Predicting Successful Aging in a Population-Based Sample of Georgia Centenarians

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Research Article
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Used a population-based sample (Georgia Centenarian Study, GCS), to determine proportions of centenarians reaching 100 years as (1) survivors (43%) of chronic diseases first experienced between 0–80 years of age, (2) delayers (36%) with chronic diseases first experienced between 80–98 years of age, or (3) escapers (17%) with chronic diseases only at 98 years of age or older. Diseases fall into two morbidity profiles of 11 chronic diseases; one including cardiovascular disease, cancer, anemia, and osteoporosis, and another including dementia. Centenarians at risk for cancer in their lifetime tended to be escapers (73%), while those at risk for cardiovascular disease tended to be survivors (24%), delayers (39%), or escapers (32%). Approximately half (43%) of the centenarians did not experience dementia. Psychiatric disorders were positively associated with dementia, but prevalence of depression, anxiety, and psychoses did not differ significantly between centenarians and an octogenarian control group. However, centenarians were higher on the Geriatric Depression Scale (GDS) than octogenarians. Consistent with our model of developmental adaptation in aging, distal life events contribute to predicting survivorship outcome in which health status as survivor, delayer, or escaper appears as adaptation variables late in life.

1. Introduction

With the expected lifespan of humans increasing at a rate of 2.5 years per decade [1], it will not be uncommon for individuals born in developed countries in this decade to live into the next century (Figure 1(a)) [2]. This observation poses a substantial challenge to health care and other entitlement systems because chronic diseases, which are the cause of 60 percent of deaths worldwide, often dictate the conditions of our later lives. Here we develop a means to predict the health-related survivorship outcomes of centenarians entering the next century.

The GCS obtained a population-based sample of 244 centenarians and near-centenarians (98 years old or older) and 80 octogenarians [3] through voter registration roles, and sampling from a complete list of nursing homes (NH) and personal care homes (PCH) in a 44-county area of northeast Georgia [3]. The GCS sample was drawn from
2. Materials and Methods

The recruitment rate (i.e., the percentage of those participating out of those contacted) was 67.2% for centenarians and 46.0%, for octogenarians. Data on GCS participants were collected under Institutional Review Board approval and Human Subjects consent and are deposited in the Georgia Centenarian Database [5]. In contrast to Phase 1 and Phase 2 of the GCS, centenarians in Phase 3 here spanned a wide range of functional capacity from being bedbound in a nursing home to living independently in the community [3]. Demographic and medical histories of GCS participants were collected onto computer generated questionnaires and completed in 4, ~2 hour interviews with GCS participants. Sources for answers on the health
questionnaire were participants, their legal proxy, care professionals in NHs or PCHs, and medical charts at NHs or PCHs. The health questionnaire included medical history, current problems (such as, bedbound status, assistive devices, and restricted activity days), medications/oxygen, physical examination (including vital signs, skin fold/Arm Circumference and hand grip, hearing, vision, fine motor testing, lower leg extension, foot sensory, weight/height, and shoulder flexion and vision test), EPESE and PPME tests of functional capacity (including standing balance, 8-foot walk, chair stands, step-up, and Bed Mobility), gross physical abnormalities, global assessment of physical health, and GDS [6]. International Disease Classification 9 (ICD-9) provided a framework for constructing the health questionnaire. More details on data collected have been previously given [3]. The instruments available at http://qa.genetics.uga.edu/ were then scanned into a Teleform database [5], checked, corrected, and verified and saved as individual pdf images for loading into the Georgia Centenarian Database [5].

### Table 1: Demographics of 2000 Census in Georgia and GCS study participants.

| Age Range | Participants | 2000 Census |
|-----------|--------------|-------------|
|            | Number | Percent | Number | Percent |
| 98         | 61 | 25% | 362 | 30% |
| 99         | 48 | 20% | 275 | 23% |
| 100–104    | 126 | 52% | 526 | 42% |
| 105+       | 9 | 4% | 81 | 6% |
| TOTAL      | 244 | 100% | 1244 | 100% |

### (b) Race Distribution, 2000 Census versus Participants

| Race    | Participants | 2000 Census |
|---------|--------------|-------------|
|         | Number | Percent | Number | Percent |
| Black   | 52 | 21% | 397 | 32% |
| Non-Black | 192 | 79% | 847 | 68% |
| TOTAL   | 244 | 100% | 1244 | 100% |

