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Dementia-Free Survival Among Centenarians: An Evidence-Based Review

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Background. The 2000 U.S. census identified 50,454 Americans older than 100 years (18 per 100,000). Increased longevity is only of benefit if accompanied by the maintenance of physical, social, and cognitive function into advanced age. The goal of this review was to identify research describing centenarians to find the prevalence of dementia-free survival.

Methods. We reviewed 650 publications to find studies that described the prevalence of dementia in centenarians, were community-based, had data that were specific to persons older than 100 years, and were published in peer-reviewed journals. For each study, we identified the prevalence of dementia, the completeness of the sample, the number of study participants, the method used to diagnose dementia, and the duration of the study.

Results. We identified 20 research groups from 14 countries with publications meeting our search criteria. The studies showed substantial variation in methods of assessing cognitive status, assuring a complete cohort, and sample size. Few studies reported longitudinal data or attempted diagnosis of the cause of dementia. The prevalence of dementia-free survival past 100 years of age varied between 0 and 50 percent.

Conclusions. The methodology used in studies regarding dementia prevalence among centenarians is sufficiently varied that combination of existing studies into a meta-analysis is not possible. Suggestions for assuring quality in future centenarian research are presented.

ALTHOUGH dementia and other disability may come to all of us if we live long enough, even very frail centenarians are often found to be healthy into their 90s (1–4). For this reason, centenarians provide models for healthy aging (4,5), and centenarian studies can guide provision of care for an aging population.

Meta-analyses of current data regarding elderly persons between the ages of 65 and 90 indicate that the rate at which new cases of dementia occur doubles every 5 years after the age of 65. For example, new cases of dementia occur in about 6% of persons in their 85th year and 12% in their 90th, with prevalence rates of 25 and 35 percent (6–9). In this article we critically review studies about the prevalence of dementia in the centenarian age group to see if a meta-analysis could show if dementia incidence and prevalence continue to increase in this age group. We also seek to identify factors that would improve the quality of future studies of centenarians.

Methods

We searched Medline and other data bases to identify studies describing centenarians. Key words used included ''centenarians,'' ''nonagenarians,'' ''prevalence,'' ''dementia,'' and ''epidemiology.'' We reviewed the citations in articles from the computerized searches to identify older studies, and sought the advice of experts to find more studies. This strategy identified 650 publications. We reviewed these publications to identify studies regarding the prevalence of dementia among centenarians. To be included, studies had to be community-based, contain prevalence data for dementia in persons older than 100 years, and be published in peer-reviewed journals. After a community-based study had been identified, every effort was made to find all articles related to the study. The studies were then rated [on the basis of accepted criteria for studies involving prognosis (10)] by two of the authors (JC and JHR) on six quality indicators as shown in Tables 1 and 2. The studies regarding the prevalence of dementia in centenarians are summarized in Table 3 (11–39).

Results

We identified 20 studies from 14 countries that met our search criteria. Other centenarian studies have indicated plans to study dementia prevalence data, but we were unable to find published results (40–42). Additional centenarian studies have not reported prevalence of dementia (43–46) or were not community-based (47), so they are not included in Table 3.

The likelihood of dementia-free survival after the age of 100 varied between 0% in smaller studies to as much as 50% in other studies (see Table 3). All the studies in Table 3 found more female than male centenarians, although in Sardinia (41,48) and among the Uygur people of China (44) the proportion of men is higher. The studies in Table 3 that reported gender data indicate that male centenarians are more likely to be intact cognitively than their female contemporaries, possibly because men tend to die more quickly after they become demented than women do

