

Translational Article

Special Issue on Extreme Longevity

Understanding Dementia Prevalence Among Centenarians

Leonard W. Poon,¹ John L. Woodard,² L. Stephen Miller,³ Robert Green,⁴ Marla Gearing,⁵ Adam Davey,⁶ Jonathan Arnold,⁷ Peter Martin,⁸ Ilene C. Siegler,⁹ Lusine Nahapetyan,¹ Young Sek Kim,¹⁰ and William Markesbery¹¹

¹Institute of Gerontology, University of Georgia, Athens.

²Department of Psychology, Wayne State University, Detroit, Michigan.

³Department of Psychology, University of Georgia, Athens.

⁴Partners Center for Personalized Genetic Medicine, Harvard University Medical School, Boston, Massachusetts.

⁵Department of Neurology, Emory University Medical School, Atlanta, Georgia.

⁶College of Health Professions, Temple University, Philadelphia, Pennsylvania.

⁷Department of Genetics, University of Georgia, Athens.

⁸Department of Human Development and Family Studies, Iowa State University, Ames.

⁹Department of Medical Psychology, Duke University Medical Center, Durham, North Carolina.

¹⁰Department of Adult Education, Dong-Eui University, Busan, South Korea.

¹¹Sanders Brown Gerontology Center, University of Kentucky, Lexington.

Address correspondence to Leonard W. Poon, PhD, Institute of Gerontology, University of Georgia, 255 East Hancock Avenue, Athens, GA 30602.
Email: lpoon@uga.edu

The goals of this article are to (a) establish the concurrent and clinical validity of the Global Deterioration scale in assessing cognitive functions and stages of dementia among centenarians, (b) identify the prevalence of all-cause dementia in representative samples of centenarians, and (c) demonstrate how variations in sample demographic characteristics could significantly affect estimates of dementia prevalence. A quarter of the 244 centenarians in a population-based sample had no objective evidence of memory deficits. Another quarter showed signs of transient confusion, and about half showed classical behavioral signs of dementia with about 15% in each of Global Deterioration scale stages 4–6 and about 5% in the most severe stage 7. Variations in age, gender, race, residence status, and education of the study sample as well as criteria used for dementia rating were found to affect prevalence.

Key Words: Dementia prevalence—Centenarians—Validation.

Received June 24, 2011; Accepted December 16, 2011

Decision Editor: Rafael de Cabo, PhD

THERE is a wide range of dementia prevalence among centenarians reported in the literature. In a review of 23 studies reporting dementia prevalence among centenarians, one study found 100% prevalence, but others reported a range between 27% and 75%, with a mean of about 60% (1–13). Two likely contributing factors for the large range of reported prevalence are (a) instruments that are not validated with centenarians might have been employed that could produce haphazard results and (b) studies might have employed convenience or nonrepresentative samples that could bias the results. These two hypotheses of contributing factors could account for large variations in the reported prevalence. Finally, the large variations could also be due to true differences across populations and cultures.

The goal of this article is to resolve the disparity among centenarian studies in reported dementia prevalence and to

understand factors that contributed to the disparity. Two studies are reported. Study 1 is designed to establish the concurrent and clinical validity of the Global Deterioration scale (GDS) used to assess clinical symptomatology in normal aging and Alzheimer's disease (AD) for centenarians. Study 2 then employs the validated instrument to assess all-cause dementia prevalence in a population-based sample of centenarians and explore how variations in sampling characteristics could differentially bias prevalence.

STUDY 1: VALIDITY OF GDS AMONG THE CENTENARIANS

In the description of cognitive decline associated with AD, Reisberg and colleagues published a series of articles in the 1980's that described the progressive nature of the clinical course and presentations of AD in its early, middle,

and late stages (14). Stages of the progressing illness were defined by their clinical characteristics in terms of observable everyday behaviors (15). Empirical evidence was presented on significant associations between the state and rate of progressive decline with independent behaviors, neuroradiologic, neurometabolic, and neuroimmunologic assessments in normal aging and progressive primary degenerative dementias (15–20). Hence, the development of an ordinal scale based on clinical observations by trained clinicians that ranks clinical characteristics in terms of observable everyday behaviors with levels of cognitive decline and levels of progression of AD was shown to have practical, clinical, patient management applications (21). The scale has particular advantage when employed with the centenarian population as cognitive performance tests are taxing and time consuming for that population.

Reisberg's GDS validation work did not include centenarians who are more frail and variable in terms of health and cognition. Study 1 addresses whether the GDS has similar diagnostic utility among centenarians (10). The study focused on four research questions on the concurrent and clinical validity of the GDS: (a) Is the ordinal ranking of the GDS staging similar to those found in other global measures of cognition such as the Mini-Mental State Examination (MMSE; 22) and the Clinical Dementia Rating (CDR) scale (23,24)? (b) Does the distribution of the GDS scores substantiate clinicians' and neuropathologists' independent dementia assessment? (c) Could the GDS ordinal ranking of dementia severity positively relate to or predict accepted standards of dementia in levels and variations in neuropsychological tests such as executive function, verbal fluency, abstract reasoning, memory, basic, and instrumental functioning? Finally, (d) are there consistencies between GDS ratings and neuropathological findings such as density of neurofibrillary tangles and cerebral atrophy? Answers to the earlier questions would provide information on the usability of GDS in terms of concurrent and clinical validity with centenarians.

