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**Month of birth influences survival
up to age 105+:
first results from the age validation study
of German semi-supercentenarians**

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Month of Birth Influences Survival up to Age 105+.

First results from the age validation study of German semi-supercentenarians.

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Centenarian Data: What We Know, What We Think We Know

Abstract

Using data from Germany, we examine if month of birth influences survival up to age 105. Since age reporting at the highest ages is notoriously unreliable we draw on age-validated information from a huge age validation project of 1487 alleged German semi-supercentenarians aged 105+. We use month of birth as an exogenous indicator for seasonal changes in the environment around the time of birth. We find that the seasonal distribution of birth dates changes with age. For 925 age-validated semi-supercentenarians the seasonality is more pronounced than at the time of their births (1880-1900). Among the December-born the relative risk of survival from birth to age 105+ is 16 per cent higher than the average, among the June-born, 23 per cent lower. The month-of-birth pattern in the survival risks of the German semi-supercentenarians resembles closely the month-of-birth pattern in remaining life expectancy at age 50 in Denmark.

Introduction

Information about survival at the highest ages has only recently become available. Robine and Vaupel present evidence that supercentenarians emerged as late as in the mid-1960s. Since the mid-1970s their number increases regularly. (Robine & Vaupel 2001).

We know little about why a person reaches age 110 (supercentenarian) or 105 (semi-supercentenarian). A recent controversial article argues that the reduction in lifetime exposure to infectious disease and other sources of inflammation made an important contribution to the historical decline in old-age mortality (Finch & Crimmins 2004). The authors show a strong association between early-age mortality and subsequent mortality in the same cohort for cohorts born in Sweden since 1751. The fetal-origins hypothesis of adult disease (Barker et al. 1989) claims that nutrition of the mother during pregnancy or in the first year of life leads to physiological or metabolic programming of the newborn and substantially determines the occurrence of pathological phenomena later in life.

We know about the importance of improvements in sanitation, nutrition, income and medicine in the reduction of mortality at young and old ages. The question arises whether survival up to such extraordinary ages such as age 105 or higher is influenced by early life conditions in addition to all these factors. This study shows that among the many possible genetical and environmental factors also the very first period of life influences the chances of becoming a semi-supercentenarian.

Since age reporting at the highest ages is notoriously unreliable we use age-validated information from a large age validation project of German semi-supercentenarians aged 105+. In Germany the number of people aged 105+ tripled within the last 10 years (Maier & Scholz 2004). Despite this impressive increase the absolute number of people reaching such high age is still low – not only in Germany but also worldwide. An international research group, therefore, gathers information about semi-supercentenarians all over the world and combines this information in the International Database on Longevity (IDL, www.supercentenarians.org). Only age-validated individuals are included in the database. The database is intriguing because it will allow us to test theories of aging and mortality at extreme ages. The German data reported here are part of the IDL.

We use the month of birth as an exogenous indicator for seasonal changes in the environment around the time of birth. Month of birth is widely available for complete populations. Contrary to other measures of early life environment such as e.g. birthweight or

socioeconomic status of the parents it is free of selection bias because it is based on population data rather than on surveys. In addition, month of birth does not have any life course interpretation and the social differences which affect month of birth tend to reduce the effect on lifespan rather than to strengthen it (Doblhammer 2004).

Month of birth affects life expectancy at age 50 in various countries of the Northern and Southern Hemisphere (Doblhammer 2004). It has been used extensively in epidemiological research, particularly in the field of schizophrenia and other diseases of the nervous and mental system (for reviews see Davies et al. 2003, McGrath & Welham 1999, Torrey et al. 1997, Fossey & Shapiro 1992, Bradbury & Miller 1985). Evidence for a month-of-birth pattern has also been found for e.g. various types of cancer, for diseases of the circulatory system, diseases of the respiratory system and infectious disease (for a review of existing studies see Doblhammer 2004).

Using data from German semi-supercentenarians, we examine if month of birth predisposes individuals to survive up to age 105. We also compare the month-of-birth pattern in survival risk of German supercentenarians with the pattern that we previously found in life expectancy of the Danish population aged 50 and above (Doblhammer 2004, Doblhammer & Vaupel 2001).

Data

The seasonal distribution of births in Germany at the end of the 19th century is given in the series of statistical yearbooks for the German Empire (Statistik des Deutschen Reiches). For the time period 1881-1898, appr. 32,5 million births with a distinct seasonal pattern are reported.