Table 1. Criteria Used to Evaluate Centenarian Studies

1. Validity: Did the study involve centenarians exclusively, and was a reliable method used to identify the centenarians in the region?
   (++) Total centenarian population for the study region was identified using an accurate database.
   (+) Unreliable database was used, but it only includes centenarians.
   (0) Data for centenarians cannot be separated from younger cohort data.
2. Inclusiveness: Was complete ascertainment achieved?
   (++) Eligible patients were accounted for, including those who died before being seen; reasons for exclusion were specified.
   (+) Most eligible participants were included in the study, but reasons for exclusion were not specified.
   (0) An attempt to account for all eligible participants was not made, or less than half of the eligible participants were included in the study.
3. Sample size: Was the sample large enough for generalizable conclusions?
   (++) Sample >100 centenarians
   (+) Sample 50–99 centenarians
   (0) Sample <50 centenarians
4. Sampling frequency: Were study participants followed longitudinally?
   (++) More than two determinations of cognitive status were made at different points in time for each participant.
   (+) At least two assessments were made.
   (0) Only one assessment was made.
5. Cognitive and functional assessment: Was dementia identified in a reliable, standardized manner?
   (++) The methods used to identify dementia were validated and widely accepted.
   (+) The method used to assess cognitive status was specified but not widely used enough to allow comparisons with other studies.
   (0) The method used to define cognitive status was not specified.
6. Diagnosis: Was an attempt made to identify the specific cause of dementia?
   (++) Each demented patient was evaluated by an accepted method to determine the cause of dementia.
   (+) Diagnosis was made, but the criteria were not specified or not applied to the whole cohort.
   (0) No attempt at diagnosis was made, only specified as dementia.

(20,49–51). Unfortunately, because of the variation in methodology used in different centenarian studies, no definitive conclusion regarding the likelihood of dementia-free survival past 100 years of age is possible.

Discussion

The small number of study participants in most of the studies in Table 3 suggests that meta-analysis, which has been used to determine the prevalence and incidence of dementia for younger age groups (5–9) could be used to combine data from the studies in Table 3. However, the inconsistency in methods in the centenarian studies in Table 3 makes meta-analysis inappropriate. The definition of dementia is not consistent from study to study. The method used to assess patients also varies; studies have shown that very elderly persons may appear intact when one method of assessment is used, but impaired when other scales are used (52). Sampling methods vary as well; some studies have convenience samples, whereas others make an effort to get a complete population sample (Table 2). The rest of the discussion follows the six criteria from Table 1.

Table 2. Scoring for Studies in Table 3 Based on Criteria From Table 1

Principal Investigator (Ref.)	1 Validity	2 Inclusiveness	3 Sample Size	4 Sampling Frequency	5 Assessment	6 Diagnosis
Beregei (11)	1	+	++	0	0	0
Homma (12)	0	++	++	0	++	0
Heeren (13)	0	++	0	+	++	0
Robine (14)	0	0	++	0	+	0
Poon (15)	0	++	+	0	++	0
Wernicke (16,17)	0	++	0	+	+	0
Liverpool (18,19)	0	++	0	++	+	6
Ebly (20)	0	++	0	0	+	0
Sobel (21)	0	++	++	0	+	0
Asada (22)	0	++	0	0	+	0
Samuelson (23)	0	++	+	0	++	0
Blansjaar (24,25)	0	++	0	0	++	0
Ott (26)	0	++	0	+	++	0
Silver (27,28)	0	++	++	0	++	0
Franceschi (29–31)	0	+	++	0	+	0
Ravaglia (32)	0	++	+	0	++	0
Anderson-Ranberg (33,34)	++	2	++	0	++	0
Von Strauss (35,36)	0	++	0	0	++	0
Rott (37,38)	0	++	+	+	+	0
Choi (39)	0	+	+	0	++	0

Validity

As only 1 in 5500 persons in developed countries lives to the age of 100, large populations must be sampled to get an adequate number for research. Formal age verification of centenarians (e.g., birth records) further challenges the ascertainment of centenarians (53). All but one (18) of the studies in Table 3 used census data to identify centenarians. Census data may accurately identify the birth date of citizens but, because of the high mortality rate in this age group, many deceased persons are listed so the total number is often unreliable. Centenarians who live in long-term care facilities are accessible (47); however, they tend to be less functional than are those persons living independently, leading to an overestimation of the prevalence of impairment. In the community, centenarians who are more intact may be more likely to be willing to volunteer to be study participants, leading to underestimation of dementia prevalence. Several ''centenarian'' studies included persons 95–99 years old; we included those studies in Table 3 (13,16,26), but these studies cloud the picture because they do not provide centenarian-specific data.

