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Methodological Considerations in Studying Centenarians: Lessons Learned From the Georgia Centenarian Studies[1]

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This chapter charts the development of the three phases of the Georgia Centenarian Study (Poon, 1992). The goal of this chapter is to share rationale, methodologies, design pitfalls, and strategies in studying centenarians. A fundamental challenge for all centenarian studies is to understand how centenarians live longer and to identify the specific biological, psychological, and sociological characteristics that make this possible (Lehr, 1991; Poon, Bramlett, Holtsberg, Johnson, & Martin, 1997; Vaillant & Mukamal, 2001). Studies of centenarians and the oldest old remain, in relative terms, a rarity within gerontological research (Vaupel et al., 1998), although interest in this area has increased steadily over the past 20 years (Lehr, 1991; Poon et al., 1997; Vaupel et al., 1998). Studies conducted in the United States (e.g., Perls, 1997; Poon, 1992), Japan (e.g., Chan, Suzuki, & Yamamoto, 1997), South Korea (Wilcox, Wilcox, & Suzuki, 2001), Italy (e.g., Capurso et al., 1997), Hungary (e.g., Regius, Beregi, & Klinger, 1994), France (e.g., Regius et al., 1994), Sweden (e.g., Samuelsson et al., 1997), Finland, and Denmark (Jeune, 1994) have added greatly to our knowledge base and provide a foundation for further hypothesis testing and an increasingly realistic and detailed picture of what it is like to be 100.

THE GEORGIA CENTENARIAN STUDIES

The Georgia Centenarian Study began in 1988 (Poon, 1992). Phase 1 (1988–1992) was cross-sectional, examining unique adaptation characteristics of community-dwelling and cognitively intact centenarians, octogenarians, and sexagenarians in Georgia. Phase 2 (1992–1998) was a longitudinal follow-up of these three cohorts. Building on the lessons learned from these earlier studies, our current study, Phase 3 (2001–2007), which is in the final phase of completion, is comprehensive and population based. It was designed to (a) identify and isolate longevity genes, (b) describe the neuropathology of dementia, (c) assess neuropsychological and physical functioning, and (d) characterize the resources and adaptations of centenarians.

Phase 1: Cross-Sectional Findings

The decision made in our first attempt of studying centenarians was to define the best possible performances among the “expert survivors”-centenarians who were cognitively intact and community dwelling-and compare their performances with control groups with

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similar inclusion criteria in their 80s and 60s (Poon et al., 1992). The problem with this approach was that only a portion of centenarians in the general population was cognitively intact and community dwelling. Further, it is not known how representative were these centenarians in the general population. The advantage of this design was that the same inclusion criteria were employed for all three groups, and a primary difference among the groups was chronological age. This design was an improvement over previous designs when comparing centenarians with younger controls in that the prevalence of dementia was much larger among centenarians, which presented a significant confounding factor, especially when measuring cognitive and other cognitively related behaviors. The disadvantage of this design was that conclusions about the centenarians' performance could only be generalized to those who were cognitively intact and community dwelling. Another potential confounding factor in this cross-sectional design is that cohort effects in addition to chronological age could demonstrate significant effects. However, this confounding factor is inherent in cross-sectional designs. Since phase 1 involved the investigation of cognitive performances and a heavy reliance on self-report of personality, health, health history, medication, and dietary measures, the selection of cognitively intact participants was imperative and justifiable.

Participants in the first phase were community-dwelling and cognitively intact (38 men and 53 women sexagenarians, 31 men and 62 women octogenarians, and 35 men and 102 women centenarians, for a total of 321 study participants). Consistent with the findings from the Alameda County Study (Breslow & Breslow, 1993) and the Harvard College Alumni Study (Paffenbarger et al., 1994), which pointed out the benefits of healthy habits in improving life expectancy, the Georgia centenarians tended to practice health habits that were found to prolong life (Johnson, Houston, Fischer, Poon, & Martin, 1995; Nickols-Richardson, Johnson, Poon, & Martin, 1996a). Few smoked, were obese, or consumed excessive alcohol. Compared to cohorts in their 60s and 80s, centenarians tended not to have more illnesses, prescription medications, or visits to a physician and longer hospital stays during a 6-month observation period. Further, these centenarians tended to escape chronic diseases during their life time.

The intake of most nutrients was similar among 60-, 80-, and 100-year-old community-dwelling groups, with a few exceptions (Johnson et al., 1995; Nickols-Richardson et al., 1996a). Centenarians consumed breakfast more regularly and avoided weight loss diets and large fluctuations in body weight. They also tended to consume more whole milk, less 2% milk and yogurt, and were less likely to avoid dietary cholesterol. In terms of personality characteristics, centenarians were more dominant, suspicious, practical, and less tense than control subjects in their 60s and 80s (Martin et al., 1992). They were less likely to use active behavioral reactions but were more likely to utilize cognitive coping behaviors compared to octogenarians (Martin et al., 1992). Centenarians were more likely to acknowledge problems than those in other age groups, and they were less likely to seek social support as a coping strategy for their problems (Martin, Poon, & Johnson, 1995).

Community-dwelling centenarians reported fewer potential visitors. They were less likely to talk on the telephone and have a spouse as primary caregiver, but more likely to have their children as caregivers and to receive help with food and meal preparation from family and friends (Martin, Poon, Kim, & Johnson, 1996). However, when they were sick or disabled, they were just as likely as those in their 60s and 80s to have someone help them, to have a confidante, and to have daily visitors.

Compared to younger community-dwelling cohorts, centenarians tended to report more somatic but not emotional symptoms. Although centenarians were found to have more

depressive symptoms compared to younger cohorts, few community-dwelling centenarians showed an indication of clinically significant levels of depressive symptoms.

African American centenarians had significantly higher levels of depression and poorer self-perceived health than their White counterparts. However, when education and income were taken into account, differences in selfperceived health were eliminated, and differences in mental health decreased but remained significant (Kim, Bramlett, Wright, & Poon, 1998). This was found for all three age groups.

Examination of cross-sectional differences showed poorer performances in most cognitive functions in centenarians compared to octogenarians and sexagenarians, except for everyday problem-solving tasks (Holtsberg, Poon, Noble, & Martin, 1995; Poon et al., 1992). The magnitude of age differences was smaller in crystallized intelligence than in fluid intelligence. Education was shown to have a profound positive effect that modulated the level of performance in all subjects, especially the centenarians. Taken together, these findings show that, although dementia-free centenarians are lower in psychometric abilities, they could use their crystallized intelligence and cumulative experience to compensate in everyday problem solving.