The data about the semi-supercentenarians in Germany (ages 105+) come from the office of the German president. The data base from the presidential office contains a total of 1.487 eligible semi-supercentenarians who survived up to the years 1989-2002. The final number that entered into the age validation study was reduced by two test cases and 80 individuals, who were still 104 years old. 393 individuals were born outside the present German border and have not been age validated, yet. Of the 1348 individuals who were born within the borders of the German Empire (Deutsches Reich), 925 have been age validated by a special procedure, which in more detail is described later. They are born between the years 1881 and 1900 (Table 1). Only 87 individuals born within the present borders of Germany are not age-validated at this point in time. The main reasons why we failed to age validate them

are (1) the local registration office refused to cooperate, (2) the place of birth could not be identified because several places in Germany carry the same name, (3) the local registration office could not find an entry for the person in question.

The Danish data consist of a mortality follow-up of all Danes who were at least 50 years old on 1 April 1968. This is a total of 1,371,003 people, who were followed up to week 32 of 1998. The study excludes 1,994 people who were lost to the registry during the observation period. Among those who are included in the study, 86% (1,176,383 individuals) died before week 32 of 1998; 14% (192,626 individuals) were still alive at the end of the follow-up.

Methods

The test whether the seasonal distribution of birth dates among the semi-supercentenarians departs from the seasonal distribution of births in 1881-1898 is based on the χ^2 -goodness-of-fit test. Standardized residuals are calculated using $(n_i - e_i)/e_i^{1/2}$ where n_i stands for the observed number of birth dates among semi-supercentenarians in month i and e_i for the expected number of births in month i on the basis of the birth distribution for the years 1881-1898.

To estimate differences in survival according to the month of birth a method called Survival-Attributes Assay (Christensen et al. 2001) is applied. Let N_0 be the number of births. Let p_0 be the proportion of births with the fixed attribute month of birth. Let p_{105} be the proportion at age 105. Let s be the survival probability from age 0 to age 105 for the individuals who have the fixed attribute. Let S be the survival probability from age 0 to 105 for the entire cohort.

Then, because

$$p_0 N_0 s = N_{105} S p_{105}, \quad [1]$$

it follows that

$$s = S p_{105} / p_0. \quad [2]$$

Thus, the relative risk of surviving from birth to age 105 for people born in a specific month is the ratio of their observed proportions at birth and at age 105.

In Denmark both the risk population and the number of deaths are known, which means that it is possible to estimate remaining life expectancy at age 50 on the basis of life tables that were corrected for left truncation. This was achieved by calculating occurrence and

exposure matrices that take into account an individual's age on 1 April 1968. For example, a person who was 70 at the beginning of the study and who died at age 80 enters the exposures for ages 70 to 80 but is not included in the exposures for ages 50 to 69. The central age-specific death rate is based on the occurrence-exposure matrix. The corresponding life-table death rate is derived by means of the Greville Method (Greville 1943).

Age validation

The German age validation study is part of the International Database on Longevity project. The aim of the German study is to obtain complete and validated lists of German semi-supercentenarians. The age validation follows a distinct procedure. In a first step, the office of the German president was asked for a list of all known persons aged 105 and older who ever received a congratulatory letter from the German president on the occasion of their 105th or a higher birthday between 1989 and 2002. This list is probably exhaustive because the local registries are required by administrative order to report every person reaching the age of 105 in their municipality. The office of the German president is thus the only institution in Germany that holds centrally a complete list of all semi-supercentenarians. In a second step, the local registry office at the place of residence was asked for information about the vital status of the person and for the person's place of birth. In a third step the local registry office at the place of birth is asked for a document certifying the date and place of birth. A person is considered age validated if both the local registries at the place of residence and at the place of birth verify the date and place of birth.

Results

A distinct seasonal pattern exists in the seasonal birth distribution of the years 1881-1898 of the German Empire (Table 2). Births peak in March (+8,74%), reach a trough in June (7,91%) and a secondary peak in September (8,61%).

The seasonal distribution of birth dates changes with age and the seasonal fluctuations in the birth dates of semi-supercentenarians are more pronounced than at the time of their births (Figure1). The distribution of birth dates of semi-supercentenarians departs from the seasonal distribution of births in their birth years (eligible: χ^2 test statistic=18.98, df=11, p=0.06; validated: χ^2 test statistic=10.998, df=11, p=0.44).