Methods

Subject recruitment.—Study participants were associated with Phase III of the Georgia Centenarian Study, a population-based multidisciplinary study examining the genetics, neuropathology, functional capacities, adaptations, and resources of centenarians. Based on census information from 44 counties in Northern Georgia, the study included a population-based sample of 244 centenarians and near centenarians (age 98–108 years) recruited from the community, personal care homes, and nursing homes (NHs) in 44 counties in Northern Georgia. At the time of recruitment, census estimated about 1,200 centenarians resided in the 44 counties. The University of Georgia Institutional Review Board approved the methodology, and all participants provided their informed consent to participate. A detailed description of the recruitment, instruments, and testing methodologies can be found in Poon and colleagues (25).

Mean age of the sample was 100.6 ± 2.04 years with range from 98.1 to 108.6 years. The majority of the sample was women (84.8%) and Caucasian (78.7%). Overall, 43% resided in NHs, 19.7% in personal care homes, and 37.3% resided in a private home/apartment. Mean years of education for the sample was 10.6 ± 3.8 years (range from 0 to 17 years, $n = 237$).

A subset of centenarian participants ($N = 51$) was enrolled in a Neuropathology Study and consented to postmortem brain donation. These subjects have agreed to longitudinal follow-up evaluation and were re-examined every 6 months in their homes with monthly phone checks to the family. Mean age of the participants in the brain donation sample was 100.8 ± 2.1 years (range from 98.1 to 105.9 years). This sample is also predominantly Caucasian (88.2%) and women (90.2%). Fifteen of the participants (29.4%) lived independently in private home/apartment, 24 lived in NH (47%), and 12 lived in personal care home (23.5%). Mean years of education were 10.4 ± 3.9 years (range from 0 to 17 years).

Measures.—Because the GDS (15) is the primary instrument of inquiry, a full description is provided. The GDS is a behavioral rating scale that is based on the premise that three major clinical phases of dementia are identifiable: forgetfulness, confusion, and dementia. These phases are further refined into seven clinically identifiable and ratable stages.

GDS stage 1 is identified as normal and shows no cognitive decline. In stage 2, there are subjective complaints of memory deficit, such as forgetting formerly well-known names and where one has placed familiar objects. There is no objective evidence of memory deficit on clinical interview and in employment/social situations. Stage 3, known as mild cognitive impairment, represents an intermediate stage between the cognitive changes of aging and fully developed symptoms of dementia. Mild cognitive impairment is not easily diagnosed and is frequently confused between age-associated normal memory decline and beginning dementia. Deficits in stage 3 manifest in more than one area: for example, getting lost when traveling to unfamiliar locations, work and name finding deficit becomes apparent to intimates/co-workers, decreased ability in remembering names of new people, concentration deficit on clinical testing, patients may read and remember relatively little material, and decreased performance in demanding employment/social settings. Objective evidence of memory deficit is obtained only with an intensive interview. The subtlety of the clinical symptoms may be increased by the denial that often begins to become manifested in these patients. Mild-to-moderate anxiety accompanies symptoms. GDS stage 4 is the earliest stage of dementia (26). On clinical interview, clear-cut deficits manifest in the following areas: decreased knowledge of current and recent events, memory of personal history, and decreased ability to travel, handle finances, and perform complex tasks. Generally, there is no deficit in time/person orientation, recognition of familiar persons and faces, or ability to travel to familiar locations. Denial is a

dominant defense mechanism. In stage 5, patients can no longer survive without some assistance. There is some disorientation to time (date, season, etc.) or place. During interviews, patients are unable to recall an address or telephone number of many years, the school from which they graduated, or the names of close family members (grandchildren). However, they know their own names and generally know their spouse's and children's names. Patients do not require assistance with toileting and eating. In stage 6, patients may occasionally forget their spouse's name, who they are entirely dependent upon for survival, but almost always recall their own name. Patients are unaware of recent events in their lives, surroundings, and time but can retain some sketchy knowledge of their past lives. Personality and emotional changes occur including: delusional behavior (may accuse their spouse of being an imposter, talk to imaginary figures, or their own reflection in the mirror); obsessive symptoms (repeat simple cleaning activities); anxiety, agitation, and violent behavior; and loss of willpower because an individual cannot carry a thought long enough to determine a purposeful course of action. Patients require some assistance with activities of daily living (ADLs). Stage 7 reflects a very severe cognitive decline: patients lose verbal abilities, basic psychomotor skills, and require assistance with all ADLs including toileting and feeding.

Procedure.—Participants were tested individually at their homes by a trained interviewer over four 2-hour sessions (25). The GDS was one of the last instruments employed after 8 hours of interaction over four sessions with the participant to provide the trained interviewer sufficient time to clinically judge the level of functioning associated with the scale. No informant was involved in the derivation of this measure.

