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Centenarians – a useful model for healthy aging? A 29-year follow-up of hospitalizations among 40 000 Danes born in 1905

Henriette Engberg,[1] Anna Oksuzyan,[1,2] Bernard Jeune,[1] James W. Vaupel[2] and Kaare Christensen[1]

[1]The Danish Aging Research Center, Epidemiology Unit, Institute of Public Health, University of Southern Denmark, Odense, Denmark

[2]Max Planck Institute for Demographic Research, Rostock, Germany

Summary

Centenarians surpass the current human life expectancy with about 20–25 years. However, whether centenarians represent healthy aging still remains an open question. Previous studies have been hampered by a number of methodological shortcomings such as a cross-sectional design and lack of an appropriate control group. In a longitudinal population-based cohort, it was examined whether the centenarian phenotype may be a useful model for healthy aging. The study was based on a complete follow up of 39 945 individuals alive in the Danish 1905 birth cohort on January 1, 1977 identified through the Danish Civil Registration System (DCRS). Data from the Danish Demographic Database and The Danish National Patient Register (in existence since 1977) were used. The 1905 cohort was followed up from 1977 through 2004 with respect to hospitalizations and number of hospital days. Survival status was available until December 2006. Danish centenarians from the 1905 cohort were hospitalized substantially less than their shorter-lived contemporaries at the same point in time during the years 1977 through 2004. For example, at age 71–74, the proportion of nonhospitalized centenarians was 80.5% compared with 68.4% among individuals who died in their early 80s. This trend was evident in both sexes. As a result of their lower hospitalization rates and length of stay in hospital compared with their contemporaries, who died at younger ages, Danish centenarians represent healthy agers. Centenarians constitute a useful study population in the search for fixed traits associated with exceptional longevity, such as genotype.

Key words: centenarians; exceptional longevity; fixed traits; healthy aging; hospitalization.

Introduction

Centenarians surpass the current human life expectancy with about 20–25 years. This remarkable accomplishment has captured the attention of researchers for decades; what does it take to make it to 100? Are centenarians able to teach us how to stay healthy even in their very advanced age? And has the road to 100 been blessed with better health compared with contemporaries who died at much younger ages?

Rowe & Kahn (1998) defined the term 'successful aging' as 'avoidance of disease and disability; maintenance of high physical and cognitive function; and sustained engagement in social and productive activities'. Other definitions of successful aging are proposed, but at present no consensual definition has been established (Depp & Jeste, 2006). Because centenarians live at the extreme of the human lifespan, they may have reached very advanced age because of a unique capability to postpone disease and disability into their later years of life and as such represent healthy aging. In the past decade, several papers have dealt with the examination of the centenarian phenotype as a model for healthy aging (Hitt *et al.*, 1999; Andersen-Ranberg *et al.*, 2001; Franceschi & Bonafe, 2003; Bernstein *et al.*, 2004; Andersen *et al.*, 2005; Berzlanovich *et al.*, 2005; Motta *et al.*, 2005; Gondo *et al.*, 2006).

The interest in centenarians as a model for healthy aging is driven by the desire to identify key factors associated with exceptional longevity in humans. Centenarians may represent a unique study population in the search for fixed traits associated with exceptional longevity, for example genotype. The quest for the genetics of exceptional longevity has initiated large and multinational research programmes such as The EU-Integrated Project GEHA (GEnetics of Healthy Aging) (Franceschi *et al.*, 2007) and the Long Life Family Study (LLFS) initiated by the National Institute on Aging (NIA), USA (Long Life Family Study, 2008). However, whether centenarians, in fact, represent a useful model for healthy aging still remains a subject of debate (Martin, 2000; Jeune, 2002; Christensen *et al.*, 2006).

A number of methodological issues are pertinent to the investigation of centenarians as prototypes of healthy aging. Previous studies have all been based on cross-sectional surveys of centenarians (Beregi & Klinger, 1989; Poon *et al.*, 1992;

Correspondence
Professor Kaare Christensen, The Danish Aging Research Center, Institute of Public Health, University of Southern Denmark, J. B. Winsløwsvej 9B, 5000 Odense C, Denmark. Tel.: +45 6550 3049; fax: +45 6550 3682; e-mail: kchristensen@health.sdu.dk

The work was carried out at The Danish Aging Research Center, Institute of Public Health, University of Southern Denmark, J. B. Winsløwsvej 9B, 5000 Odense C, Denmark.