Phase 2: Longitudinal Findings

As noted earlier, cross-sectional studies could contain significant cohort confounding effects, and convergence of cross-sectional and longitudinal findings could untangle and validate some of the confounding. Phase 2 was designed to serve that purpose. There are limited longitudinal studies in centenarian research because the mortality rate among centenarians is 50% per year. Centenarian researchers are fortunate to collect all the necessary data when the participants are still alive or before some significant disease or events preclude data collection. Methodological problems in longitudinal studies with centenarians are varied: (a) the longitudinal follow-up period cannot be long owing to the mortality rate; (b) if short longitudinal periods are employed with younger control groups, there may not be measurable changes; and (c) high dropout rates in the centenarian group may result in the overemphasis of survival effects. Given the above known limitations of longitudinal study, the design decision of phase 2 was to focus on patterns of stability and change over time for the three age groups. For centenarians, we measured change over 20 months; for octogenarians and sexagenarians, we measured change over 5 years. The differential longitudinal periods presented an analysis challenge. One of the solutions employed was to evaluate the rates of change for the three groups over the first 20 months.

When assessing personality changes for centenarians over time, our results indicated higher scores in radicalism (a measure of openness to experience) and lower scores in sensitivity after the retest time of 20 months (Martin, Long, & Poon, 2002). With regard to personality states, we noted higher scores in depression and fatigue. In comparison to the two younger groups, centenarians had lower stability coefficients in dominance, fatigue, and state extraversion. Finally, centenarians with lower Mini-Mental State Examination (MMSE) scores showed significantly higher stabilities in the personality traits radicalism and tension (Martin et al., 2002).

One of the most interesting findings in comparing longitudinal patterns is on stability and change in cognitive functions among the three groups. Centenarians were all cognitively intact at the first time of testing. However, after 20 months, the cognitive abilities of about one-third of the centenarians declined noticeably. Four patterns of change were detected among the three groups for different cognitive functions. Pattern 1 was characterized by stability for all cohorts (no age, time, or interaction effects were found) for the WAIS-R (Wechsler Adult Intelligence Scale-Revised) vocabulary test, a measure of crystallized

intelligence. Extant literature supports the stability of vocabulary over the adult life span, and our results extend that finding to healthy community-dwelling centenarians. Pattern 2 reflected stability over time for all age groups between phases 1 and 2 for the MMSE, total everyday problem-solving scores, free recall memory for recent U.S. presidents, WAIS-R arithmetic, and crystallized intelligence. The results replicated findings in the literature in that minimal or no age-related change was expected in crystallized intelligence and tertiary memory. Everyday problem solving was expected to decline with advancing age, but this hypothesis was not supported in the healthy community-dwelling centenarians or in any other age group.

Pattern 3 was characterized by stability for those in their 60s and 80s but decline for healthy community-dwelling centenarians (age × time interaction). This pattern was found for the acquisition and retrieval of new information in paired-associates learning. Memory functions were most sensitive to aging effects. We found a similar pattern in the retrieval phase, indicating the increased vulnerability for centenarians to memory loss over time.

In pattern 4, we found stability for those in their 60s and decline for those in their 80s and 100s (age × time interaction). This pattern was found in measures of fluid intelligence. Over the 20-month period, the sexagenarians remained the same (WAIS-R picture arrangement) or improved (WAIS-R block design), and octogenarians showed the greatest decline in both measures, with centenarians lower at both occasions. Significant age, time, and age × time interactions were found in block design, picture arrangement, and the combination of these two measures in fluid intelligence. The literature supports the well-known finding of age-related differences and decline in fluid intelligence, and the results extend that finding to centenarians.

In conclusion, our longitudinal results showed that cognition was stable for those in their 60s. Fluid intelligence showed deterioration for those in their 80s, and both memory and fluid intelligence declined for centenarians. It is worthwhile to note that many cognitive functions were quite stable for healthy centenarians. A list of the nearly 100 publications generated from the first two phases of the study can be found at http://www.geron.uga.edu/pdfs/CentStudyBooklet.pdf.

Phase 3: A Population-Based Study

As noted earlier, methodological problems were present for both cross-sectional and longitudinal designs in the study of the oldest old. Central to both designs is the sampling of participants. In phase 1, the selection of cognitively intact and community-dwelling centenarians presented a challenge to generalization to the overall centenarian population. However, the selection of cognitively intact centenarians in phase 1 was found to be an advantage for phase 2, in that we were able to observe the change in cognition and other functions over time when the participants were cognitively intact at baseline. Our current phase 3 project addresses the generalization issue by selecting a population-based sample of centenarians and near-centenarians (age 98 and older). A population-based sample allows us to compare and contrast differences in performances among those centenarians who were cognitively intact and community dwelling in phase 1 to a population-based sample with a distribution of cognitive abilities, living situations, health, and functional capacities. It allows us a diverse and representative sample to examine the genetic contribution to longevity; relationships between neuropathology and cognition; behavioral, health, and disease contributions to functions; and supportive resources and personality and environmental factors to adaptation. While the collected data are being analyzed at present, the following is a description of our methodologies, hypotheses, as well as challenges and solutions presented in a population-based study of centenarians.

METHODS

Participants

To achieve the objectives of phase 3 of the Georgia Centenarian Study, we drew samples from specific target populations: (a) centenarians and nearcentenarians (age 98 and older), (b) octogenarians, and (c) younger controls (age 20–59) from a 44-county area of northeast Georgia. The elderly who were recruited for phase 1 were limited to those living in households and who were cognitively intact, thereby failing to represent not only the substantial proportion of centenarians who are living in nursing homes and assisted living facilities but also the large number of centenarians in households who have physical or cognitive limitations that prevent them from participating in such a study. Another factor that limited the generalizability of findings from phase 1 is that centenarians were identified using a variety of methods (e.g., culling names from newspaper articles and other media, requesting names from local area agencies on aging, and word-of-mouth advertising), none of which allow the probability of selection to be assessed. Some individuals may be much more readily found through these methods than others-for example, those who are or have in the past been active in churches or other organizations or those who have well-connected family members.

Centenarians

A plan for a representative sampling of centenarians was conceived by requesting the Center for Medicare and Medicaid Services (CMS) for names of centenarian Medicare enrollees for research purposes. It was estimated that upward of 95% of older adults in the United States are Medicare enrollees, and a sample of centenarian Medicare enrollees would provide a reasonable representative sample of centenarians in northern Georgia. Unfortunately, a change of CMS policy precluded the use of this strategy after the request to the CMS was approved, and the list had to be returned.