The study research questions focused on centenarians and whether and how GDS relate to (a) *other global tests of cognitive status* such as the MMSE (22) and the CDR (23), (b) *neuropsychological tests* such as executive function (*Behavioral Dyscontrol scale*) (27), verbal fluency (*Controlled Oral Word Association Test*; 28), abstract reasoning (*Wechsler Adult Intelligence Scale—III Similarities*; 29), memory (*Fuld Object–Memory Evaluation*; 30), (c) *functional abilities* such as ADLs (31), instrumental activities of daily living (32), *Direct Assessment of Functional Status* (33), *Physical Performance and Motility Examination* (34), (d) *neuropathological findings* such as density of neurofibrillary tangles and plaques and cerebral atrophy, and (e) *concordance with clinical and neuropathological assessments*. Detailed descriptions of these instruments can be found in Poon and colleagues (25) and will not be provided here. Hence, our analysis strategy was to evaluate the concordance through correlations among the ordinal ranking of GDS with the performances of the tests noted previously.

A subset of 51 centenarians consented for the neuropathology study. Longitudinal data collection was initiated 6 months after the main data collection and every 6 months after

with three frequently used global dementia scales: the CDR (23), Consortium to Establish a Registry for Alzheimer's Disease (35), and MMSE, along with a brief neurological examination until the participants' deaths. The goal was to gather as much global cognitive status data as possible. After death, fresh brain weight was determined and 1 cm sections were removed from the left frontal, temporal, and occipital poles and rapidly frozen on metal plates. Then the brains underwent MRI scanning for data associated with white matter volume, gray matter volume, lateral ventricular volume, volume of specific lobes, and volume of infarcts. Following MRI, neuropathological assessment of the fixed brain was independently conducted by a neuropathologist (W.M.), who was unaware of all clinical and neuropsychological data. First, cortical atrophy was assessed macroscopically. Following macroscopic assessment, densities of postmortem diffuse plaques, neuritic plaques, and neurofibrillary tangles as well as Lewy bodies and vascular changes (atherosclerosis and arteriosclerosis, previous infarcts and hemorrhages) were measured in the cerebral cortex, hippocampus, amygdala, and entorhinal cortex. Extant neuropathological diagnostic criteria that were frequently used for the diagnosis of AD were employed, and they were Khachaturian (36), Consortium to Establish a Registry for Alzheimer's Disease (37), Braak (38), and National Institute on Aging–Reagan Institute criteria (39). Consensus conferences were held among neurologists, neuropsychologists, and neuropathologists on diagnosis based on respective clinical and neuropathology data sets.

Results

Missing data.—In the initial sample, the GDS scores were missing for four centenarians (1.6%, $n = 244$). In the subset of centenarians with neuropathology data ($n = 51$), the GDS score for one female centenarian (1.9%), and the CDR scores for 17 centenarians (33.3%) were missing, mostly because the participants died before they were tested for CDR ($n = 15$). Participants with missing data were not included in the analyses.

The distributions of global, neuropsychological, and functional measures by the stages of dementia severity are displayed in Table 1. Correlations of these tests with GDS are displayed in Table 2.

Concordance with global measures.—Table 2 shows the bivariate (Spearman's) correlations between the GDS and the other concomitant measures. The left panel shows correlations for the entire sample ($N = 240$), and the right panel shows correlations for the subset of participants ($N = 50$) who participated in the neuropathology study. It is noted that the two sets of correlations show parallel and robust patterns of results. The GDS exhibits a high and significant association with MMSE ($r = -.9, p < .001$) and CDR ($r = .8, p < .01$), two instruments commonly used in global dementia assessment. Although GDS and CDR are similar instruments reflecting clinicians' judgment of dementia severity,

Table 1. Distribution of Mean and SD of Neuropsychological and Functional Measures by GDS Levels

| GDS Levels | MMSE (<i>M</i> ± <i>SD</i>) | WAIS (<i>M</i> ± <i>SD</i>) | DAFS (<i>M</i> ± <i>SD</i>) | COWAT (<i>M</i> ± <i>SD</i>) | BDS (<i>M</i> ± <i>SD</i>) | ADLs (<i>M</i> ± <i>SD</i>) | IADLs (<i>M</i> ± <i>SD</i>) |
|----------------|-------------------------------|-------------------------------|-------------------------------|--------------------------------|------------------------------|-------------------------------|--------------------------------|
| 1 | 27.9 ± 1.4 | 16.1 ± 7.4 | 73.9 ± 5.3 | 9.4 ± 2.9 | 17.2 ± 2.1 | 13.4 ± 1.9 | 12.1 ± 2.1 |
| 2 | 24.9 ± 3.5 | 12.9 ± 8.9 | 64.1 ± 15.1 | 6.9 ± 3.2 | 14.8 ± 3.3 | 12.5 ± 2.3 | 9.4 ± 3.2 |
| 3 | 20.8 ± 4.9 | 9.2 ± 7.8 | 54.3 ± 17.5 | 4.9 ± 3.1 | 12.0 ± 3.8 | 11.9 ± 3.0 | 9.3 ± 3.3 |
| 4 | 18.3 ± 5.1 | 7.5 ± 8.5 | 47.1 ± 13.9 | 4.5 ± 3.2 | 8.0 ± 5.5 | 11.3 ± 2.2 | 8.8 ± 2.9 |
| 5 | 14.2 ± 4.1 | 5.5 ± 5.2 | 37.5 ± 16.8 | 2.9 ± 2.3 | 5.4 ± 4.4 | 11.1 ± 3.1 | 8.8 ± 3.7 |
| 6 | 6.4 ± 5.1 | 0.7 ± 1.8 | 14.9 ± 14.1 | 0.7 ± 1.2 | 1.1 ± 1.8 | 8.9 ± 5.3 | 6.9 ± 5.3 |
| 7 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| Total <i>N</i> | 240 | 237 | 231 | 233 | 232 | 221 | 221 |

Notes: ADLs = activities of daily living; BDS = Behavioral Dyscontrol scale; COWAT = Controlled Oral Word Association Test; DAFS = Direct Assessment of Functional Status scale; GDS = Global Deterioration scale; IADLs = instrumental activities of daily living; MMSE = Mini-Mental State Examination; WAIS = Wechsler Adult Intelligence Scale.

