

Predictors of Exceptional Longevity: Effects of early-life childhood conditions, mid-life environment and parental characteristics

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Approach

To study “success stories” in long-term avoidance of fatal diseases (survival to 100 years) and factors correlated with this remarkable survival success

An example of incredible resilience

Winnie ain't quitting now.

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Smith G D Int. J. Epidemiol. 2011;40:537-562

Exceptional longevity in a family of Iowa farmers

- Father: Mike Ackerman, Farmer, 1865-1939 lived 74 years
 - Mother: Mary Hassebroek 1870-1961 lived 91 years
1. Engelke "Edward" M. Ackerman b: 28 APR 1892 in Iowa **101**
 2. Fred Ackerman b: 19 JUL 1893 in Iowa **103**
 3. Harmina "Minnie" Ackerman b: 18 SEP 1895 in Iowa **100**
 4. Lena Ackerman b: 21 APR 1897 in Iowa **105**
 5. Peter M. Ackerman b: 26 MAY 1899 in Iowa 86
 6. Martha Ackerman b: 27 APR 1901 in IA 95
 7. Grace Ackerman b: 2 OCT 1904 in IA **104**
 8. Anna Ackerman b: 29 JAN 1907 in IA **101**
 9. Mitchell Johannes Ackerman b: 25 FEB 1909 in IA 85

**Studies of centenarians
require careful design and
serious work on age
validation**

**The main problem is to find an
appropriate control group**

Approach

- **Compare centenarians and shorter-lived controls, which are randomly sampled from the same data universe: computerized genealogies**

Approach used in this study

- **Compare centenarians with their peers born in the same year but died at age 65 years**
- **It is assumed that the majority of deaths at age 65 occur due to chronic diseases related to aging rather than injuries or infectious diseases (confirmed by analysis of available death certificates)**

Case-control study of longevity

Cases - 765 centenarians survived to age 100 and born in USA in 1890-91

Controls – 783 their shorter-lived peers born in USA in 1890-91 and died at age 65 years

Method: Multivariate logistic regression

Genealogical records were linked to 1900 and 1930 US censuses providing a rich set of variables

Age validation is a key moment in human longevity studies

- **Death dates of centenarians were validated using the U.S. Social Security Death Index**
- **Birth dates were validated through linkage of centenarian records to early U.S. censuses (when centenarians were children)**

A typical image of 'centenarian' family in 1900 census

Ross, William	Head	M	M	May	1872	28	M	10		
—, Lizzie	Wife	M	F	Nov	1876	23	M	10	5	4
—, William A.	Son	M	M	Aug	1891	8	M			
—, Daniel	Son	M	M	Jan	1894	6	M			
—, Virginia	Daughter	M	F	Dec	1897	2	M			
—, Callie	Daughter	M	F	Oct	1899	1/2	M			

Genealogies and 1900 and 1930 censuses provide three types of variables

- **Characteristics of early-life conditions**
- **Characteristics of midlife conditions**
- **Family characteristics**

Early-life characteristics

- **Type of parental household (farm or non-farm, own or rented),**
- **Parental literacy,**
- **Parental immigration status**
- **Paternal (or head of household) occupation**
- **Number of children born/survived by mother**
- **Size of parental household in 1900**
- **Region of birth**

Midlife Characteristics from 1930 census

- **Type of person's household**
- **Availability of radio in household**
- **Person's age at first marriage**
- **Person's occupation (husband's occupation in the case of women)**
- **Industry of occupation**
- **Number of children in household**
- **Veteran status, Marital status**

Family Characteristics from genealogy

- **Information on paternal and maternal lifespan**
- **Paternal and maternal age at person's birth,**
- **Number of spouses and siblings**
- **Birth order**
- **Season of birth**

Example of images from 1930 census (controls)

Burke Bernard A	Head	Bookkeeper	Retail cigar
— Erica	Wife #	none	
— Raymond B	Son	none	

Coy Mace A.	Head	superintendent	oil field
— Willie J.	Wife #	none	
— M. Lucille	Daughter	none	
— Billie L.	Daughter	none	

Parental longevity, early-life and midlife conditions and survival to age 100. Males