Among the December-born validated semi-supercentenarians the relative risk of survival from birth to age 105+ is 16 per cent higher than the average, among the June-born, 23 per cent lower (Figure 2, Table 2). The month-of-birth pattern in the survival risks of the semi-supercentenarians in Germany is highly correlated (Spearman's rank-order correlation $\rho=0.80$, $p<.01$ for validated semi-supercentenarians; $\rho=0.77$, $p<.01$ for eligible semi-supercentenarians) with the respective pattern for Denmark, which shows the deviation in remaining life expectancy at age 50 by month of birth from the average life expectancy (Figure 2).

For June-born the value of the standardized residual is -2 (Table 2): under the assumption of normal distributed residuals this indicates a significant deviation from the expected value. Among the eligible semi-supercentenarians the standardized residuals for June and December indicate a significant deviation from the expected value.

Discussion

The results of this study show that the environment early in life influences the chances of an individual to survive up to the highest ages. We use month of birth as an exogenous indicator for seasonal changes in the environment at the time of birth. Based on the seasonal birth distribution of the semi-supercentenarians' birth cohorts and the seasonal distribution of the birth dates at ages 105+ we find that the June-born have a significantly lower risk of surviving up to age 105+ while the December-born have a higher risk. The month-of-birth pattern among supercentenarians is highly correlated with the pattern observed in remaining life expectancy at age 50 in Denmark.

Previous studies (Doblhammer 2004) showed that the month of birth pattern in life expectancy is not caused by socioeconomic confounding or an interaction between the seasonal distribution of deaths and the increasing mortality risk with age. The month of birth effect is indeed linked to the earliest period in life around the time of birth.

The month of birth pattern in Danish infant mortality at the beginning of the 20th century rules out the explanation that the lifespan pattern is caused by mortality selection (Doblhammer & Vaupel 2001). Mortality selection implies that among the fall-born only the more robust individuals would survive the first year of life, and would then have lower mortality later in life. Danish data on historical infant mortality between the years 1911 and 1915, however, show the contrary effect. June-born infants have a 30 percent higher death rate during the first year of life than the December-born. Selective survival can therefore not explain the month-of-birth pattern in life span.

The month-of-birth pattern in Danish infant mortality rather points to another explanation. For Denmark the correlation between infant mortality in the first year of life and adult mortality after age 50 is 0.87 and highly significant. This result indicates those factors that contributed to the high infant mortality of the past are also the factors that cause the differences in lifespan by month of birth.

Unfortunately, no data exist for the German Empire in the 19th century about infant mortality by month of birth. However, historical data for Belgium and New York (Huntington 1936) yield similar results, namely that the spring- and summer-born infants experience higher mortality during the first year of life than the fall- and winter-born.

Public health experts at the beginning of the 20th century considered mothers' health status and whether the mothers breastfed their babies as two important factors that were closely linked with the survival of the infants (Preston & Haines 1991, Kuh & Davey Smith 1993). The health status of pregnant women depends largely on their diet and on the general disease load. Breastfeeding the infant is primarily related to a lower incidence of infectious disease of the gastrointestinal tract, which historically is the major cause of infant mortality.

Both nutrition, particularly at the beginning of the 20th century, and infectious disease are highly seasonal. Peak growth of the fetus *in-utero* happens during the third trimester. For infants born in spring the third trimester coincides with a period of largely inadequate nutrition; for those born in fall, with a period of plenty.

The incidence of infectious disease depends on the climate and on the seasons of the year. The incidence of waterborne infectious disease, which mainly affects the gastrointestinal tract, is correlated with warmer temperatures and flooding. Peak climatological temperatures coincide with the incidence of foodborne diseases. Many childhood diseases are highly seasonal; airborne diseases that affect the respiratory tract usually peak in fall and winter.

The effect of nutrition of the mother during pregnancy on health of the child at adult ages is highly contested. Nutrition is considered to be the central causal mechanism in the fetal-origins hypothesis, which claims that inadequate nutrition of the mother during pregnancy leads to growth retardation *in-utero* and to an increased risk of heart disease later in life. A series of studies (for a review see Joseph & Kramer 1996) find a significant relationship between birth weight, an indicator of growth retardation in utero, and later life health outcomes. These findings, however, are inconsistent with the results from studies that look at old-age mortality of cohorts born shortly after periods of famine and that supposedly were affected by severe malnutrition of the mother during their gestational period (Kannisto et

al. 1997, Stanner et al. 1997, Rosenboom et al. 2001). Generally, those born shortly before, during or after a famine had similar mortality rates at older ages.