Our revised sampling plan had two components. The first called for a census of all skilled nursing facilities (SNFs) and personal care homes (PCHs) located in the 44-county area and for the identification of all residents of a sample of those facilities who are age 98 and older. The second component relied on lists of registered voters, again across the entire 44-county area, and using the date-of-birth information contained on those lists to identify individuals who were age 98 and older. There was some overlap between these components (that is, some residents of SNFs and PCHs were also found on voter registration lists), but the voter registration lists contained a much higher proportion of the noninstitutionalized than of the institutionalized.

To achieve control over the number of participants and maximize the proportion of respondents who were over age 100, the 44 counties were divided into four strata, defined to be mostly contiguous and with approximately the same number of centenarians according to the 2000 census population enumeration. The target population for each of the four strata was defined as persons residing within the geographic boundaries of the stratum who were age 98 or older by the beginning of the field period for that stratum. Some parameters of this design-in particular, the sampling fractions-were intentionally left flexible to permit modifications to be made over the data collection period to allow the targeted sample sizes to be achieved while maintaining control over costs.

Lists were generated of SNFs and PCHs in each of the 44 counties and of the number of beds in each of those facilities. Interviewers called on each of the selected facilities, explained the study, and requested the names of all centenarians and (if called for by the sample specifications) near-centenarians currently residing in that facility.

To implement the second component of the sample design, we listed all centenarians and near-centenarians (that is, all individuals who had their 98th birthday on or before the date of the start of data collection in a given stratum), who were on the voter registration file and whose address indicated that they resided in one of the counties in that stratum.

Development of Sampling Weights for Centenarians

In a population-based study, it is imperative to ascertain that the obtained sample contains pertinent characteristics of the population. Hence, several steps were involved in developing weights for the centenarians in this study. It is important to note that, unlike the typical sample survey, the goal of this study was, with some minor exceptions, to identify all centenarians in a specific geographic area, to contact each of those identified, and to recruit as many of them as possible as participants in the data collection activities. There were minor exceptions: first, that random samples were taken from small personal care homes to reduce the large upfront costs of contacting and securing the cooperation of many of these small facilities, most often only to learn that they had no resident centenarians; and, second, initially residents age 98 and 99 were identified in only a random fourth of the skilled nursing facilities and personal care homes in which those age 100 and older were identified, but this differentiation between near-centenarians and centenarians was later abandoned. The process of developing the weights was intended to take account of the sampling of small personal care homes and, therefore, of their residents.

Second, we made no attempt to take account specifically of differences in the response rate for different parts of the population, because of practical considerations. Obtaining the cooperation of a sample member depended on a long and often complex series of steps, especially for those in nursing homes and personal care facilities. Initially, an appropriate administrator had to be identified in each facility, and then the study had to be explained to that person. A request was then made of that administrator for a list of all residents age 98 and older (or, in some of the initial cases, those age 100 and older). Often this request was not met directly; instead, the administrator sometimes agreed to contact a relevant family member of each such resident and to ask them to contact study staff if they were willing for them to approach the resident, and only then could we identify those residents, try to contact them, and ask them if they would participate.

In the case of household residents, the information on voting rolls was often incorrect or out of date, and thus many of the individuals on the voter rolls who were designated as eligible (age 98 or older) were never contacted. Many of these were likely ineligible because they had died or had moved out of the designated geographic area, but it was impossible for us to estimate what proportion of the selected cases were actually eligible, and therefore we could not estimate the response rate.

We took the 2000 census data for centenarians and near-centenarians living in the designated geographic area as a reasonable substitute for the target population as it was over the period of data collection. The creation of weights, therefore, depended primarily on poststratification as a sequence designed to bring the weighted sample distribution into close agreement with the target population with respect to the five characteristics (geographic substratum, age, gender, race, and type of residence) that we could obtain from the 2000 census. Partly because we did not have a five-way cross-tabulation of the census data, but primarily because the number of cells in such a detailed cross-tabulation would have been very large (and the resulting weights highly variable), we approximated the same result through an iterative (raking) process. That is, we adjusted first on one of the five characteristics (substratum), readjusted on cross-tabulation of successive pairs of the remaining four characteristics, and repeated these steps until achieving a stable set of weights from one iteration to the next. Results based on mean square errors were compared

for 67 key study variables under each of four different weighting schemes (unweighted, untruncated weights, truncated weights, and adjusted truncated weights). The results suggested that, for most applications, weights truncated at the 5th and 95th percentiles are preferable to unweighted analysis or the other weighting schemes. For purposes of description, and because the process of constructing weights for octogenarians and young controls is still underway, this chapter presents unweighted values for study variables.

Octogenarians

The sample design that we developed for the control sample of 80 octogenarians, like that of the centenarians, had two components. Based on the proportion of octogenarians who were classified as institutionalized according to the 2000 census, our intention was to draw 85% of the sample of octogenarians from the voter registration rolls for the 44 counties and the remainder from SNFs and PCHs in those same counties. As with the sample of centenarians, we used a stratified sample design, with the same four sets of counties, and with data collection in each stratum taking place in the same period as for the centenarians. Due to the much larger number of 80-year-olds than of centenarians on the voter rolls and the fact that we did not need as many recruits, we randomly selected a sample of octogenarians for recruitment. Given the small sample size (about 20 per stratum) and the relatively small proportion of octogenarians who reside outside of households (about 15%), in each of the four strata we identified a sufficient number of octogenarians to provide three participants who resided in a small subset of the SNFs that were selected for the sample of centenarians.

Samples of octogenarians (that is, individuals who had their 80th birthday on or before the date of the start of data collection in a given stratum but had not yet had their 90th birthday as of that date and who were listed as resident in one of the counties in that stratum) were drawn from the voter registration file.

Young Controls

Our objective was to obtain DNA and family longevity data from samples of 100 participants in each of four age ranges: 20–29, 30–39, 40–49, and 50–59. Because the proportion of the population that is in these age ranges is much higher than that of octogenarians and centenarians, we specified a design whereby eligible individuals would be identified by making telephone calls to a random sample of households, using a standard random digit dial procedure. Informants in households contacted in this way were asked to enumerate members, and a random selection was made of one member from those in the eligible age range. To improve the efficiency of the data collection, the 44 counties were first divided into the same four strata specified in the sample designs for the centenarians and octogenarians; and then the counties in these strata were further divided into substrata, and one county was selected from each of these substrata with probability proportional to the number of centenarians enumerated in the county in the 2000 census.

Raw values of demographic characteristics for GCS participants are shown in Table 12.1.