MMSE is a performance-based instrument that is also highly associated with the GDS.

Concordance with neuropsychological tests.—Table 2 also shows that GDS correlated significantly with central

executive functioning (Behavioral Dyscontrol scale, $r = -.8$, $p < .001$), word fluency (*Controlled Oral Word Association Test*, $r = -.7$, $p < .001$), memory (Fuld Object–Memory Evaluation, $r = -.7$, $p < .001$), and abstract reasoning (Wechsler Adult Intelligence Scale similarity, $r = -.6$, $p < .001$).

Table 2. Bivariate Correlations (Spearman’s Correlation) Between the GDS and Neuropsychological, Functional, Neuropathological, and Global Measures of Cognition with Total Sample ($N = 240$, left panel) and Subset of Participants in Neuropathological Study ($N = 50$)

| Measures | GDS | | GDS | |
|-----------------------------|--------------|------------------|--------------|------------------|
| | Correlations | Total <i>N</i> * | Correlations | Total <i>N</i> † |
| Global measures | | | | |
| MMSE | –0.9*** | 240 | –0.9*** | 50 |
| CDR | | | 0.8*** | 33 |
| Neuropsychological measures | | | | |
| COWAT | –0.7*** | 233 | –0.7*** | 50 |
| BDS summary score | –0.8*** | 232 | –0.8*** | 50 |
| FOME delayed recall | –0.7** | 232 | –0.8*** | 49 |
| FOME delayed recognition | –0.3** | 232 | –0.3* | 49 |
| FOME retention estimate | –0.7*** | 232 | –0.8*** | 49 |
| WAIS similarities subscale | –0.6*** | 237 | –0.7*** | 50 |
| Functional measures | | | | |
| ADLs | –0.4*** | 221 | –0.3 | 44 |
| ADLs, proxy report | –0.6*** | 215 | –0.7*** | 44 |
| IADLs | –0.3*** | 221 | –0.4* | 44 |
| IADLs, proxy report | –0.7*** | 238 | –0.8*** | 49 |
| DAFS | –0.8*** | 231 | –0.8*** | 50 |
| PPME | –0.5*** | 240 | –0.6*** | 49 |
| Neuropathology measures | | | | |
| Fresh brain weight | | | –0.4** | 50 |
| Cerebral atrophy | | | 0.5*** | 50 |
| Braak | | | 0.5** | 46 |
| CERAD | | | 0.3 | 50 |
| NIA–Reagan | | | 0.5*** | 43 |

Notes: ADL = activities of daily living; BDS = Behavioral Dyscontrol scale; Braak = Braak neuropathological staging of Alzheimer-related changes; CDR = Clinical Dementia Rating scale; CERAD = consortium to establish registry for Alzheimer’s disease; COWAT = Controlled Oral Word Association test; DAFS = Direct Assessment of Functional Status scale; FOME = Fuld Object–Memory Evaluation; GDS = Global Deterioration scale; IADL = instrumental activities of daily living; MMSE = Mini-Mental State Examination; NIA–Reagan = National Institute on Aging–Reagan institute criteria for neuropathological diagnosis of Alzheimer’s disease; PPME = physical performance and motility examination; WAIS = Wechsler Adult Intelligence Scale.

* *N* ranged between 221 and 240 due to missing data.

† *N* ranged between 33 and 50 due to missing data.

* $p < .05$, ** $p < .01$, *** $p < .001$.

Concordance with basic and instrumental functions and mobility.—GDS was able to predict in a statistically significant manner ADL ($r = -.4$, $p < .001$) and instrumental activities of daily living ($r = -.3$, $p < .001$), as well as mobility performances (Physical Performance and Motility Examination, $r = -.5$, $p < .001$). It is also noted that the mean performances of the Direct Assessment of Functional Status, a direct observational measure of ADL and instrumental activities of daily living, in each of the seven stages of the GDS are statistically different and distinct.

Concordance with neuropathological findings.—Variations of the GDS was significantly correlated with variations in neuropathologic findings in the Braak score ($r = -.5$, $p < .01$), cerebral atrophy ($r = .5$, $p < .001$), brain weight ($r = -.4$, $p < .01$), and National Institute on Aging–Reagan Institute criteria for dementia ($r = .5$, $p < .01$).

Concordance with clinical and neuropathological assessments.—Among the 51 participants who participated in the neuropathology study, it is interesting to note that clinical and neuropathological assessments are not in perfect agreement as found by a number of studies (40–42). In nine cases, the subjects were found demented clinically; however, no neuropathological evidence of dementia was found. In two cases, subjects were judged to be cognitively intact; however, the subjects met criteria for dementia neuropathologically. It may be possible that some centenarians have more premorbid cognitive reserves or that neuropathology may have different clinical significance among centenarians. These are important research issues for the next phases of centenarian research. It is important to note that clinical and neuropathological agreement was found in 39 of the 51 cases. Table 3 shows the concordance between GDS and the consensus diagnoses among the 39 cases.