Multivariate logistic regression, N=714

Variable	Odds ratio	95% CI	P-value
Father lived 80+	1.82	1.33-2.50	<0.001
Mother lived 80+	1.97	1.44-2.70	<0.001
Farmer in 1930	1.80	1.30-2.49	<0.001
Age at first marriage	1.01	0.99-1.03	0.204
Born in North-East	1.89	1.16-3.10	0.011
Born in the second half of year	1.43	1.05-1.96	0.022
Radio in household, 1930	0.92	0.67-1.28	0.620

Parental longevity, early-life and midlife conditions and survival to age 100

Women

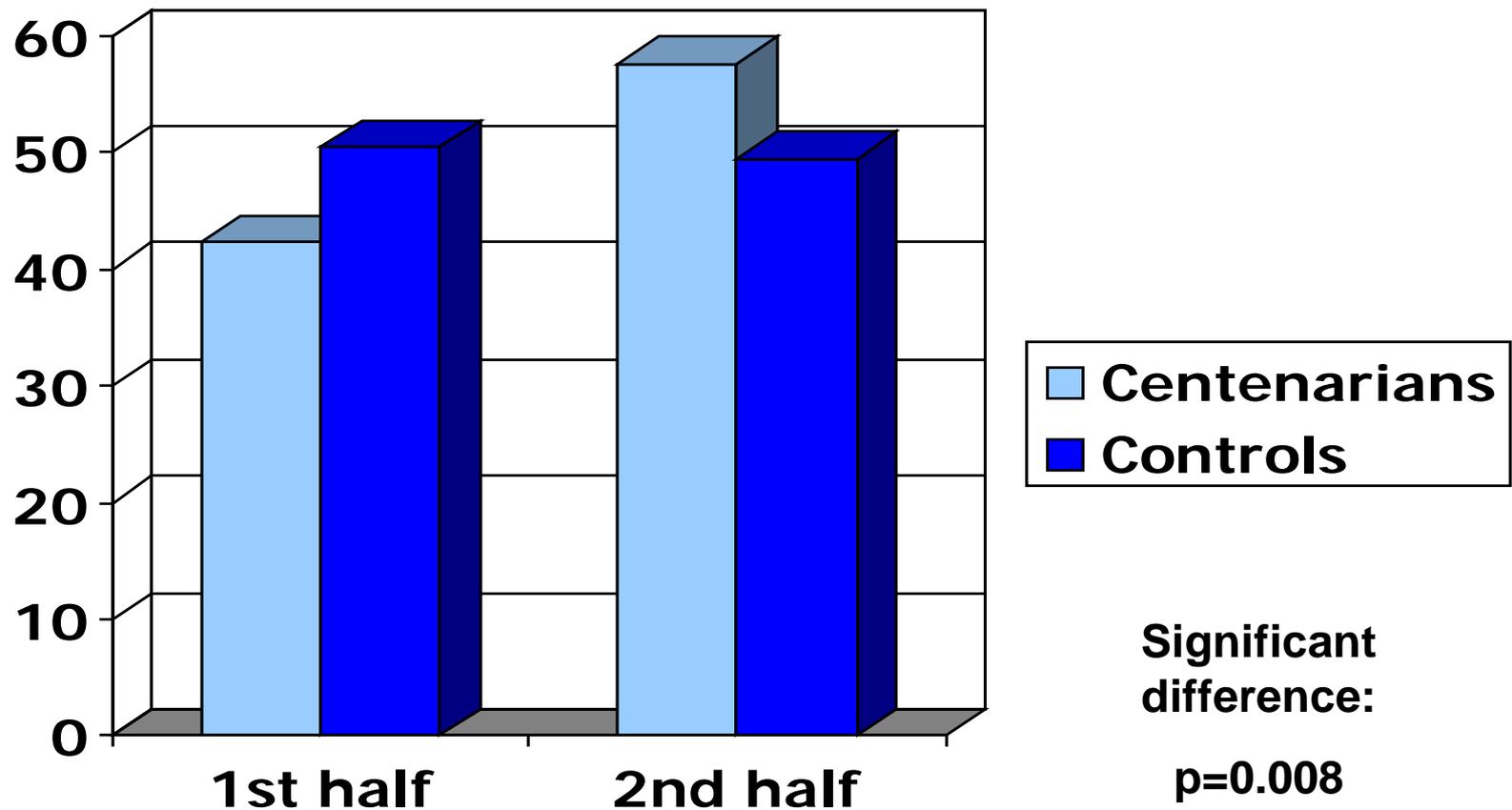
Multivariate logistic regression, N=750			
Variable	Odds ratio	95% CI	P-value
Father lived 80+	2.04	1.48-2.81	<0.001
Mother lived 80+	2.33	1.71-3.17	<0.001
Husband farmer in 1930	1.23	0.89-1.70	0.210
Age at first marriage	1.02	1.001-1.04	0.013
Radio in hh, 1930	1.60	1.16-2.23	0.005
Born in the second half of year	0.99	0.69-1.43	0.966
Born in North-East	1.02	0.62-1.65	0.950