PROCEDURES

Data Acquisition and Measures

Data collection for young controls was minimal and included a blood draw and completion of a demographics and family longevity questionnaire in a communal laboratory setting in the community. Data collection for octogenarians was limited to variables relevant for neuropsychological and physical functioning; no blood samples were obtained from octogenarians. The comprehensive nature of the Georgia Centenarian Study required that a data collection team meet centenarians at their place of residence. To keep the testing burden

to a minimum, data collection was divided into four sessions, each of which could be completed within 2 hours. On the first visit, after explaining the aims of the study and obtaining informed written consent, information was collected regarding demographics and family longevity and mental status. A second session included a blood draw, the 15-item Geriatric Depression Scale, dietary information, a physical examination, and mobility performance measures. The third session focused on neuropsychological functioning, including the Behavioral Dyscontrol Scale, Controlled Oral Word Association Task, Fuld Object Memory Evaluation, the Severe Impairment Battery, WAIS Similarities, and a measure of hand-tapping speed. A fourth session focused on physical functioning and included the Direct Assessment of Functional Status, Global Deterioration Rating Scale, Health and Safety questionnaire, and the Older Americans Resources Scale. At the end of the last interview, an attempt was made by a specially trained member of the data collection team to recruit participants into the neuropathology component of the study, described in greater detail below. A total of 66 individuals agreed to neuropsychological follow-up and brain donation postmortem.

Additional information was also collected regarding resources and adaptations of centenarians, both directly from the centenarian and through a proxy according to a set of selection criteria. When a proxy provided information, the mental status, depressive symptoms, and functioning of the proxy were also assessed. The following domains were assessed for resources and adaptation: personality traits, coping, social resources, and levels of fatigue. Furthermore, a number of mental health dimensions (in addition to depression) were assessed: life satisfaction, affect balance, and loneliness. Distal resources were assessed through life events and questions about past achievement (e.g., education, occupation, volunteering). Finally, a number of questions related to economic dependence and health care utilization were assessed.

Blood Sample Collection, Processing, and Storage

A core cell, blood, and DNA laboratory was established at the University of Georgia to efficiently manage the collection, processing, storage, and distribution of biological materials collected and derived from centenarians and control subjects participating in phase 3 of the Georgia Centenarian Study. Centralization of blood sample processing, storage, and distribution by this core laboratory permitted standardization of sample handling procedures, coordination of sample distribution to the various projects, and control of sample inventories.

Blood samples were collected from centenarians in their residences by a skilled phlebotomist at the time of the physical examination. Due to varying times of collection and the frail nature of some participants, blood was collected in the nonfasted state. This precluded the determination of some parameters, including lipid profiles, which are typically measured after an overnight fast. Samples were transported to the core laboratory soon after collection to ensure that blood samples were processed within 4 hours after collection. This time window was chosen as the maximum travel time needed to transport samples from any location in the 44-county area. In addition, preliminary analysis had indicated a rapid deterioration of several blood components between 4 and 6 hours after collection (Johnson et al., 1995). The time interval between blood collection and processing was recorded and provided to the Data Management and Analysis Core to evaluate the effects of time variation on blood chemistry measurements.

To ensure a successful blood draw, all participants were encouraged to drink ample fluids on the day of sample collection to maintain hydration. Successful blood draws were also facilitated by the use of multiple sample blood collection needles or winged “butterfly” collection sets and an experienced geriatric phlebotomist. Under these collection conditions,

sufficient blood to meet all project needs was obtained from more than 80% of the centenarian participants.

Whole blood, plasma, and serum, required for hypothesis testing on genetic and functional contributions to longevity, were processed. These tests will be detailed in future publications specific to these components of the project. Any residual serum or plasma samples collected from the centenarians are banked in −80° C freezers at the University of Georgia. The clotted red blood cell fraction from the serum separation is also stored at −80° C. While there was no immediate need for these red blood cells, they are being stored for possible future studies, such as RBC isozyme analysis or mitochondrial DNA purification.

Cell Immortalization

In most cases, the short life expectancy of the centenarian study population precludes resampling of study members beyond 1 or 2 years after the first sample is collected. However, lymphoblastoid cell lines prepared directly from peripheral blood samples or from cryopreserved lymphocytes provide a renewable supply of genomic DNA and RNA that can be used for follow-up studies of informative genotypes and for typing new candidate genes that may become of interest. Thus, contractual arrangements were made with Coriell Institute for Medical Research (Camden, NJ) to prepare immortalized cell lines and DNA from blood samples received from the Georgia Centenarian Study on a fee-for-services basis. For cell immortalization, two tubes of whole blood were drawn from study participants in 10 ml yellow-top Vacutainer tubes, placed directly into the shipping containers provided by Coriell, shipped overnight at room temperature (~25° C), and received the following day. Use of specialized packing to hold and ship the samples, overnight shipment, and initiation of isolation and cryopreservation of lymphocytes or cell immortalization immediately upon sample receipt helped maintain the integrity of the lymphocytes and allowed for greater efficiency of transformation of cells from the blood samples of the centenarians.

The cell lines, cryopreserved lymphocytes, and extracted DNA are banked at the National Institute of Aging (NIA) Cell Repository at Coriell Institute (http://ccr.coriell.org). The NIA Cell Repository facilitates research on aging by providing research investigators with high quality, well-characterized, and uncontaminated cell lines that would not normally be available to the research community. Coriell maintains a comprehensive computerized data management system for the Aging Cell Repository and is responsible for maintaining the cell stocks in liquid nitrogen and establishing new cell lines and distributing cultures as directed. Genetic material from the Georgia Centenarian Study will be available for distribution to qualified investigators approximately 1 year after the end of the project period.

Data Management and Analysis

Specific components of the study required in-depth biostatistical support. These are described in detail within the particular projects. To coordinate the overall requirements of the program project and promote synergistic collaborations, an integrated study data base was developed and made available in an online format. Results of this endeavor have been presented in detail elsewhere (Dai et al., 2007) and include development of a variety of data screening and analysis tools, as well as results from newly developed methods for assessing statistical power in a $2 \times 2 \times 2$ table where certain marginals are fixed.

GENETIC CONTRIBUTIONS TO LONGEVITY

There are several approaches to discerning genetic variations that play roles in exceptional longevity. The approach utilized in this study is the selection of candidate genes and

comparing the frequencies of variations of these genes among centenarians and controls. Our focus is on candidate genes whose involvement in the intrinsic aging process has at least been documented in a model system. Furthermore, we will ultimately be able to parse out the contribution of genetic factors to complex phenotypes associated with aging that will be analyzed in the other component projects of the Georgia Centenarian Study. The candidate genes chosen for analysis are apolipoprotein E (APOE), HRAS1, and LASS1/LAG1.