Table 3. Concordance of GDS Ratings With the Consensus (clinical/neuropathological) Diagnoses

| Consensus Diagnoses | GDS = 4–7 (Yes Dementia) | GDS = 3 (Maybe Dementia) | GDS = 1–2 (No Dementia) | Total |
|---------------------|-----------------------------|-----------------------------|----------------------------|-------|
| Yes dementia | 18* | 6 | 2 | 26 |
| Maybe/MCI | 1 | 2* | 1 | 4 |
| No Dementia | 1 | 1 | 7* | 9 |
| Total | 20 | 9 | 10 | 39 |

Notes: MCI = mild cognitive impairment. Fisher's Exact Test of association, $p = .0003$.

* Concordant cells.

There is a perfect concordance between the GDS ratings and consensus diagnoses in 27 of 39 cases (69.2%), and Fisher's Exact Test shows this concordance is statistically significant, $p = .0003$.

Discussion

The primary question posed in Study 1 focused on whether the GDS has sufficient concurrent and clinical validity for its use with centenarians. The results showed favorable outcomes. One, GDS is highly correlated with the MMSE and CDR, two commonly used and validated instruments in the assessment of cognition and dementia. Two, GDS has significant concordance with neuropsychological tests of cognitive functions that are related to AD as well as assessment of basic and instrumental functioning. Three, the GDS scores are indicative of changes in neuropathological indices in AD such as the Braak score, cerebral atrophy, brain weight, and National Institute on Aging–Reagan Institute criteria for dementia. Finally, GDS ratings are in concordance in 27 of 39 cases in terms of independent, clinical, and neuropathological consensus ratings of dementia.

The GDS was derived from clinical observations over the time course of patients with primary degenerating disease of the Alzheimer's type (43). As the onset of AD is insidious, family members could detect gradual decline of cognitive function over time. The GDS denotes the seven stages of decline from normal to early incipient to mild, moderate, moderately severe, and severe stages. The results from Study 1 showed the scale can be appropriately employed with centenarians and contains concurrent and clinical validity in its application.

STUDY 2: POPULATION-BASED STUDY OF DEMENTIA PREVALENCE

The goals of Study 2 are to employ the GDS with centenarians to (a) identify the prevalence of all-cause dementia in a representative sample of centenarians, (b) differentiate the distribution of behavioral staging of forgetfulness, confusion, and dementia in this population-based sample, and (c) demonstrate how variations in sampling characteristics could differentially bias the observed prevalence. Participant recruitment, methods, and procedures are described in Study 1.

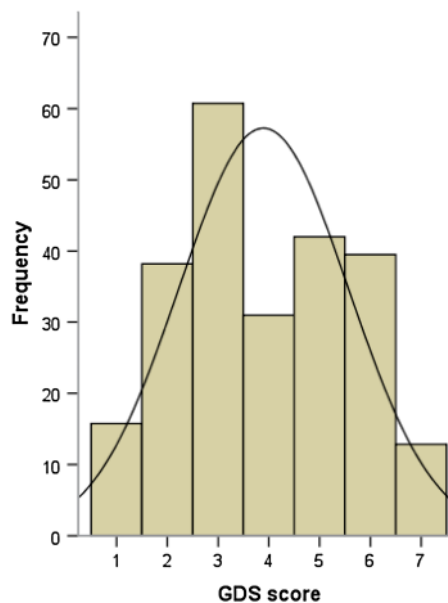


Figure 1. The frequency distribution of dementia severity for centenarians (mean = 3.9, $SD = 1.7$).

Results

Missing data.—The GDS scores for four female centenarians were missing (1.6%). We did not report the results on this category because of the small numbers. Analyses were conducted on both weighted (adjusted to population values) and unweighted (unadjusted) means. Results were generally identical. The weighted values are reported here.

Patterns of dementia prevalence.—Figure 1 shows the pattern of frequency distribution of GDS severity. The distribution of GDS among centenarians is evenly distributed in the middle ranges, with a median of 4 and a mean of 3.9 ($SD = 1.7$); 6.6% of centenarians had a GDS stage 1 and 15.9% had stage 2; 25.3%, 12.9%, 17.5%, 16.5%, and 5.4% of centenarians had stages 3–7, respectively.

Impact of gender, race, living arrangements, and education on dementia prevalence.—Table 4 shows the proportion of centenarians without dementia, with mild cognitive impairment, or with dementia, by gender, race, living arrangements, and educational attainment. African American centenarians ($\chi^2(2) = 11.1, p = .004$) and NH residents had a significantly higher frequency of dementia, compared with Caucasians and community or personal care home residents ($\chi^2(2) = 24.8, p < .001$). Based on the t test, female centenarians had a slightly higher dementia severity (mean GDS = 4) compared with males (mean GDS = 3.5; $t(237) = -2.3, df = 237, p < .05$). When female and male centenarians were divided into three categories of severity, the gender difference was only marginally different ($\chi^2(2) = 4.1, p = .13$). Higher educational attainment was associated with lower likelihood of dementia ($\chi^2(4) = 20.4, p < .001$).

