The Consortium to Establish a Registry for Alzheimer’s Disease (CERAD) was established in 1986 by a grant from the National Institute on Aging (NIA), to standardize procedures for the evaluation and diagnosis of patients with Alzheimer’s disease (AD). Patients and nondemented control subjects were recruited from 24 NIA-sponsored Alzheimer’s Disease Research Centers and other university programs in the US. Using standardized diagnostic criteria and assessment instruments, CERAD subjects were examined at entry and annually thereafter, to observe the natural progression of AD. Autopsy examination of the brain was included, to the extent possible, to obtain neuropathologic confirmation of the clinical diagnosis.

The major standardized instruments developed by CERAD are now used by many AD research centers in the US and abroad, by physicians in clinical practice, and in population-based surveys. They have been translated into Bulgarian, Chinese, Dutch, Finnish, French, German, Italian, Japanese, Korean, Portuguese, and Spanish. Approximately 75 papers describing CERAD findings have been published in English-speaking scientific medical journals. While focusing on the standardization of assessment instruments and methods, the CERAD study obtained information on the natural history of AD, its clinical, neuropsychological, and neuropathological correlations; its family history; and behavioral and associated personality changes. Data were obtained on 1,094 carefully screened, nationally distributed White and African-American patients with AD and on 463 nondemented controls, many of whom were observed for periods as long as seven years. The clinical diagnosis of AD was confirmed in 87% of autopsied cases.
CERAD – Contact

A complete listing of CERAD assessment instruments and related materials available for purchase is listed on our Order Form. The assessment instruments and data are available on request for use by non-CERAD investigators.

Written inquiries are welcome

Contact:

<table>
<thead>
<tr>
<th>Albert Heyman, MD</th>
<th>Gerda Fillenbaum, PhD</th>
</tr>
</thead>
<tbody>
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<td>e-mail: <a href="mailto:Gerda.Fillenbaum@duke.edu">Gerda.Fillenbaum@duke.edu</a></td>
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<tr>
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<td>Box 3003 DUMC</td>
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<tr>
<td>Phone: (919) 286-6406</td>
<td>Durham, NC 27710</td>
</tr>
<tr>
<td>FAX: (919) 286-9219</td>
<td>Phone: (919) 660-7530</td>
</tr>
<tr>
<td></td>
<td>FAX: (919) 684-8569</td>
</tr>
</tbody>
</table>

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CERAD ASSESSMENT INSTRUMENTS

CERAD developed the following standardized instruments to assess the various manifestations of Alzheimer’s disease:

- Clinical/Neuropsychology
- Neuropathology
- Behavior Rating Scale for Dementia
- Family History Interviews
- Assessment of Service Needs

Members of the clinical staff at participating clinical sites were trained and certified in the uniform administration of these assessments. Data were gathered from carefully screened patients with Alzheimer’s disease and from control subjects, who were also enrolled in the CERAD study. The CERAD database comprises 1094 patients and 463 non-demented elderly control subjects who were evaluated annually for as long as seven years. This case material has been a valuable resource for information on Alzheimer’s disease and is the basis for some 75 publications describing the CERAD research findings. Autopsy examination of the brain was carried out, to the extent possible, in an effort to obtain neuropathologic confirmation of clinical diagnoses.

A complete listing of CERAD assessment instruments and related materials available for purchase is listed on our Order Form. The assessment instruments and data are available on request for use by non-CERAD investigators. Written inquiries are welcome.
CERAD Clinical and Neuropsychology Assessment

This Clinical Assessment Packet consists of a battery of brief evaluations designed to gather demographic, clinical, neurological and neuropsychological data on cognitively impaired subjects, sufficient to establish a clinical diagnosis of dementia based on CERAD criteria.