Variables found to be non-significant in multivariate analyses

- **Parental literacy and immigration status, farm childhood, size of household in 1900, percentage of survived children (for mother), sibship size, father-farmer in 1900**
- **Marital status, veteran status, childlessness**
- **Paternal and maternal age at birth, loss of parent before 1910**

Season of birth and survival to 100

Birth in the first half and the second half of the year among centenarians and controls died at age 65

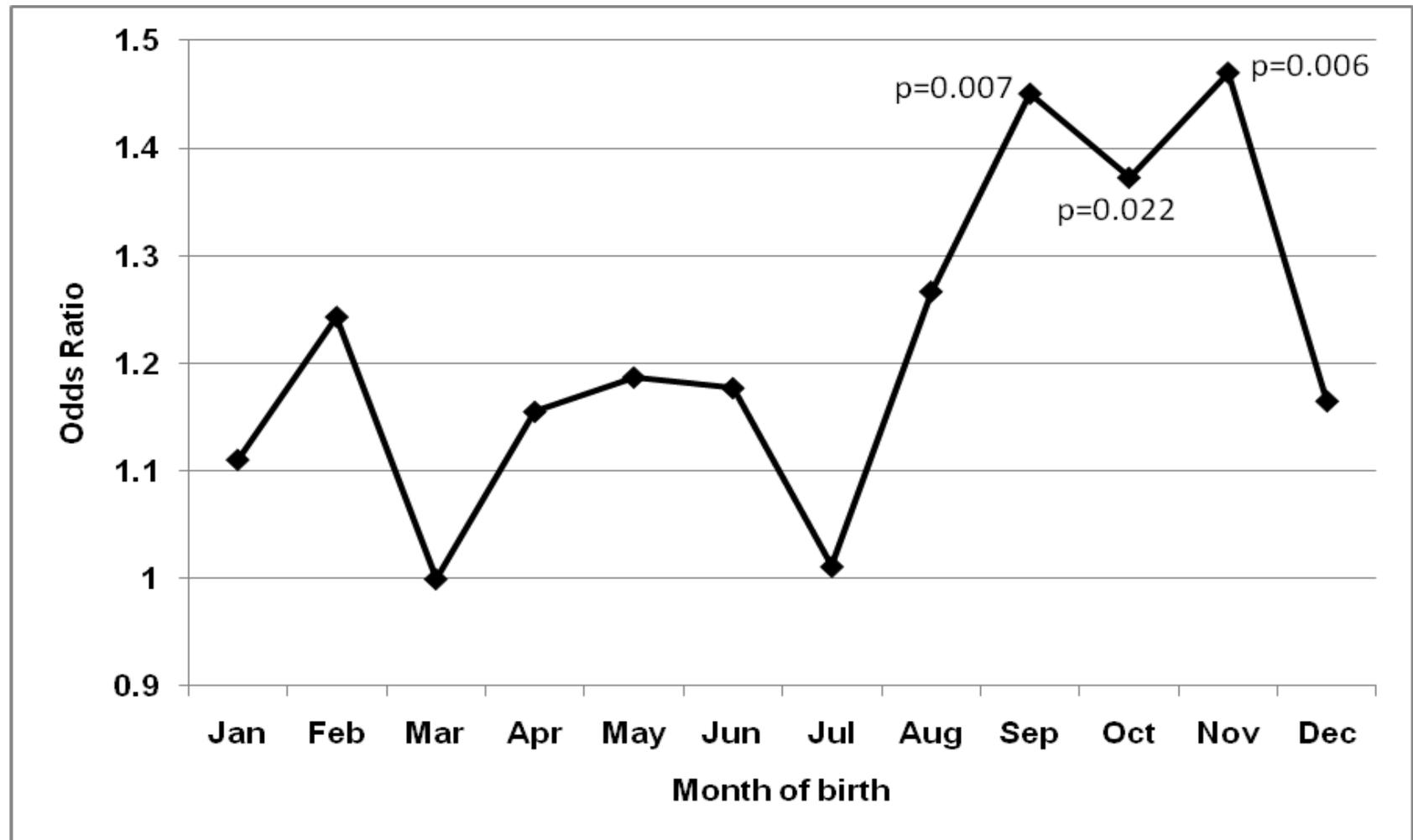


Within-Family Study of Season of Birth and Exceptional Longevity

**Month of birth is a useful proxy
characteristic for environmental
effects acting during in-utero
and early infancy development**

Siblings Born in September-November Have Higher Chances to Live to 100

Within-family study of 9,724 centenarians born in 1880-1895 and their siblings survived to age 50



Possible explanations

These are several explanations of season-of-birth effects on longevity pointing to the effects of early-life events and conditions:

- **seasonal exposure to infections,**
- **nutritional deficiencies,**
- **environmental temperature and sun exposure.**

All these factors were shown to play role in later-life health and longevity.

Conclusions

- Both midlife and early-life conditions affect survival to age 100
- Parental longevity turned out to be the strongest predictor of survival to age 100
- Information about such an important predictor as parental longevity should be collected in contemporary longitudinal studies

Study of biological and non-biological relatives of centenarians

- **Numerous studies showed that biological relatives of centenarians have substantial survival advantage compared to biological relatives of shorter-lived individuals**

Who lives longer in centenarian families? Siblings > Spouses > Siblings-in-law

Relatives of 1,711 centenarians born in 1880-1895

Relatives:	Men		Women	
	N	LS50*	N	LS50*
Parents	1590	76.2	1557	77.2
Spouses	877	75.4	283	81.4
Siblings	5324	77.6	4877	82.4
Siblings in law	2363	75.1	2410	79.5
1900 US birth cohort		73.3		79.4

*Mean lifespan conditional on survival to age 50

**Little is known about effects
of centenarian's sex on