### (c) Gender Distribution, 2000 Census versus Participants

| Gender | Participants | 2000 Census |
|--------|--------------|-------------|
|        | Number | Percent | Number | Percent |
| Male   | 37 | 15% | 237 | 19% |
| Female | 207 | 85% | 1007 | 81% |
| TOTAL  | 244 | 100% | 1244 | 100% |

To validate medical histories on centenarians, nonfasting blood samples were drawn by a skilled phlebotomist as previously described [3]. From these blood samples, glycated hemoglobin (HbA1c) and hemoglobin levels were assessed by a clinical diagnostic laboratory (LabCorp, Inc., Burlington, NC) and used for diagnosis of diabetes and anemia, respectively. Dementia status was also cross-validated by a combined neuropathological and clinical consensus report on 66 centenarians, who consented to neuropsychology followup and brain donation postmortem [3]. Results are to be reported elsewhere.

A multinomial logistic response model was fitted to the study data [13] with SPSS Software at (http://www.spss.com/). The response was whether or not a centenarian is a survivor (S), delayr (D), escaper (E), or other (O) with probability $\pi_{ij}$, where $i$ indexes all levels of the independent variables, sex, race, institutional status, education, body mass index, use of tobacco (i.e., the $ih$ subpopulation), and the 11 indicators of chronic diseases found in Figure 1(b) and $j = S$, D, E, or O. Using a “[[" for closed and ‘)’ for open as a standard mathematical notation, a survivor of chronic diseases is a centenarian who first experiences chronic diseases in earlier years from [0,80), a delayr is a centenarian who only first experiences chronic diseases late in life from [80,98), and an escaper is a centenarian who only encounters chronic diseases at the very end of life at 98 or older. These definitions of survivor, delayr, and escaper differ slightly from those in [4] by using a cutoff of 98 (instead of 100) for the escaper category and by using a different list of chronic diseases in Figure 1(b). For the multinomial response model here, we use all 11 chronic diseases in Figure 1(b) to define survivor, delayr, or escaper. More restrictive definitions for particular disease classes are also examined in the Results and Discussion (see Table 3).

The log-likelihood is product-multinomial and proportional to

$$l(B) = \sum_{i}^{m} \sum_{j}^{f} n_{ij} \ln \left( \pi_{ij} \right).$$

(1)

The cell probabilities $\pi_{ij}$ are determined by the independent variables and given by

$$\pi_{ij} = \frac{\exp \left( x'_{i} \beta_{j} \right)}{1 + \sum_{k=1}^{J-1} \exp \left( x'_{i} \beta_{k} \right)},$$

(2)

where $x'_{i}$ is the vector of observations on the $ith$ subpopulation and $\beta_{j}$ is the vector of regression coefficients for the $jth$ response. The reference response is $J$. The Other (O) category arose when there were missing data, and the reference response was survivor (S). The model was fitted by the method of maximum likelihood [13].

3. Results and Discussion

Will we be cognitively intact? The prevalence of cognitively intact centenarians is still being debated. There is broad variation (27%–100%) in the literature [3] about the
Table 2: The lifetime prevalences of psychiatric disorders other than dementia in centenarians versus octogenarian control group in GCS [3] do not differ.

| Disease* | Octogenarians (%) | Centenarians (%) | Total # |
|----------|-------------------|------------------|---------|
| Dementia | 13 (14%)*         | 136 (57%)*       | 321     |
| Depression| 14 (17.5%)        | 36 (14.8%)       | 324     |
| Anxiety  | 5 (6.3%)          | 17 (7.0%)        | 324     |
| Psychosis| 1 (1.3%)          | 6 (2.5%)         | 324     |
| Total    | 33                | 185              | 324     |

*The row categories are not mutually exclusive, but dementia tends to be positively associated with psychiatric disorders (Figure 1(b)). The association of Dementia with age (Control versus Centenarian) is significant with \( P < .00001 \) by Fisher’s Exact test [14] for a \( 2 \times 2 \) table, but the associations of Depression, Anxiety, and Psychosis individually with age (Control versus Centenarian) are not significant with \( P > .05 \). If we combine mental health across Depression, Anxiety, and Psychosis and test for association with age (Control versus Centenarian) by Fisher’s Exact test [14] for a \( 2 \times 2 \) table, the association of the aggregate variable indicating Depression, Anxiety, or Psychosis with age is not significant. The percents reported in this table are among 80 octogenarians or 244 centenarians.