Table of contents of CERAD Protocol 5: Assessment Packet for Probable Alzheimer’s Disease (AD):

A. DEMOGRAPHIC DATA
   SUBJECT

B. DEMOGRAPHIC DATA
   INFORMANT

C. CLINICAL HISTORY
   C1 Clinical History
      A) Cognitive Impairment/Dementia
      B) Systemic Illnesses
      C) Cerebrovascular Disease
      D) Parkinson’s Disease
   C2 Blessed Dementia Scale (ADL)
   C3 Behavior Rating Scale
   C4 Short Blessed Test
   C5 Calculation, Clock and Language

D. CLINICAL EXAMINATIONS
   D1 Physical Examination
   D2 Neurologic Examination

E. LABORATORY AND IMAGING STUDIES
   A) Clinical laboratory studies
   B) Neuroimaging studies

F. CLINICAL DIAGNOSIS
   F1 CDR Staging

INFORMANT

F2 Diagnostic Impression
   A) Cognitive Function Normal
   B) Impaired Cognition

F3 Diagnostic Impression
   A) Alzheimer’s Disease
   B) AD with Other Illness
   C) Other Disorders

J. NEUROPSYCHOLOGICAL FORMS
   J0 Summary of J Tests
   J1 Verbal Fluency
   J2 Boston Naming Test
   J3 Mini-mental State Exam
   J4 Word List Memory
   J5 Constructional Praxis
   J6 Word List Recall
   J7 Word List Recognition
   J8 Recall of Constructional Praxis

See the CERAD list of publications on clinical and neuropsychological findings in AD. For information regarding purchase of this assessment material, check the Order Form.
CERAD Neuropathology Assessment

The CERAD neuropathology criteria are widely used in the US and abroad for studies of Alzheimer’s disease and other dementias of the elderly. This assessment was developed to fulfill the following aims and purposes:

- To establish accurate, reliable, and standardized neuropathological criteria for the diagnosis of Alzheimer’s disease (AD) and other dementias;

- To develop a practical protocol for postmortem examination of the brain and provide standard, reliable measures for determining the neuropathological spectrum and heterogeneity of Alzheimer’s disease and other dementias;

- To extend the CERAD assessments to include dementias associated with other disorders such as vascular disease, Parkinson’s disease, alcoholism, and depression;

- To establish a data base for pooling the neuropathological findings of Alzheimer’s disease and other dementias with clinical information on demented and cognitively normal subjects.

The Neuropathology assessment packet includes the following data forms:
A. Demographic Data
B. Clinical History
C. Gross Examination of the Brain
D. Cerebral Vascular Disease: Gross Findings
E. Microscopic Vascular Findings
F. Major Non-vascular Microscopic Findings
G. Microscopic Evaluation of Hippocampus and Neocortex
H. Assessment of Neurohistological Findings
I. Neuropathological Diagnosis
J. Final Assessment

This assessment packet includes a detailed manual, The CERAD Guide to the Neuropathological Assessment of Alzheimer’s Disease and Other Dementias.

See the CERAD list of publications on neuropathological findings in AD. For information regarding purchase of this assessment material, check the Order Form.
CERAD Behavior Rating Scale for Dementia (BRSD)

The CERAD Behavior Rating Scale for Dementia (BRSD) is a standardized instrument for rating behavioral abnormalities in demented or cognitively impaired subjects. Descriptive items are scaled according to frequency of psychopathological behavior.

In a pilot test, the initial 51-item scale was administered by trained examiners to informants for 303 subjects with probable AD who had undergone standardized clinical evaluation by CERAD. Wide variability was found in the nature of the behavioral disturbances; factor analysis indicated eight preliminary factors that mapped onto the following clinically relevant domains:

- depressive features
- psychotic features
- defective self-regulation
- irritability/agitation
- vegetative features
- apathy
- aggression
- affective lability

This scale was found to be reliable with high interrater agreement. It has since been modified slightly on the basis of this study. The questionnaire is now available for purchase in either a 46-item version or a shorter 17-item version, together with an instruction manual. A video training tape is also available.

See the CERAD list of publications on behavioral changes in AD.

For information regarding purchase of materials, check the Order Form.
CERAD Family History Assessment

In response to the need for a uniform family history assessment in genetic and epidemiological studies of AD, CERAD developed a standardized Family History Assessment of AD. This assessment consists of interview instruments, coding forms, and hierarchical rating systems designed to determine the presence of AD, Parkinson's disease, and Down syndrome among relatives of cases of AD and their spouse controls.

These instruments are relatively brief (taking about 45 minutes to complete) and easy to administer.

This assessment was used in a multi-center family history study of AD to evaluate 118 cases with AD and their non-demented spouses, enrolled at 11 different CERAD sites in the US. The study found that first-degree relatives of patients with AD had a significantly greater cumulative risk of AD than did the relatives of spouse controls. Furthermore, the cumulative risk of AD was significantly greater among female relatives than among male relatives. The numbers of affected first-degree relatives with Parkinson’s disease or Down syndrome did not differ between the families of cases and those of controls.