Inclusiveness

A number of unique challenges lead to a high refusal rate when centenarians identified by census data are contacted. Elderly survivors tend to be socially isolated because their peer group is deceased. The principal social contact of

Table 3. Studies Assessing the Cognitive Status of the Oldest Old

Project Name (Ref.) Authors (Date, Setting)	Population	Tests Used	Results (Nondemented is CDR 0 or 0.5)
Hungarian Centenarian Study (11) (Beregei et al.) Hungary, 1989	123/218 centenarians identified by national census	Not specified	26% of men and 63% of women demented; total demented and *N* for gender not specified
Japan Centenarian Study (12) (Homma et al.) Japan, 1990	218/509 (43%) of centenarians in Tokyo consented to be interviewed, no data on 12, total = 206	CDR scale, Hasegawa Dementia Scale	67% (137/206) demented, 48% (27/56) of men and 73% (110/150) of women
Dutch Aging Study (Heeren et al.) (13) The Netherlands, 1991	Of 1259 persons >85 y in Leiden, 28 were >95 y	Screened with MMSE: if <24, GMS and MBPC and CDR	100% (28/28) at least mildly demented (tables in article inconsistent)
French Centenarian Study (14) (Robine et al.) France, 1991	756/3800 centenarians identified by French census	PSPMSQ	62% of 756 demented; 65% (431/663) of women and 42% (39/93) of men
Georgia Centenarian Study (15) (Poon et al.) Unites States, 1992	84 persons >100 years, 23 males	WAIS, various memory tests, MMSE	Some not demented, specific numbers not given
Berlin Aging Study (16,17) (Wernicke et al.) Germany, 1994	26 persons ≥95	GMS-A2 DSM-III	42% (11/26) demented; 6 women and 5 men; totals not given for gender
Liverpool MRC-ALPHA study (18,19) (Saunders et al.) England, 1992	15/5222 elderly persons from records of general practitioners, followed every 2 years until death	MMSE and AGECAT	47% (7/15) demented; 0/1 men, 7/14 women
Canadian Study of Health and Aging (CSHA; 20) (Ebly et al.) Canada, 1994	13/2800 persons >85 y, national random sample	3MS score	85% (11/13) demented; gender data not given
Finnish Centenarian Study (21) (Sobel et al.) Finland, 1995	Census data used to find 271 centenarians; 179 examined fully; 86 died before being seen	DSM-III clinical criteria and PSPMSQ	33% (59/179) demented, 18% (5/28) of men and 36% (54/151) of women (authors excluded mild dementia)
Yamanashi prefecture study (22) (Asada et al.) Japan, 1996	47/50 persons >100 y in Yamanashi prefecture; 8 were men; 3 died before being seen	ADLs, Hasegawa Dementia Scale, personal interview	70% (33/47) demented; gender data not given
Swedish Centenarian Study (23) (Sameulsson et al.) Sweden, 1997	98/143 eligible persons agreed to be studied on 100th birthday	DSM-III-Revised, WAIS, other functional and memory tests	73% (72/98) demented; 56% (10/18) of men and 80% (65/82) of women
Dutch Centenarian study (24,25) (Blansjaar et al.) The Netherlands, 1998–2000	1998: 9 (1 male) 2000: 17 (2 males) examined; participants were described in detail	IQCODE, ADS-3, CDT, Proverbs	1998: All 9 demented 2000: 100% (17/17) demented, 2/17 mildly demented
Rotterdam Study (26) (Ott et al.) Holland, 1998	24 persons >95 y had both baseline and follow-up testing 3 y later	Screened with MMSE and GMS-A; if MMSE < 26, CAMDEX and neurologic assessment	3/21 women and 0/9 men developed dementia; baseline prevalence not stated
New England Centenarian Study (27,28) (Silver et al.) United States, 1994–present	1998: 69 centenarians studied 2001: 36/43 studied; 31 women	CDR, MMSE, Boston Naming, MDRS, CERAD battery	1998: 80% (55/69) demented; no gender data 2001: 68% (23/34) demented; no gender data
Italian Multicenter Study on Centenarians (29–31) (Franchesci et al.) Italy, 2000–2005	382/1162 Italian centenarians, random sample	If MMSE, score < 5, proxy used; CDT used also; 3 outcome levels: A: Healthy B: Indeterminate C: Unhealthy	Group A: 22% (85/382), 19% (58/303) of women, 34% (27/79) of men Group B: 30% (113/382), 30% (92/303) of women, 27% (21/79) of men Group C: 41% (159/382), 46% (139/303) of women, 26% (20/79) of men (some of group C not demented) Not grouped 7%: 14 women, 11 men
Northern Italian Centenarian Study (32) (Ravaglia et al.) Italy, 1999	92/154 centenarians identified by census data	ADL assessment, MMSE, CDR scale used	62% (57/92) demented, 50% (18/36) of men and 70% (39/56) of women