prevalence of dementia in centenarians partially due to differences in assessment methods and partially due to age, gender, race, educational attainment ratios, and sampling techniques (e.g., convenience samples versus population-based samples). Sampling methods can be vital to the results when one considers that the functional capacity of Nobel Laureate [15], Dr. Rita Levi-Montalcini, who serves currently in the Italian Senate, to someone needing the support of a nursing home. A Global Deterioration Scale (GDRS) battery [12] was administered to GCS participants. Dementia is scored when an individual receives a score of 4–7 on the GDRS. As shown in Figure 1(d), approximately half of centenarians (57%) scored as having dementia, while the majority of octogenarians were cognitively intact.

What will be our emotional state once we reach 100? Based on a health history questionnaire, centenarians do not appear to experience more depression, anxiety, or psychoses relative to octogenarian controls (Table 2). This is surprising because the prevalence of dementia, which is associated with psychiatric and neurological diseases (Figure 1(b)), is significantly higher in centenarians versus octogenarians (Figure 1(d)). To validate concurrently these findings, centenarians and the control group were compared on the Geriatric Depression Scale (GDS) [6] short form (Figure 2(f)). The short form GDS has a range from 1 to 15, with 6–10 suggestive of depression and 11–15 almost always indicative of depression. In Figure 2(f), there is a significant difference by a \( t \)-test \( (t = 3.68, \text{df} = 296, P < .001) \) in the mean GDS between centenarians and octogenarians. What this means is that while there is no evidence for a difference in lifetime prevalences of psychiatric disorders (other than dementia) in Table 2, there is a subclinical difference in level of depression.

How likely is it that we will be coping with a chronic disease? There are three mutually exclusive avenues to 100 in this study [4]. We can be survivors of chronic diseases in earlier years from 0–80. Alternatively, we can be delayers and only first experience chronic disease late in life from 80–98, or we can be escapers and only encounter chronic disease at the very end of life at 98 or older. The avenue by which we achieve 100 years of age depends on the chronic disease encountered (Table 3c). There are significantly different outcomes with respect to cardiovascular disease and cancer when it comes to how we reach 100. For example, cardiovascular disease (i.e., congestive heart failure, myocardial infarction, high blood pressure, peripheral vascular disease, stroke, transient ischemic attack (TIA), or any other heart problems) has a more even distribution across the three avenues, while centenarians with cancer are mostly escapers (73%). Both categories, cardiovascular disease and cancer, aggregate across 8 or more distinct forms of cardiovascular disease or cancer.

We compared the avenues to 100 in the New England Centenarian Study (NECS) and GCS. These two studies differ in population, sampling methods, and chronic disease categories. Despite these differences, the NECS [4] percentage of survivors, delayers, and escapers is 38, 42, and 19%, respectively in Table 3a, which is similar (not significantly different by an exact test [14] in Table 3a) to the corresponding percentages in the GCS of 43, 36, and 17%, respectively. Matching to the NECS chronic disease, selection did not change this outcome (Table 3b). When all chronic diseases in Figure 1(b) are considered, the fraction
Figure 2: The factors of cardiovascular disease (a), cancer (b), pneumonia (c), psychiatric disorders (d), and living arrangement (e) determine the fraction of survivors, delayers, and escapers [4] among centenarians. The observed (in blue) and expected proportions (in red) track each other in that the logistic multinomial model well predicts the outcome of a being a survivor (S), delayer (D), or escaper (E) [4]. In panels (a)–(e), a square indicates the presence of a disease and a circle, the absence of a disease. (f). Centenarians were higher (with mean of 3.21 and standard deviation of 2.56) on the Geriatric Depression Scale (GDS) [6] than the control group of octogenarians (with mean of 2.13 and standard deviation of 2.62). The proportion (15.5%) of centenarians with GDS from 6–15 is significantly different from that proportion (4.6%) in octogenarians ($Z = 3.13, P < .001$).
of escapers is relatively small among centenarians (17–24% in Table 3). This percentage is also very similar to a Danish nearly complete longitudinal, 1905 birth cohort study of successful aging in 40,000 Danes with 19% escapers [16].