The situation is different concerning the effect of infectious disease. There exists ample evidence that infectious disease early in life affects later life health and mortality. Historically, people born in years with extremely high infant mortality primarily caused by whooping cough and smallpox tend to have higher mortality later in life (Bengtsson et al. 2001). Tuberculosis in late adulthood is believed to originate in infections during childhood (Elo & Preston 1992). *H pylori* infections in childhood are responsible for peptic ulcer-morbidity later in life (Susser 2001). Increased *H pylori* infections in childhood caused by poor living circumstances before and during World War II seem to be responsible for the high rates of stomach cancer in Japan today (Gersten & Wilmoth 2002). Chronic respiratory disease later in life seems to be related to lower respiratory tract infection in childhood (Elo & Preston 1992).

Conclusion

German semi-supercentenarians, similar to those in other countries, are a highly selected group of people who survived despite adverse living conditions throughout much of their life. They were born at a time of extremely high infant mortality: in Southern Germany about every fourth infant died during the first year of life. They survived two World Wars and the Great Depression in the 30th. In the 1980's in East Germany they survived despite the generally much higher mortality there as compared to the West. Nevertheless, we find an effect of the early life environment independent of later life experiences. In our study we cannot assess its magnitude as compared to other life course factors. This challenge has to be faced by future studies.

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Table 1: Year of birth and number of German Semi-supercentenarians who attained age 105+ in the years 1989-2002.

Year of birth	Total		Born in the German Empire		Born in the German Empire and age validated	
	Number	Percent	Number	Percent	Number	Percent
1880	1	0.1	1	0.1		
1881	2	0.1	2	0.1	1	,1
1882	4	0.3	4	0.3	2	,2
1883	16	1.1	14	1.0	12	1,3
1884	31	2.1	27	2.0	19	2,1
1885	59	4.0	54	4.0	28	3,0
1886	68	4.6	61	4.5	43	4,6
1887	66	4.4	60	4.5	48	5,2
1888	84	5.6	73	5.4	48	5,2
1889	87	5.9	75	5.6	52	5,6
1890	84	5.6	74	5.5	50	5,4
1891	112	7.5	102	7.6	71	7,7
1892	115	7.7	109	8.1	72	7,8
1893	115	7.7	103	7.6	73	7,9
1894	126	8.5	112	8.3	83	9,0
1895	165	11.1	151	11.2	94	10,2
1896	158	10.6	148	11.0	110	11,9
1897	191	12.8	175	13.0	118	12,8
1898	2	0.1	2	0.1	1	,1
1900	1	0.1	1	0.1		
Total	1487	100.0	1348	100,0	925	100,0

Table 2: Seasonal distribution of births, relative risk of survival and standardized residuals; German Empire 1881 to 1898 and age-validated semi-supercentenarians born in the German Empire.

	Births		Semi-supercentenarians				Age validated			
	German Empire		born in the German Empire				Semi-supercentenarians			
	1881-1898						born in the German Empire			
	Number	Percent	Number	Percent	Relative Risk of survival	Standardized Residuals	Number	Percent	Relative Risk of survival	Standardized Residuals
Jan	2826175	8.69	110	8.16	0.94	-0.63	77	8.3	0.96	-0.37
Feb	2622762	8.06	113	8.38	1.04	0.39	82	8.9	1.10	0.86
Mar	2843700	8.74	121	8.98	1.03	0.29	78	8.4	0.96	-0.32
Apr	2674474	8.22	98	7.27	0.88	-1.23	72	7.8	0.95	-0.46
May	2702507	8.31	96	7.12	0.86	-1.51	70	7.6	0.91	-0.78
Jun	2573261	7.91	86	6.38	0.81	-2.00	56	6.1	0.77	-2.01
Jul	2672654	8.21	105	7.79	0.95	-0.57	70	7.6	0.93	-0.69
Aug	2733265	8.40	117	8.68	1.03	0.34	80	8.6	1.02	0.26
Sep	2800130	8.61	136	10.09	1.17	1.86	93	10.1	1.17	1.50
Oct	2720225	8.36	114	8.46	1.01	0.11	83	9.0	1.08	0.64
Nov	2632740	8.09	112	8.31	1.03	0.32	74	8.0	0.99	-0.10
Dec	2732161	8.40	140	10.39	1.24	2.55	90	9.7	1.16	1.40
Total	32534054	100.00	1348	100.00			925	100.0		

Sources: Statistische Jahrbücher. Deutsches Reich

Figure1: Distribution of birth dates of the 1348 eligible and the 925 age validated semi-supercentenarians born in the German Empire and seasonal distribution of births 1881-1898 in the German Empire.