Table 3. Studies Assessing the Cognitive Status of the Oldest Old (*Continued*)

Project Name (Ref.) Authors (Date, Setting)	Population	Tests Used	Results (Nondemented is CDR 0 or 0.5)
''Longitudinal Study of Danish Centenarians (LSDC)'' (33,34) (Anderson-Ranberg et al.) Denmark, 1999	207/276 persons who turned 100 over a 1-year period; 78% (162) women	CDR, MMSE, ADL	51% (105) were demented; no gender data
Kungsholmen Project (35,36) (von Strauss et al.) Sweden, 2000	94/145 persons >95 y; 8 were centenarians, data not given separately	MMSE; detailed clinical interviews, neuropsychological battery	48% (45/94) had CDR of 2 or 3; 30% (3/10) of men and 50% (42/84) of women
Heidelberg Centenarian Study (37,38) (Rott C et al.) Germany, 2001	91/156 (58%) of centenarians studied; in a follow-up visit 18 months later 36 were studied, 54% (49/91) had died	MMSE GDS	71% (65/91) were demented at the first visit and 75% (31/41) at second visit; gender data not given
Korean Centenarian Study (39) (Choi et al.) Korea, 1999	89/103 centenarians identified from census data	CDR	62% (55/89) demented, 46% (5/11) of men and 64% (50/78) of women

Notes: The Dutch Aging Study (10), Berlin Aging Study (16,17), Rotterdam Study (26), and Kungsholmen Project (35,36) did not separate data regarding data from 90- to 99-year-old participants from centenarian data. For the totals in the ''Results'' column, we used a Clinical Dementia Rating (CDR) scale score of ≥ 1 to define dementia when possible; some authors used a different cutoff in their publications or did not use the CDR scale.

AGECAT = Automatic Geriatric Examination for Computer Assisted Taxonomy; GMS = Geriatric Mental State Schedule; MMSE = Mini-Mental State Examination; MBPC = Memory and Behavior Problem Checklist; CAMDEX = Cambridge Examination for Mental Disorders in the Elderly; MDRS = Mattis Dementia Rating Scale; GDS = Global Deterioration Score; PSPMSQ = Pfeiffer's Short Portable Mental Status Questionnaire; BRMC = Blessed Roth Memory-Concentration Test; CDT = Clock Drawing Test; DSM-III = Diagnostic and Statistical Manual of Mental Disorders, Third Edition; 3MS = Modified Mini-Mental Status Examination; ADLs = Activities of Daily Living; WAIS = Wechsler Adult Intelligence Test; IQCODE = Informant Questionnaire on Cognitive Decline in the Elderly; ADS-3 = Amsterdam Dementia Screening Text; CERAD = Consortium to Establish a Registry of Alzheimer Disease.

centenarians is typically a child or other relative who is protective of ''their'' centenarian. They may view participation as too demanding of a frail elderly persons (54). Elderly persons are generally not attracted by any personal health benefits that might result from participation in medical research, although the idea of ''being useful to someone'' may motivate them to volunteer to be a research participant (55).