See the CERAD list of publications on Family History.

For information regarding purchase of this material, contact the main CERAD office.
CERAD Assessment of Service Needs

Large sums of money are currently spent for health care and for other services needed for persons with Alzheimer's disease and other dementias of the elderly. Precise information is lacking, however, as to the specific services needed and used in the long-term care of these persons.

For this reason, CERAD developed a questionnaire for administration to caregivers of CERAD subjects with AD. It assesses the need for and the extent of use of the most common services for care of persons with dementia. This questionnaire usually takes about 15 minutes to administer and includes questions on:

- The caregiver’s current situation
- Overnight care for the patient outside the home
- Day care for the patient outside the home
- Care required for the patient in the home
- Help for the caregiver
- Need for other services.

For information regarding purchase of this material, see the Order Form.
### CERAD Study Population (Database)
Basic Characteristics of cases with Alzheimer's Disease (N=1094) and Control Subjects (N=463) at Entry into CERAD

<table>
<thead>
<tr>
<th>Year Entered</th>
<th>CASES</th>
<th>CONTROLS</th>
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<tbody>
<tr>
<td>1987</td>
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<td>1988</td>
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<td>1992-95</td>
<td>146</td>
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<th>Stage of Dementia (CDR Scale)</th>
<th>CASES</th>
<th>CONTROLS</th>
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<td>No Dementia</td>
<td>0</td>
<td>460</td>
</tr>
<tr>
<td>Uncertain</td>
<td>37</td>
<td>3</td>
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<tr>
<td>Mild</td>
<td>564</td>
<td>0</td>
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<tr>
<td>Moderate</td>
<td>425</td>
<td>0</td>
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<tr>
<td>3</td>
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<table>
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<th>Age at Entry (Years)</th>
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<td>65 - 74</td>
<td>423</td>
<td>226</td>
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<td>More than 74</td>
<td>484</td>
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<td>Black</td>
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<td>636</td>
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<th>CASES</th>
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<td>160</td>
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<td>Female</td>
<td>646</td>
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<td>0 - 8</td>
<td>234</td>
<td>36</td>
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<td>9 - 11</td>
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<td>12</td>
<td>324</td>
<td>136</td>
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<td>Greater than 12</td>
<td>413</td>
<td>252</td>
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<table>
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<th>Entered Nursing Home</th>
<th>CASES</th>
<th>CONTROLS</th>
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<td>No</td>
<td>575</td>
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<table>
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<th>Death</th>
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<tr>
<td>Yes</td>
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<td>25</td>
</tr>
<tr>
<td>No</td>
<td>683</td>
<td>438</td>
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<table>
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<th>Brain Autopsy</th>
<th>CASES</th>
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<td>202</td>
<td>8</td>
</tr>
<tr>
<td>No</td>
<td>209</td>
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</table>
Clinical
Reliable information on the rate of progression of cognitive impairment was obtained in a well-characterized group of patients with AD who were followed using standardized CERAD assessments. Rate of decline was slower for patients with less severe dementia. Significant weight loss was found to be more frequent in patients than in controls. CERAD studies also reported the impact of depression on AD, those with early- vs. late-onset dementia, and comparisons of patients with AD and those with schizophrenia.


**Neuropsychology**

The Neuropsychology Battery developed by CERAD includes tests of verbal fluency (naming animals); a modified 15-item Boston Naming Test; Mini-Mental State Examination; word list memory, recall, and recognition; constructional praxis; and recall of constructional praxis. Word list recall was found to distinguish best between AD patients and normal controls.


**Neuroimaging**
Although the CERAD attempt to standardize neuroimaging measures of AD suggests that uniform reading of brain scans at any one clinical site was possible, uniform reading across multiple sites proved difficult to achieve.


**Neuropathology**
Findings obtained using the CERAD neuropathology protocol confirmed the clinical diagnosis of AD in 87% of autopsied CERAD patients. This widely-used protocol has since been modified for use by general pathologists for the diagnosis of dementia. (See also section on Associated Dementias.)


Minority Studies
In CERAD, as in other longitudinal studies, recruitment and retention of African American subjects often required special measures. When age, education, and severity of disease at entry were controlled, race was found to have only a very mild effect on progression of dementia.