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Louhija *et al.*, 1994; Candore *et al.*, 1997; Samuelsson *et al.*, 1997; Allard, 1998; Andersen-Ranberg *et al.*, 1999, 2001; Perls *et al.*, 1999; Motta *et al.*, 2005; Selim *et al.*, 2005; Gondo *et al.*, 2006; Ozaki *et al.*, 2007; Willcox *et al.*, 2007; Darviri *et al.*, 2008; Martin *et al.*, 2008). Some use retrospective data collection to estimate the level of morbidity and disability before the respondents' 100th birthday (Hitt *et al.*, 1999; Andersen-Ranberg *et al.*, 2001; Willcox *et al.*, 2007) and others compare centenarians with younger age groups (Candore *et al.*, 1997; Andersen-Ranberg *et al.*, 1999; Selim *et al.*, 2005; Martin *et al.*, 2008). A few of these studies indicate that centenarians have been healthy or well functioning throughout most of their lives (Samuelsson *et al.*, 1997; Hitt *et al.*, 1999; Willcox *et al.*, 2007; Darviri *et al.*, 2008). Key issues are the risk of high attrition rates and difficulties in identifying and locating every potential respondent for a survey (Hitt *et al.*, 1999; Ozaki *et al.*, 2007; Darviri *et al.*, 2008), potentially leading to a selected study population. Age validation is crucial to the correct reports of centenarian prevalence (Jeune & Vaupel, 1999). Ideally, to avoid cohort effects, centenarians should be compared with members of their own birth cohort. Moreover, the trajectories of healthy aging are most preferably studied in a longitudinal framework, where information on relevant markers of aging processes is collected prospectively. Finally, a follow-up study requires a well-defined study population and careful ascertainment of each participant to minimize the risk of selection bias.

In the present study, we examined whether centenarians represent a useful model for healthy aging by following the complete Danish 1905 birth cohort from 1977, when there were 40 355 individuals alive in the cohort, until 2005 regarding hospitalizations and length of stay in hospital. We showed that centenarians in their 70s and 80s were hospitalized substantially less than their shorter-lived contemporaries.

Methods

In Denmark, every citizen is listed in the Civil Registration System (CRS) by his/her unique civil person registration number (CPR number). The CPR number identifies each individual, and through Statistics Denmark, it can be linked to several sociodemographic and health related registries. We used information from the Danish Demographic Database and the Danish National Patient Registry. Since 1977, when the register was established, every hospital admission and length of stay in hospital has been recorded and linked to each individual CPR number.

Study population

The study was based on the entire Danish 1905 birth cohort identified through the CRS. All individuals alive and living in Denmark on January 1, 1977 were included in the study, i.e. a total of 40 355 people aged 71–72 years. Individuals who permanently (n = 193) migrated from Denmark during the period April 1, 1968, through January 1, 2003, were excluded from the study population. In addition, individuals who temporarily (n = 217) migrated from Denmark during the period before or after January 1, 1977, and returned some time between 1977 and 2003, were excluded from the study population. Thus, the study population consisted of 39 945 individuals, and of these 22 264 were women and 17 681 men. The 1905 cohort was followed up from 1977 through 2004 concerning hospitalizations and number of hospital days.

Measures

Vital statistics data

Information on the date of birth and the date of death was retrieved for every person in the cohort until December 2006. The cohort was then divided into 5-year-age groups, except for the first and the last one, according to age at death. The age groups were 71–74, 75–79, 80–84, 85–89, 90–94, 95–99, 100+ years of age.

Hospitalization

Denmark has a free healthcare system, and the Danish National Patient Registry contains information about somatic hospitalizations, the number of hospital days and diagnoses for each individual admitted to a hospital in Denmark (Andersen *et al.*, 1999). Information on hospitalization was available during the period January 1, 1977, through December 31, 2004, for every individual included in the study. Hospitalization was a binary variable indicating whether or not the participant had been hospitalized, and only inpatients qualified as hospitalized individuals. Except from the ICD-8 Y00-Y96 diagnoses (general medical examination or observation of different organ systems or in relation to child birth and pregnancy), and the ICD-10 Z00-Z99 diagnoses (factors influencing health status and contact with health services) and U00-U99 diagnoses (codes for special purposes such as SARS or contact with bacterial agents resistant to antibiotics), all hospital admissions were included in the study.

Length of stay in hospital was calculated as the mean number of hospital days per individual per year during the period 1977 through 2004. The information on length of stay in hospital was grouped according to the age at death and age at hospitalization for each individual. If the period of stay in hospital included the turn of the year, the number of hospital days was divided according to the corresponding year. The mean number of hospital days was calculated for the total sample and for hospitalized individuals only.