Apolipoprotein E phenotypes were examined in a Finnish population (Holtsberg et al., 1995; Poon, 1992; Poon et al., 1992). The frequency of the E4 isoform was reduced in nonagenarians. Another Finnish study (Louhija et al., 1994) confirmed the APOE results at the genetic level and found, in addition, that the E2 allele has a higher frequency in centenarians. The APOE results of this study have been replicated in a French population (Schachter et al., 1994). The APOE association has been replicated in numerous studies (Blanche, Cabanne, Sahbatou, & Thomas, 2001).

Mitochondrial genotypes have also been examined for their association with longevity (Tanaka, Gong, Zhang, Yoneda, & Yagi, 1998). It has been shown that HRAS1 is associated with longevity (Bonafe et al., 2002). Interestingly, there is evidence of an interaction between this gene and mitochondrial genotype in this association.

LAG1 is the first gene cloned as a longevity-determining gene (D'mello et al., 1994). It was identified in a screen for genes that may play a role in yeast aging (Egilmez, Chen, & Jazwinski, 1989). The human homologue of LAG1 was cloned and given the name LASS1 (Jiang, Kirchman, Zagulski, Hunt, & Jazwinski, 1998). Laglp operates ceramide synthesis in yeast as a component of ceramide synthase (Guillas et al., 2001; Schorling, Vallee, Barz, Riezman, & Oesterhelt, 2001). Human homologues perform the same function (Guillas et al., 2003). Besides its validation as a longevity gene in a model system, LAG1 has functional implications that are particularly noteworthy for this study. Ceramide is not only a structural component of sphingolipids, which are particularly prevalent in the nervous system, but it is also an important signaling molecule, which affects cell proliferation, differentiation, stress responses, and apoptosis and modulates the function of the immune, endocrine, vascular, and nervous systems (Mathias, Pena, & Kolesnick, 1998).

In performing association studies, we are testing the hypothesis that alleles of certain genes are associated with longevity. This is an approach that is uncomplicated theoretically and statistically. A control group is required, however. A positive result, if it is not confounded as described below, represents a correlation and must, therefore, be subjected to further validation (Glazier, Nadeau, & Aitman, 2002). All other factors being equal, associative analyses have the advantage of allowing the assignment of an allele to a trait even if that allele is responsible for only a fraction of the variance for that trait (Lander & Schork, 1994). This is the major feature that is attractive to us in our analysis of the complex trait of longevity. The case group comprises 242 centenarians, while the young control group includes 400 individuals in the age range of 20 to 60. The choice of an extreme phenotype tends to enhance statistical power. As pointed out before, the study of rare survivors (here centenarians) mitigates the high levels of locus and allelic heterogeneity in the analysis of polygenic traits (Perls, Kunkel, & Puca, 2002; Wright, Charlesworth, Rudan, Carothers, & Campbell, 2003). In our study, we have focused on single-nucleotide polymorphisms (SNPs), which are the largest source of variation in the human genome.

By way of example, we have calculated the required sample sizes as the log pca varies from 0.1 to 1.0 with an interval of 0.1 (Figure 12.1). The sample size necessary to detect the associations between factors of interest increases from 4 to more than 900 as the log ρ^sub ca^ varies from 1.0 to 0.1. In this example, ρ^sub 1^ is fixed at −0.6592. The results showed

that the required sample size changes dramatically as the log ρ^sub ca^ varies from a small number to a relatively large number. For the 17th SNP, an association with longevity can be detected down to about log ρ^sub ca^ [congruent with] 0.86, as shown in Figure 12.1. It indicates that the probability table of the control group plays an important role in determining the power of the statistical test when other parameters are fixed. We can also see that when the log odds ratios are close to zero (i.e., systematic associations are very small), a large sample size is required to detect associations.

The SNPs will also be used to reconstitute haplotypes, which will be subjected to similar analyses. Population admixture is a major confounding factor in our study. The Georgia population is primarily of European and African descent, with admixes of other origins present as well. The general approach of using marker loci unlinked to the candidate locus to detect population stratification in association studies has been recently validated using a simulation procedure (Pritchard & Rosenberg, 1999). The population stratification will be performed using 100 well-characterized Alu insertion polymorphisms that have already been shown to be sufficient for the reclassification of individuals to the appropriate geographic origin with 98% to 100% accuracy (Bamshad et al., 2003; Ray et al., 2005).

NEUROPATHOLOGY OF DEMENTIA IN CENTENARIANS

The relationship between late-life aging and cognitive impairment is not well understood. For example, it is not known which cognitive changes occur with age alone and which are due to the presence of neuropathologic changes in the brain such as cerebral infarcts or Alzheimer's disease. In the Neuropathology (Project 2) of the Georgia Centenarian Study, we are exploring these questions by gathering clinical, cognitive, and neuropathologic data from a subset of the subjects characterized in the Georgia Centenarian Study. The overall aim of Project 2 is to explore relationships among senile plaque and neurofibrillary tangle counts, brain infarcts, functional abilities, cognitive measures, and the presence of dementia in a racially and educationally diverse sample of centenarians.

Studies of centenarians are particularly valuable because of their potential to offer insights into fundamental questions about the cognitive toll of normal aging and the ultimate clinical expression of neuropathologic findings. Most clinical studies have suggested that a large proportion (50% to 75%) of centenarians have cognitive impairment (Allard, 1991; Blansjaar, Thomassen, & Van Schaick, 2000; Forette, 1997; Ivan, 1990; Louhija et al., 1994; Powell, 1994; Silver, Newell, Brady, Hedley-White, & Perls, 2002). Interestingly, several neuropathologic studies have found Alzheimer's disease pathology in fewer subjects than expected (Delaere, He, Fayet, Duyckaerts, & Hauw, 1993; Mizutani & Shimada, 1992; Silver et al., 1998), and in one study, 4 out of 14 centenarians showed discrepancies between their antemortem neuropsychological performance and the neuropathologic findings in their brains at autopsy (Silver et al., 2002). Only two of these studies included meaningful antemortem neuropsychological testing, few utilized quantitative neuropathologic assessment measures, and none had sufficient numbers of subjects to draw empirical inferences. In Project 2 of the Georgia Centenarian Study, we utilize careful clinical and neuropsychological studies of centenarians during life coupled with thorough neuropathologic evaluation of their brains upon death to address the following three hypotheses:

Hypothesis 1

The clinical syndrome of dementia should be expressed only in those centenarians who meet neuropathologic criteria (National Institute on Aging and Reagan Institute Working Group, 1997) for the diagnosis of Alzheimer's disease, those who have cerebral infarcts in critical

brain regions, or those who have other identifiable gross and/or histopathologic brain lesions.