Table 4. Dementia Distribution of Centenarians by Gender, Race, Living Status, and Education

| | Centenarians (N = 240) | | | Total N | p Value |
|------------------|-------------------------|---------------|----------------------|---------|---------|
| | No Dementia (GDS = 1–2) | MCI (GDS = 3) | Dementia (GDS = 4–7) | | |
| Gender, n (%) | | | | | |
| Male | 9 (20.9) | 16 (37.2) | 18 (41.9) | 43 | .13 |
| Female | 45 (22.7) | 45 (22.7) | 108 (54.5) | 198 | |
| Race, n (%) | | | | | |
| White | 45 (26.8) | 47 (28.0) | 76 (45.2) | 168 | <.004 |
| African American | 9 (12.5) | 14 (19.4) | 49 (68.1) | 72 | |
| NH | 6 (8.8) | 11 (16.2) | 51 (75.0) | 68 | <.001 |
| PCH | 13 (41.9) | 7 (22.6) | 11 (35.5) | 31 | |
| PH/A | 36 (25.2) | 43 (30.1) | 64 (44.8) | 143 | |
| Education, n (%) | | | | | |
| Less than HS | 11 (13.1) | 13 (15.5) | 60 (71.4) | 84 | <.001 |
| Some HS | 7 (26.0) | 11 (40.7) | 9 (33.3) | 27 | |
| HS graduate | 36 (28.8) | 37 (29.6) | 52 (41.6) | 125 | |

Notes: GDS = Global Deterioration scale; HS = high school; MCI = mild cognitive impairment; NH = nursing home; PCH = personal care home; PH/A = private home/apartment.

Discussion

The first two goals of Study 2 were to examine the prevalence and distribution of dementia in a representative sample of centenarians with an average age of about 100 years in Northern Georgia. In this representative sample, we found that about a quarter of the centenarians (22.5%) have no cognitive impairment or objective evidence of memory deficits on clinical interview and in employment or social situations (stages 1 and 2). Among these individuals, about 16% exhibited some form of mild forgetfulness. About a quarter of the centenarians (25.3%) were identified as having difficulty in remembering names, getting lost in familiar settings, difficulty in learning new information, and problems in concentration in work or social situations (stage 3). As noted earlier, stage 3 is commonly known as the mild cognitive impairment stage in which an individual exhibits some form of transient confusion. About half of the centenarians (52.3%) were identified having some form of dementia ranging from exhibiting clear-cut deficits in recent and familial information, traveling, finances, time/person disorientation (stage 4 or early dementia) to needing assistance for some ADLs and to delusional behaviors and severe cognitive dysfunction requiring assistance to all ADLs (stages 5–7 or moderate to severe stages).

It has been reported that investigators have used different criteria in judging dementia prevalence (7). This can be demonstrated using the distribution of severity from this study. If one uses a criterion of adequacy of everyday functioning (GDS stages 1–3), then the prevalence is 52.2%. However, if one uses a strict criterion of any sign of mild confusion to severe dementia (GDS stages 3–7), then the prevalence is 77.5%. The range of prevalence is similar to the 42% to 75% reported by many studies. Hence, it is important to clearly state the criteria used to judge the presence of dementia in reporting prevalence. Variation in the decision criteria may be sufficient to produce the large variability in reported prevalence (44).

The second goal of the study was to examine how sampling characteristics could affect the prevalence of dementia. Race, residence status, and education were found to significantly affect prevalence while gender contributed a marginal effect. African American centenarians had a higher frequency of dementia compared with Caucasians. The results replicated findings reported with older adults who are not centenarians. Although the reasons for race differences in dementia prevalence are not clear, it has been hypothesized that there are potential associations with differences in genetic background, known disease risk factors such as hypertension, diabetes mellitus, stroke, education levels, socioeconomic status, and cultural differences in the perceptions of dementia (45).

As expected, education also affected dementia prevalence. Our results replicated the robust findings that among older adults education is negatively related to dementia prevalence. Further, centenarians in NHs were more demented than those living in the community. Although this finding seems to be logical and expected, convenience samples of centenarians living in the community would underestimate dementia prevalence in the population, but the opposite is true with the oversampling of centenarians living in institutions.

Gender differences seemed to exert a marginal effect. Severity of dementia was found to be slightly higher for women compared with men; however, this difference disappeared when we examined gender differences across the three levels of severity. Our findings may explain why some investigators found gender differences, but others did not.

The study of centenarians has progressed from simple descriptive studies to multi- and interdisciplinary population-based studies to systematically unravel the secrets of longevity (46). The question still persists on the rate of change of cognition among centenarians and whether centenarians are statistical outliers or expert survivors who could test the applicability of our current aging theories and

models. As centenarians at the end of life tended to be frail and have limited ability to stand up to the vigor of biomedical and psychosocial studies, they are also well protected by their families and communities. Hence, it stands to reason that early researchers tended to employ convenience samples to get as much information as possible even if the methodologies were flawed for generalizations.

WHAT HAVE WE LEARNED?