Results

Individuals who died as nonagenarians and centenarians had the lowest level of hospitalization at all time points compared with their shorter-lived contemporaries (Table 1) (columns). In

Table 1 Proportion of nonhospitalized individuals (%) by age period (years) and age at death (years) in the 1905 Cohort†

		Not hospitalized at age:					
Age at death	*N*	71–74	75–79	80–84	85–89	90–94	95–99
Total sample – men and women (*n* = 39 945)							
71–74	5484	19.1					
75–79	9012	57.2	13.7				
80–84	9494	68.4	41.3	14.4			
85–89	8506	74.9	53.1	35.7	20.1		
90–94	5261	79.3	62.6	49.2	34.0	30.2	
95–99	1829	81.7	68.1	57.5	44.7	33.6	38.9
100+	359	80.5	68.8	60.2	52.4	45.4	43.5
Male subjects (*n* = 17 681)							
71–74	3247	20.1					
75–79	4873	56.6	13.9				
80–84	4346	67.8	41.3	13.1			
85–89	3221	74.2	53.2	36.3	18.1		
90–94	1544	79.0	63.9	50.6	35.6	27.1	
95–99	400	78.3	63.0	59.8	46.3	35.8	33.8
100+	50	76.0	64.0	52.0	60.0	40.0	30.0
Female subjects (*n* = 22 264)							
71–74	2237	17.7					
75–79	4139	57.9	13.6				
80–84	5148	69.0	41.2	15.5			
85–89	5285	75.3	53.1	35.4	21.3		
90–94	3717	79.4	62.1	48.6	33.3	31.5	
95–99	1429	82.6	69.6	56.8	44.3	33.0	40.3
100+	309	81.2	69.6	61.5	51.1	46.3	45.6

†Individuals with a migration status were excluded from the analysis (*n* = 410).

Table 2 Mean number of hospital days per individual per year by age at death (years) in the 1905 Cohort†

		Hospitalized at age:											
		71–74		75–79		80–84		85–89		90–94		95–99	
Age at death	*N*	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Total sample – men and women (*n* = 39 945)													
71–74	5484	17.2	0.3										
75–79	9012	5.5	0.1	15.1	0.2								
80–84	9494	3.1	0.1	5.6	0.1	14.0	0.2						
85–89	8506	2.0	0.1	3.2	0.1	5.5	0.1	11.5	0.2				
90–94	5261	1.4	0.1	2.1	0.1	3.1	0.1	5.1	0.1	7.2	0.2		
95–99	1829	1.3	0.1	1.3	0.1	1.7	0.1	2.9	0.1	3.8	0.2	4.8	0.2
100+	359	1.0	0.2	1.5	0.2	1.4	0.2	1.6	0.2	2.7	0.3	2.8	0.3
Male subjects (*n* = 17 681)													
71–74	3247	16.0	0.4										
75–79	4873	5.1	0.2	14.1	0.3								
80–84	4346	2.8	0.1	4.9	0.1	13.4	0.3						
85–89	3221	1.8	0.1	2.6	0.1	4.3	0.1	10.7	0.3				
90–94	1544	1.3	0.1	1.6	0.1	2.3	0.1	4.1	0.2	7.6	0.4		
95–99	400	1.6	0.3	1.3	0.2	1.1	0.1	1.9	0.2	2.7	0.2	4.8	0.4
100+	50	1.2	0.6	0.9	0.2	1.1	0.4	1.1	0.4	2.2	0.4	2.8	0.6
Female subjects (*n* = 22 264)													
71–74	2237	18.9	0.5										
75–79	4139	6.0	0.2	16.2	0.3								
80–84	5148	3.3	0.1	6.1	0.2	14.5	0.3						
85–89	5285	2.2	0.1	3.5	0.1	6.1	0.1	12.0	0.3				
90–94	3717	1.5	0.1	2.2	0.1	3.5	0.1	5.6	0.2	7.1	0.2		
95–99	1429	1.2	0.1	1.3	0.1	1.9	0.1	3.2	0.2	4.1	0.2	4.7	0.3
100+	309	1.0	0.2	1.6	0.2	1.5	0.2	1.7	0.2	2.7	0.3	2.7	0.3

†Individuals with a migration status were excluded from the analysis (*n* = 410).