Hypothesis 2

Among brain-autopsied centenarians, we expect antemortem dementia severity to be significantly correlated with the presence of lacunar or larger infarcts in basal ganglia, thalamus, deep white matter, hippocampus, or other brain regions critical to cognitive function (adjusting for the presence and quantity of neuropathologic features of Alzheimer's disease).

Hypothesis 3

Among brain-autopsied centenarians, a relationship between clinical and pathologic markers of neurocognitive reserve (head circumference, educational level, occupational attainment, brain weight, synapse number, neuron number) and the degree of antemortem cognitive decline, adjusted for the presence and quantity of neuropathologic features of Alzheimer's disease, can be expected.

Subjects who participated in the Georgia Centenarian Study were asked to consider participating in the neuropathology project. Based on reports by others (Silver et al., 1998) and our own pilot study, we anticipated that 25% to 30% of subjects in the Georgia Centenarian Study would consent to brain donation, for a projected enrollment of 60 to 72 subjects, and this level of enrollment was successfully achieved. The subjects enrolled in the neuropathology project are being followed longitudinally with the MMSE (Folstein, Folstein, & McHugh, 1975), CERAD (Consortium to Establish a Registry for Alzheimer's Disease) battery (Morris et al., 1989), and Clinical Dementia Rating Scale (Morris, 1993) administered at 6-month intervals, along with a brief neurological examination.

Neuropathological examination of the postmortem brain includes magnetic resonance imaging followed by detailed gross and microscopic neuropathologic evaluation, including assessment of cerebral atrophy and ventricular dilatation; grading of the degree of atherosclerotic change in the major arteries of the Circle of Willis; recording of the sizes and specific locations of infarcts, hemorrhages, or lacunar infarcts; quantitation of diffuse and neuritic plaques and neurofibrillary tangles in the amygdala, hippocampal CA1 region, subiculum, entorhinal cortex, and in the frontal, temporal, parietal, and occipital lobes; quantitation of Lewy bodies; assessment of small vessel disease, congophilic angiopathy, white matter pallor, inflammatory changes, and the number and age of microinfarcts; and quantification of synapses in frozen tissue specimens from the frontal, temporal, and occipital poles.

NEUROPSYCHOLOGICAL AND HEALTH PREDICTORS OF FUNCTIONAL CAPACITY

The measurement, evaluation, and prediction of functional capacity, defined as the ability to perform basic activities of daily living (BADLs) and instrumental activities of daily living (IADLs), has been a largely neglected area of study in the oldest old. Centenarians are particularly at risk of becoming functionally dependent, which has repeatedly been shown to result in the greatest utilization of health care resources (Krach, DeVaney DeTurk, & Zink, 1996; Muller, Fahs, & Schechter, 1989; Rock et al., 1996) and is a strong predictor of both institutionalization and mortality (Fried et al., 1998; Inouye et al., 1998; Ogawa, Iwasaki, & Yasumura, 1993; Sonn, 1996; Worrall, Chaulk, & Briffett, 1996). Cognitive, physical, and sociodemographic factors contributing to the preservation or decline of IADL and BADL competency are not well understood but are nevertheless of critical importance in

maintaining a satisfactory quality of life at the limits of longevity. Knowledge of critical factors that influence everyday functioning would permit development of effective interventions that capitalize on or enhance preserved abilities, facilitating recovery, maintenance, or improvement of functional capacity (e.g., Fortinsky Covinsky Palmer, & Landefeld, 1999). By understanding how different types of BADL and IADL performance may be affected by cognitive impairment, compensatory strategies permitting recovery, preservation, or improvement in everyday functioning can be developed. Such approaches might include making use of maximal environmental cuing strategies (e.g., notepad, voice recorder), repetition of important information in multiple sensory modalities, behavioral rehearsal, or other similar memory support procedures. Our goal is to examine the relative and combined contributions of neuropsychological, physical, and nutritional factors to functional capacities of the oldest old.

In light of known age-related changes in cognition (Frieske & Park, 1993; Park, Smith, Dudley, & Lafronza, 1989; Poon, 1985), neuropsychological assessment of cognitive abilities in the elderly has assumed a prominent role in determining whether an individual's cognitive performance is ageappropriate, or possibly related to an underlying disease state, such as dementia (Flicker, Ferris, Crook, Bartus, & Reisberg, 1986). However, results of cognitive assessment are also commonly used to make determinations regarding functional capacity (Heaton & Pendleton, 1981; Poon et al., 1986), inferring that cognitive capacities are inevitably tied to the ability to perform BADLs and IADLs (Loewenstein, Rubert, et al., 1992; Loewenstein, Rubert, Argiielles, & Duara, 1995; Loewenstein, Ardilla, et al., 1992; Poon, Rubin, & Wilson, 1989). Despite this common practice, this premise is largely untested among the oldest old, but it remains a critical issue. Our understanding of the complex relationships between cognitive and functional ability is limited, particularly among elderly individuals for whom physical/sensory cognitive, and functional abilities show varying degrees of compromise.

Functional abilities, such as management of finances, driving an automobile, and living independently, tend to be overlearned, highly practiced, and rely on the interaction between a number of cognitive abilities (which may permit capitalization on viable cognitive skills to compensate for other failing abilities). Therefore, one might predict that functional capacity for certain routine tasks (e.g., BADLs) may be more age resistant than discrete cognitive abilities that are evaluated routinely during neuropsychological assessment (Corey-Bloom et al., 1996). Alternatively, the prevalence of physical and sensory disability is high among elderly persons (Blazer, Burchett, Service, & George, 1991; Cornoni-Huntley et al., 1985; Manton, 1989; Miles & Bernard, 1992), resulting in the contrary prediction that physical and sensory impairments exert a substantial negative impact on level of both cognitive and adaptive functioning in the oldest old (Guralnik & Simonsick, 1993; Heath & Fentem, 1997; Laukkanen, Sakari-Rantala, Kauppinen, & Heikkinen, 1997; Salen, Spangfort, Nygren, & Nordemar, 1994; Sonn, 1996; Sonn, Frandin, & Grimby 1995).

Specific cognitive resources have been directly tied to level of adaptive functioning in the elderly both with and without dementia using direct assessment techniques (Loewenstein, Ardilla, et al., 1992; Loewenstein, Rupert, et al., 1992; Loewenstein et al., 1995; Loewenstein, Argiielles, Barker, & Duara, 1993; Nadler, Richardson, Malloy Marran, & Hosteller Brinson, 1993; Richardson, Nadler, & Malloy, 1995; Rozzini et al., 1997; Vitaliano, Breen, Albert, Russo, & Printz, 1984) and likely contribute to maintenance of independence in the community with an acceptable quality of life. The ability to successfully carry out BADLs and IADLs is contingent on a complex interplay between numerous cognitive abilities as well as adequate physical/sensory functioning.