What have we learned from these two studies that could assist future investigators in the study of cognition and dementia among centenarians? First, we established that the GDS has concurrent and clinical validity for the assessment of dementia for centenarians. Second, the criteria used in the determination of dementia are critical to the resultant dementia prevalence. If one uses a criterion of adequacy of everyday functioning (GDS stages 1–3), then the prevalence is 52.2%. However, if one uses a strict criterion of any sign of mild confusion to severe dementia (GDS stages 3–7), then the prevalence is 77.5%. Finally, we have shown the variation in demographic characteristics of the sample could definitely influence the observed prevalence of dementia among centenarians. Hence, convenient samples may over- or underestimate prevalence, and this may explain the large disparity of dementia prevalence reported in the literature. Many of the first generations of centenarian studies are descriptive studies of convenient samples from which caution must be exercised in the generalization of reported dementia prevalence (46).

On the other hand, population-based studies have limitations as well. A common example is the limited number of men and minorities in a representative sample that could reduce statistical reliability in examining gender and race differences. Two practices are commonly employed to address the situation, although these practices have cost-effectiveness trade-offs. The first is to oversample the variable that is underrepresented. Given the difficulty in recruitment of protected centenarians, significantly more resources are needed to execute this practice. The second is to ensure that the obtained data are representative of the population by applying a weight correction to adjust differences between census and sample characteristics. This method was employed in Study 2. Greater confidence in the result could be achieved even though the numbers of men and minorities are small in the sample.

FUNDING

Phase 3 of the Georgia Centenarian Study is funded by the National Institute on Aging (P01AG17553, 2001–2009, L.W.P., PI).

ACKNOWLEDGMENTS

The authors acknowledge the original design effort from S.M. Jazwinski, M.A. Johnson, W.L. Rodgers, D.B. Hausman, I.S. Siegler, L. Burrell, and Z. Burrell; data collection effort from Molly Burgess, Kim Grier, Elizabeth Jackson, Erick McCarthy, Kathy Shaw, Lisha Strong, and Sandra

Reynolds; data management from Shayne Anderson; and manuscript preparation from M. Cristina Isales.

REFERENCES

- Blansjaar BA, Thomassen R, Van Schaick HW. Prevalence of dementia in centenarians. *Int J Geriatr Psychiatry*. 2000;15(3):219–225.
- Andersen-Ranberg K, Vasegaard L, Jeune B. Dementia is not inevitable: a population-based study of Danish centenarians. *J Gerontol B Psychol Sci Soc Sci*. 2001;56(3):P152–P159.
- Ravaglia G, Forti P, De Ronchi D, et al. Prevalence and severity of dementia among northern Italian centenarians. *Neurology*. 1999; 53(2):416–418.
- Engberg H, Christensen K, Andersen-Ranberg K, Jeune B. Cohort changes in cognitive function among Danish centenarians. A comparative study of 2 birth cohorts born in 1895 and 1905. *Dement Geriatr Cogn Disord*. 2008;26(2):153–160.
- Thomassen R, van Schaick HW, Blansjaar BA. Prevalence of dementia over age 100. *Neurology*. 1998;50(1):283–286.
- Corrada MM, Brookmeyer R, Berlau D, Paganini-Hill A, Kawas CH. Prevalence of dementia after age 90: results from the 90+ study. *Neurology*. 2008;71(5):337–343.
- Gondo Y, Poon LW. Cognitive function of centenarians and its influence on longevity. In: Poon LW, Perls T, eds. *Biopsychosocial Approaches to Longevity: Annual Review of Gerontology and Geriatrics*. Vol. 27. New York: Springer; 2007:129–149.
- von Strauss E, Viitanen M, De Ronchi D, Winblad B, Fratiglioni L. Aging and the occurrence of dementia: findings from a population-based cohort with a large sample of nonagenarians. *Arch Neurol*. 1999;56(5):587–592.
- Samuelsson SM, Alfredson BB, Hagberg B, et al. The Swedish Centenarian Study: a multidisciplinary study of five consecutive cohorts at the age of 100. *Int J Aging Hum Dev*. 1997;45(3):223–253.
- Hagberg B, Bauer Alfredson B, Poon LW, Homma A. Cognitive functioning in centenarians: a coordinated analysis of results from three countries. *J Gerontol B Psychol Sci Soc Sci*. 2001;56(3):P141–P151.
- Gondo Y, Hirose N, Arai Y, et al. Functional status of centenarians in Tokyo, Japan: developing better phenotypes of exceptional longevity. *J Gerontol A Biol Sci Med Sci*. 2006;61(3):305–310.
- Silver MH, Jilinskaia E, Perls TT. Cognitive functional status of age-confirmed centenarians in a population-based study. *J Gerontol B Psychol Sci Soc Sci*. 2001;56(3):P134–P140.
- Ott A, Breteler MM, van Harskamp F, et al. Prevalence of Alzheimer's disease and vascular dementia: association with education. The Rotterdam study. *BMJ*. 1995;310(6985):970–973.
- Reisberg B. *Brain Failure: An Introduction to Current Concepts of Senility*. New York: Free Press/Macmillan; 1981.
- Reisberg B, Ferris SH, de Leon MJ, Crook T. The Global Deterioration Scale for assessment of primary degenerative dementia. *Am J Psychiatry*. 1982;139(9):1136–1139.
- Johansson B, Zarit SH. Dementia and cognitive impairment in the oldest old: a comparison of two rating methods. *Int Psychogeriatr*. 1991;3(1):29–38.
- Paul RH, Cohen RA, Moser DJ, et al. The Global Deterioration Scale: relationships to neuropsychological performance and activities of daily living in patients with vascular dementia. *J Geriatr Psychiatry Neurol*. 2002;15(1):50–54.
- de Leon MJ, Ferris SH, George AE, et al. Computed tomography and positron emission transaxial tomography evaluations of normal aging and Alzheimer's disease. *J Cereb Blood Flow Metab*. 1983;3(3):391–394.
- Ferris SH, de Leon MJ, Wolf AP, et al. Positron emission tomography in the study of aging and senile dementia. *Neurobiol Aging*. 1980; 1(2):127–131.
- Nandy K, Reisberg B, Ferris SH, de Leon MJ. Brain reactive antibodies and progressive cognitive decline in the aged. *J Am Aging Assoc*. 1981;4:145.