The high mortality rate among very old persons can also affect research results; deaths which occur during the study period can lead to an underestimation of dementia rates because impaired participants may die before they can be assessed. Longitudinal studies indicate that the interval between the onset of dementia and death shortens with increasing age. This means that populations that survive into extreme old age might be expected to have a lower prevalence of dementia, because demented centenarians tend to die after the onset of dementia with less delay than do younger cohorts (2,4,56).

Another limitation of the studies in Table 3 is that most took place in industrialized nations among urban populations. Little research about centenarians in developing countries has been done. Sample sizes for minorities and other special populations are generally small in centenarian studies, so distinctions between these and the majority population are not possible. Rural areas may contain a higher proportion of elderly persons than metropolitan areas (54), but the rural elderly population is underrepresented in research (1), and most published studies include few rural centenarians.

Perhaps because of the reasons cited above, many studies use information obtained from proxies rather than from the centenarians themselves. It is unclear whether information from proxies is more or less accurate than that obtained from the elderly participants themselves. The Heidelberg study group compared proxy and study participant interviews in a group of 85 centenarians and found that centenarians tended to overrate their Activities of Daily Living capability and that their self-ratings were highly mood-dependent (57). This finding occurs in younger elderly persons as well (58).

Sample Size

Sample size in the community-based studies in Table 3 varied from 13 to more than 700. The logistical difficulties outlined above and the time involved in performing a careful assessment of a centenarian are barriers to achieving adequate sample size. Small samples may limit the generalizability of prevalence estimates; however, smaller samples may allow a more thorough and accurate assessment.

Cognitive and Functional Assessment

Detailed cognitive assessment is not always performed in centenarian studies. Some of the studies in Table 3 used screening measures such as the Mini-Mental State Examination rather than more comprehensive tools. The Clinical Dementia Rating scale, which may vary in its administration and is difficult to use in field studies, was the most commonly used test. Although cognitive function is the most important driver of the final score, performing a Clinical Dementia Rating involves an assessment of Activities of Daily Living, physical health, and cognitive function, whereas other scales may provide only an assessment of mental status. However, physical health and cognitive function are closely interrelated in this age group, so it is

important to assess both (2,23). Failure to recognize the normal cognitive and physical changes in very old persons leads to an overestimation of the prevalence of dementia or physical impairment among centenarians (2). Similarly, special assessment scales and great patience are required to provide an accurate assessment of a motorically, visually, or hearing-impaired elderly person (33,55).

Need for Multiple Assessments

Increasing age is associated with increased variability on testing, so that studies that involve only one assessment of elderly persons tend to give a less accurate assessment than do those that involve multiple assessments over time. The increased mortality rate of about 50% annually in centenarians makes follow-up more difficult in this age group (37); another factor is the extended interview time needed because centenarians tire so easily. Few of the studies in Table 2 used longitudinal assessments. Some studies indicate that they are following patients longitudinally, but longitudinal data have not been published (27,32,40).

Diagnosis

Few of the studies in Table 3 tried to identify the specific cause of dementia. Existing data indicate that the majority of cases of dementia in younger age groups are due to Alzheimer dementia (8,20); however, the causes of cognitive decline in very old persons are not known. Diagnosis is a particularly challenging problem while study participants are alive, although criteria are available for clinical diagnosis of common causes of dementia (16). Even neuropathologic examination of brains after death, often considered the gold standard of diagnosis, may show evidence of more than one form of dementia or be inconclusive in other ways (59).