Table 3 Proportion of individuals (%) with > 5 hospital days by age period (years) and age at death (years) in the 1905 Cohort†

		Hospitalized at age:					
Age at death	*N*	71–74	75–79	80–84	85–89	90–94	95–99
Total sample – men and women (*n* = 39 945)							
71–74	5484	59.2					
75–79	9012	26.9	60.1				
80–84	9494	17.1	29.3	57.6			
85–89	8506	12.3	18.4	30.2	50.3		
90–94	5261	9.3	12.4	18.2	29.4	35.8	
95–99	1829	7.6	7.7	10.3	17.1	23.6	26.5
100+	359	6.4	8.6	8.6	10.6	17.8	18.9

†Individuals with a migration status were excluded from the analysis (*n* = 410).

proximity to death, the proportion of nonhospitalized individuals decreased (rows). These trends were similar in both sexes. Twenty-eight (7.8%) of 359 centenarians had not been hospitalized from 71 years of age until age 100; of these 27 (8.7%) were women and one (2%) was a man.

Table 2 depicts the mean length of stay in hospital for the entire 1905 birth cohort, in total and stratified by sex. The mean number of hospital days per individual per year declined with increasing age at death in a dose–response fashion across all time periods (columns) and in both sexes. For example, at age 71–74, the length of stay in hospital declined from six hospital days per individual per year for women who died in their mid to late 70s to just 1 day for those who died as centenarians. The only exception in all age and death groups was for females at age 75–79 where later centenarians had a slightly higher mean number of hospital days compared to individuals dying in their late 90s. In proximity to death, the number of hospital days increased (rows), and also among those who died at advanced ages. However, with increasing age at death, the number of hospital days in the period prior to death declined (diagonal). These trends were similar for men and women. To examine the robustness of our analyses where all migrated people were excluded, we performed a sensitivity analysis including the temporarily migrated individuals (data not shown). However, no changes to the outcome of the study were observed.

Compared to birth cohort members, who died at younger ages, centenarians generally had the lowest proportion of individuals with more than five hospital days per period across all time periods (columns) (Table 3). In proximity to death, the proportion of individuals with more than five hospital days increased across all age groups (rows), and these trends were similar in both sexes (data not shown).

Focusing on the length of stay among hospitalized individuals, centenarians again had the lowest number of hospital days compared with shorter-lived members of the birth cohort (columns) (Table 4). For example, at age 71–74 among individuals who died in their late 70s, the mean number of hospital days per individual per year was 12.9 compared with 5.1 among centenarians. These trends were similar for men and women (data not shown). When the analyses were performed using the median instead of the mean, a similar pattern was observed in Table 4.

Discussion

Danish centenarians from the 1905 birth cohort compared with their shorter-lived contemporaries experienced fewer hospitalizations and fewer hospital days at the same point in time during the years 1977 through 2004, and this trend was evident in both sexes. Not only were centenarians less hospitalized than their shorter-lived contemporaries, they also spent fewer days in hospital. This may reflect two important aspects of the health of the oldest old: first, centenarians seem to be able to postpone critical disease into their later years of life, and second, the diseases and co-morbidities that centenarians incur may be less severe, or influence the individual to a lesser extent, compared with their contemporaries who died at younger ages.

In proximity to death, there was a gradient of increasing number of hospital days in both sexes across all ages. This is

Table 4 Mean number of hospital days per individual per year among hospitalized individuals by age at death (years) in the 1905 Cohort†

		Hospitalized at age:																	
		71–74			75–79			80–84			85–89			90–94			95–99		
Age at death	*N*	*n*	Mean	SE	*n*	Mean	SE	*n*	Mean	SE	*n*	Mean	SE	*n*	Mean	SE	*n*	Mean	SE
Total sample – men and women (*n* = 39 945)																			
71–74	5484	4434	21.3	0.4															
75–79	9012	3859	12.9	0.3	7773	17.5	0.3												
80–84	9494	2997	9.7	0.2	5577	9.5	0.2	8125	16.4	0.2									
85–89	8506	2137	8.0	0.3	3987	6.7	0.1	5467	8.5	0.1	6796	14.4	0.2						
90–94	5261	1090	6.9	0.2	1965	5.5	0.2	2673	6.2	0.2	3472	7.8	0.2	3672	10.4	0.2			
95–99	1829	335	6.9	0.5	583	4.1	0.2	778	4.1	0.2	1011	5.3	0.2	1215	5.7	0.2	1118	7.8	0.3
100+	359	70	5.1	0.7	112	4.8	0.5	143	3.6	0.4	171	3.4	0.3	196	4.9	0.4	203	4.9	0.4

†Individuals with a migration status were excluded from the analysis (*n* = 410).

consistent with a number of health economic studies that show that during the last year of life, healthcare expenditures markedly increase because of the high 'cost of dying' (Miller, 2001; Madsen *et al.*, 2002a,b). The mean number of hospital days prior to death decreased with higher age at death. This may on one hand indicate a fairly rapid decline in health before death in very old age, or on the other hand that the oldest old are less likely to be admitted to hospital, partly because of less aggressive medical care and treatment among the oldest-old population and the frequent use of long-term care facilities in this segment of the population (Lubitz & Riley, 1993; Perls & Wood, 1996; Levinsky *et al.*, 2001; Seshamani & Gray, 2004). Finally, the change may partly reflect change in hospital practice because, over the study period, the length of hospital admissions has been reduced substantially.