longevity of relatives**

**In this study effects of centenarian's
sex were used to explore genetic and
environmental effects on longevity**

Dataset

We have developed and analyzed a new computerized database on 1,711 validated centenarians born in 1880-1895 in the the United States, their parents and 13,185 shorter-lived siblings.

Having centenarian brother is 'better' than centenarian sister (for males only)

Siblings of centenarians	Male centenarians		Female centenarians		P-value
	N	LE50	N	LE50	
Brothers	1268	29.25	4056	27.09	<0.001
Sisters	1071	32.06	3806	32.45	0.328

Life expectancy of siblings at age 50 depending on the sex of centenarian

Survival of male siblings of centenarians, by sex of centenarian



Having centenarian son is 'better' than centenarian daughter (for fathers only)

	Male centenarians		Female centenarians		P-value
	N	LE50	N	LE50	
Fathers	374	27.22	1216	25.93	0.023
Mothers	362	27.97	1195	27.03	0.176

Life expectancy of parents at age 50 depending on the sex of centenarian

Using siblings-in-law as a control group

Siblings-in-law do not share genetic background and living conditions with centenarians

On the other hand, they usually come from a similar socio-economic background, so may be a good control group

Sex of centenarian is important for siblings but not for siblings-in-law

Married relatives:	Male centenarians		Females centenarians		P-value
	N	LE50	N	LE50	
Brothers	784	29.53	2437	27.12	<0.001
Sisters	650	31.36	2378	32.40	0.045
Brothers in law	492	24.95	1857	25.06	0.846
Sisters in law	611	29.22	1796	29.55	0.539

Life expectancy of relatives at age 50 depending on the sex of centenarian

Only women benefit from having centenarian spouse

	Centenarian spouses		Sibling spouses		P-value
Sex of spouse	N	LE50	N	LE50	
Men	875	25.40	2349	25.04	0.411
Men (married to 103+ centenarians)	214	25.36	2349	25.04	NS
Women	283	31.40	2407	29.46	0.007

Life expectancy of spouses at age 50 depending on the sex of centenarian

Conclusion

Familial factors in human longevity are likely to be sex-specific.

Exploring complex environmental and genetic effects in longevity could be facilitated by further analysis of sex-specific effects

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