Conclusion

Current evidence does not provide robust estimates of the prevalence of dementia among centenarians because of inconsistency of the methods used in various studies. Application of consensus standards regarding the optimal assessment methods for centenarian research would improve our understanding of the dynamic demographics of the oldest old and provide direction for future research on the health of this important population.

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A more complete reference list is available on request from the authors.

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REFERENCES

1. Clayton GM, Dudley WN, Patterson WD, et al. The influence of rural/urban residence on health in the oldest-old. *Int J Aging Hum Dev*. 1994;38:65–89.
2. Hagberg B, Bauer Alfredson B, Poon LW, et al. Cognitive functioning in centenarians: a coordinated analysis of results from three countries. *J Gerontol Psychol Sci*. 2001;56B:P141–P151.
3. Thomae H. *Patterns of Aging: Findings from the Bonn Longitudinal Study of Aging*. New York: Karger; 1976.
4. Perls T, Levenson R, Regan M, et al. What does it take to live to 100? *Mech Ageing Dev*. 2002;123:231–242.
5. Ritchie K, Kildea D, Robine JM. The relationship between age and the prevalence of senile dementia: a meta-analysis of recent data. *Int J Epidemiol*. 1992;21:763–769.
6. Ankri J, Poupard M. Prevalence and incidence of dementia among the very old. Review of the literature. *Revue d Epidemiologie et de Sante Publique*. 2003;51:349–360.(Full text in English on www.e2med.com/resp)
7. Gao S, Hendrie HC, Hall KS, et al. The relationships between age, sex, and the incidence of dementia and Alzheimer disease: a meta-analysis. *Arch Gen Psychiatry*. 1998;55:809–815.
8. Jorm AF, Jolley D. The incidence of dementia: a meta-analysis. *Neurology*. 1998;51:728–733.
9. Fratiglioni L, Launer LJ, Andersen K, et al. Incidence of dementia and major subtypes in Europe: a collaborative study of population-based cohorts. Neurologic Diseases in the Elderly Research Group. *Neurology*. 2000;54(11 suppl 5):S10–S15.
10. Sackett DL. Haynes RB, Tugwell P: Making a prognosis. *In: Clinical Epidemiology: A Basic Science for Clinical Medicine*. Boston: Little, Brown and Company; 1981:159–169.
11. Beregi E, Klinger A. Health and living conditions of centenarians in Hungary. *Int Psychogeriatrics*. 1989;1:195–200.
12. Homma A, Nakazato K, Shimonaka Y. Centenarians in Japan: a gerontopsychiatric survey. In: Hasagawa K, Homma K, eds. *Psychogeriatrics: Biological and Social Advances*. Amsterdam, The Netherlands: Excerpta Medica; 1990:351–356.
13. Heeren T, Lagaay A, Hijmans W. Prevalence of dementia in the 'oldest old' of a Dutch community. *J Am Geriatr Soc*. 1991;39:755–759.
14. Robine JM, Romieu I, Allard M: Les centenaires français et leur état de santé fonctionel. *Presse Med*. 2003;32:360–364.
15. Martin P, Long MV, Poon LW. Age changes and differences in personality traits and states of the old and very old. *J Gerontol Psychol Sci*. 2002;57B:P144–P152.
16. Wernicke TF, Reischies FM. Prevalence of dementia in old age: clinical diagnoses in subjects aged 95 years and older. *Neurology*. 1994;44: 250–253.
17. Wernicke TF, Linden M, Gilberg R, et al. Ranges of psychiatric morbidity in the old and the very old–results from the Berlin Aging Study (BASE). *Eur Arch Psychiatry Clin Neurosci*. 2000;250:111–119.
18. Dewey ME, Copeland JR. Dementia in centenarians. *Int J Geriatr Psychiatry*. 2001;16:538–539.
19. Saunders PA, Copeland JR, Dewey ME, et al. The prevalence of dementia, depression and neurosis in later life: the Liverpool MRC-ALPHA Study. *Int J Epidemiol*. 1993;22:838–847.
20. Ebly EM, Parhad IM, Hogan DB, et al. Prevalence and types of dementia in the very old: results from the Canadian Study of Health and Aging. *Neurology*. 1994;44:1593–1600.
21. Sobel E, Louhija J, Sulkava R, et al. Lack of association of apolipoprotein E allele epsilon 4 with late-onset Alzheimer's disease among Finnish centenarians. *Neurology*. 1995;45:903–907.
22. Asada T, Yamagata Z, Kinoshita T, et al. Prevalence of dementia and distribution of ApoE alleles in Japanese centenarians: an almost-complete survey in Yamanashi Prefecture, Japan. *J Am Geriatr Soc*. 1996;44:151–155.
23. 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;45:223–253.
24. Thomassen R, van Schaick HW, Blansjaar BA. Prevalence of dementia over age 100 [see comment]. *Neurology*. 1998;50:283–286.
25. Blansjaar BA, Thomassen R, Van Schaick HW. Prevalence of dementia in centenarians. *Int J Geriatr Psychiatry*. 2000;15:219–225.
26. Ott A, Breteler MM, van Harskamp F, et al. Incidence and risk of dementia. The Rotterdam Study. *Am J Epidemiol*. 1998;147:574–580.
27. Silver M, Newell K, Hyman B, et al. Unraveling the mystery of cognitive changes in old age: correlation of neuropsychological evaluation with neuropathological findings in the extreme old. *Int Psychogeriatrics*. 1998;10:25–41.