In the present study, only approximately 8% of centenarians had not been hospitalized in the age of 71 through 100 years. However, centenarians, compared with their shorter-lived contemporaries, were hospitalized substantially less at the same point in time, indicating a postponement of critical disease into later years of life. A previous study by Evert *et al.* (2003), based on retrospective methodology, characterizes centenarians according to three different morbidity profiles: survivors (age-associated disease before the age of 80 years), delayers (age-associated disease after the age of 80 years), and escapers (without common age-associated disease before 100 years of age). Of the 424 centenarians included in the study, 19% fit the escaper profile whereas 43% were delayers and 38% were survivors (Evert *et al.*, 2003). Our study suggests that only a smaller proportion of centenarians seem to escape critical disease measured as hospitalization throughout life.

The comparison between studies of morbidity profiles among the oldest old may, however, have certain constraints because the inclusion of different types and numbers of diagnoses, variations in definition of disease and different time frames, affect the prevalence estimates of morbidity. For example, in the present study, the relatively low prevalence of nonhospitalized centenarians during the 29-year period prior to their 100th birthday may arise because of the inclusion of practically all inpatient diagnoses. Had we included fewer diagnoses, a different prevalence estimate may have been evident.

A few of the earlier studies have indicated that centenarians may represent healthy aging (Hitt *et al.*, 1999; Willcox *et al.*, 2007). However, these studies were based on retrospective data collection and did not include any control group. The present study lends support to these previous studies on the basis of improved methodology. By using a longitudinal design and an entire birth cohort as our study population, we were able to compare the centenarians with their most appropriate controls, namely individuals belonging to their own birth cohort. Intra-cohort comparison eliminates cohort effects in health and healthcare utilization. For example, the improvements in healthcare technology and medical care and treatment over time may introduce bias in the comparison of individuals belonging to different birth cohorts.

The cohort was population based with only a small number of individuals migrating to and from Denmark during the period 1968 through 2003. A sensitivity analysis including the temporarily migrated individuals did not change the outcome of the study.

We used hospitalization and number of hospital days as markers of healthy aging. During the 29-year follow up, the Danish healthcare system has undergone considerable changes. First, the outpatient care and service have improved considerably, and as a consequence, this has in recent years led to fewer hospitalizations per patient and a higher proportion of medical care and treatment relocated to both the general practitioners (GPs) and to specialized medical care units (Ministry of Prevention and Health, 2007; The Danish National Board of Health, 2007). Second, the average number of hospital days per patient has decreased, possibly because of accelerated continuity of care, enhanced treatment methods and diagnostic procedures (Ministry of Prevention and Health, 2007). Third, over the 29-year follow-up period, the Danish healthcare system has moved towards an era of less agism, i.e. compared with 20 years ago, today it is not un-common for a nonagenarian to have a hip replacement or undergo major heart surgery. The above-mentioned reorganizations within the Danish healthcare system influence the pattern of hospitalization and the number of hospital days over time. However, the reorganizations largely work in the same direction, i.e. towards fewer hospitalizations and number of hospital days per patient in recent years, and because we compare the same cohort (1905) for the same calendar years, our analyses are not sensitive to these time trends.

The use of hospitalization and length of stay in hospital as markers of health is widely accepted, especially in a country like Denmark, which is well known for its social welfare system including free health insurance coverage for each citizen. The welfare system covers every individual, independent of income, social class and civil status. This makes Danish hospitalization data less confounded by for example socio-economic status than in most other settings. However, in using hospitalization as the only marker of health, the study may be too restrictive because hospitalization mainly reflects critical illness and disease. We cannot rule out that different trends may have been found if we would have had information for other aspects of health, for example GP visits and medication use.

In conclusion, our study showed that centenarians have been healthier than their contemporaries who died at younger ages. Within a longitudinal framework, we found a clear and consistent inverse relationship between being hospitalized and length of stay in hospital and age at death. Nonagenarians and centenarians had the lowest number of hospitalizations and hospital days at practically all time points during the 29-year follow up. This underscores the importance of centenarians as a unique subgroup of the population and supports the use of centenarians as a useful model for healthy aging

with respect to the identification of fixed traits associated with exceptional longevity, such as genotype.

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