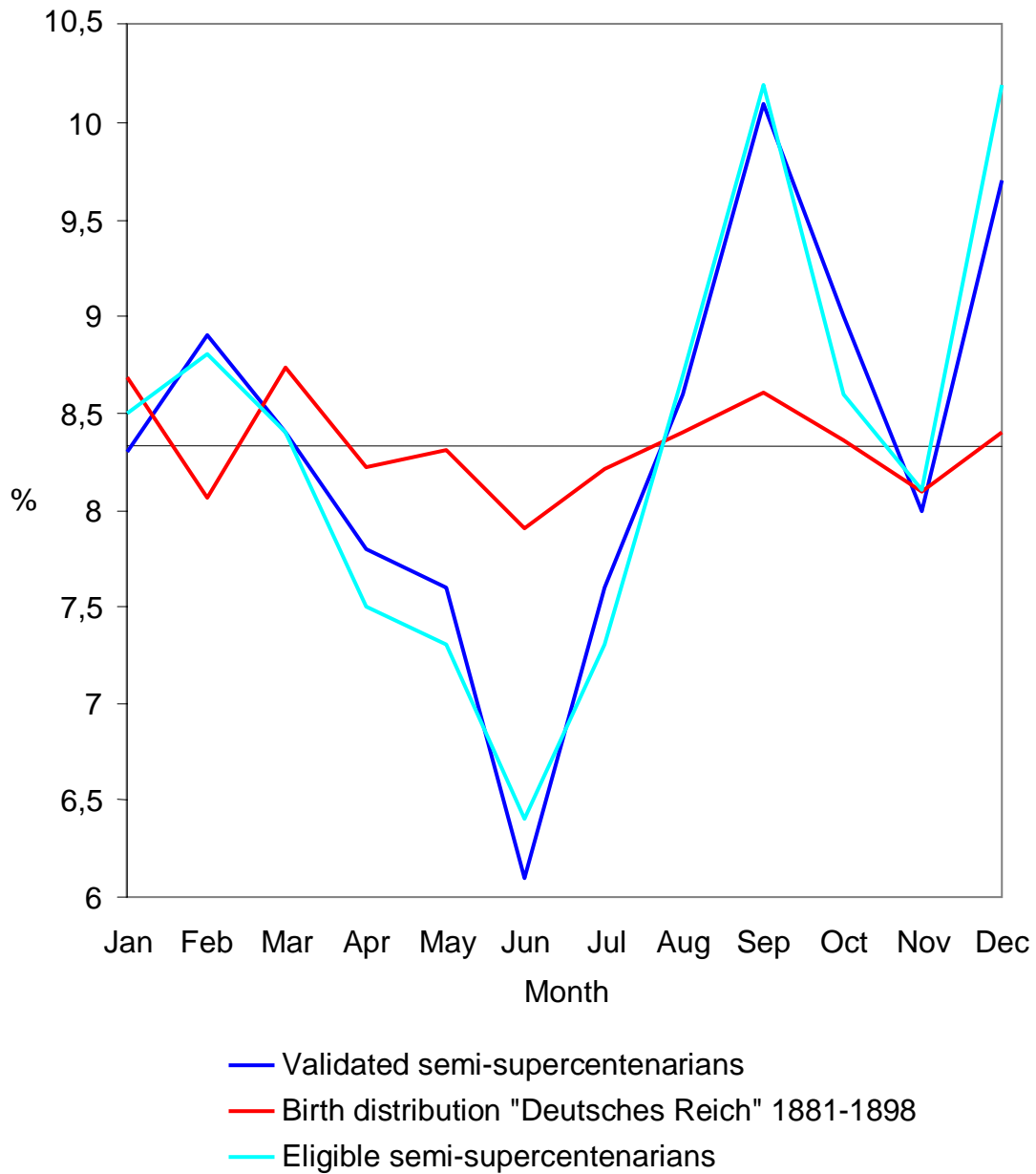


Figure 2: Relative risks of survival from birth to age 105+ by month of birth for the 1348 eligible and the 925 age validated semi-supercentenarians born in the German Empire and deviation in remaining life expectancy at age 50 by month of birth in Denmark.