Health Economics
AD is reported to be the third most expensive disease in the US, after heart disease and cancer. There are few published studies on Medicare-reimbursed services for patients with an accurate diagnosis of AD. CERAD studies indicated that the frequency and duration of hospitalization were greater for AD subjects than for matched controls. These studies further indicate that multiple years of Medicare-based data are needed to identify persons with AD.


Family History
In our study comparing the families of 118 patients with AD and their nondemented spouses, we found a significantly greater risk for AD among families of patients than among those of controls. There was also a greater risk of AD among female relatives than among males.


Outcomes
Age, sex, and severity of dementia were found to be the major predictors of survival of
patients with AD, whereas race, education, and marital status were not important predictors. The major predictors of time to nursing home admission were sex, age, marital status (men only), and severity of dementia. Death certificates were found to be poor sources of information regarding the presence of dementia, since dementia was not mentioned in nearly a third of the death certificates of CERAD patients who had an overt clinical diagnosis of AD.


Associated Dementias
Neuropathologic examination of the brains of CERAD cases with autopsy-confirmed AD disclosed coexisting lesions of Parkinson's disease in 21% of them, and of cerebrovascular disease in an additional 28%. Patients with cerebrovascular lesions tended to be older, more severely demented, and performed more poorly on neuropsychology testing.


Welsh-Bohmer KA, Gearing M, Saunders AM, et al. Apolipoprotein E genotypes
Behavioral Studies
The CERAD Behavior Rating Scale for Dementia (BRSD) identified eight behavioral domains that may be related to AD, including agitation, depression, and hallucinatory phenomena. Both a full (46 item) and a short (17 item) version of this scale are available.


Studies In Foreign Languages
Considerable attention has been given to equivalence in translating CERAD assessment instruments into foreign languages. Such translations are currently being used in German-speaking populations in Switzerland, Austria, and Germany, and in a standardized national population study in Finland. The following studies showed the French- and English-language versions to be comparable.


Statistics and Data Management
CERAD has developed improved methods for analyzing longitudinal data, which maximize the amount of information provided by a sample with rolling enrollment and
different lengths of time in the study. Less conventional approaches to examining data, based on fuzzy set theory, have also been examined.


Sampling Issues
Characteristics of the measures used and of the study population can influence findings. We found that the widely-used Clinical Dementia Rating Scale is indeed valid. While the most ill patients are more likely to drop out of longitudinal studies of non-demented elderly, studies of persons with AD showed that the most ill are more likely to stay. Continued participation of control subjects who are spouses of enrolled patients is interdependent. Not surprisingly, the continued participation of one is related to the continued participation of the other.


Theses and Dissertations


Additional Publications
The authors of most of the following papers were not members of the original CERAD group. They have, however, published important studies based on CERAD data and concepts.

Behavioral Studies


Clinical


Epidemiology


Lee DY, Lee JH, Ju YS, et al. The prevalence of dementia in older people in an


**Neuropathology**


**Neuropsychology**


**Statistical Analyses**


**Translations**


CERAD - Materials

Following its organization in 1986, the Consortium to Establish a Registry for Alzheimer’s Disease enrolled 24 university medical centers in the U.S. engaged in Alzheimer’s disease (AD) research. The purpose of this consortium at that time was to develop brief, standardized and reliable procedures for the evaluation and diagnosis of patients with AD and other dementias of the elderly. These procedures included data forms, flipbooks, guidebooks, brochures, instruction manuals and demonstration tapes, which are now available for purchase. The CERAD assessment material can be used for research purposes as well as for patient care.

Purchase orders should be accompanied by a brief description of the proposed use of the assessment instruments, the approximate number of subjects to be tested each year as well as plans, if any, for publication. CERAD material purchased by the approved applicant is restricted to his or her use only and must not be sold or redistributed to others without authorization.

CERAD has developed several basic standardized instruments, each consisting of brief forms designed to gather data on normal persons as well as on cognitively impaired or behaviorally disturbed individuals. Such data permit the identification of dementia based on clinical, neuropsychological, behavioral or neuropathological criteria.