Functional ability was assessed using both self-report and performance-based measures. The performance-based physical function supports the rating of global assessment of health and provides insight into how the impairments affected function. The Established Populations Epidemiological Studies of the Elderly (EPESE) Short Physical Performance Battery (Guralnik et al., 1994) is a balance and mobility test predictive of nursing home placement and institutionalization when scores are lower than 4 on a 0- to 12-point scale. As one would expect, the 54% of the community dwellers compared to 2% of the SNF residents scored 5 or better on the EPESE. Over 98% of the SNF residents used an assistive device compared to 70% of the community dwellers. However, very few (less than 7%) of either the community dwellers or the SNF residents were bed bound, and both populations were similar in their frequency of falls in the past month (−10%). The Physical Performance Mobility Exam (PPME; Winograd et al., 1994) provides information on lower levels of function and includes bed mobility, transfer from bed to chair, and ability to stand. In SNF residents, 78% scored 0 on the PPME 6-point scale compared to 9% of the community dwellers. Surprisingly, no participants in either group reported difficulty balancing while walking. One of our research foci was to ascertain the contributions of physical performances to functional capacities of the oldest old.

Height, weight, and body mass index (BMI) were similar in the community dwellers and the SNF residents. Community dwellers required fewer physician visits with 84% having fewer than three visits in the past 6 months compared to 68% of the SNF residents. Fewer community dwellers (13%) were hospitalized in the past 6 months compared to SNF residents (22%). On the global assessment of health, 38% of community dwellers were reported as mildly physically impaired compared to 48% of the SNF residents reported as severely impaired. Approximately 30% of both populations were moderately impaired. Impairment is reflected in capacity measures, in which the community dwellers were better than 50% higher than the SNF residents in grip strength (community dwellers: average of right and left hands 19.72 pounds; SNF, 8.56 pounds). Surprisingly, leg extension was similar for both groups. This may be a function of the manual muscle manometer that was used to assess strength. Community dwellers (137 degrees) have more passive right shoulder flexion than SNF residents (110 degrees). Active shoulder flexion is about 10 degrees lower for each group, reflecting lower accessible flexibility for function. One possible explanation may be low strength to lift the arm restricts the person’s shoulder flexibility. Interestingly less than 25% of either group reported feeling weak. This may be due to the appropriate match between the support residents receive to manage the demand of the environment in the face of waning strength.

Dietary habits were explored by examining the primary means of feeding (e.g., typical foods, pureed foods, etc.), as well as the frequency of intake of food groups, including protein foods (meat, poultry, fish), dairy foods, fruits, fruit juices, and vegetables. Because of common functional problems in the very old, such as difficulty procuring or chewing food, it cannot be assumed that current diet reflects past dietary habits and that the current diet accounts for the exceptional longevity of centenarians, and it should not be assumed that centenarians have better dietary habits when living at home than in long-term care settings (e.g., Johnson, Davey Hausman, Park, & Poon, 2006). Also, there may be cohort differences in food preferences and dietary factors for longevity. For example, in our previous study in Georgia, centenarians and octogenarians, compared to sexagenarians, were less likely to skip breakfast and consumed a more varied diet, with more frequent consumption of milk and grain foods (Houston, Johnson, Poon, & clayton, 1994). However, centenarians also consumed high-fat foods, such as whole milk and biscuits, and coffee more frequently than the two younger cohorts (Houston et al., 1994). Thus, in our ongoing study, data describing dietary patterns will be used primarily for explaining variability in current physical and mental function rather than as indicators of lifelong dietary patterns that might be predictive

of exceptional longevity. Genetic differences in nutrient metabolism (Ames, Elson-Schwab, & Silver, 2002) may be more likely to account for differences in longevity than current food intakes.

ADAPTATION AND RESOURCES IN CENTENARIANS

Examining factors, especially genetic and biomedical ones, that contribute to reaching the age of 100 years or more has always been a central topic in centenarian research (e.g., Jeune, 2002). Interestingly, few researchers have addressed the equally important question of how well these very long-lived individuals are able to adapt to the enormous physical, cognitive, social, and economic strains that they are facing, which may put their mental health at risk, and whether some combinations of attributes are over- or underrepresented among centenarians (e.g., Martin et al., 2006). This issue is of increasing societal significance, because becoming a centenarian will no longer be a rarity but quite normal at least for women (Vaupel, 2000). Investigations have demonstrated that some centenarians continue to function well and live independently in their communities, whereas many depend greatly on others for their care and support (Anderson-Ranberg, Schroll, & Jeune, 2001; Poon, 1992; Rott, d'Heureuse, Kliegel, Schonemann, & Becker, 2001).

One of the central questions in research with centenarians is why some centenarians continue to adapt very well, whereas others are quite impaired. Although there are many criteria one might use to distinguish well-adapted from poorly adapted centenarians, our work focuses on four critical areas of adaptation: functional capacity, cognitive impairment, mental health problems, and economic-financial dependency. Whether centenarians score high or low on these critical domains may depend on psychosocial demands and resources available to centenarians. We propose that lifelong experiences and accomplishments, stress, personality, and coping, as well as social and economic resources determine how well centenarians adapt to challenges in late life. The following section highlights the importance of four critical areas of adaptation (i.e., functional capacity, cognitive impairment, mental health problems, and economic cost and dependence) and then suggests important resources that may help to answer the primary adaptation question of why some centenarians adjust well and others do not.