Based on these survivorship outcomes and their apparent stability across three studies, we can make predictions about the cohort beginning in the year 2060. To do so we add one more category, the attritor, who never survives to be a centenarian. For the original cohort yielding the GCS participants (97) were all of these distal variables available. The number of major life events was significant (P < .014) in a stepwise fitting procedure to predict a centenarian's outcome as survivor, delay, or escaper (see Materials and Methods). Goodness of fit remained adequate with the addition of this distal variable (Pearson \( \chi^2 = 75.9 \) with \( df = 90 \)). The Cox and Snell pseudo-\( R^2 \) increased to 0.51 with this one additional independent variable, indicating distal variables do help to predict survival outcome.

**What chronic diseases will we need to cope with?** Individuals in the GCS were characterized by their history of chronic diseases based on medical histories and an extensive battery of psychosocial tests. The positive associations (edges) between the 11 most frequent chronic diseases (nodes) of centenarians are graphically rendered by multidimensional scaling and network software [9, 10] (Figure 1(b)). There appear to be two clusters of chronic diseases: one resembles a multicausal cluster having such common causes/determinants as smoking, imbalanced nutrition, sedentary lifestyle, and includes cardiovascular disease, pneumonia, osteoporosis, anemia, and cancer; and a second cluster including dementia, psychiatric disorders, and neurological disorders. Those diseases that are connected are significantly associated by an exact test [14] (\( \alpha = 0.05 \)) of diseases X and Y, in which centenarians are classified by disease status for diseases X and Y in a 2 × 2 table. The two clusters were independently generated by clustering using average linkage [11] (Figure 1(c)).

The fact that dementia does not correlate with cardiovascular disease may at first sight seem surprising. This is, however, not the first time this observation has been made. In the Nun study [23], dementia did not necessarily correlate
Table 5: Lifetime Prevalence of chronic diseases among centenarians in the GCS.

| Chronic Disease | Male (%) | Female (%) | Pooled over sexes (%) | Number of centenarians |
|-----------------|----------|------------|-----------------------|------------------------|
| cardiovascular  | 27 (73)  | 169 (82)  | 196 (80)              | 244                    |
| dementia        | 15 (41)  | 121 (60)* | 136 (57)              | 240*                   |
| pneumonia       | 15 (43)  | 90 (43)   | 105 (43)              | 244                    |
| cancer          | 14 (38)  | 59 (29)   | 73 (30)               | 244                    |
| osteoporosis    | 1 (3)    | 58 (28)** | 59 (24)               | 244                    |
| psychiatric     | 2 (5)    | 45 (22)*  | 47 (19)               | 244                    |
| anemia          | 5 (14)   | 37 (18)   | 42 (17)               | 244                    |
| diabetes        | 3 (8)    | 18 (9)    | 21 (9)                | 244                    |
| kidney          | 7 (19)   | 11 (5)**  | 18 (7)                | 244                    |
| neurological    | 4 (11)   | 11 (5)    | 15 (6)                | 244                    |
| COPD            | 2 (5)    | 2 (1)     | 4 (2)                 | 244                    |

*P < .05 by Fisher’s Exact Test of disease associated with sex [19]; **P < .01 by Fisher’s Exact Test of disease associated with sex [19]; ***P < .001 by Fisher’s Exact test of disease associated with sex [19].

Four centenarians had missing data.

Distal influences | Proximal influences | Developmental outcomes

Parent’s education

Education

Proximal stress

Health and survivorship outcome

Cumulative life events

Individual and social resources

A summary of the prevalent chronic diseases among centenarians is summarized in Table 5. Cardiovascular disease and dementia are the most prevalent chronic diseases among centenarians. For some conditions, such as osteoporosis, dementia, and psychiatric disorders, the prevalence differs significantly between the sexes.