21. Mace NL, Rabins PV. *The 36-Hour Day*. Baltimore, MD: Johns Hopkins University Press; 1981.
22. Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State." A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189–198.
23. Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. A new clinical scale for the staging of dementia. *Br J Psychiatry*. 1982;140:566–572.
24. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology*. 1993;43(11):2412–2414.
25. Poon LW, Jazwinski M, Green R, et al. Methodological considerations in studying centenarians: lessons learned from the Georgia Centenarian Studies. In: Poon LW, Perls T, eds. *Biopsychosocial Approaches to Longevity: Annual Review of Gerontology and Geriatrics*. Vol. 27. New York: Springer; 2007:231–264.
26. Reisberg B, Ferris SH, Kluger A, Franssen E, Wegiel J, de Leon MJ. Mild cognitive impairment (MCI): a historical perspective. *Int Psychogeriatr*. 2008;20(1):18–31.
27. Grigsby J, Kaye K, Robbins LJ. Reliabilities, norms and factor structure of the Behavioral Dyscontrol Scale. *Percept Mot Skills*. 1992;74(3 Pt 1):883–892.
28. Benton AL, Hamsher K, Sivan AB. *Multilingual Aphasia Examination*. 3rd ed. Iowa City, IA: AJA Associates; 1994.
29. Wechsler D. *Wechsler Adult Intelligence Scale-III (WAIS-III)*. San Antonio, TX: The Psychological Corporation; 1997.
30. Fuld PA. *The Fuld Object-Memory Evaluation*. Chicago, IL: Stoelting Instrument Company; 1981.
31. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. *JAMA*. 1963;185:914–919.
32. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist*. 1969;9(3):179–186.
33. Loewenstein DA, Amigo E, Duara R, et al. A new scale for the assessment of functional status in Alzheimer's disease and related disorders. *J Gerontol*. 1989;44(4):P114–P121.
34. Winograd CH, Lemsky CM, Nevitt MC, et al. Development of a physical performance and mobility examination. *J Am Geriatr Soc*. 1994;42(7):743–749.
35. Morris JC, Heyman A, Mohs RC, et al. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part I. Clinical and neuropsychological assessment of Alzheimer's disease. *Neurology*. 1989;39(9):1159–1165.
36. Khachaturian ZS. Diagnosis of Alzheimer's disease. *Arch Neurol*. 1985;42(11):1097–1105.
37. Mirra SS, Heyman A, McKeel D, et al. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part II. Standardization of the neuropathologic assessment of Alzheimer's disease. *Neurology*. 1991;41(4):479–486.
38. Braak H, Braak E. Neuropathological staging of Alzheimer-related changes. *Acta Neuropathol*. 1991;82(4):239–259.
39. Newell KL, Hyman BT, Growdon JH, Hedley-Whyte ET. Application of the National Institute on Aging (NIA)—Reagan Institute criteria for the neuropathological diagnosis of Alzheimer disease. *J Neuropathol Exp Neurol*. 1999;58(11):1147–1155.
40. Nelson PT, Braak H, Markesbery WR. Neuropathology and cognitive impairment in Alzheimer disease: a complex but coherent relationship. *J Neuropathol Exp Neurol*. 2009;68(1):1–14.
41. Geddes JW, Tekirian TL, Soutanian NS, Ashford JW, Davis DG, Markesbery WR. Comparison of neuropathologic criteria for the diagnosis of Alzheimer's disease. *Neurobiol Aging*. 1997;18(4 suppl):S99–S105.
42. Silver M, Newell K, Hyman B, Growdon J, Hedley-Whyte ET, Perls T. Unraveling the mystery of cognitive changes in old age: correlation of neuropsychological evaluation with neuropathological findings in the extreme old. *Int Psychogeriatr*. 1998;10(1):25–41.
43. Reisberg B, Ferris SH, Borenstein J, Sinaiko E, de Leon MJ, Buttinger C. Assessment of presenting symptoms. In: Poon LW, ed. *Clinical Memory Assessment of Older Adults*. Washington, DC: American Psychological Association; 1986:108–128.
44. Calvert JF, Hollander-Rodriguez J, Kaye J, Leahy M. Dementia-free survival among centenarians: an evidence-based review. *J Gerontol A Biol Sci Med Sci*. 2006;61(9):951–956.
45. Froehlich TE, Bogardus ST, Inouye SK. Dementia and race: are there differences between African Americans and Caucasians? *J Am Geriatr Soc*. 2001;49(4):477–484.
46. Poon LW, Perls T, eds. *Biopsychosocial Approaches to Longevity: Annual Review of Gerontology and Geriatrics*. New York: Springer; 2007:27.