for all participants enrolled in ADCs supported by the National Institute on Aging, Bethesda, Maryland. Education was coded as the highest grade or number of years of regular school completed. Participants in the data set were not evaluated or enrolled using a uniform protocol, and therefore variables in the Minimum Data Set may reflect slightly different information. The age at onset variable refers to the reported onset of dementia symptoms rather than the age at diagnosis. Data from participants enrolled in the Washington University Alzheimer’s Disease Research Center were removed from the NACC sample, as these data were analyzed separately.

**WASHINGTON UNIVERSITY SAMPLE**

Participants were enrolled in the longitudinal studies of Washington University (WU) Alzheimer’s Disease Research Center. Details concerning participant recruitment, enrollment, and assessment have been published. Amount of formal education was recorded as the total number of years of education completed.
Identification of factors that delay recognition of dementia symptoms is important in targeting individuals for treatment. Like others,3,4 we found that duration of education has a modest association with age at onset, in that reported onset of dementia symptoms is slightly earlier for participants with more education. Together with the finding that the time from reported onset of symptoms to first assessment does not vary by education, these results suggest that individuals of varying educational levels do not differentially delay seeking medical attention after noticing symptoms, but that symptoms are recognized later among those with less education, as suggested by an earlier report.4

Persons with more education may be more likely to be engaged regularly in cognitive tasks or occupational roles that emphasize subtle changes in cognitive functions, leading to earlier detection.4 Therefore, in assessing for dementia among persons with less formal education, clinicians may need to individualize their assessment procedures, so that changes attributable to memory and thinking problems in cognitive, recreational, and social activities in which the individual regularly engages are detected. Because recognition of early

STATISTICAL ANALYSES

PROC LIFETEST (SAS Institute Inc, Cary, North Carolina) was used to estimate the survival curves of reported age at onset of dementia symptoms for the education groups using the Kaplan-Meier product-limit method. Cox proportional hazard models5 using PROC PHREG (SAS Institute Inc) were used to test the effect of education together with demographic variables (sex, race, and birth cohort) on the survival functions of age at onset. Three categories were used to reflect amount of education: low (<8 years), moderate (8-11 years), and normative (≥12 years). Two birth cohorts were created (birth <1920 and ≥1920) based on a median split of the birth years in the NACC sample. To adjust for differences across the centers, ADC was used as a stratum in the proportional hazard models (SAS Institute Inc) conducted with the NACC sample.

Reported onset of dementia symptoms occurred prior to first ADC assessment for most participants in both the NACC (97.6%) and WU (97.9%) samples. Analysis of variance was used to examine education group differences in time from reported age at onset to first assessment. Mini-Mental State Examination6 (MMSE) and CDR scores were used to assess differences between the education groups in the degree of cognitive impairment at first assessment. Mini-Mental State Examination data were available for 86% of the NACC sample, but because the MMSE was not administered at WU until 1996, these data were available for only 35% of WU participants. Clinical Dementia Rating data were available for all WU participants, but were not reported to the NACC until September 2005 and therefore were not available in the 2003 NACC data set used here.

RESULTS

NACC SAMPLE (N=21 880)

Sixty-five percent of NACC participants were women, 83% were white, and 51% were born before 1920. Seventy-three percent of participants had 12 or more years of education, 19% had 8 to 11 years, and 8% had less than 8 years. Reported age at onset was younger with increasing amount of education (log-rank test, P < .001) (Figure). This finding was confirmed in the Cox proportional hazards analysis when differences between the individual survival curves were tested controlling for sex, race, birth stratum, and ADC (Table). The moderate and normative education groups showed a slightly faster rate of reported age of AD onset over time compared with the low education group, and the normative group had a slightly faster rate than the moderate group (Table). Male sex and white race were associated with earlier age at onset, and birth before 1920 was associated with later age at reported onset. The mean (SD) number of years from age at onset to age at first assessment at the ADC was similar for the normative (4.25 [3.3] years), moderate (4.29 [3.2] years), and low (4.28 [3.5] years) education groups (P = .71), though mean (SD) MMSE scores at first assessment differed (P < .001) across the groups (normative, 18.0 [7.2]; moderate, 15.3 [6.7]; low, 12.9 [6.3]).
dementia symptoms may be associated with amount of formal education, these results also suggest that researchers should be cautious when using self-reports or proxy reports of memory impairment; statistical adjustment for level of education may be appropriate depending on the research question.

As has been found in other studies, later birth years were associated with younger ages at reported onset.3 Greater awareness of dementia, increasing recognition that AD is not an inevitable consequence of normal aging, and the development of better diagnostic tools throughout the years may account for earlier reported age at onset in the later birth cohort.

Limitations of the study include differences across the ADCs in how age at onset was assessed. Unfortunately, there is currently no universal, standardized way to measure age at onset of dementia symptoms. Furthermore, reports of age at onset are likely to be imprecise. The study sample consisted of individuals with an AD diagnosis who were enrolled in an ADC, and thus it is unclear the extent to which these results would generalize to all individuals with an AD diagnosis. In addition, enrollment in

Figure. Reported age at onset of dementia with time in each sample.
Table. Results of Cox Proportional Hazard Models Testing Rate of Reported Age of AD Onset Over Time

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>NACC Sample Hazard Ratio (95% Confidence Interval)</th>
<th>WU Sample Hazard Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-11 vs &lt; 8</td>
<td>1.12 (1.06-1.18) a</td>
<td>1.18 (0.92-1.5)</td>
</tr>
<tr>
<td>≥ 12 vs &lt; 8</td>
<td>1.18 (1.12-1.24) a</td>
<td>1.16 (0.91-1.46)</td>
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<tr>
<td>≥ 12 vs 8-11</td>
<td>1.05 (1.02-1.09) b</td>
<td>0.98 (0.87-1.11)</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.10 (1.07-1.13) b</td>
<td>1.33 (1.19-1.48) a</td>
</tr>
<tr>
<td>White race</td>
<td>1.07 (1.03-1.11) b</td>
<td>1.35 (1.14-1.60) a</td>
</tr>
<tr>
<td>Birth &lt; 1920</td>
<td>0.198 (0.191-0.204) a</td>
<td>0.15 (0.14-0.16) a</td>
</tr>
</tbody>
</table>

Abbreviations: AD, Alzheimer disease; NACC, National Alzheimer’s Coordinating Center; WU, Washington University.

a P < .001.
b P < .01.

an ADC may itself be influenced by factors related to education, such as economic status.

Accepted for Publication: April 16, 2007.

Correspondence: Catherine M. Roe, PhD, Department of Neurology, Washington University School of Medicine, 4488 Forest Park Ave, Ste 101, St Louis, MO 63108 (cathyr@wubahios.wustl.edu).

Author Contributions: Catherine Roe had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Roe and Morris. Acquisition of data: Roe. Analysis and interpretation of data: Roe, Xiong, Grant, Miller, and Morris. Drafting of the manuscript: Roe and Morris. Critical revision of the manuscript for important intellectual content: Roe, Xiong, Grant, Miller, and Morris. Statistical analysis: Roe, Xiong, Grant, and Miller. Obtained funding: Roe. Administrative, technical, and material support: Morris. Study supervision: Morris.

Financial Disclosure: None reported.

Funding/Support: This study was supported by grants P50 AG05681, P01 AG03991 (WU Alzheimer’s Disease Research Center), and U01 AG016976 (NACC) from the National Institute on Aging and by the Charles and Joanne Knight Alzheimer Research Initiative.

Additional Contributions: We are grateful to the staff of the NACC for their contributions.

REFERENCES