28. Silver MH, Jilinskaia E, Perls TT. Cognitive functional status of age-confirmed centenarians in a population-based study. *J Gerontol Psychol Sci.* 2001;56B:P134–P140.
29. Franceschi C, Motta L, Valensin S, et al. Do men and women follow different trajectories to reach extreme longevity? Italian Multicenter Study on Centenarians (IMUSCE). *Aging Clin Exp Res.* 2000;12: 77–84.
30. Motta M, Bennati E, Ferlito L, et al. Successful aging in centenarians: myths and reality. *Arch Gerontol Geriatrics.* 2005;40:241–251.
31. Gueresi P, Troiano L, Minicuci N, et al. The MALVA (MAntova LongeVA) study: an investigation on people 98 years of age and over in a province of Northern Italy. *Exp Gerontol.* 2003;38:1189–1197.
32. Ravaglia G, Forti P, De Ronchi D, et al. Prevalence and severity of dementia among northern Italian centenarians. *Neurology.* 1999;53: 416–418.
33. Andersen-Ranberg K, Vasegaard L, Jeune B. Dementia is not inevitable: a population-based study of Danish centenarians. *J Gerontol Psychol Sci.* 2001;56B:P152–P159.
34. Andersen-Ranberg K, Schroll M, Jeune B. Healthy centenarians do not exist, but autonomous centenarians do: a population-based study of morbidity among Danish centenarians. *J Am Geriatr Soc.* 2001;49: 900–908.
35. von Strauss E, Viitanen M, De Ronchi D, et al. Aging and the occurrence of dementia: findings from a population-based cohort with a large sample of nonagenarians. *Arch Neurol.* 1999;56:587–592.
36. von Strauss E, Fratiglioni L, Viitanen M, et al. Morbidity and comorbidity in relation to functional status: a community-based study of the oldest old (90+ years). *J Am Geriatr Soc.* 2000;48:1462–1469.
37. Rott C, d'Heureuse V, Kliegel M, et al. [Heidelberg Centenarian Study: theoretical and methodological principles for social science research of the oldest old]. *Zeitschrift fur Gerontologie und Geriatrie.* 2001; 34:356–364.
38. Kliegel M, Sliwinski M. MMSE cross-domain variability predicts cognitive decline in centenarians. *Gerontology.* 2004;50:39–43.
39. Choi YH, Kim JH, Kim DK, et al. Distributions of ACE and APOE polymorphisms and their relations with dementia status in Korean centenarians. *J Gerontol Biol Sci Med Sci.* 2003;58A:227–231.
40. Sikora E. Studies on successful aging and longevity: Polish Centenarian Program. *Acta Biochimica Polonica.* 2000;47:487–489.
41. Deiana L, Ferrucci L, Pes GM, et al. AKEntAnnos. The Sardinia Study of Extreme Longevity. *Aging Clin Exp Res.* 1999;11:142–149.
42. Gonos ES, Agrafiotis D, Dontas AS, et al. Ageing research in Greece. *Exp Gerontol.* 2002;37:735–747.