When will we experience a chronic disease? For centenarians, the development of chronic diseases varies by type. It is clear from Figure 1(d) that the prevalence of dementia rises sharply between the ninth and eleventh decade of life. A similar question is addressed about age of onset for cancers and cardiovascular disease among centenarians in Table 4b. Cancers (with the exception of skin cancers) tend to have early onset in the eighth decade (seventies) of life, and as a consequence we saw no difference in their frequency between octogenarians and centenarians (Table 4b). In contrast, cardiovascular disease has a later onset in the ninth decade of life in GCS (Table 4a). This presents a puzzle for why there is no difference in proportions between centenarians and octogenarians in cardiovascular disease (Table 4b). To correct for right censoring and to address this puzzle, we performed a separate Cox-regression analysis [17] on age at onset for cancer and cardiovascular disease as a function of the covariates used in the multinomial response modeling with race being a significant factor in a stepwise Cox-regression analysis of cancer age at onset. The effect of the Cox regression was to shift the estimated means of cancer and cardiovascular disease earlier to 60 and 77 years with neuropathology. There are in fact at least two forms of dementia, Alzheimer’s disease and vascular dementia [24] with the latter being much less prevalent and correlated with vascular disease. In centenarians, only 12% of the cases of dementia were reported as vascular dementia [25]. The low prevalence of vascular dementia could be one explanation for the lack of correlation with dementia as scored by the GDRS in Figure 1(d), which does not distinguish the two forms of dementia. As discussed in the next section, cancer and cardiovascular disease have an earlier presentation than dementia. It is possible that other factors, such as coping mechanisms with stress and lifestyle (Figure 3), can also intervene to affect dementia status at 80 years of age and beyond and weaken the association further.

In some cases, the chronic condition reported in medical histories could be independently validated. For example, diabetes can be independently validated by glycated Hemoglobin (HbA1C) levels (a cutoff >7% is indicative of diabetes), and a declaration of diabetes by HbA1C levels is highly associated with reports from medical histories by Fisher’s Exact test in both centenarians and octogenarians (P < .005). As a second example hemoglobin (Hb) levels (in grams/deciliter or g/dL) were determined on centenarians and octogenarians. When GCS participants are classified as anemic using a cutoff of 12 g/dL in females and 13 g/dL in males, an exact test of association between these two classifications of GCS participants for anemia is P = .05. There is underreporting of anemia from medical histories relative to anemia defined from participant Hb levels.

Figure 3: Developmental Adaptation: The influence of distal variables (e.g., cumulative life events, parents’ education, education, and childhood health) on adaptational outcomes in very late life.
of age, respectively. The earlier mean onset corrected for right censoring then explains why in Table 4b there is no difference in lifetime prevalence of cardiovascular disease between octogenarians and centenarians. In that GCS is a cross-sectional study, there is a need to validate this temporal pattern of barriers to successful aging being cancer and then cardiovascular disease in cohort studies [16, 18].

In summary, our data show that there are 11 chronic diseases that centenarians are likely to experience late in life. These diseases fall into two morbidity clusters, one involving diseases as cardiovascular disease, cancer, anemia, and osteoporosis, and another cluster associated with dementia. These chronic diseases pose three major barriers to successful aging. In their sixties centenarians are at risk for cancer. In their seventies they are at risk for cardiovascular disease. In their eighties and beyond they are at risk for dementia. Approximately half (43%) of the centenarians did not experience dementia. Approximately 17% of the GCS centenarians escaped chronic disease till near the end of their life, while 36% delayed the onset into the 80’s and 90’s and 43% survived chronic diseases acquired earlier in life (<80 years of age). These proportions of escapers, delayers, and survivors serve as predictions for the 2060 cohort with median life expectancy of 100 in this population. The caveats on such a prediction include no cohort effects (i.e., war, disease, major health advance, or changes in the predictors in Figure 2) beyond those leading to the increase in life expectancy of 2.5 years per decade. With the exception of dementia, mental health status did not differ between centenarians and octogenarians, although levels of depressive symptomatology appeared to be higher on the GDS scale in centenarians than octogenarians. Consistent with our model of developmental adaptation [22] (Figure 3), distal life events contribute to predicting survivorship outcome. The morbidity classification put forth by the NECS [4] and current health status are critical adaptation variables in very late life.

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Authors Contributions

J. Arnold contributed to study design, analysis and interpretation, wrote the paper, and contributed to overall design of the study. S. M. Jazwinski contributed to study design, framed some of the questions addressed in this paper, advised on data collection, analysis, and interpretation. W. L. Rodgers developed and supervised the study sampling design. J. Dai developed software for study design and data analysis. A. Davey, I. C. Siegler, and L. W. Poon developed measures from the demographic and medical histories. A. K. and L. Nahapetyan carried out data analysis. M. A. Johnson and D. Hausman collected blood chemistry data in particular and supervised questionnaire collection in general. R. Hensley, P. Martin, and M. MacDonald formulated a study and collected data on distal variables, such as education, affecting health of centenarians. L. W. Poon led the design of the study, supervised the study, supervised data collection, advised on data analysis and interpretation, and supervised the design and analysis of cognitive measures employed.

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