Staff at participating CERAD sites were trained and certified to administer the assessment instruments and to evaluate the subjects enrolled in the study. Cases and controls were evaluated at entry and annually thereafter including (when possible) autopsy examination of the brain to track the natural progression of AD and to obtain neuropathological confirmation of the clinical diagnosis. The CERAD data base has become a major resource for research in Alzheimer’s disease. It contains longitudinal data for periods as long as seven years on the natural progression of the disorder as well as information on clinical and neuropsychological changes and neuropathological manifestations.
CERAD - Materials

1. Clinical/Neuropsychological Assessment for Alzheimer’s Disease - $65

The clinical forms request information from the subject (and, where appropriate, from a knowledgeable informant) regarding the patient’s clinical history, systemic disorders, cerebrovascular disease, parkinsonism, depression, the Blessed Dementia Rating Scale, Short Blessed Test, calculation, clock and language tests, physical examination, laboratory studies, the Clinical Dementia Rating scale and finally, a diagnostic impression of either AD alone, AD associated with other disorders or non-AD dementia.

The neuropsychological assessment includes measures of verbal fluency, confrontational naming (15-item Boston Naming Test), the Mini-Mental State examination, measures of verbal learning, recall and recognition, and constructional praxis performance and recall.

Spiral-Bound Flipbooks: For use with neuropsychological battery -$30 each
1A -Modified Boston Naming Test : 15 line drawings for identification
1B -Word List Memory, Recall and Recognition Test

2. CERAD Video Demonstration Tapes - $75 each
2A -Administration of the Neuropsychological Battery (J Forms and L Forms)
2B -Demonstration of Behavior Rating Scale for Dementia
2C -French Language Tape: Administration de la Batterie Neuropsychologique

3. CERAD Neuropathological Assessment for Alzheimer’s Disease - $85

This assessment is a highly respected instrument which is widely used in the U.S. and abroad for clinical studies of AD and other progressive dementias of the elderly. Its purpose is to establish more accurate and standardized neuropathological criteria for the diagnosis of AD. It is a practical protocol for post-mortem examination of the brain and provides measures for determining the neuropathological spectrum and heterogeneity of AD and other dementias. This assessment packet includes forms for collecting information on demographic data and gross and microscopic findings on cerebrovascular disease. It also includes an assessment of the neurohistological findings and final neuropathological diagnoses. It is accompanied by a detailed manual, the CERAD Guide to Neuropathological Assessment of AD and Other Dementias.

4. The Behavior Rating Scale for Dementia (BRSD) - $85

This assessment is a standardized instrument for rating behavioral abnormalities in demented or cognitively impaired individuals. Items are scaled according to their frequency of occurrence. The scale is informant-based and consists of 46 items which can be categorized into clinically relevant domains, i.e., depressive features, psychotic symptoms, behavioral dysregulation, irritability/agitation, vegetative features, aggression and affective lability. A shorter 17 item version is also available. The BRSD includes an additional packet containing a comprehensive instruction manual including results of factor analysis, scoring forms, scoring tables, instructions to informant and response cards.

5. Assessment of Service Needs of Patients with Dementia - $25
A questionnaire is available for administration to caregivers of subjects with AD. It assesses the need for and extent of use of the most common services required for care of persons with dementia. The questionnaire includes questions on the caregiver’s current situation, day and over-night care for the patient outside the home and care of the patient at home.

6. Autopsy Resource Packet - $20
This is a set of guidelines, sample correspondence, and forms available for medical centers interested in obtaining brain autopsies. It includes educational pamphlets designed to encourage autopsy examination.

7. CD-ROM: The CERAD Database and Assessment Instruments - $600
The CERAD study population includes 1094 patients with a clinical diagnosis of AD and 463 control subjects who were enrolled at 24 university medical centers in the U.S. These patients and controls were evaluated annually between 1987 and 1996. The resulting longitudinal data include clinical findings and neuropsychological test scores, behavioral manifestations of dementia, time to death or admission to a nursing home and neuropathological findings. Standardized neuropathological confirmation of the clinical diagnosis was made at autopsy in approximately half of the decedents.

The CD-ROM contains:
- The complete CERAD dataset;
- CERAD assessment batteries: data-gathering forms and testing instructions;
- Condensed versions of the data forms with variable names;
- Selected ancillary and educational materials;
- A Manual of Operations giving the history of the CERAD study and information on the database.

- Shipping and handling cost of $15 will be added to all orders.
- Prices are current as of June, 2003 but are subject to change at any time.

Please contact CERAD for information regarding the availability of CERAD assessment instruments in additional languages, e.g., Bulgarian, Chinese, Dutch, Finnish, French, German, Italian, Japanese, Korean, Portuguese, Spanish.

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