Functional capacity refers to the basic capabilities of individuals to carry out tasks that are essential to independent and self-sufficient living (e.g., the ability to run errands, cook, and do housework). Previous research has indicated that even the top 20% to 25% of American centenarians are particularly vulnerable to decline in these basic living tasks (Martin et al., 1996; Poon, 1992). Cognitive impairment refers to the level of deterioration in such mental processes as thinking, remembering, speaking, abstracting, and evaluating (Holtsberg et al., 1995). Some decline in cognitive functioning is inevitable in extreme old age (Poon, 1985). For example, a high prevalence of impairment (51%) was obtained in the Danish Longitudinal Centenarian Study (Andersen-Ranberg, Vasegaard, & Jeune, 2001). However, previous research has also documented strong individual differences in the cognitive capacities of centenarians (cf. Holtsberg et al., 1995). A total of 37% of the Danish centenarians had no signs of cognitive impairment at all (Andersen-Ranberg et al., 2001). Mental health problems can also be critical risk factors for centenarians, particularly when associated with low levels of social support. For example, centenarians typically score high on depressive symptoms and loneliness (Martin, Hagberg, & Poon, 1997; Martin, Rott, Kerns, Poon, & Johnson, 2000). Furthermore, depression, low morale, and loneliness significantly predict levels of functional capacity, health, and well-being in centenarians (e.g., Adkins, Martin, & Poon, 1996; Martin et al., 1997). Economic cost represents the estimated costs associated with living expenses, health care, and miscellaneous life expenses. Previous research has indicated that up to one-half of centenarians live below the

poverty line (Goetting, Martin, Poon, & Johnson, 1996; Martin et al., 1996). It is likely that the oldest old will have an increasingly substantial impact on health care and social service systems throughout the world (Morgan, 2000; Suzman, Willis, & Manton, 1995), even though recent research suggests that the increase in health care expenditures may be less than expected, because of the concentration of expenditures at the end of life, rather than during the extra years of relatively healthy years (Yang, Norton, & Stearns, 2003).

Individual, social, and economic resources figure prominently in effective adaptation models in the oldest old (Martin et al., 2002). While the oldest old, particularly centenarians, are exposed to major risk factors that influence vulnerability to stress associated with life events (Kaplan, 1996), not all in this age group draw from lower levels of physical, psychological, social, and economic resources when compared to other age groups (Goetting et al., 1996; Martin et al., 1992, 1996, 1997; Nickols-Richardson, Johnson, Poon, & Martin, 1996b; Poon, 1992). We therefore propose a differential resources hypothesis suggesting that those centenarians who can draw from sufficiently high available personal and social resources adapt significantly better than those with lower resources. Those resources include personality, past experiences, and achievements.

Centenarians show differences in personality traits when compared to other age groups (Martin et al., 1992, 1996). For example, centenarians scored higher on dominance, suspiciousness, and shrewdness, while they scored lower on imagination and tension (Martin et al., 1992, 1996) when compared to other age groups. Among centenarians, the personality configuration of low neuroticism, high competence, and high extraversion traits was especially distinctive (Martin et al., 2006). In mortality studies, survivorship was negatively related to neuroticism and positively to conscientiousness (Wilson, Mendes de Leon, Bienas, Evans, & Bennett, 2004). Continuity of personality characteristics may explain how some centenarians preserve functional autonomy, subjective health, and subjective well-being.

Other important resources include past experiences and achievements, as well as behavioral skills that predict differential levels of adaptation. While many studies concerning the oldest old focus on specific deficits, our work on resources and adaptation emphasizes areas of personal strengths (such as personality, coping, experiences). The contribution of such factors to the understanding and prediction of centenarian well-being represents an integral component in the study of the oldest old.

SUMMARY

The goal of this chapter was to share methodological concerns and pitfalls in the study of centenarians. In so doing, we outlined the designs, hypotheses, problems, and findings from the three phases of the Georgia Centenarian Study. Each phase presented its own challenges. As noted in the list of authors and investigators of this chapter, the study of biopsychosocial aspects of the oldest old requires a multidisciplinary team that must work in an interdisciplinary manner to resolve problems and issues. The team must learn to work across disciplines and to depend on each other for new solutions to existing designs and methodological problems. The solutions might not be perfect, and some were compromises. Lessons learned from these experiences may be used for the next generations of centenarian research. Over the last 20 years, we have been confronted with issues of (a) generalization from a convenience sample of centenarians, (b) methodological issues in obtaining a representative sample, (c) determination of proper control groups for centenarian research, (d) recruitment for research of a population that is well protected by their family and community, (e) testing a frail population with a high mortality rate, (f) methodological issues in cell immortalization of centenarian blood, (g) issues relating to how much testing time and how many sessions are appropriate in order not to fatigue the participant, (h)

ethical issues in requesting brain donations, (i) methods of transportation of blood samples from the field to the laboratory, (j) quality control on data acquisition and efficient methods for data sharing, and many more.

We brought attention to the cross-sectional and longitudinal designs on centenarian research; each has their distinct advantages and disadvantages. Neither of these designs could provide conclusions on the definitive, replicable, or enduring characteristics of centenarians. Perhaps if and when the opportunity exists, a time-sequential design (Schaie, 1994) could be applied to answer a number of needed questions on the influence of time, cohort, and time of measurement issues among the oldest old.

This chapter is written for the next generations of centenarian researchers. May they learn from our experience and dilemma.

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Appendix

Now in its 12th year, and funded by the National Institute on Aging, the New England Centenarian Study is the largest genetic and social study of centenarians and their families in the world (www.bumc.bu.edu/centenarian).

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Ilene C. Siegler, PhD, Professor, Medical Psychology and Neuroscience, Duke University Medical Center, Durham, North Carolina

John L. Woodard, PhD, Associate Professor, Department of Psychology, Wayne State University, Detroit, Michigan

Biographies

Leonard W. Poon, PhD, DPhiL, he, is professor of public health in the Department of Health Policy and Management, professor of psychology in the Department of Life Span Developmental Psychology, chair of the faculty of gerontology, and director of the Institute of Gerontology at the University of Georgia. He is also the director of the Georgia Geriatric Education Center. Dr. Poon is the principal investigator of the Georgia Centenarian Study, which was funded by the National Institute of Mental Health (1988–1992–1992–1997) and the National Institute on Aging (2001–2008). He is the founder and executive director of the International Centenarian Consortium since 1994. Aside from his primary interests of functional, cognitive, and behavioral correlates of longevity and adaptation, his research includes normal and pathological changes of memory with age, early detection of dementia, and the impact of exercise and activities on cognitive functions among older adults. Dr.

Poon is a fellow of the Gerontological Society of America, the American Psychological Association, the American Psychological Society, and the Association for Gerontology in Higher Education.

Thomas T Perls, MD, MPH, completed his undergraduate degree in biology at Pitzer College in Claremont, California. He graduated from the University of Rochester School of Medicine in 1986, followed by internship in internal medicine at Harbor UCLA Medical Center in Torrance, California. He was a geriatrics registrar (fellow) at Mount Royal Hospital in Melbourne, Australia. After completing a 3-year geriatrics fellowship at Harvard Medical School, he joined the staff at Beth Israel Deaconess Medical Center, where he founded the New England Centenarian Study. He moved to Boston University School of Medicines Geriatrics section in 2001 as an associate professor. Dr. Perls is board certified in internal medicine with special qualifications in geriatrics, and he is a fellow of the American College of Physicians.