43. Tanaka M, Takeyasu T, Fuku N, et al. Mitochondrial genome single nucleotide polymorphisms and their phenotypes in the Japanese. *Ann N Y Acad Sci.* 2004;1011:7–20.
44. Jumabay M, Ozawa Y, Kawamura H, et al. Ambulatory blood pressure monitoring in Uygur centenarians. *Circ J.* 2002;66:75–79.
45. Zheng ZX, Wang ZS, Zhu HM, et al. Survey of 160 centenarians in Shanghai. *Age Ageing.* 1993;22:16–19.
46. Atzmon G, Gabriely I, Greiner W, et al. Plasma HDL levels highly correlate with cognitive function in exceptional longevity. *J Gerontol Med Sci.* 2002;57A:M712–M715.
47. Fries BE, Morris JN, Skarupski KA, et al. Accelerated dysfunction among the very oldest-old in nursing homes. *J Gerontol Med Sci.* 2000;55A:M336–M341.
48. Poulain M, Pes GM, Grasland C, et al. Identification of a geographic area characterized by extreme longevity in the Sardinia island: the AKEA study. *Exp Gerontol.* 2004;39:1423–1429.
49. Passarino G, Calignano C, Vallone A, et al. Male/female ratio in centenarians: a possible role played by population genetic structure. *Exp Gerontol.* 2002;37:1283–1289.
50. Franceschi C, Bonafe M. Centenarians as a model for healthy aging. *Biochem Soc Trans.* 2003;31:457–461.
51. Perls T, Terry D. Understanding the determinants of exceptional longevity. *Ann Intern Med.* 2003;139(5 pt 2):445–449.
52. Pioggiosi P, Forti P, Ravaglia G, et al. Different classification systems yield different dementia occurrence among nonagenarians and centenarians. *Dement Geriatr Cogn Disord.* 2004;17:35–41.
53. Perls TT, Bochen K, Freeman M, et al. Validity of reported age and centenarian prevalence in New England. *Age Ageing.* 1999;28: 193–197.
54. Rosenthal TC, Fox C. Access to health care for the rural elderly. *JAMA.* 2000;284:2034–2036.
55. Leahy MJ, Thurber D, Calvert Jr JF. Benefits and challenges of research with the oldest old for participants and nurses. *Geriatr Nurs.* 2005;26:21–28.
56. Fries JF. Compression of morbidity in the elderly. *Vaccine.* 2000; 18:1584–1589.
57. Schonemann-Gieck P, Rott C, Martin M, et al. [Similarities and differences between self-rated and proxy-rated health in extreme old age]. *Zeitschrift fur Gerontologie und Geriatrie.* 2003;36: 429–436.
58. Magaziner J. Use of proxies to measure health functional outcomes in effectiveness research in persons with Alzheimer disease and related disorders. *Alzheimer Dis Assoc Disord.* 1997;(suppl 6): 168–174.
59. Snowdon DA, Nun S. Healthy aging and dementia: findings from the Nun Study. *Ann Intern Med.* 2003;139(5 pt 2):450–454.

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